Washington State Health Care Authority

Upper Endoscopy for Gastroesophageal Reflux Disease (GERD) and Upper Gastrointestinal (GI) Symptoms

Evidence Update

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Health Technology Assessment Program (HTA)

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This evidence update report is based on research conducted by the Center for Evidence-based Policy (Center) under contract to the Washington State Health Care Authority (HCA). This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the authors, who are responsible for the content. These findings and conclusions do not necessarily represent the views of the Washington HCA and thus, no statement in this report shall be construed as an official position or policy of the HCA.

The information in this assessment is intended to assist health care decision makers, clinicians, patients, and policymakers in making evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

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Bottom Line

This evidence review provides an update on studies published since the original evidence review was conducted in 2012.[1] That evidence review informed the coverage policy for the use of upper endoscopy for gastroesophageal reflux disease (GERD) and upper gastrointestinal (GI) symptoms adopted by the Washington State Health Technology Clinical Committee in April 2012.[1] After summarizing the eligible studies in this evidence update, we have determined that new studies likely will not change the conclusions of the 2012 evidence report.[1]

Background

Upper GI disease can present with a variety of symptoms including swallowing difficulties, dyspepsia, reflux, acute abdominal pain, retrosternal chest pain, nausea and vomiting, belching, or hiccoughs, most of which are nonspecific.[2] And while upper GI symptoms may be linked to significant morbidity,[2] many people with upper GI issues have no abnormal findings upon examination.[2]

Gastroesophageal reflux disease (GERD) is one of the possible upper GI issues, and is characterized by episodes of stomach acid and stomach contents returning back up into the esophagus.[3] Symptoms can include heartburn, regurgitation, chest discomfort, tooth erosions, cough, asthma, and layrngitis.[3,4] GERD is a severe and ongoing condition that may lead to complications such as esophagitis, Barrett esophagus, or cancer of the esophagus.[3,4] GERD affects between 18% and 28% of adults in the US and affects slightly more men than women.[4]

Diagnosis of GERD can often be based on clinical symptoms alone if the patient reports classic symptoms such as heartburn or regurgitation.[3,5] The diagnostic evaluation, including the use of upper endoscopy, aims to identify those patients who have developed complications related to GERD or to confirm the diagnosis if it is unclear (e.g., in a patient who does not respond to appropriate medication).[3,5] Upper endoscopy can also be part of the diagnostic process in people with alarm symptoms, such as GI bleeding (hematemesis, melena, hematochezia, occult blood in stool) or unexplained weight loss.[3,5]

Treatment for upper GI symptoms or GERD is often a multifaceted approach and should be tailored to the individual patient. Options include over-the-counter medications, lifestyle changes (e.g., weight loss), eating 2 to 3 hours before lying down, or avoiding foods that cause symptoms.[3]

In 2012, the WA Health Technology Clinical Committee determined that upper endoscopy for GERD and GI symptoms is a covered benefit with conditions.[1] The limitations of coverage state that, among adults with initial presenting complaints of upper GI symptoms or symptoms consistent with GERD, upper endoscopy is a covered benefit when the following conditions are met[1]:

- Failure of adequate trial of medical treatment to improve or resolve symptoms (recurrence of symptoms after initial treatment indicates treatment failure)[1]; or
- Presence of alarm symptoms[1]

The focus of this evidence update is on the use of upper endoscopy to diagnose GERD and other gastrointestinal (GI) symptoms.

Policy Context

Due to recent legislative changes in Washington State, topics subject to certain coverage conditions need to be assessed for new evidence (i.e., via a signal search) on an annual basis. Therefore, to meet the new legal requirements, this signal search focuses on upper endoscopy for GERD and GI symptoms.

