Management of Dyspepsia: A Decision Analysis Model

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Abstract

The purpose of this study was to evaluate the costs and outcomes associated with five management strategies for patients with dyspepsia: endoscopy; upper gastrointestinal (GI) radiographic series; a serologic test for *H pylori;* empiric acute antisecretory therapy followed by endoscopy upon recurrence; and empiric acute antisecretory therapy followed by serology on recurrence. A decision-analysis model was used to simulate patient costs and outcomes (ie, time with active dyspepsia and percentage of gastric cancers diagnosed early) for a demographically representative sample of the U.S. population over a 5-year period. Serologic testing followed by antimicrobial/ antisecretory therapy for patients who are positive for *H pylori* is associated with costs of $1,670 per patient treated and 3.1 months with active dyspepsia. Compared with serology, endoscopy costs 17% more, but patients' time with active dyspepsia is 36% less and 98% of cancers are diagnosed early. An upper-GI series costs 6% more than serology but is associated with 19% less time with active dyspepsia for patients; 96% of cancers are diagnosed early. The remaining two management options were never preferred. Based on costs and outcomes, serologic testing for *H pylori* in patients with dyspepsia is preferable to empiric acute antisecretory therapy. Spending an additional 6% to 17% to use endoscopy or an upper-GI series for a more accurate diagnosis can be expected to decrease time with active dyspepsia and increase the number of cancers detected early. If physicians are willing to prescribe empiric antimicrobial/antisecretory therapy without testing for *H pylori,* this option is preferred to serology only if the savings of $50 per patient treated are assumed to exceed the cost associated with unnecessary use of antibiotics (eg, antibiotic-resistant bacteria).

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In 1992, approximately 5.5% of the U.S. population reported that they experienced dyspepsia (examples of related digestive conditions are ulcer, gastritis, duodenitis, and frequent indigestion).[1] Physicians must choose from a variety of accepted management options used to diagnose and treat this common symptom. In an effort to decrease costs and improve outcomes associated with dyspepsia, health plans are interested in reducing this variation in practice patterns through the development of best-practice protocols. The goal of this study is to inform health plans and physicians of the relative costs and outcomes associated with five approaches to the management of dyspepsia so that these plans can begin to develop guidelines or to refine existing protocols.

Dyspepsia is defined as upper-abdominal pain, discomfort, heartburn, nausea, vomiting, or other symptoms referable to the upper-gastrointestinal (GI) tract.[2] Physicians usually further classify patients who have dyspepsia by symptom pattern or by underlying disease. Classification by symptom pattern can result in a qualified diagnosis of refluxlike dyspepsia, ulcerlike dyspepsia, dysmotilitylike dyspepsia, or nonspecific dyspepsia. When making differential diagnoses, physicians must use mainly symptom patterns, yet it may be more informative were they to classify patients by underlying disease, as this scheme tells us more about how patients will respond to different treatment options.[3]

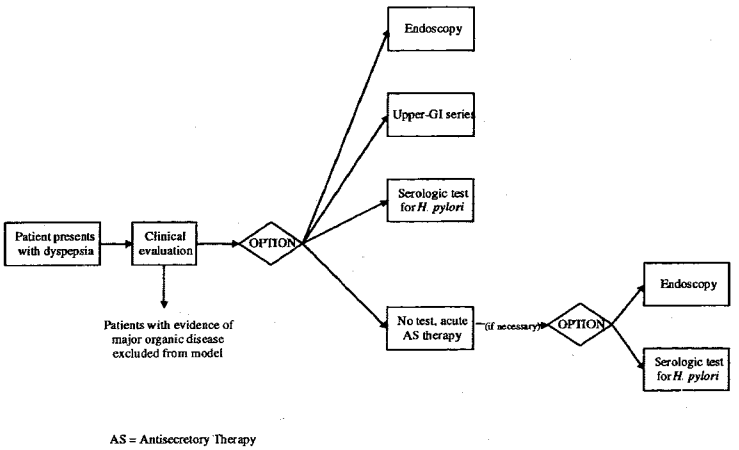
Most studies categorize dyspepsia into the following four underlying diseases: peptic ulcer disease (PUD), gastroesophageal reflux disease (GERD), gastric cancer, and functional dyspepsia. A diagnosis of PUD includes both gastric and duodenal ulcers, GERD includes all the symptoms and mucosal lesions

that result from abnormal reflux of gastric contents,[4] and gastric cancer refers to carcinomas of the stomach.

