



Complete Summary

GUIDELINE TITLE

Dyspepsia and GERD.

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Dyspepsia and GERD. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 Jul. 50 p. [102 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: Dyspepsia. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Jan. 48 p.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

- Dyspepsia, including gastric ulcer dyspepsia; duodenal ulcer dyspepsia; or non-ulcer (functional) dyspepsia
- Gastroesophageal reflux disease (GERD)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine
Radiology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To increase the use of recommended methods for evaluating dyspepsia
- To increase appropriate pharmaceutical treatment of patients with dyspepsia
- To decrease complications associated with peptic ulcer disease
- To improve functional outcomes and satisfaction of patients with dyspepsia
- To increase the use of initial treatment recommendations for evaluating gastroesophageal reflux disease (GERD)
- To increase appropriate treatment for patients who have ongoing symptoms after initial treatment recommendations

TARGET POPULATION

Adult males and nonpregnant adult females with symptoms of epigastric pain or discomfort on greater than 25% of days over the past 4 weeks. Individuals with nausea, heartburn or acid regurgitation are eligible.

This guideline does not stipulate the exact symptoms that define dyspepsia, thus allowing the clinician some latitude in identifying the patients to whom this guideline can be applied.

This guideline does not apply to patients whose symptoms are characteristic of biliary tract disease, pancreatic disease or irritable bowel syndrome.

INTERVENTIONS AND PRACTICES CONSIDERED

Dyspepsia

Diagnostic Assessment

1. Medical history including history of prior documented ulcer
2. Evaluate symptoms, with particular attention to presence of alarm features
3. Endoscopy
4. Multiphase upper gastrointestinal (UGI) studies
5. Helicobacter pylori (H. pylori) serology or urea breath testing (UBT)

6. Fasting serum gastrin (to rule out Zollinger-Ellison in patients who do not use nonsteroidal anti-inflammatory drugs [NSAIDs])
7. Evaluation for increased risk of gastric cancer
8. Biopsy for *H. pylori*

Treatment

1. Eradicative therapy for *H. pylori*
 - Proton pump inhibitor (PPI) drugs, such as omeprazole (Prilosec®), lansoprazole (Prevacid®), rabeprazole (Aciphex®), pantoprazole (Protonix®), or esomeprazole (Nexium®)
 - Clarithromycin
 - Amoxicillin
 - Tetracycline
 - Metronidazole
 - Bismuth
2. Discontinuation of nonsteroidal anti-inflammatory drugs
3. Smoking cessation

Gastroesophageal Reflux Disease (GERD)

Diagnostic Assessment

1. Flexible esophagogastroduodenoscopy
2. 24-hour pH monitoring

Treatment

1. Behavioral/lifestyle modifications
 - Dietary changes (avoid caffeine, chocolate, fats, alcohol, decaffeinated tea and coffee, caffeinated soft drinks, citrus juices, peppermint, and spearmint)
 - Weight loss
 - Avoiding large meals
 - Body positioning (avoid lying down after eating, elevating head of bed)
 - Tobacco cessation
2. Changing medications that can lower the lower esophageal sphincter (LES), such as theophylline, calcium channel blockers, and barbiturates
3. Use of antacids and over-the-counter proton pump inhibitors (PPIs)
4. Step-down therapy
5. Proton pump inhibitors for patients with erosive esophagitis or worse

MAJOR OUTCOMES CONSIDERED

- Efficacy of *Helicobacter pylori* testing (positive or negative)
- Sensitivity, specificity, positive and negative predictive value of diagnostic instruments
- Efficacy/side effects of medications
- Recurrence of peptic ulcer disease
- Recurrence of esophagitis
- Incidence and risk factors of gastric cancer

- Patient symptoms
- Healing rates
- Costs of diagnostic tests and treatments

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

No additional description of literature search strategies is available.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to

the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Study Quality Designations:

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The guideline developer reviewed published cost analyses.