Objectives

The primary aim of this assessment is to determine whether there is new evidence that would likely change the conclusions of the most recent health technology assessment report in 2012.[1]

Methods

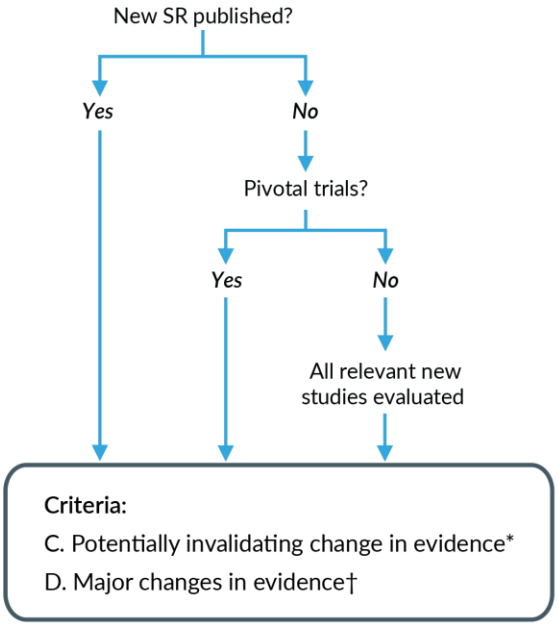
To identify studies published since the 2012 evidence update,[1] we conducted updated searches of Ovid MEDLINE All, Cochrane Database of Systematic Reviews, and the Cochrane Controlled Trials Register database (through December 11, 2024; see Appendix A). Further, we searched the reference lists of all identified systematic reviews, meta-analyses, and guidelines for relevant studies.

To determine whether a signal exists (i.e., there is new evidence that may change the current coverage determination), we followed a modified Ottawa approach (Figure 1) and examined full texts of new systematic reviews, published in the past 5 years. If a treatment or technology is not currently covered, the signal search centered on efficacy and looked at peer-reviewed abstracts of trials for newly identified randomized controlled trials (RCTs) published since any relevant systematic reviews. Conversely, if a treatment or technology of interest is currently covered based on a previous decision by the Washington State Health Technology Clinical Committee, this signal search focuses on harms as reported in systematic reviews only.

To assess whether the conclusions might need updating, we used an algorithm based on a modification of the Ottawa method[6]; see Figure 1. Our approach to screening and reviewing eligible studies was as follows:

- We screened the retrieved references and ongoing study records against the inclusion criteria (see Appendix B).
- We assessed the likelihood, by indication, of recent evidence triggering an update to the 2012 coverage determination for endoscopy for GERD and upper GI symptoms.

Figure 1. Algorithm of the Modified Ottawa Method[6] of Identifying Signals for Update



*A-1. Opposing findings: Pivotal trial or SR including at least one new trial that characterized the treatment in terms opposite to those used earlier

A-2. Substantial harm: Pivotal trial or SR whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making

A-3. Superior new treatment: Pivotal trial or SR whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm

†B-1. Important changes in effectiveness short of "opposing findings"

B-2. Clinically important expansion of treatment

B-3. Clinically important caveat

B-4. Opposing findings from discordant meta-analysis or nonpivotal trial

Source. Adapted from Washington State signal search guidance.

Abbreviation. SR: systematic review.

We summarized the findings of any eligible published systematic reviews and health technology assessments in the following manner: if we identified more than 1 comparable reviews, and 1 or more is more recent or more comprehensive, then the other review(s) were not summarized, and we documented the rationale for selection. However, we did not assess the risk of bias of the eligible reviews or primary studies.

We reported a narrative description of the search results along with key study characteristics of the included reviews and primary studies:

- The number of studies (for systematic reviews) and number of participants (for all study designs)
- The intervention studied
- Comparators to the intervention
- Relevant outcomes reported in the publication

We also highlighted any discrepancies and differences across systematic reviews and individual primary studies.

We assessed the evidence for harms, as the technology is currently covered, along with any potential effects on the 2012 coverage decision.[1] The summary assessment at the end of this report aims to give the WA Health Technology Assessment team and the Agency Medical Directors succinct information on whether there is new evidence that may warrant a reconsideration of the existing coverage policy.

PICO

Appendix B lists the detailed inclusion and exclusion criteria we used to select eligible studies.

Populations

- Adults with upper GI symptoms

Interventions

- Upper GI endoscopy

Comparators

- Medical management without endoscopy
- Usual care

Outcomes

- Clinical symptom resolution (e.g., as measured by symptom scoring tools)
- Health care resource use
- Development of serious GI pathology (e.g., malignancy, Barrett esophagus, esophageal stricture)
- Quality of life, as measured using a validated tool
- Other economic outcomes, such as costs

Key Questions for This Evidence Update

KQ1. For what diagnoses and within what time frames, is repeat endoscopy indicated versus other tests or no follow-up tests for surveillance of disease progression or treatment response? Does repeat endoscopy change treatment and outcome?

