

The following abstracts—from medical journals containing the most recent literature on gastrointestinal disorders, H. pylori infections, GERD, and duodenal ulcers—were selected for their relevance to a managed care perspective.

Continuous Maintenance Treatment of Reflux Esophagitis

Fundamental questions were addressed regarding the natural history and complications of erosive esophagitis and the need for maintenance treatment in patients with severe disease and the impact of such treatment on the course of disease and its complications. It was determined that the immediate goal should be to keep patients asymptomatic providing them with an acceptable quality of life, and consequently preventing recurrent erosion of the esophageal mucosa. Patients should be encouraged to make lifestyle modifications in diet, weight reduction, and sleeping position and should be advised of the necessity of long-term treatment with agents to reduce gastric acid secretion. H₂-receptor antagonists (H₂RAs) in the higher-dosage regimens are approved for the treatment of reflux esophagitis. Proton pump inhibitors are also successful in controlling symptoms of reflux esophagitis and in healing esophageal erosions, proving superior to standard doses of H₂RAs for this condition. Since 80% of patients may experience symptomatic recurrence of disease within 6 months in the absence of adequate maintenance therapy, continuous treatment or repeated courses of short-term treatment have been recommended. Since maintenance of healing is an important factor in treatment, continuous treatment, as opposed to short-term treatment, may prove to be the therapy of choice.

Howden CW, Castell DO, Cohen S, et al. The rationale for continuous maintenance treatment of reflux esophagitis. *Arch Intern Med* 1995;155:1465-1471

Prevalence of GERD

Estimating the prevalence of GERD is difficult, since there is no precise definition or standard for the disease. Symptoms are variable and even occur in healthy people. If a diagnosis is to be made from typical symptoms, they must be troublesome in the least to justify the term "disease," and may even be further qualified based on the need for treatment. GERD may be said to affect 10% of the adult population (defined as those who demonstrate reflux symptoms and who use antacids). The 1-year incidence of endoscopic esophagitis has been shown to be 1.2%. Esophagitis was also found in about 10% of the population; however, owing to disputable criteria, the prevalence is more likely about 5% and is found more often in men than in women. The severity of GERD with regard to symptoms and esophagitis tends to increase with age.

Petersen H. The prevalence of gastroesophageal reflux disease. *Scand J Gastroenterol* 1995;30:5-6

Cost Effectiveness of Treatment Alternatives for Refractory GERD

Despite the introduction of H₂-receptor antagonists, a percentage of GERD patients have not responded well to medical treatment. Omeprazole has become a treatment option, offering relief for patients with Grade III or Grade IV esophagitis. However, cessation of treatment results in rapid relapse. An alternative treatment is surgery (Nissen fundoplication) and is performed most frequently in The Netherlands. A meta-analysis of published articles was conducted to compare maintenance treatment with omeprazole with open and laparoscopic Nissen fundoplication from a health-economic perspective. The goal of medical treatment is to reduce gastric acidity; surgery attempts to restore lower esophageal sphincter pressure. The absence of esophagitis is the central comparative factor (study and results were restricted to this factor). Surgery appears to be a cost-effective treatment option for patients with severe or refractory GERD compared with medical treatment (omeprazole) that lasts longer than 4 years. If effectiveness is based solely on keeping patients in full remission of esophagitis, surgery will lead to substantial savings from this point onwards. A laparoscopic Nissen procedure might be even more cost effective owing to a reduced hospital stay and would be more cost effective than medical treatment, if this treatment is to last longer than 17 months. In addition to potential superiority because of its associated decrease in postoperative morbidity, laparoscopic surgery is also likely to be more cost effective.

van den Boom G, Go PMMYH, Hameeteman W, Dallemagne B. Cost effectiveness of medical versus surgical treatment in patients with severe or refractory gastroesophageal reflux disease in The Netherlands. *Scand J Gastroenterol* 1996;31:1-9

Preventing Relapse in Reflux Esophagitis

Recurrence rates of reflux esophagitis following endoscopic healing were compared using daily omeprazole (20 mg every morning; n=53), weekend omeprazole (20 mg three consecutive days per week, n=55), and daily ranitidine (150 mg twice daily, n=51). Patients were assessed for relapse by endoscopy at 6 and 12 months, or at recurrence of symptoms, and serum gastrin was monitored. At 12 months, the estimated proportion of patients in remission was 89% when receiving daily omeprazole compared with 32% when receiving weekend omeprazole. Median gastrin concentrations increased slightly during healing, but remained within the normal range and did not change during the maintenance phase. A relationship was demonstrated between the amount of acid suppression and successful maintenance of healing and symptom control. Acute treatment with omeprazole 20 mg each morning was found to be safe and highly effective long-term for preventing relapse of reflux esophagitis and associated symptoms.

