

The following abstracts, from peer-reviewed journals containing literature on H pylori testing and eradication were selected for their relevance to this seminar and to a managed care perspective.

Costs and Efficacy of Eight Antibiotic Regimens vs Maintenance Therapy

The authors of this report evaluated the costs and outcomes of eight antibiotic regimens and compared them with the costs and outcomes of maintenance therapy with H₂-receptor antagonists in patients with H pylori-induced duodenal ulcer. They first determined aggregate eradication rates by performing a meta-analysis of 119 studies involving 6416 patients. They then used the complexity of each regimen to determine actual effectiveness and the anticipated rate of compliance, as well as a decision analytic model to determine health outcomes and annual costs. Average annual total costs of H pylori testing and antibiotic therapy ranged from \$223 to \$410 and prevented ulcer recurrence in 70% to 86% of the patients under study. Maintenance therapy cost \$424 and prevented ulcer recurrence in 72% of patients. Of the eight regimens evaluated, all had documented activity against H pylori and all resulted in lower costs compared with maintenance therapy. Three of the eight regimens were associated with the lowest costs and the lowest recurrence rates. They were: standard triple therapy (BMT) for 14 days (\$233; 18% recurrence), triple therapy with a PPI, metronidazole, and clarithromycin for 7 days (\$235; 15% recurrence), and standard triple therapy plus a PPI for 7 days (\$236; 14% recurrence). The authors conclude that all patients with duodenal ulcer induced by H pylori should have their infection eradicated, preferably by regimens with consistently lower costs and better outcomes.

Taylor JL, Zagari M, Murphy K, Freston JW. Pharmacoeconomic comparison of treatments for the eradication of *Helicobacter pylori*. *Arch Intern Med* 1997;157:87-97.

Screening and Eradication in Dyspeptic Patients Under 45

In this study, the authors compared two interventions to assess the cost effectiveness of H pylori screening and eradication treatment in patients under the age of 45 presenting with peptic-type dyspepsia. The interventions were: conventional empiric treatment with healing and maintenance doses of cimetidine vs eradication solely in patients with confirmed peptic ulcer; and conventional empiric therapy for all patients with dyspepsia vs the use of a serology test to identify patients with H pylori. The latter group of patients then underwent endoscopy and, when peptic ulcer disease was found, were treated with an eradication regimen. A urea breath test was subsequently done to confirm successful eradication of the organism. The main outcome measures were the expected cumulative costs over 10 years and the proportion of time the patients spent without ulcer recurrence. A decision analytic model was used to represent the epidemiology of dyspepsia; a Markov process was used to model the outcomes of the treatment interventions. Patients with a confirmed ulcer spent an average of 99% of their time free from recurrence after receiving eradication therapy. By comparison, patients treated with cimetidine spent an average of 95% of their time being recurrence-free. Moreover, the authors found that eradication therapy was less costly than cimetidine treatment. However, when the initial cost of identifying which patients should receive eradication therapy was added to the analysis, the cost savings took almost 8 years to accrue. Thus, enthusiasm for testing and eradication in dyspeptic patients seen in general practice should be tempered by the fact that cost savings are not realized until many years later.

Briggs AH, Sculpher MJ, Logan RP, Aldous J, Ramsay ME, Baron JH. Cost effectiveness of screening for and eradication of *Helicobacter pylori* in management of dyspeptic patients under 45 years of age. *Br Med J* 1996;312:1321-1325.

Impact of Eradication on Ulcer Drug Use and Complications

In this British study of the clinical consequences and financial implications of H pylori eradication, the authors assessed the use of ulcer-healing medications and antacids in a total of 175 patients with peptic ulcer disease by means of a quarterly questionnaire. The organism had been successfully eradicated in 106 of these patients for a mean of 3.2 years, but not in 69, who remained infected. In the former group, gastrointestinal hemorrhage during the 344 patient years after eradication was 18-fold lower (0.003 per patient year) than during the 912 patient years before eradication (0.056 per patient year). In addition, fewer patients in this group used ulcer-healing medication (12%-18%) during any one quarter of the year-long survey than did those with residual infection (34%-51%). Similarly, the average cost of the ulcer-healing drugs used during the survey was lower for those in whom infection had been eradicated (£30.59) than in those who remained positive (£99.05). Antacid consumption was also lower in those who were free of infection. Thus, successful eradication significantly reduced the annual cost of ulcer-healing drugs, and maintenance of ulcer remission after eradication significantly reduced the occurrence of ulcer complications.