KQ2. What are the potential harms of performing upper endoscopy in the diagnostic or treatment planning workup of adults with upper GI symptoms? What is the incidence of these harms? Include consideration of progression of treatment in unnecessary or inappropriate ways.

KQ3. What is the evidence that upper endoscopy has differential efficacy or safety issues in sub populations? Including consideration of:

a. Gender
b. Age
c. Psychological or psychosocial co-morbidities
d. Other patient characteristics or evidence-based patient selection criteria, especially comorbidities of diabetes, high body mass index (BMI), and chronic ingestion of alcohol
e. Provider type, setting or other provider characteristics
f. Payer or beneficiary type: including worker's compensation, Medicaid, state employees

KQ4. What is the evidence of cost and cost-effectiveness of endoscopy compared to other treatment strategies when used in diagnostic or treatment planning workups of adults with upper GI symptoms?

Findings

We identified 489 unique publications in our updated searches, with 14 articles screened at the full-text stage. Of these, 1 study was eligible for inclusion in this report. Appendix C summarizes the systematic review we prioritized for inclusion. The list of studies excluded at the full-text level, with reasons, may be found in Appendix E. We did not identify any pivotal studies for inclusion in this report.

Effectiveness of Early Endoscopy

As of the 2012 coverage determination, endoscopy is currently covered as a diagnostic tool.[1] We therefore focused on harms only for this evidence update.

Harms

We did not identify any eligible systematic reviews or pivotal randomized controlled trials (RCTs) on the harms of endoscopy for upper GI symptoms or GERD in adults, as currently covered. Based on the prior evidence review and the lack of newly identified evidence, the conclusions of the 2012 evidence review are unlikely to change.

Differential Efficacy of Endoscopy in Sub Populations

We did not identify any eligible systematic reviews or pivotal RCTs on the differential efficacy of endoscopy in subpopulations, including gender, age, psychological or psychosocial comorbidities, other patient characteristics, provider type, setting, other provider characteristic, payer, or beneficiary type. Based on the prior evidence review and the lack of newly identified evidence, the conclusions of the 2012 evidence review are unlikely to change.

Repeat Endoscopy

We identified 1 systematic review (Appendix C), published in 2024, evaluating the effectiveness of second-look (or repeat) endoscopy in patients with acute peptic ulcer bleeding.[7] The review included 10 RCTs, including 8 published studies and 2 conference abstracts, with a total of 1,513 participants.[7] Of the 10 included studies, none were included in the 2012 report.[1]

Across the 10 RCTs, the initial endoscopy was usually performed within the first 24 hours after hospital admission.[7] The scheduled second-look endoscopy occurred at 24 to 36 hours after the first endoscopy, in most cases.[7] There were no significant differences between single or second-look endoscopy after treatment.[7] When compared with the initial endoscopy, a second-look endoscopy at 30 days showed[7]:

- No difference in the rate of rebleeding (13% vs. 10%; risk ratio [RR], 0.78; 95% confidence interval [CI], 0.53 to 1.14)
- No difference in the rate of surgery (4% vs. 2%; RR, 0.58; 95% CI, 0.29 to 1.15)
- No difference in mortality (4% vs. 3%; RR, 0.89; 95% CI, 0.46 to 1.71)
- No difference in the number of blood units transfused (0 vs. 0.01; mean difference, −0.01 units; 95% CI, −0.30 to 0.28)

The authors rated the certainty of the evidence as moderate for rebleeding, surgery, and mortality because of wide confidence intervals (i.e., imprecision), and as low for the number of units of blood transfused because of wide confidence intervals and some heterogeneity (i.e., inconsistency).[7]

Bottom Line

Based on the prior evidence review and the single systematic review on repeat endoscopy, there is no evidence to support scheduled second-look endoscopy for GERD and upper GI symptoms.

Costs and Cost-Effectiveness of Endoscopy

We did not identify any eligible studies about the cost or cost-effectiveness of endoscopy as a diagnostic tool for upper GI symptoms or GERD for this evidence update. Based on the prior evidence review and the lack of newly identified evidence, the conclusions of the 2012 evidence review are unlikely to change.