Helicobacter pylori testing appears to be a cost-effective approach for long-term dyspepsia management. (See Discussion Appendix C in the original guideline document.) A decision-analytic model shows that an approach utilizing a combination of empiric therapy for Helicobacter pylori and antisecretory therapy was superior to antisecretory therapy alone. In addition, initial therapy for Helicobacter pylori guided by serological testing was the most cost-effective option. When endoscopy can be provided for less than \$500 including all fees, immediate endoscopy is more cost-effective.

A second decision analysis comparing the costs and outcomes of initial anti-Helicobacter pylori treatment to initial endoscopy among those who are

Helicobacter pylori antibody positive shows initial therapy as the most cost-effective management strategy.

Additional cost-benefit analyses have been performed. Refer to the original guideline document for all citations.

METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline annotation, discussion and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member groups during an eight-week review period.

Each of the Institute's participating member groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating member groups following implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

Guideline Work Group

Following the completion of the review period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary and a written response is prepared to address each of the responses received from member groups. Two members of the Committee on Evidence-Based Practice carefully review the input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of four questions: (1) Is there consensus among all ICSI member groups and hospitals on the content of the guideline document? (2) Has the drafting work group answered all criticisms reasonably from the member groups? (3) Within the knowledge of the appointed reviewer, is the evidence cited in the document current and not out-of-date? (4) Is the document sufficiently similar to the prior edition that a more thorough review (critical review) is not needed by the member group? The committee then either approves the guideline for release as submitted or negotiates changes with the work group representative present at the meeting.

Pilot Test

Member groups may introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer and other practice systems. Evaluation and assessment occur throughout the pilot test phase, which usually lasts for three-six months. At the end of the pilot test phase, ICSI staff and the leader of the work group conduct an interview with the member groups participating in the pilot test phase to review their experience and gather comments, suggestions, and implementation tools.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline; the Committee on Evidence-Based Practice reviews the revised guideline and approves it for release.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations for the management of dyspepsia are presented in the form of a primary algorithm, [Dyspepsia](#), with 20 components, and a secondary algorithm, [Gastroesophageal Reflux Disease \(GERD\)](#), with an additional 13 components (for a total of 33 components), accompanied by detailed annotations. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) and conclusion grade (I-III and Not Assignable) definitions are repeated at the end of the Major Recommendations field.

Clinical Highlights

1. Send patients with dyspepsia plus one of the following alarm features for urgent endoscopic evaluation. Suggested time frames for the urgency of endoscopy are provided with each of the alarm features listed. (Annotations #3, 4)
 - Melena (within 1 day if ill)
 - Hematemesis (within 1 day if ill)
 - Persistent vomiting (7-10 days)
 - Anemia (7-10 days)
 - Acute onset of total dysphagia (within 1 day)
 - Weight loss greater than 5% (involuntary) (7-10 days)
2. Patients 50 years of age and older with symptoms of uncomplicated dyspepsia should be evaluated with nonurgent upper endoscopy. (Annotation #8)
3. Patients with dyspepsia but no alarm features or reflux symptoms, should receive *Helicobacter pylori* (*H. pylori*) testing and if positive, eradication therapy. (Annotations #5, 6, 10, 11)
4. Patients with dyspepsia and negative testing results for *H. pylori* should be treated empirically with Proton Pump Inhibitors (PPIs). (Annotation #12)
5. Patients age 50 or older and who have had symptoms of GERD for 10 years or more should be considered for endoscopy during initial management. (Annotation #24)
6. Patients with gastroesophageal reflux should receive single trial step-down therapy. (Annotations #24, 28, 29, 30, 33)
7. Patients with GERD usually require long-term PPI therapy. (Annotation #33)

Dyspepsia Algorithm Annotations

1. Symptoms of Dyspepsia or GERD

Dyspepsia

Dyspepsia is defined as pain or discomfort felt to arise in the upper gastrointestinal (GI) tract with symptoms on greater than 25% of days over the past 4 weeks. Patients with epigastric pain or discomfort, or nausea are eligible.