Functional dyspepsia, also called idiopathic, essential, or nonulcer dyspepsia, is the term used to characterize dyspepsia for which no underlying disease process has been identified to explain the symptoms.

Since its introduction in the 1960s, endoscopy has been the standard diagnostic mechanism for dyspepsia because it allows physicians to visually inspect the mucosa.[5] To avoid the expense associated with endoscopy, some clinicians have supported the use of empiric treatment for dyspeptic patients. However, empiric therapy may prolong symptoms and delay the diagnosis of gastric cancer. The present analysis evaluates the costs and outcomes associated with both endoscopy and empiric therapy as well as other approaches to management of dyspepsia, such as an upper-GI series or *H pylori* serology.

Figure 1. Overview of Management Strategies

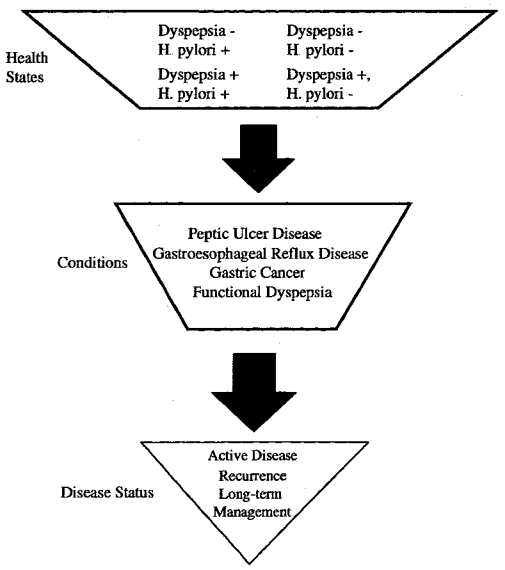


··· METHODS ···

Data from the published literature as well as expert clinical opinions were integrated into a clinically relevant decision-analysis model built using *i think* software (High Performance Systems, Hanover, NH). This software is particularly useful for disease management simulations, as it permits modeling of patient flow over time in addition to costs and outcomes.

Our decision-analysis model begins when a patient with dyspepsia seeks out a physician. The model then assumes that the physician conducts a history and physical examination, which enable the physician to identify individuals with major organic disease and those who do not require treatment with antisecretory agents (eg, those with gallstone disease or lactose intolerance). These patients receive no further analysis. The model allows the physician to select one of the following five initial management alternatives (Figure 1): (1) endoscopy; (2) an upper-GI radiographic series; (3) serologic testing for *H pylori*; (4) empiric acute antisecretory therapy with serology on recurrence; and (5) empiric acute antisecretory therapy with endoscopy on recurrence.

Figure 2. Overview of Decision Analysis Model



States of Health

The clinical model allows for patients in four states (Figure 2): (1) no dyspepsia, *H pylori* absent; (2) no dyspepsia, *H pylori* present; (3) active dyspepsia, *H pylori* absent; (4) active dyspepsia, *H pylori* present. Each dyspepsia-positive state contains four subsets that correspond to the following underlying conditions: peptic ulcer disease (PUD), gastroesophageal reflux disease (GERD), gastric cancer, and functional

dyspepsia. Within each of these four conditions, patients flow through a third level of health states based on disease status, namely active disease, recurrence, and long-term management.

Our model begins with dyspepsia-free patients distributed between two states: (1) no dyspepsia, *H pylori* absent and (2) no dyspepsia, *H pylori* present according to the prevalence of *H pylori* in the U.S. population. Every month, patients move through the various health states according to the key model parameters (ie, the incidence of dyspepsia; the incidence of *H pylori* infection; the prevalence of PUD, GERD, gastric cancer, and functional dyspepsia; the probability of recurrence following treatment; and the probability of long-term maintenance therapy) detailed in Table 1. We run the model for a 5-year time period to reflect the time frame typically reported in studies of long-term maintenance therapy. The model assumes that patients without dyspepsia accrue no costs and that patients who develop dyspepsia accrue costs according to the assumptions in Table 2.

Management Strategies

We evaluate the five approaches to diagnosis and treatment of dyspepsia noted earlier: endoscopy; upper-GI radiographic series; serologic tests for *H pylori*; empiric acute antisecretory therapy with serology on recurrence; and empiric acute antisecretory therapy with endoscopy on recurrence.