Dent J, Yeomans ND, Mackinnon M, et al. Omeprazole v ranitidine for prevention of relapse in reflux esophagitis. A controlled double blind trial of their efficacy and safety. *Cut* 1994;35:590-598

H. pylori in Gastric Ulcer Disease

Short- and medium-term experience in patients with *H. pylori* associated gastric ulcers treated with omeprazole and antibiotics was reported to demonstrate the role of anti-*H. pylori* treatment in gastric ulcer disease. Patients (N=83) presenting with *H. pylori*-positive active gastric ulcer disease were treated with omeprazole and antibiotics in seven different clinical protocols designed to eradicate *H. pylori* infection and to evaluate the post-therapeutic course of ulcer disease. In patients available for follow-up (53 of 78), *H. pylori* eradication was 67.9%. Optimal results were obtained with 2-week treatment regimens comprising omeprazole 20 mg bid and amoxicillin 500 mg qid, or 1000 mg bid (eradication 80%). Eradication of *H. pylori* was found to hasten ulcer healing, with a 6-week healing rate of 84.9% compared with 60% of patients with persistent infection (P=0.0148). Fifty patients with healed ulcers were followed for 1 year. *H. pylori* eradication was associated with a statistically significant reduction in ulcer recurrences (3.1 v 55.6%, P). Eradicating *H. pylori* not only changes the natural history of *H. pylori* associated gastric ulcer disease, but also hastens ulcer healing and is associated with healing previously refractory ulcers. Amoxicillin/omeprazole should be considered the treatment of choice to eradicate *H. pylori* in duodenal and gastric ulcers that are caused by this micro-organism.

Labenz J, Borsch G. Evidence for the essential role of *Helicobacter pylori* in gastric ulcer disease. *Cut* 1994;35:19-22.

Cost Comparison of PPIs and H2RAs for Erosive GERD

Nearly 2% of patients with GERD suffer from erosive GERD, a more severe variant with potential complications such as esophageal strictures, hemorrhage, Barrett's esophagus, and esophageal cancer. Although it has become more evident that proton pump inhibitors (PPIs) are the most effective agents for healing and preventing recurrence of erosive GERD, many physicians still prefer to use H2-receptor antagonists (H2RAs) as initial therapy, possibly resulting from the misconception that PPIs are more costly. To aid physicians in treatment decisions for erosive esophagitis, a 15-member panel including gastroenterologists, primary care physicians from both academic and community settings, and healthcare economists and pharmacists met to construct a decision-analysis model. The results of the model indicate that the cost of using PPIs as initial treatment for erosive GERD was approximately equal over a 1-year period to that of using generic H2RAs (\$1,192 and \$1,152 respectively). The cost of using branded H2RAs was \$1,495 per year. A threshold analysis was performed to calculate the percentage of generic H2RAs that would be prescribed in a patient population so that the annual cost of H2RA treatment would equal the annual cost of PPI treatment. Although this analysis was biased against PPIs whenever doubt existed over data sources, treatment protocols, or analysis plans, treatment of erosive esophagitis initially with PPIs was found to be more effective and less costly than treating initially with H2RAs over a 1-year period.

Zagari M, Villa KF, Freston JW. Proton pump inhibitors versus H2-receptor antagonists for the treatment of erosive gastroesophageal reflux disease: A cost-comparative study. *Am J Man Care* 1995;1:247-255