Alignment With International Guidelines

In addition to our survey of systematic reviews and pivotal primary studies, we reviewed recent clinical practice guidelines related to our review, published in the last 5 years (Appendix D) in countries rated as *very high* on the United Nations Human Development Index.[8] Guidelines publication dates range from 2019 to 2024. One of these is an international guideline,[9] 2 guidelines come from the US,[10,11] 1 is from Europe,[12] 1 is a joint US and European guideline,[13] along with 1 guideline each from the Japan,[14] Korea,[15] and the UK.[16] We did not assess the methodological quality of the practice guidelines but we do summarize the methods used for developing the recommendations (Appendix D).

The international guidelines disagree about whether upper endoscopy is required for functional dyspepsia,[12,14] but recommend the following actions:

- Endoscopy should be performed 2 to 4 weeks after discontinuation of antisecretory therapy[9,10]
- Endoscopy is recommended to diagnose GERD and to exclude other diseases, especially if proton pump inhibitor (PPI) therapy is not effective or after other testing has ruled out other serious diseases and disorders[10-13,15,16]
- Endoscopy should be used for evaluation of patients presenting with dysphagia, alarm symptoms, or multiple risk factors for Barrett esophagus[10,12,13]
- Patients with gastric ulcer and Helicobacter pylori (H. pylori) infection should have repeat endoscopy 6 to 8 weeks after beginning treatment, depending on the size of the lesion[14,16]
- Clinicians should evaluate the appropriateness and dosage of PPIs within 12 months after initiation, and offer endoscopy to establish appropriateness of long-term PPI therapy[11]

Common alarm symptoms mentioned in international guidelines include new onset of symptoms at an advanced age, weight loss, recurrent vomiting, bleeding, dysphagia, painful swallowing, abdominal masses, fever, family history of esophageal or gastric cancer, lack of response to initial treatment, or symptom flare-up after discontinuation of treatment.[11,14]

The Canadian Association of Gastroenterology and Crohn's and Colitis Canada published joint recommendations in Choosing Wisely Canada on 12 gastroenterology tests and treatments to question.[17] Their recommendations, specific to upper GI endoscopy are:

- Avoid using an upper-GI series to investigate dyspepsia[17]
- Avoid performing an endoscopy for dyspepsia without alarm symptoms for patients under the age of 60 years[17]

The Choosing Wisely Canada recommendation to avoid the use of upper-GI series (a series of X-ray images that use a barium swallow to map the upper digestive tract) was based on 1 health technology assessment from 2003 and a technical review on evaluating dyspepsia from 2005.[17] Based on these cited sources, Choosing Wisely Canada says that upper GI series have a significant proportion of false positive and false negative results compared with endoscopy, and studies have consistently found that this is not a cost-effective approach compared with other strategies of managing dyspepsia.[17]

The rationale for the second recommendation was as follows:[17]

- Endoscopy is an accurate test for diagnosing dyspepsia, but organic pathology that does not respond to acid suppression or H. pylori eradication therapy is rare under the age of 60
- Most guidelines therefore recommend as the first line approach for managing dyspepsia either empirical PPI therapy or a noninvasive test for H. pylori and then offering therapy if the patient is positive
- If the patient has alarm features such as progressive dysphagia, anemia or weight loss, endoscopy may be appropriate

The cited source for this second recommendation is the 2017 joint guideline from the American College of Gastroenterology and the Canadian Association of Gastroenterology.[18]

Bottom Line

Based on a review of these guidelines, Washington's current coverage determination is in line with international guidelines and is unlikely to need updating.

Summary

Upper GI symptoms and GERD can cause significant morbidity and are associated with swallowing difficulties, dyspepsia, reflux, acute abdominal pain, retrosternal chest pain, nausea and vomiting, belching, hiccoughs, and decreased quality of life.

Treatment for upper GI symptoms or GERD is often a multifaceted approach and should be tailored to the individual patient. Endoscopy is a commonly accepted diagnostic tool for upper GI symptoms and GERD.

Because endoscopy has been an accepted diagnostic tool for many years, there are almost no new systematic reviews or primary studies. After summarizing in this evidence update the single eligible systematic reviews for harms of second-look endoscopy, we determined the new studies are unlikely to change the conclusions of the 2012 evidence report for endoscopy for upper GI symptoms or GERD.