GERD

GERD is the probable diagnosis if the patient has heartburn (retrosternal pain) or acid regurgitation (a sour or bitter taste in mouth) as the dominate symptom. These symptoms are sought because their presence is associated with a probability of 89% and 95%, respectively, of GERD based on studies using esophageal pH monitoring as the reference standard. The goal is to minimize the number of patients with ulcer referred to the GERD algorithm.

Evidence supporting this recommendation is of classes: C, R

3. Are There Alarm Features?

Alarm features should be sought in all patients presenting with dyspepsia. If alarm features are present, endoscopy should be performed (suggested time frames for urgency of endoscopy are provided with each of the alarm features listed). Alarm features is a term that is used frequently in the dyspepsia literature to describe clinical features that may suggest underlying disease that should be diagnosed and treated without the delay of an empiric therapeutic trial. Alarm features frequently cited are:

- Anemia (7-10 days)
- Acute onset dysphagia (within 1 day)
- Hematemesis (within 1 day if ill)
- Melena (within 1 day if ill)
- Persistent vomiting (7-10 days)
- Weight loss greater than 5% (involuntary) (7-10 days)

Evidence supporting this recommendation is of class: D

4. Endoscopy for Alarm Features/Out of Guideline

Endoscopy is the procedure of choice for evaluation of dyspepsia. A single contrast barium study is not an acceptable alternative. Multiphase upper gastrointestinal (UGI) studies performed by radiologists with specific training in gastrointestinal radiology are an acceptable alternative to endoscopy.

If specialty radiologic expertise with multiphase barium UGI is available, UGI study should be viewed as an alternative to endoscopy. Otherwise, endoscopy provides greater sensitivity for the diagnosis of peptic ulcer disease.

[Conclusion Grade III: See Conclusion Grading Worksheet - Appendix A of the original guideline document, - Annotation #4]

Evidence supporting this recommendation is of classes: A, C

5. Prior Documented Ulcer?

In patients presenting with dyspepsia and a prior documented ulcer, referral to a gastroenterologist is appropriate. Documentation of the prior ulcer must include an endoscopy or barium UGI report confirming the presence of an ulcer.

6. H. pylori Testing, Eradication/Case Management

Case management should begin with H. pylori testing. Several tests are available with different sensitivity, specificity, and costs (refer to the Diagnostic Tests for Helicobacter Pylori Table in the original guideline document). Those who are positive should receive eradication therapy. (Refer to Main Algorithm Annotation #10, "Is H. pylori Testing Positive?" and Annotation #11, "Treatment for H. pylori.").

Patients who continue nonsteroidal anti-inflammatory drugs (NSAIDs) during treatment for peptic ulcers should have the duration of PPI treatment extended to twelve weeks total.

Symptoms continuing for a month or more into treatment should prompt endoscopy regardless of initial treatment. Further evaluation may be necessary.

Maintenance PPI treatment is not indicated for those experiencing symptom resolution after treatment. Patients with complicated peptic ulcer disease may be considered for maintenance treatment using PPI at one-half the therapeutic dose after successful treatment. Documenting H. pylori eradication should be limited to those with a history of complicated peptic ulcer disease.

Evidence supporting this recommendation is of classes: A, C, D, M, R

8. Is Patient Age 50 or Older, or at Increased Risk of Gastric Cancer?

Environmental and genetic factors along with a number of disorders are associated with an increased risk of gastric cancer. The precursor conditions associated with increased risk for gastric cancer include chronic atrophic gastritis and intestinal metaplasia, pernicious anemia, benign gastric ulcer disease, Helicobacter pylori infection, Menetrier's disease, gastric adenomatous polyps, immunodeficiency syndromes, and Barrett's esophagus.

Genetic and environmental factors for an increased risk of gastric cancer include a family history of gastric cancer, blood type A, hereditary nonpolyposis colon cancer syndrome, low consumption of fruits and

vegetables, consumption of salted, smoked, or poorly preserved foods, cigarette smoking, alcohol use, and obesity.