UBT for *H. pylori*

The urea breath test (UBT) is an important non-invasive test for *H. pylori*. Used mainly after *H. pylori* eradication, it is easy to perform, reliable, inexpensive, and poses no risk to patients. UBT is already used widely in research and deserves greater use in clinical practice. Urea isotopically labeled with the radioactive isotope ¹³C or ¹⁴C is given orally. If *H. pylori* is present in the stomach, its urease enzyme hydrolyses the urea producing isotopically labeled CO₂. This diffuses into blood, is excreted by the lungs, and can be detected in the breath. For the primary diagnosis of gastroduodenal pathology, endoscopic tests are indicated rather than UBTs, since endoscopy gives more information than just to determine the presence of *H. pylori*. The main indication for UBTs occurs after attempted *H. pylori* eradication and where follow-up endoscopy is unnecessary. Confirming eradication is important, since treatment failure is common. However, UBT is also important for checking for infection when an ulcer is found at endoscopy but biopsy specimens cannot be taken because of anticoagulant treatment. To avoid inaccuracies in testing, UBTs should not be given within one month after a course of antibiotics, bismuth, or omeprazole or immediately following gastric surgery because of rapid emptying of urea from the stomach.

Atherton JC, Spiller RC The urea breath test for *Helicobacter pylori* Gut 1994;35:723-725

Guidelines for Management of Gastrointestinal Reflux Disease in Managed Care

Gastrointestinal reflux disease (GERD) is a common problem in primary care practice and results in high rates of healthcare use. Management often has been based on patient preferences and physician biases. A diverse group of experts assembled to consider recommendations for the evaluation and treatment of patients with symptoms of GERD in a managed care setting, and to identify outcomes that would require additional research. Two algorithms based on endoscopic findings were designed—one for the treatment of complicated GERD, and the second for treatment of uncomplicated GERD. The experts advised that the choice of treatment strategy be based on benefits achieved in long-term follow-up. The goals of therapy in a managed care or fee-for-service environment were identified as eliminating symptoms, healing esophageal injury, managing and preventing of complications (eg, strictures), and preventing recurrence. In cases of GERD with esophagitis, treatment goals included eliminating symptoms, healing esophagitis, preventing and controlling complications, and maintaining remission. In the absence of esophagitis, the goal is effective treatment using the lowest cost-effective dose of an antisecretory or prokinetic agent.

Fennerty MB, Castell D, Fendrick M, et al The diagnosis and treatment of gastroesophageal reflux disease in a managed care environment. Arch Intern Med 1996;156:477-484.

Costs of GI-Tract Illness Associated with Day-Care Attendance

The risk of diarrheal illness has been estimated from several studies to be from 2.2 to 3.5 times higher for children in day-care centers (DCCs) than for children cared for at home. To estimate the total cost of gastrointestinal-tract illness contracted in DCCs, data was collected during a 16-month cohort study of rotavirus diarrhea in four DCCs. Parents were surveyed to assess factors affecting cost of illness and the range of child-care options employed. The DCC study population included children between ages 1 to 18 months with no known underlying disease. A research nurse visited each DCC daily to record attendance and the occurrence of diarrhea in the study children. If a child were absent, child-care providers reported the reason for absence and made follow-up calls to parents to confirm the reason for absence when it was not previously reported. Diarrhea was defined as an episode lasting more than 24 hours with two or more loose or watery stools in a 24-hour period, or with a change in the child's normal stool pattern to twice the usual frequency. A new episode was determined if there were 7 or more symptom-free days since the previous episode. Direct costs were determined based on estimates for physician care and hospitalization, representing a total probable cost of \$20.70 per episode of diarrhea per child (\$5.50 per episode for physician office visits and \$15.20 per episode for hospitalization), considering that there was a 10% chance that an episode would lead to a physician visit and a 6% chance that an episode would lead to hospitalization. Indirect costs were determined from responses on the parent-questionnaire. The mean total cost of diarrheal illness in this cohort was \$172.01 per child-year among children under 3 years of age. The primary component of the cost of all diarrheal illness among children attending DCCs, however, may not be medical, but associated with ill-child care.