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Appendix A. Search Strategies

Search for Systematic Reviews:

Ovid MEDLINE(R) ALL <1946 to December 11, 2024>

1. Endoscopy, Digestive System/ 10036
2. (Esophagogastroduodenoscop$ or EGD or endoscop$ or gastroscop$ or esophagoscop$ or duodenoscop$).ti. 120546
3. or/1-2 126251
4. Gastroesophageal Reflux/ 29280
5. (GERD or GORD or "Esophageal Reflux" or "Gastric Acid Reflux" or "Gastro-Esophageal Reflux" or "Gastro-oesophageal Reflux").ti,ab. 16949
6. Heartburn/ or (heartburn or Pyrosis).ti,ab. 6834
7. Dyspepsia/ or (Dyspepsi$ or indigestion).ti,ab. 17016
8. Nausea/ or nausea$.mp. or Vomiting/ or vomit$.mp. or emesis.mp. or hematemesis.ti,ab. 137909
9. Abdominal Pain/ or ((upset$ or sore$ or ache$ or pain$ or complain$ or symptom$ or bother$) adj3 (stomach$ or esophag$ or belly or abdomen$)).ti,ab. 32676
10. Gagging/ or gagging.mp. or "pharyngeal reflex".ti,ab. 1035
11. ('peptic ulcer' or 'gastrointestinal bleed' or 'gastrointestinal bleeding').ti,ab. 45004
12. Peptic Ulcer/ 32624
13. or/4-12 273538
14. 3 and 13 9395
15. 'review'.ti. 806199,
16. 14 and 15 345
17. limit 16 to (english language and yr="2012 -Current") 236

Search for Randomized Controlled Trials

Ovid MEDLINE(R) ALL <1946 to December 12, 2024>

1. Endoscopy, Digestive System/ 10037
2. (Esophagogastroduodenoscop$ or EGD or endoscop$ or gastroscop$ or esophagoscop$ or duodenoscop$).ti. 120602
3. or/1-2 126308
4. Gastroesophageal Reflux/ 29287
5. (GERD or GORD or "Esophageal Reflux" or "Gastric Acid Reflux" or "Gastro-Esophageal Reflux" or "Gastro-oesophageal Reflux").ti,ab. 16961

6. Heartburn/ or (heartburn or Pyrosis).ti,ab. 6837
7. Dyspepsia/ or (Dyspepsi$ or indigestion).ti,ab. 17022
8. Nausea/ or nausea$.mp. or Vomiting/ or vomit$.mp. or emesis.mp. or hematemesis.ti,ab. 137989
9. Abdominal Pain/ or ((upset$ or sore$ or ache$ or pain$ or complain$ or symptom$ or bother$) adj3 (stomach$ or esophag$ or belly or abdomen$)).ti,ab. 32691
10. Gagging/ or gagging.mp. or "pharyngeal reflex".ti,ab. 1036
11. 'peptic ulcer'.ti,ab. 23528
12. Peptic Ulcer/ 32622
13. or/4-12 254219
14. 3 and 13 7219
15. limit 14 to randomized controlled trial 481
16. limit 15 to yr="2012-current" 193
17. limit 16 to English 187