Esophagogastroduodenoscopy, performed within 4 weeks, may be appropriate in patients age 50 or over because the incidence of gastric cancer is increased, but no study to date has shown improved outcomes. [Conclusion Grade II: See Conclusion Grading Worksheet - Appendix B of the original guideline document, - Annotation #9.]

Initial endoscopy may be cost-effective in this age group; however, sensitivity analysis shows the cost effectiveness is driven by the cost of endoscopy and so will vary.

Evidence supporting this recommendation is of classes: A, C, D

10. Is H. pylori Testing Positive?

An approach to possible gastric or duodenal ulcer disease should include a strategy to eliminate *Helicobacter pylori*. Sensitive and specific point-of-care testing is commercially available and can provide 5 to 10 minute turnaround using whole blood, serum or plasma. *Helicobacter pylori* urea breath testing (UBT) has similar sensitivity and superior specificity. If the cost and availability of urea breath testing is similar to serology in the local practice environment, it would be the preferred test.

Helicobacter pylori testing appears to be a cost-effective approach for long-term dyspepsia management. [Conclusion Grade II: See Conclusion Grading Worksheet - Appendix C of the original guideline document, - Annotation #10.]

Evidence supporting this recommendation is of classes: A, C, M, R

11. Treatment for H. pylori

There are multiple regimens Food and Drug Administration (FDA) approved for treatment of *Helicobacter*. In addition, many more are published in the literature. The two following therapies are equally effective in eradicating *H. pylori* (95% effective) and in preventing gastrointestinal ulcer recurrence (80% effective). These two therapies represent a combination of ease of compliance and cost. Patient compliance is very important. The patient can and should take all drugs simultaneously. The choice of regimen may be influenced by frequency of dosing or patient tolerance or highly variable local acquisition costs.

Regardless of which therapy course is chosen, patients with significant symptoms at presentation may continue to use a standard dose of a PPI for 3 extra weeks at the end of the combination drug treatment.

Treatment choice #1: 7-day treatment

- PPI standard dose twice daily x 7 days

- Clarithromycin: 500 mg twice daily x 7 days**
- Amoxicillin: 1 gram twice daily x 7 days*

Treatment choice #2: 7-day treatment

- PPI standard dose twice daily x 7 days
- Tetracycline: 250 mg four times daily (qid) x 7 days*
- Metronidazole: 500 mg twice daily x 7 days**
- Bismuth: chew 2 tablets four times daily x 7 days

*Substitute metronidazole 500 mg twice daily x 7 days if patient is intolerant to tetracycline or amoxicillin.

**Substitute amoxicillin 1 gram twice daily x 7 days if suspect H. pylori resistance to metronidazole.

Proton Pump Inhibitors (PPI)—Generic Names, Trade Names, and Usual Adult Dose

- Esomeprazole (Nexium®) -- 40 mg daily
- Lansoprazole (Prevacid®) -- 30 mg daily
- Omeprazole (Prilosec®) -- 20 mg daily
- Pantoprazole (Protonix®) -- 40 mg daily
- Rabeprazole (Aciphex®) -- 20 mg daily

12. Empiric Trial of Full Dose PPI /Address NSAID Use

Empiric Trial

The available proton pump inhibitors (PPIs) appear to be equivalent in efficacy and in adverse event profiles in the management of acid-peptic disorders when given in equipotent acid-suppressive doses. Full-dose therapy for four weeks as an empiric trial is recommended.

Evidence supporting this recommendation is of classes: A, D, R

Patients on nonsteroidal anti-inflammatory drugs (NSAIDs)

Patients on NSAIDs should have these discontinued if possible. If it is not possible to discontinue NSAIDs, a duration of therapy of 12 weeks is recommended. This recommendation is based on well documented higher healing rates in patients with gastric as well as duodenal ulcers treated for a duration of twelve weeks compared to eight weeks. (See also Main Algorithm Discussion and References #16 in the original guideline document).