Powell KU, Bell GD, Bolton GH, et al. *Helicobacter pylori* eradication in patients with peptic ulcer disease: Clinical consequences and financial implications. *Q J Med* 1994;87:283-290.

Benefits of Eradication in Ulcer Disease, Recurrence, and Gastritis

The author of this review from The Netherlands addresses the role of H pylori and the effect of its eradication not only on peptic ulcer disease, but also on gastritis, atrophic gastritis, and gastric cancer. In the review, the author places special emphasis on the various factors that influence the clinical course of H pylori infection, including severity of inflammation, bacterial factors such as *cag A* pathogenicity, and host factors such as acid production. The author points out that H pylori induces chronic gastritis in virtually all infected patients, with the inflammation leading to peptic ulceration and atrophic gastritis in a considerable number of infected individuals, and eventually to gastric cancer in a minority of those infected. The author concludes that eradication of the organism is required for patients with peptic ulcer disease and may also be advocated for patients on profound acid suppressive therapy, noting that eradication has been shown to cure gastritis and prevent ulcer recurrence. However, the author calls for further study to determine the efficacy of eradication in the primary and secondary prevention of atrophic gastritis and gastric carcinoma.

Kuipers EJ. *Helicobacter pylori* and the risk and management of associated diseases: Gastritis, ulcer disease, atrophic gastritis and gastric cancer. *Aliment Pharmacol Ther* 1997;11(suppl 1):71- 88.

Cost-Effectiveness of Nine Eradication Strategies

In this Canadian study, the authors used published data and decision analysis techniques to estimate the cost effectiveness of nine eradication strategies in the management of patients with uncomplicated duodenal ulcer. Two strategies utilized intermittent therapy with either omeprazole or ranitidine, one strategy employed continuous maintenance therapy with ranitidine, and six strategies used ulcer-healing drugs plus antibiotics to eradicate H pylori infection. The authors first estimated curves of ulcer healing time on the basis of published data and estimation of expected time for acute healing episodes. They then combined these data on healing time with the probability of ulcer recurrence to estimate the expected number of weeks to heal per patient. They found that patients who received any of the six eradication regimens containing antibiotics had fewer days per year with ulcer than did those who received maintenance of intermittent therapy with ranitidine. In addition to better outcomes, four of these six eradication regimens also had lower costs than ranitidine therapy. The authors also found that two regimens using omeprazole plus one antibiotic (either amoxicillin or clarithromycin) were more costly than two other regimens using omeprazole plus two antibiotics (amoxicillin and metronidazole or clarithromycin and metronidazole), although the outcomes with all four were similar. While omeprazole-based regimens were more costly than ranitidine/bismuth triple therapy, they were associated with fewer ulcer recurrences and fewer days with symptoms. The analysis did not take compliance and metronidazole resistance into account. However, as the authors point out, compliance is becoming less of an issue as eradication regimens become simpler to comply with and shorter in duration.

O'Brien B, Goeree R, Hunt R, Wilkinson J, Levine M, William A. Cost effectiveness of alternative *Helicobacter pylori* eradication strategies in the management of duodenal ulcer. *Can J Gastroenterol* 1997;11:323-331.

Short-Term, Low-Dose Therapy with Lansoprazole and Two Antibiotics

In an effort to improve standard eradication treatment (with omeprazole plus two antibiotics) by reducing both the number of pills required each day and the total cost of therapy, the investigators for this Italian study evaluated a new, short-term, low-dose triple-therapy regimen (LAM) consisting of lansoprazole (30 mg a day for 7 days), azithromycin (500 mg a day for 3 days), and metronidazole (250 mg twice a day for the same 3 days). Patient compliance, drug tolerance, and drug costs were also considered in the evaluation. The LAM regimen was given to 60 patients presenting with H pylori-positive gastritis (with or without peptic ulcer) and compared with the classic OCT regimen (omeprazole/clarithromycin/tinidazole) given to 60 matched patients. H pylori infection was evaluated before and after eradication by rapid urease assay and conventional histology. Biopsies from the corpus and antrum were taken before eradication therapy and again 7 to 8 weeks after treatment was discontinued to confirm eradication. In the LAM group, H pylori was eradicated in 56 of the 60 patients (93.3%); in the OCT group, the organism was eradicated in 52 of the 57 patients who completed the treatment (91.2%). The difference between the eradication rates for the two groups was not statistically significant. Ulcer healing was observed in all patients with gastric or duodenal ulcer. The authors conclude that the short-term, low-dose LAM regimen is as effective as the OCT regimen in terms of eradication. More important, the new LAM regimen also appears to have advantages over OCT with regard to drug tolerance, patient compliance, and cost of therapy.