Appendix B. Detailed Inclusion and Exclusion Criteria

Table B. Detailed Inclusion and Exclusion Criteria for This Evidence Review

Study Component	Inclusion	Exclusion
Populations	• Adults with upper GI symptoms	• Studies in children with GI symptoms • Studies in adults without GI symptoms
Interventions	• Upper GI endoscopy	• Upper GI endoscopy as treatment (i.e., not for diagnosis or treatment planning)
Comparators	• Medical management, without endoscopy • Usual care	• Comparators other than those stated • No comparator
Outcomes	• Clinical symptom resolution (e.g., as measured by symptom scoring tools) • Health care resource use • Development of serious GI pathology (e.g., malignancy, Barrett esophagus, esophageal stricture) • Quality of life, as measured using a validated tool • Other economic outcomes, such as costs	• Studies that do not report outcomes of interest • Economic outcomes from studies performed in non-US countries • Economic outcomes from studies performed in the US published more than 5 years ago
Timing	• As part of diagnostic work-up or treatment planning	• None stated
Setting	• Any outpatient or inpatient clinical setting in countries categorized as very high on the UN Human Development Index	• Nonclinical settings (e.g., studies in healthy volunteers, animal models of disease, cell culture, xenografts, organoids) • Countries categorized other than very high on the UN Human Development Index
Study Design	• Clinical practice guidelines • Systematic reviews and meta-analyses • Comparative primary studies	• Abstracts, conference proceedings, posters, editorials, letters • Studies without a comparator • Non-comparative association or correlation studies • Development of novel diagnostic endoscopy techniques • Proof-of-principle studies (e.g., technique modification)
Sample Size	• None specified	• Studies that do not meet the minimum sample size
Publication	• Published, peer-reviewed, English-language articles	• Studies with abstracts that do not allow study characteristics to be determined • Studies that cannot be located • Duplicate publications of the same study that do not report different outcomes or follow-up times, or single site reports from published multicenter studies • Studies published in languages other than English

Abbreviations. GI: gastrointestinal; UN: United Nations.

Appendix C. Included Systematic Reviews

Table C. Summary Characteristics of Systematic Reviews of Repeat Endoscopy in Patients With Upper GI Symptoms or GERD

Author, Year	Evidence Base Used	Effectiveness and Harms	Author Conclusions
Benites,Goni et al.,[7] 2024	8 RCTs plus 2 RCT abstracts N = 1,513 participants Spanning 1994 to 2022	No significant differences: • Rebleeding (RR, 0.78; 95% CI, 0.53 to 1.14) • Surgery (RR, 0.58; 95% CI, 0.29 to 1.15) • Mortality (RR, 0.89; 95% CI, 0.46 to 1.71) • Number of units of blood transfused (MD, −0.01 units; 95% CI, −0.30 to 0.28)	Second-look endoscopy is not more effective than a single endoscopy in patients with peptic ulcer bleeding

Abbreviations. CI: confidence interval; GERD: gastroesophageal reflux disease; GI: gastrointestinal; MD: mean difference; RCT: randomized controlled trial; RR: risk ratio.

Appendix D. Summary of Clinical Practice Guideline Recommendations

Table D. Summary of Clinical Practice Guideline Recommendations

Author, Year Society Location	Guidelines Method	Condition	Relevant Recommendations	Notes
Gyawali et al.,[9] 2024 Lyon Consensus 2.0 International	• Update • Literature review (not provided) • Expert consensus	GERD	• To maximize the diagnostic yield, endoscopy should be performed 2 to 4 weeks after discontinuation of antisecretory therapy in unproven GERD	Other recommendations focus on endoscopic findings
Jung et al.,[15] 2021 Seoul Consensus (Korean Society of Neurogastroenterology and Motility; and Asian Neurogastroenterology and Motility Association) Korea	• Systematic review with meta-analysis • GRADE • Patient survey • Expert consensus	GERD	• Statement 10: Endoscopy with or without biopsy can be recommended to diagnose gastroesophageal reflux disease and exclude other organic diseases ○ QoE: very low. SoE: strong • Experts' opinions: agree strongly (53.3%), agree with some reservations (42.2%), undecided (2.2%), disagree (2.2%), and disagree strongly (0.0%)	Endoscopic surveillance recommended in patients with long-segment Barrett esophagus
Katz et al.,[10] 2022 American College of Gastroenterology US	• Systematic literature review (not provided) • Expert consensus	GERD	• In patients with chest pain who have had adequate evaluation to exclude heart disease, objective testing for GERD (endoscopy and/or reflux monitoring) is recommended ○ QoE: Low; SoE: Conditional • We recommend endoscopy as the first test for evaluation of patients presenting with dysphagia or other alarm symptoms (weight loss and GI bleeding) and for patients with multiple risk factors for Barrett esophagus ○ QoE: Low; SoE: Strong	Endoscopy should be performed after PPIs have been discontinued for 2-4 weeks
Miwa et al.,[14] 2022 Japanese Society of Gastroenterology Japan	• Systematic literature review (not provided)	FD	• Upper gastrointestinal endoscopy is not required to diagnose FD • FD should be diagnosed based on a comprehensive evaluation of symptoms, age, medical history, presence of Helicobacter pylori infection, and laboratory history. However, endoscopy or other	Alarm symptoms: • New onset of symptoms at an advanced age • Weight loss • Recurrent vomiting • Bleeding