Evidence supporting this recommendation is of classes: A, C, D, M

13. Symptoms Persist >4 Weeks?

Although ulcer healing may take 8 weeks or more, the majority of patients with a gastric or duodenal ulcer have improvement in symptoms at 4 weeks.

Evidence supporting this recommendation is of classes: A, D

15. Endoscopy Positive?

Endoscopy is the procedure of choice in most situations for evaluation of dyspepsia. If an ulcer is seen, a biopsy for *H. pylori* should be taken. A single contrast barium study is not an acceptable alternative. Multiphasic UGI studies performed by radiologists with specific training in gastrointestinal radiology are an acceptable alternative to endoscopy.

16. Case Management

Patients with an ulcer should have an *H. pylori* breath test if their stomach was not biopsied at the time of endoscopy. Treatment to eradicate *H. pylori* should be provided to those infected. If previously treated for *H. pylori*, a different regimen should be used and provided for 14 days, not 7. Metronidazole should be substituted for amoxicillin in the patient who has received amoxicillin previously. If not infected with *H. pylori*, review NSAID use and smoking history as appropriate. If esophagitis is seen, refer to the GERD Algorithm (#22).

Evidence supporting this recommendation is of class: C

17. Continue Treatment for 8 Weeks Total Course and Then Stop

Data on healing rates in both gastric and duodenal ulcers suggest that treatment with antiulcer agents should be continued to complete a course of eight weeks. The most effective agents for the majority of patients are PPIs. Patients who continue NSAIDs during treatment for peptic ulcers, particularly gastric ulcers, should have the duration of PPI treatment extended to twelve weeks total.

Evidence supporting this recommendation is of classes: A, R

18. Functional Dyspepsia

Most patients who undergo endoscopy for dyspepsia will not have a positive finding to explain the symptoms. The terms "non-ulcer" or "functional dyspepsia" have been used to label this situation. No medical treatment is clearly of proven benefit. On a case-by-case basis, elimination of certain foods (e.g., caffeine, alcohol, fat, etc.) or medications (e.g., NSAIDs) may help. On a similar individual basis, eradication of *Helicobacter pylori* (if not already done), treatment with a PPI (if not already done), prokinetic or low-dose tricyclic antidepressant, and exploration of the contribution of psychologic distress may prove beneficial. Additional testing may be necessary, but over testing, overtreatment, and over referral should be avoided. Short-term empiric trials could be considered.

Evidence supporting this recommendation is of classes: A, R

21. Symptoms of GERD

GERD is the probable diagnosis if the patient has heartburn (retrosternal pain) or acid regurgitation (a sour or bitter taste in mouth) as the dominant symptom. These symptoms are sought because their presence is associated with a probability of 89% and 95%, respectively, of GERD based on studies using esophageal pH monitoring as the reference standard. The goal is to minimize the number of patients with ulcer referred to the GERD algorithm.

22. Are there Alarm Features?

Alarm features should be sought in all patients presenting with dyspepsia. If alarm features are present, endoscopy should be performed (suggested time frames for urgency of endoscopy are provided with each of the alarm features listed). Alarm features is a term that is used frequently in the dyspepsia literature to describe clinical features that may suggest underlying disease that should be diagnosed and treated without the delay of an empiric therapeutic trial. Alarm features frequently cited are:

- Anemia (7-10 days)
- Acute onset dysphagia (within 1 day)
- Hematemesis (within 1 day if ill)
- Melena (within 1 day if ill)
- Persistent vomiting (7-10 days)
- Weight loss greater than 5% (involuntary) (7-10 days)

For further discussions, please refer to Discussion and reference #3 in the original guideline document.

24. Initial Management (8 Weeks)

Initial treatment of GERD should consist of an eight-week trial of PPI therapy, more long-term behavioral modifications, and possibly endoscopy, designed to help reduce reflux both structurally and promoting proper function of the lower esophageal sphincter (LES), and also reducing acidity of gastric juices.