Hardy AM, Lairson DR, Morrow AL Costs associated with gastrointestinal-tract illness among children attending day-care centers in Houston, Texas. Pediatrics 1994;94:1091-1093

Costs of Alternative Strategies for Duodenal Ulcer

A cost comparison using decision analysis was used to determine the optimal management strategy for duodenal ulcer and to determine if there were cost savings associated with initial eradication of *H. pylori* in comparison to traditional acid suppression; to determine the necessity of urease testing and its effect on cost; and to determine if the optimal treatment strategy was affected by factors such as the prevalence of *H. pylori* infection and concomitant cost and side effects. Probability estimates were derived from published clinical trials, cohort studies of patients at low risk for malignant ulcer, and expert opinion. Side effects from combination therapy, antibiotics and H₂-receptor antagonists (H₂RAs), and resulting costs were included from the perspective of a model HMO. Initial therapy with antibiotics for *H. pylori* plus an H₂RA proved least costly when the prevalence or likelihood of *H. pylori* infection exceeded 66% to 76%. Costs ranged from \$284 for re-treatment with empiric antibiotic and H₂RA to \$398 for endoscopy-guided secondary treatment. The consensus concluded that treatment of ulcer disease, whether first presentation or recurrence, should include antimicrobial agents in addition to an H₂RA, to realize not only cost savings but also lower recurrence rates. *H. pylori* eradication should be part of the initial treatment for duodenal ulcer.

Imperiale TF, Speroff T, Cebul RD, McCullough AJ. A cost analysis of alternative treatments for duodenal ulcer. *Ann Intern Med* 1995;123:665-672

Treating Acute Duodenal Ulceration

A double-blind, controlled study was conducted to compare the efficacy and safety of lansoprazole (15 mg or 30 mg) with ranitidine (300 mg) and placebo in relieving symptoms and promoting healing of acute duodenal ulceration and to examine the effects of these agents on serum gastrin levels, ECL density, and *H. pylori* colonization. Patients (N=280) with one or more endoscopically confirmed duodenal ulcer crater at least 3 mm in diameter, either in the duodenal or pyloric canal, were randomized into four groups: 80 patients entered into each active treatment group and 40 into the placebo group. Endoscopies were performed and blood and urine tests were repeated at 2- and 4-week intervals following initial treatment. Patients were provided diary cards to record symptoms. The occurrence and severity of adverse events and their relationship to study medication were evaluated. After 4 weeks of treatment, 19 of 40 (47.5%) patients receiving placebo had healed compared with 55 of 78 (70.5%) receiving ranitidine (*p* vs placebo), 61 of 76 (80.3%) receiving lansoprazole 30 mg (*p* vs placebo), and 72 of 78 (92.3%) receiving lansoprazole 15 mg (*p* vs placebo and ranitidine). Lansoprazole 15 mg and 30 mg were equally effective and well tolerated. Treatment with lansoprazole 30 mg produced superior 4-week healing rates and symptom relief to those produced by placebo or standard dose ranitidine (300 mg).

Lanza F, Goff J, Scowcroft C, et al. Double-blind comparison of lansoprazole, ranitidine, and placebo in the treatment of acute duodenal ulcer. *Am J Gastroenterol* 1994;89:1191-1200.

Cost Benefit of GERD Management

GERD symptoms involve a variety of organs, including chest, lungs, throat, and intestines and affect as many as 40% of the general adult population monthly and 7% daily. The duration of symptoms in patients seeking help for reflux is often more than 5 years in an unselected population. GERD exerts a great influence on quality of life (QoL), since the symptoms impose themselves on victims throughout daily activities. QoL is low in patients with reflux esophagitis and upper dyspepsia. Values normalize during medical treatment or after surgery for reflux esophagitis. The impact of GERD is reflected in medical use and consultation; thus, cost is an important factor to consider when evaluating treatment options. Cost of treatment is complex and includes direct costs of therapy, consultations, endoscopy, and surgery, as well as indirect costs, such as loss of productivity, further consultations, sick leave, and decreased working capacity. Based on results of clinical healing trials, omeprazole has been found the most cost-effective drug for treating reflux esophagitis. No evaluations have been made for patients with reflux symptoms only. Consequences for the patient and society should be evaluated to optimize future therapy.

Glise H. Quality of life and cost of therapy in reflux disease. *Scan J Gastroenterol* 1995;30:38-42.

CME QUESTIONS: TEST #0296S5

Instructions

After reading this Educational Roundtable special report, select the best answer to each of the following questions. In order to receive 1 CME credit, at least 7 of the 10 answers must be correct. Estimated time for this activity is one hour. CME credits are distributed on a yearly basis.