Table 1. Key Parameters (%)

	%
Epidemiology	
Annual incidence of dyspepsia[6,7]	1
Distribution of underlying conditions:[2]	
Peptic ulcer disease (PUD)	17
Gastroesophageal reflux disease (GERD)	31
Early gastric cancer	3
Functional dyspepsia	50
Point prevalence of *H pylori* infection—general population[8]	25
Point prevalence of *H pylori* infection—all dyspepsia patients[9]	50
Prevalence of *H pylori* infection in dyspepsia subgroups:[10,11]	
PUD (includes both gastric and duodenal ulcers)	79.7
GERD	28.1
Early gastric cancer	81.0
Functional dyspepsia	50
Annual incidence of bleeding ulcer in general population[12]	0.07
Distribution of bleeding ulcers:[12]	
Clean base	48
Blood spot	23
Nonbleeding clot	13
Active bleed	15
Diagnosis	
Diagnosis of *H pylori* infection (sensitivity, specificity):[13]	
Endoscopy with histology	96, 97
Serology	93.5, 90.5
Diagnosis of PUD (sensitivity, specificity):	
Endoscopy[14-16]	92, 100
Upper-GI series[15]	54, 91
Diagnosis of GERD (sensitivity, specificity):[17]	
Endoscopy	57.5, 100
Upper-GI series	75.8, 55
Diagnosis of early gastric cancer (sensitivity, specificity):	
Endoscopy[18]	98.5, 100
Upper-GI series[14]	96.0, 91
Treatment	
Eradication rate for antimicrobial triple therapy[19]	84
Ulcer healing rates:[20]	
After 8 wk H2-receptor antagonist therapy	92
After 12 wk H2-receptor antagonist therapy	100
Bleeding ulcers requiring therapeutic endoscopy:[12]	
Spot or clot ulcers	10
Actively bleeding ulcers	100
Actively bleeding ulcers requiring surgery[12]	10
Recurrences	
Ulcer recurrence rates for *H pylori*-positive patients after acute therapy[21-23]	
0–3 mo	50
3–6 mo (cumulative)	65
6–9 mo (cumulative)	75
9–12 mo (cumulative)	80
Ulcer recurrence rates for *H pylori*-positive patients with bleeding ulcer who are misdiagnosed as being *H pylori*-negative and are placed on long-term maintenance antisecretory therapy[24-26]	
Year 1	8
Year 2 (cumulative)	13
Year 3 (cumulative)	17
Year 4 (cumulative)	21
Year 5 (cumulative)	22
Relapse rate for GERD patients over one year[27]	75

(Table 1 continued on next page)

Table 1. Key Parameters (%) *(continued from previous page)*

	%
Recurrences *(continued)*	
Patients with functional dyspepsia with symptoms resolved (cumulative):[24,25]	
Immediately after initial physician encounter	16
After 2 mo	22
After 3 mo	25
After 17 mo	30
Long-Term Management	
H pylori-negative patients with ulcer requiring long-term therapy[27]	20
H pylori-negative patients with bleeding ulcer requiring long-term therapy	100

Table 2. Direct and Indirect Costs ($)

Purpose	Costs ($)
Physician visits:	
Initial physician visit, new patient, 30 min (CPT 99203)	59
Physician visit, established patient, 25 min (CPT 99214)	23
Follow-up visit, established patient, 10 min (CPT 99212)	51
Diagnoses:	
Upper GI endoscopy with biopsy (CPT 43239)	623*
Surgical Pathology, Level IV (CPT 88305)	62*
Special Stains, Group I (CPT 88312)	27*
Radiological examination, upper GI tract (CPT 74246)	95*
Serologic test for *H pylori*	80§
Drugs:	
Acute antisecretory therapy (4 wk)	70
Maintenance antisecretory therapy for PUD (4 wk)	35
PRN maintenance therapy for GERD (4 wk)	15†
PRN maintenance therapy for FD (4 wk)	31‡
Combination antimicrobial/antisecretory therapy (4 wk)	90
Complications (eg, bleeding ulcer):	
Blood spot or nonbleeding clot	2,034
Clean-base ulcer	1,118
Active bleed	5,274
Productivity loss associated with model events:	Time
Ulcer, GERD, cancer, or functional dyspepsia relapse	8 hr
Physician visit	2 hr
Outpatient endoscopy	8 hr
Upper-GI series	4 hr
Economic costs associated with productivity loss	$4.25/hr