Proton Pump Inhibitors (PPI) Generic Names, Trade Names, and Usual Adult Dose

- Esomeprazole (Nexium®) -- 40 mg daily
- Lansoprazole (Prevacid®) -- 30 mg daily
- Omeprazole (Prilosec®) -- 20 mg daily
- Pantoprazole (Protonix®) -- 40 mg daily
- Rabeprazole (Aciphex®) -- 20 mg daily

1. Dietary changes

- A. Avoid caffeine, chocolate, fats, alcohol, caffeinated and decaffeinated tea and coffee, caffeinated soft drinks, citrus juices, peppermint, and spearmint.
- B. Weight loss if indicated.
- C. Avoid large meals that may increase intraabdominal pressure.

2. Avoid lying down after eating for 2 to 3 hours.
3. Elevate the head of the bed by 6 to 8 inches.
4. Avoid use of tobacco, with promotion of tobacco and nicotine cessation. Also consider changing medications that can lower the LES pressure (i.e., Theophylline, calcium channel blockers, and barbiturates).
5. Use of antacids on an as needed basis as well as the use of over-the-counter PPI may be of benefit.

These modifications may also take longer than four weeks to implement for the best effect (i.e., weight loss and tobacco and alcohol abuse). These factors should be rediscussed with the patient in each subsequent phase of treatment for GERD.

For patients age 50 and more or who have had symptoms for 10 years or more, consider endoscopy prior to treatments to evaluate for Barrett's esophagus.

Following up at 8 weeks to see if there has been some improvement in symptoms may be done. If there is no improvement, the patient should be referred for endoscopy.

If these modifications have already been tried by the patient and have been successful, then advancement to maintenance therapy would be appropriate.

Evidence supporting this recommendation is of class: R

26. Endoscopy

Flexible esophagogastroduodenoscopy should be used for the initial evaluation of esophageal symptoms in patients suspected of having GERD with refractory heartburn, odynophagia, or extra-esophageal symptoms. Endoscopy permits direct inspection and biopsy of the esophageal lining, aiding detection of grade 1 or grade 2 esophagitis--changes not apparent on x-rays. Endoscopy also permits detection and biopsy of Barrett's esophagus.

Evidence supporting this recommendation is of classes: C, D

27. Positive?

Patients with erosions, ulcerations, strictures or intestinal metaplasia (Barrett's esophagus) are considered to have a positive endoscopy. Patients who have either a normal esophageal examination or only distal esophageal erythema are considered to have a negative endoscopy.

Evidence supporting this recommendation is of class: C

28. Case Management for Negative Endoscopy

Diagnosing gastroesophageal reflux disease (GERD) can be difficult in patients with atypical symptoms, noncardiac chest pain, or normal endoscopy. Many

diagnostic tests to find pathological reflux have been developed. Few of them have withstood rigorous scientific testing and lack relevance to clinical management. Twenty-four hour pH monitoring has been adopted as the diagnostic test of choice in patients with symptoms of unknown cause. pH testing should be done after the patient has discontinued therapy for a week. Alternatively, a trial and practical experience suggest short-term administration of high-dose proton pump inhibitors (PPIs) can reduce symptoms and offer a reasonably accurate diagnostic discrimination in selected groups of patients with suspected GERD. All patients with complaints of heartburn do not necessarily have GERD. Patients who don't respond to therapy, and have negative pH studies should be considered to have functional heartburn. These patients should be individually managed, as are patients with other functional gastrointestinal disorders (i.e., irritable bowel syndrome, non-ulcer dyspepsia.)

Evidence supporting this recommendation is of class: C

29. Case Management for Refractory Reflux

Patients with erosive esophagitis or worse should be treated with proton pump inhibitors (PPI) in a double therapeutic dose. If Esomeprazole (Nexium®) has not been used at this point, it would be reasonable to try a therapeutic trial. Patients intolerant of PPIs may receive a quadruple therapeutic dose of histamine-2 receptor antagonists (H₂RA). Failure to respond should prompt doubling the dose of the antisecretory medication and referral to gastroenterology. Duration of treatment should be indefinite within a single trial of step-down.