1. **Acid-related disorders are costly mainly because:**
 - a) complications are common
 - b) the necessary medications and other therapies are expensive
 - c) they are widely prevalent and often require lifelong management
 - d) they frequently necessitate surgical intervention
 - e) patients need frequent testing and monitoring

2. **Studies show reflux disease symptoms are completely and quickly relieved with:**
 - a) sulcrafate and a cytoprotective agent
 - b) proton pump inhibitors (PPIs)
 - c) H2-receptors (H2RAs)
 - d) bismuth-based triple therapy
 - e) liquid antacids and antibiotics

3. **For duodenal and gastric ulcers, the most cost-effective approach may be to:**
 - a) heal the ulcer with antisecretory drugs
 - b) educate the patient about diet and lifestyle changes
 - c) pursue surgical intervention with the initial presentation
 - d) eradicate *Helicobacter pylori*
 - e) advise the patient to pursue an aggressive self-treatment program

4. **Choosing a regimen that is easy for patients to comply with is cost-effective for all but one these reasons: (choose the "wrong" answer)**
 - a) complex regimens are associated with decreased compliance
 - b) if compliance is decreased, efficacy is decreased
 - c) an easy-to-comply-with regimen will encourage repeat office visits
 - d) decreased compliance leads to recurrence
 - e) treatment costs increase as compliance rates decrease

5. **Looking at all costs over a 1-year period, the most effective regimen for an H. pylori associated ulcer would be:**
 - a) an H2RA alone for 21 days
 - b) PPI-based triple therapy for 7 to 10 days
 - c) a PPI alone for 3 to 6 weeks
 - d) dual therapy for 14 to 21 days
 - e) bismuth-based triple therapy for 14 days

6. **Appropriate and cost-effective management of upper gastrointestinal disorders requires:**
 - a) a long-term outlook and possibly long-term maintenance
 - b) emphasis on outcomes after 6 months to 1 year
 - c) utilization of the least expensive acute therapy
 - d) restrictive utilization of therapies and testing procedures
 - e) immediate treatment with rapid resolution of the disorder

7. **Costs calculated in 1994 for gastrointestinal diseases include all except: (choose the "wrong" answer)**
 - a) hospitalizations (\$1.78 billion in direct costs)
 - b) office visits (\$127 million)
 - c) prescription drugs (\$56 million)
 - d) lost work time (\$304 million)
 - e) testing procedures (\$250 million)

8. **Proper ICD-9 coding for gastrointestinal disorders is important because:**
 - a) correct coding will yield accurate and reliable data about these disorders
 - b) improper coding may result in reduced capitation rates
 - c) correct coding can increase the number of patient referrals
 - d) incorrect coding may lead to more restrictive formularies
 - e) proper coding can create more precise diagnostic categories

9. **Panel consensus is that the most cost-effective diagnostic test for GERD is:**
 - a) an upper GI series
 - b) guaiac test of the stool
 - c) one-time endoscopy
 - d) 24-hour pH monitoring
 - e) careful history taking

10. **The most important cost-effectiveness consideration in choosing a regimen is:**
 - a) cost of acquiring the medication
 - b) dosing schedule; more frequent dosages cost more
 - c) effectiveness, because ineffectiveness will end up costing more
 - d) the safety profile, because side-effects are expensive to treat
 - e) whether or not the manufacturer offers bundling and value-added services

<p>AMA/CME TEST FORM</p> <p>AJMC Test #0296S5</p> <p>Shifting Paradigms in the Treatment of Acid-Related Disorders</p> <p><i>Application for 1 Credit Hour of AMA Category I</i></p> <p>(Test valid through May 31, 1997 No credit will be given after this date.)</p>	<p>Please circle your answers:</p> <p>1 a b c d e</p> <p>2 a b c d e</p> <p>3 a b c d e</p> <p>4 a b c d e</p> <p>5 a b c d e</p> <p>6 a b c d e</p> <p>7 a b c d e</p> <p>8 a b c d e</p> <p>9 a b c d e</p> <p>10 a b c d e</p>	<p>(PLEASE PRINT CLEARLY)</p> <p>Name _____</p> <p>Address _____</p> <p>City _____</p> <p>State/Zip _____</p> <p>Phone # _____</p> <p>Please enclose a check for \$10, payable to American Medical Publishing, LLC, and mail with this form to:</p> <p style="text-align: center;">The AJMC CME Test American Medical Publishing 322-D Englishtown Road, Suite 101 Old Bridge, NJ 08857</p>
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yes no

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yes no

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yes no

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