Caselli M, Trevisani L, Tursi A, et al Short-term low-dose triple therapy with azithromycin, metronidazole, and lansoprazole appears highly effective for the eradication of *Helicobacter pylori*. *Eur J Gastroenterol Hepatol* 1997;9:45-48.

Cost-Effectiveness of Three Eradication Regimens vs H₂ Antagonists

After creating a decision analysis tree with a managed care perspective for three widely used eradication regimens, the authors determined the cost effectiveness of these regimens in comparison to traditional therapy with H₂-receptor antagonists. At the initial node of the decision tree, all patients in the analysis were known to be infected with H pylori, and all were assumed to have documented duodenal ulcer. Thus, costs of the methods by which the presence of infection and ulcer was confirmed were not included in the analysis. Probabilities for eradication, compliance, and metronidazole resistance were determined from published data, and a 2-year period was chosen for study to allow sufficient time for relapse and to evaluate the effect of relapse on each treatment strategy. The three eradication regimens were: 2 weeks of triple therapy with bismuth, metronidazole, and tetracycline plus an H₂ antagonist; 2 weeks of therapy with omeprazole and amoxicillin (OA); and 2 weeks of therapy with omeprazole and clarithromycin (OC). Triple therapy was least expensive (\$720), followed by OC (\$768) and OA (\$1028). Conventional therapy with H₂ antagonists was most expensive (\$1791). The authors conclude that each of the eradication regimens was less expensive than H₂-antagonist therapy. They also note that: triple therapy is the optimal regimen in areas where metronidazole resistance rates are below 36% and compliance is above 53%; OA is not cost-effective unless eradication rates are higher than 74%; and OC is effective in areas with high rates of metronidazole resistance or where poor compliance with the more complex triple-drug regimen is anticipated.

Vakil N, Fennerty MB. Cost-effectiveness of treatment regimens for the eradication of *Helicobacter pylori* in duodenal ulcer. *Am J Gastroenterol* 1996;91:239-245.

Costs and Outcomes of Initial Eradication Therapy vs Initial Endoscopy

In this decision analysis, the costs and outcomes of initial eradication therapy were compared with those of initial endoscopy in patients with uncomplicated dyspepsia who were positive for H pylori. Cost estimates were obtained from the Medicare reimbursement schedule and a health maintenance organization pharmacy, and probability estimates for ulcer, esophagitis, nonulcer dyspepsia, gastric cancer, antibiotic side effects, complications from antibiotics and endoscopy, and other clinical scenarios in H pylori-positive patients with dyspepsia were derived from the medical literature. Patients with complicated dyspepsia, history of peptic ulcer disease, previous eradication therapy, use of nonsteroidal anti-inflammatory drugs within 1 month prior to the study, or typical symptoms of gastroesophageal reflux disease were not considered in the analysis. Average costs per patient were \$820 for initial eradication therapy (which included several regimens tailored to the specific cause of the dyspeptic symptoms) and \$1276 for initial endoscopy. The authors conclude that initial eradication is more cost effective than initial endoscopy in H pylori-positive patients with dyspepsia and that endoscopy-related costs must be reduced by 96% before the two strategies become equally cost effective. Although the increase in antibiotic use for initial eradication was 252%, its financial impact was more than offset by the 53% reduction in the endoscopy workload.

Ofman JJ, Etchason J, Fullerton S, Kahn KL, Soll AH. Management strategies for *Helicobacter pylori*-seropositive patients with dyspepsia: Clinical and economic consequences. *Ann Intern Med* 1997;126:280-291

Cost-Effectiveness of Eradication for Long-Term Management of Duodenal Ulcer

The investigators for this Canadian study assessed the cost-effectiveness of H pylori eradication in relation to other pharmacologic strategies in the long-term management of patients with confirmed duodenal ulcer. They used a decision analysis model to estimate the expected costs and symptomatic ulcer recurrences during a 1-year period for three treatment strategies. In doing so, they compared two H pylori eradication regimens as well. The strategies were immediate H pylori eradication, eradication at first ulcer recurrence, and continuous maintenance therapy with ranitidine. The eradication regimens were classic triple therapy (bismuth, metronidazole, and tetracycline for 14 days) and omeprazole plus amoxicillin for 14 days. Probabilities for ulcer recurrence were derived from a meta-analysis of randomized trials reported in the literature. Symptomatic and asymptomatic recurrence of duodenal ulcer at 6 months was 65.4% for placebo and 12.8% with maintenance therapy. At 12 months, the recurrence rate was only 3.7% in patients in whom H pylori eradication was successful (85%). The expected 1-year cost of immediate eradication was \$235 (Canadian) with triple therapy and \$272 (Canadian) with omeprazole plus amoxicillin. Recurrence was the same for both regimens: 15 symptomatic recurrences per 100 patients. The authors conclude that immediate eradication with either eradication regimen was less costly and had better outcomes than either intermittent or continuous maintenance with ranitidine or delayed eradication.