Patients requiring long-term maintenance therapy, or those who are incompletely controlled on maintenance therapy with a single trial of step-down, may wish a surgical opinion regarding fundoplication or bariatric surgery (body mass index [BMI] greater than 35), or GI opinion regarding endoscopic approaches.

Evidence supporting this recommendation is of classes: A, M, R

30. Encourage Single Trial Step-Down Therapy

Patients with uncomplicated reflux may benefit from step-down therapy. Step-down therapy gradually reduces the intensity of treatment as tolerated to maintain the patient in remission. Lifestyle modifications should be continued indefinitely. Patients whose initial symptoms were controlled by lifestyle measures initially may require only occasional PPIs.

Evidence supporting this recommendation is of classes: A, D, R

33. Return to Chronic PPI Therapy

Most patients with typical reflux symptoms will respond to acid suppressive therapy. This guideline encourages trying to reduce the therapy over time but

many patients will stay on such therapy for months if not years. As long as these patients are not symptomatic, they do not require an endoscopy.

Some groups have suggested, however, that patients with reflux should have an endoscopy to screen for Barrett's esophagus (BE). BE is a change in the lining of the esophagus from the normal squamous mucosa to a metaplastic intestinal columnar mucosa. Patients with BE are at increased risk of adenocarcinoma of the esophagus and thus patients with BE are placed into endoscopic surveillance programs.

The American College of Gastroenterology recommends: "Patients with chronic GERD symptoms are those most likely to have Barrett's esophagus and should undergo endoscopy."

At present there are no data to demonstrate the cost-effectiveness of such a strategy. Patients with longer duration of symptoms (greater than 10 years) are more likely to have BE. White men are at increased risk. Selecting patients on the basis of risk would improve the cost effectiveness but has not been incorporated into guidelines. Given the absence of clear evidence of benefit, screening for Barrett's esophagus in patients with GERD cannot be advocated in all patients.

Patients requiring long-term maintenance therapy, or those who are incompletely controlled on maintenance therapy with a single trial of step-down, may wish a surgical opinion regarding fundoplication or bariatric surgery (BMI greater than 35), or GI opinion regarding endoscopic approaches.

Evidence supporting this recommendation is of class: R

Definitions:

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to

the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided for:

- [Dyspepsia](#)
- [Gastroesophageal Reflux Disease \(GERD\)](#)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The guideline contains an annotated bibliography and discussion of the evidence supporting each recommendation. The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations (i.e., choice among alternative therapeutic approaches) is graded for each study.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate evaluation of epigastric discomfort and management of gastroesophageal reflux disease (GERD)
- Appropriate diagnosis of underlying disease in patients with upper gastrointestinal tract pain or discomfort, such as duodenal ulcer, gastric ulcer, non-ulcer dyspepsia, or GERD.
- Timely management and treatment of patients with dyspepsia, including relief of symptoms

POTENTIAL HARMS

The PPIs are metabolized via hepatic cytochrome P450 enzymes, with CYP2C19 having the dominant role. However, the dominance of this route varies significantly among the PPIs. The specific P450 enzymes involved in PPI metabolism and the potential for interactions among these agents shows variation. Omeprazole is metabolized largely via CYP2C19, and the potential for interactions thus appears to be the greatest among the PPIs. If this metabolic pathway becomes saturated, there is the possibility for interactions with many drugs, including warfarin, diazepam, and phenytoin. While rabeprazole is also metabolized by this isoenzyme, it apparently possesses significant affinity for CYP3A4; very few interactions have been documented with rabeprazole. Lansoprazole is metabolized principally via CYP3A4, and interactions with theophylline have been reported. As the metabolism of pantoprazole primarily involves CYP2C19 O-demethylation, significant CYP3A4 and CYP1A induction is not

seen. This agent has the lowest potential for P450 metabolism and drug interactions.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for release, a member group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment and tobacco cessation.

The following detailed measurement strategies are presented to help close the gap between clinical practice and the guideline recommendations.