Author, Year Society Location	Guidelines Method	Condition	Relevant Recommendations	Notes
			investigations should be performed when organic disease is suspected because of a positive alarm sign	• Dysphagia • Painful swallowing • Abdominal mas • Fever • Family history of esophageal or gastric cancer • Lack of response to initial treatment • Symptom flare-up after discontinuation of treatment
NICE,[16] 2019 NICE United Kingdom	• Systematic review with meta-analysis and GRADE, available on website	GERD	• Do not routinely offer endoscopy to diagnose Barrett esophagus, but consider it if the person has GERD. Discuss the person's preferences and their individual risk factors (for example, long duration of symptoms, increased frequency of symptoms, previous esophagitis, previous hiatus hernia, esophageal stricture or esophageal ulcers, or male gender). [new 2014] • Offer people with gastric ulcer and H. pylori infection repeat endoscopy 6 to 8 weeks after beginning treatment, depending on the size of the lesion. [2004, amended 2014]	First-line treatment is PPI, but if alarm symptoms occur or initial treatment fails, refer to specialist. Inference is that endoscopy follows PPI treatment and/or referral to specialist for clinical review

Wauters et al.,[12] 2021
United European Gastroenterology; European Society for Neurogastroenterology and Motility
Europe
	• Systematic literature review (not provided)
	• Expert consensus
	• Citations provided for recommendation statements
		FD	• 5.1. Upper GI endoscopy is mandatory for establishing a diagnosis of Functional Dyspepsia. Endorsed
			  ○ QoE: High
			• 5.2. In primary care, uninvestigated dyspepsia can be managed without endoscopy if there are no alarm of risk factors. Endorsed
			  ○ QoE: High
			• 5.3. Upper GI endoscopy is mandatory if there are alarm symptoms or risk factors. Endorsed
			  ○ QoE: High
				Endoscopy recommended for patients aged older patients (≥60 years) to rule out neoplasia and in younger patients with alarm symptoms

Author, Year Society Location	Guidelines Method	Condition	Relevant Recommendations	Notes
Yadlapati et al.,[11] 2022 American Gastroenterological Association US	• Expert Consensus	GERD	• Best Practice Advice 5: If PPI therapy is continued in a patient with unproven GERD, clinicians should evaluate the appropriateness and dosing within 12 months after initiation, and offer endoscopy with prolonged wireless reflux monitoring off PPI therapy to establish appropriateness of long-term PPI therapy • Best Practice Advice 6: If troublesome heartburn, regurgitation, and/or non-cardiac chest pain do not respond adequately to a PPI trial or when alarm symptoms exist, clinicians should investigate with endoscopy	Best Practice Advice 7 describes endoscopic findings; endoscopy should be performed in patients with alarm symptoms • Reflux symptoms, heartburn, regurgitation, or non-cardiac chest pain non-responsive to PPIs • Extra-esophageal symptoms • Prolonged PPI treatment
Zerbib et al.,[13] 2021 European Society for Neurogastroenterology and Motility; American Neurogastroenterology and Motility Society Europe and US	• Expert Consensus	Refractory GERD	• Statement 14: In patients with proven GERD, both persistent typical symptoms and persistent atypical symptoms (non-cardiac chest pain, extraesophageal symptoms) on PPI therapy deserve further investigation to evaluate for poorly controlled GERD, functional esophageal disorders, motility disorders, and specific pulmonary or pharyngo-laryngeal etiologies as appropriate • Statement 18: Endoscopic and/or radiologic evaluation of EGJ morphology should be performed in patients with refractory GERD symptoms • Statement 20: Patients with persistent esophageal and/or extraesophageal symptoms on PPI therapy and no previously documented GERD should be investigated with endoscopy and ambulatory pH or pH-impedance monitoring off therapy to document presence or absence of baseline abnormal reflux	Failure of PPI to resolve symptoms indicates objective testing such as endoscopy

Abbreviations. FD: functional dyspepsia; GERD: gastroesophageal reflux disease; GRADE: Grading of Recommendations Assessment, Development and Evaluation approach; NICE: National Institute for Health and Care Excellence; PPI: proton pump inhibitor; QoE: quality of evidence; SoE: GRADE strength of evidence.