O'Brien B, Goeree R, Mohamed AH, Hunt R. Cost-effectiveness of *Helicobacter pylori* eradication for the long-term management of duodenal ulcer in Canada. *Arch Intern Med* 1995;155:1958-1964.

Cost-Benefit of Serologic Testing in Dyspepsia

To determine whether serologic screening and empiric treatment for *H pylori* is a beneficial option for patients with symptoms of dyspepsia (or whether such patients require radiologic or endoscopic procedures to establish the diagnosis of peptic ulcer), the author of this cost-benefit analysis used a decision tree to analyze the outcomes of serologic testing in dyspeptic patients. Since successful eradication is associated with such potential benefits as healing dyspepsia and preventing peptic ulcer or gastric cancer, a sensitivity analysis, in which transition rates and benefits were varied over a wide range to test the robustness of the calculated decision outcomes, was done as well. The analysis found that the cost-benefit relationship of serologic screening for *H pylori* in patients with dyspepsia was influenced primarily by the response rate of nonulcer dyspepsia to eradication. The relationship was also influenced by the cost benefit of ulcer prevention and the prevalence of peptic ulcer in patients who were positive for *H pylori*. Screening and treatment for *H pylori* were considered a beneficial option if only 5% to 10% of all patients with nonulcer dyspepsia responded to eradication therapy even if there were no other potential benefits. The analysis also found that serologic screening would be cost effective under the following circumstances: if ulcer prevention were associated with a long-term benefit of \$4000 or more, and if ulcer prevalence rates were higher than 10% in all patients with dyspepsia. However, since there is no definitive evidence that nonulcer dyspepsia responds to eradication therapy, the author concludes that treating all *H pylori*-positive patients with dyspepsia cannot be recommended at this time. For now, he recommends that antibiotic therapy for eradication be reserved for patients with proven ulcer or those with nonulcer dyspepsia who have not responded to other treatment measures.

Sonnenberg A. Cost-benefit analysis of testing for *Helicobacter pylori* in dyspeptic subjects. *Am J Gastroenterol* 1996;91:1773-1777.

Cost Effectiveness of Endoscopy vs Noninvasive Diagnostic and Treatment Strategies

In this cost-effectiveness analysis, the authors used a decision analytic model to estimate the clinical and economic effects of five available strategies for the management of peptic ulcer and *H pylori* in patients with symptoms suggesting peptic ulcer disease. Two of the strategies were invasive: immediate endoscopy for peptic ulcer and biopsy for *H pylori*; and immediate endoscopy without biopsy. The remaining three strategies were noninvasive: serologic testing for *H pylori*; empiric treatment with an antisecretory agent; and empiric therapy with an antisecretory agent plus antibiotics to eradicate *H pylori*. The economic measurements were cost per ulcer cured and cost per patient treated. The estimated costs per ulcer cured were \$8045 for endoscopy and biopsy, \$6984 for endoscopy without biopsy, \$4541 for serologic testing, \$4835 for empiric antisecretory therapy, and \$4155 for empiric therapy with an antisecretory agent plus antibiotics. The predicted costs per patient treated were \$1584 for endoscopy and biopsy, \$1376 for endoscopy without biopsy, \$894 for serologic testing, \$952 for empiric therapy with an antisecretory agent, and \$818 for empiric therapy with an antisecretory agent plus antibiotics. The authors pointed out that the cost-effectiveness advantage of the three noninvasive strategies decreased as the cost of endoscopy decreased or as the probability of recurrent symptoms increased in patients who were initially treated with a noninvasive strategy. The authors conclude that endoscopy, although costly, precisely guided diagnosis and treatment and, as a result, reduced the number of patients who received inappropriate treatment. However, they emphasize, the safety and efficacy of the less expensive noninvasive strategies strongly support their use as initial treatment in patients with symptoms that suggest peptic ulcer disease.

Fendrick AM, Chernew ME, Hirth RA, Bloom BS. Alternative management strategies for patients with suspected peptic ulcer disease. *Ann Intern Med* 1995;123:260-268.