Priority Aims and Suggested Measures for Health Care Systems

1. To increase the use of recommended methods for evaluating dyspepsia.

Possible measures of accomplishing this aim:

- a. Percentage of patients evaluated for dyspepsia with testing for *Helicobacter pylori* (*H. pylori*).
- b. Percentage of patients evaluated for dyspepsia without standard single-phase contrast studies.

- c. Percent of patients evaluated for dyspepsia with endoscopy prior to receiving a therapeutic trial who do not have an alarm feature present.
2. To increase appropriate pharmaceutical treatment of patients with dyspepsia.

Possible measures of accomplishing this aim:

- a. Percentage of patients with dyspepsia with positive H. pylori who receive antibiotic therapy.
 - b. Percentage of patients with dyspepsia treated with antibiotics for positive H. pylori who receive effective therapy.
 - c. Percentage of patients with dyspepsia treated with a proton pump inhibitor (PPI) or long-term histamine-2 receptor agonist (H₂RA) without previous endoscopic examination.
3. To decrease complications associated with peptic ulcer disease.

Possible measure of accomplishing this aim:

- a. Number (or rate) of hospital admissions for ulcer hemorrhage.
4. To improve (functional) outcomes and satisfaction of patients with dyspepsia.

Possible measures of accomplishing this aim:

- a. Percentage of patients evaluated with dyspepsia with improved symptoms following treatment as measured by a dyspepsia-specific health status instrument.
 - b. Percentage of patients with dyspepsia who report that they are satisfied or very satisfied following treatment for dyspepsia.
5. Increase the use of initial treatment recommendations for evaluating gastroesophageal reflux disease (GERD).

Possible measures for accomplishing this aim:

- a. Percentage of patients with GERD following behavioral modification recommendations.
 - b. Percentage of patients with GERD treated with PPI for an 8-week period.
 - c. Percentage of patients with GERD reporting relief of symptoms after 8-week trial of PPI.
 - d. Percentage of patients with GERD and control of symptoms with a PPI who have had a trial of step down therapy.
6. To increase appropriate treatment for patients who have ongoing symptoms after initial treatment recommendations.

Possible measures for accomplishing this aim:

- a. Percentage of patients with continued symptoms of GERD after an 8-week trial of PPI having an endoscopy.

- b. Percentage of patients age 50 (and over) who have GERD or a history of GERD for 10 years or more who have been evaluated with endoscopy.
- c. Percentage of patients with ongoing symptoms of GERD (see annotation #1) and a body mass index [BMI] greater than 35 referred for surgical opinion regarding fundoplication, bariatric surgery and/ or endoscopic approaches.

Note: There are no specifications written for the possible measures listed above. The Institute for Clinical Systems Improvement (ICSI) will seek input from medical groups on what measures are of most use as they implement the guideline. In a future revision of the guideline, measurement specifications may be included.

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Dyspepsia and GERD. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 Jul. 50 p. [102 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Oct (revised 2004 Jul)

GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT SpecialtyCare, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, Hamm Clinic, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hennepin Faculty Associates, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Health Care, North Suburban Family Physicians, NorthPoint Health & Wellness Center, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, St. Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Winona Health

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GUIDELINE COMMITTEE

Committee on Evidence-Based Practice

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, ICSI has adopted a policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

G. Richard R. Locke, MD is a consultant for Glaxo Wellcome and Novartis and receives grant support from AstraZeneca, Forest Laboratories, Glaxo Wellcome, Janssen Pharmaceutica, SmithKline Beecham, and Solvay.

No other work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at www.icsi.org.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: Dyspepsia. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Jan. 48 p.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ICSI pocket guidelines. April 2004 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2004. 404 p.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on October 9, 2002. The information was verified by the guideline developer on October 21, 2002. This summary was updated by ECRI on October 13, 2000, December 4, 2002 and most recently on April 18, 2003. The updated information was verified by the guideline developer on May 22, 2003. This summary was updated again by ECRI on September 16, 2004.

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