Appendix E. Excluded Studies

Table E. Excluded Studies at Full Text Level With Reasons

Citation	Reason for Exclusion
Alamro S M, Alanazi MM, Suwayyid WK. Capsule endoscopy for the risk stratification and management of acute upper gastrointestinal bleeding in emergency departments: a systematic review on triage, risk stratification, and management. *Cureus*. 2024;16:e71530. doi: 10.7759/cureus.71530	Intervention
Aziz M, Dasari CS, Zafar Y, et al. Does timing of endoscopy affect outcomes in patients with upper gastrointestinal bleeding: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol*. 2021;33:1055-1062. doi: 10.1097/MEG.0000000000001975	Aim
Bai L, Jiang W, Cheng R, Dang Y, Min L, Zhang S. Does early endoscopy affect the clinical outcomes of patients with acute nonvariceal upper gastrointestinal bleeding? A systematic review and meta-analysis. *Gut Liver*. 2023;17:566-580. doi: 10.5009/gnl220291	Aim
Bilder HG, Soccini C, Lasa JS, Zubiaurre I. Impact of time to esophagogastroduodenoscopy in patients with nonvariceal upper gastrointestinal bleeding: A systematic review and meta-analysis. *Rev Gastroenterol Mex (Engl Ed)*. 2022;87:320-329. doi: 10.1016/j.rgmxen.2021.11.010	Comparator
Chapelle N, Martel M, Bardou M, Almadi M, Barkun AN. Role of the endoscopic Doppler probe in nonvariceal upper gastrointestinal bleeding: Systematic review and meta-analysis. *Dig Endosc*. 2023;35:4-18. doi: 10.1111/den.14356	Comparator
Chung CS, Chen CC, Chen KC, et al. Randomized controlled trial of early endoscopy for upper gastrointestinal bleeding in acute coronary syndrome patients. *Sci Rep*. 2022;12:5798. doi: 10.1038/s41598-022-09911-5	Setting
Ejtehadi F, Sivandzadeh GR, Hormati A, et al. Timing of emergency endoscopy for acute upper gastrointestinal bleeding: a literature review. *Middle East J Dig Dis*. 2021;13:177-185. doi: 10.34172/mejdd.2021.223	Setting
Guy A, Eppler K, Moe J. Timing of endoscopy for acute upper gastrointestinal bleeding: journal club review. *CJEM*. 2022;24:20-22. doi: 10.1007/s43678-021-00233-5	Study Design
Jonasson C, Moum B, Bang C, Andersen KR, Hatlebakk JG. Randomised clinical trial: a comparison between a GerdQ-based algorithm and an endoscopy-based approach for the diagnosis and initial treatment of GERD. A*liment Pharmacol Ther*. 2012;35:1290-300. doi: 10.1111/j.1365-2036.2012.05092.x	Intervention
Merola E, Michielan A, de Pretis G. Optimal timing of endoscopy for acute upper gastrointestinal bleeding: a systematic review and meta-analysis. *Intern Emerg Med*. 2021;16:1331-1340. doi: 10.1007/s11739-020-02563-1	Aim
Park SJ, Park H, Lee YC, et al. Effect of scheduled second-look endoscopy on peptic ulcer bleeding: a prospective randomized multicenter trial. *Gastrointest Endosc*. 2018;87(2): 457-465. doi: 10.1016/j.gie.2017.07.024	Timing
Tarar ZI, Zafar MU, Farooq U, Ghous G, Shoukat HMH, Kuwajima V. Does performing endoscopy sooner have an impact on outcomes in patients with acute nonvariceal upper gastrointestinal hemorrhage? A systematic review. *Cureus*. 2021; 13(7):e16092. doi: 10.7759/cureus.16092	Aim
Tassone D, Kazi S, Lee T, Gilmore R, Ding N. Systematic review and meta-analysis of endoscopic versus medical management of peptic ulcers with adherent clots. *J Gastroenterol Hepatol*. 2024;39(10):2031-2042. doi: 10.1111/jgh.16611	Intervention