CPT = current procedure terminology; GI = gastrointestinal; DRG = diagnosis-related group; PUD = peptic ulcer disease; GERD = gastroesophageal reflux disease; FD = functional dyspepsia.
*Figures include both professional component and facility (technical) component.
†The model assumes the following distribution for PRN maintenance for GERD: 15% receive omeprazole 20 mg bid annually, 50% receive cimetidine 400 mg bid annually, and 35% receive cimetidine 400 mg bid for 4 weeks per year.
‡The model assumes the following distribution for PRN maintenance of functional dyspepsia: 10% receive cisapride 10 mg qid annually, 67.5% receive cimetidine 400 mg bid for three fourths of the year, and 22.5% receive cimetidine 400 mg bid for one half of the year.
§SmithKline Beecham Clinical Laboratories.

Endoscopy. Patients visit their physician and are scheduled for an endoscopy. If the endoscopy reveals PUD, a biopsy is performed, followed by a histologic test for *H pylori*. Patients are treated according to their *H pylori* status: if *H pylori* positive, patients receive combination antisecretory/antimicrobial therapy, or if *H pylori*-negative, patients receive an acute course of antisecretory therapy. If, following endoscopy, GERD or functional dyspepsia are diagnosed, patients are given acute antisecretory therapy, as the model assumes that to be optimal treatment for GERD.

Patients diagnosed with gastric cancer are assumed to receive appropriate treatment, but we do not quantify the cost of gastric cancer. In addition, we do not assign a cost differential between early diagnosis of gastric cancer and a diagnosis delayed 2 months because of the uncertainty in the literature related to costs. Although some studies have demonstrated a small difference in outcomes between early cancer detection and a 2-month delay,[27] no literature quantifies this difference, based on actual cost data. We, therefore, report only the percentage of cancers detected early.

If symptoms recur in a patient with PUD, an endoscopic reexamination is performed. The majority of patients with PUD who remain *H pylori*-positive following acute therapy will experience a recurrence of symptoms over a 1-year period.[21-23] If a patient with GERD or functional dyspep-

sia relapses after completion of acute therapy, he/she is placed on maintenance therapy.

Upper-Gastrointestinal Series Followed by Endoscopy on Recurrence. Patients who have dyspepsia are scheduled for an upper-GI double-contrast barium radiographic series. If the upper-GI series shows PUD, patients receive a serologic test for *H pylori* and are treated according to their *H pylori* status. If the upper-GI series reveals GERD or functional dyspepsia, patients are given a course of acute antisecretory medication. If the upper-GI series reveals cancer, the model assumes that patients will receive an endoscopy with biopsy to confirm the diagnosis. Patients with GERD who relapse after completing acute therapy are placed on a maintenance therapy regimen. If symptoms recur in patients diagnosed with PUD or functional dyspepsia, an endoscopic examination is performed. Patients are treated according to the endoscopic result.

Serology Followed by Endoscopy on Recurrence. When patients with dyspepsia visit the physician, they are first given a serologic test (IgG enzyme-linked immunosorbent assay) for *H pylori* and are treated according to their *H pylori* status. If symptoms recur after completion of acute therapy, the patients are given an endoscopy, followed by appropriate treatment based on the endoscopic diagnosis.

Acute Antisecretory Therapy Followed by Endoscopy on Recurrence. Patients with dyspepsia go to their physician and receive acute antisecretory therapy without a diagnostic test or a test for *H pylori*. If symptoms recur after completion of acute therapy, the patients are given an endoscopy, followed by appropriate treatment based on the endoscopic diagnosis.

Acute Antisecretory Therapy Followed by Serology on Recurrence. Patients with dyspepsia visit the physician and are given acute antisecretory therapy without having had a diagnostic test or a test for *H pylori*. All patients whose dyspepsia recurs after completion of drug therapy are administered a serologic test for *H pylori* and are treated with a second course of acute therapy according to the test results. If symptoms again recur after completion of this second course, patients are given an endoscopy followed by the appropriate treatment indicated by the endoscopic diagnosis.

Costs and Outcomes

For each of the five management alternatives, the model estimates direct medical costs and indirect costs (lost wages) per patient treated. Direct and indirect costs are inflated annually to reflect a real growth of 5% for physician and hospital costs, of 4% for pharmaceutical costs, and 2% for wages. All costs are discounted to 1994 dollars assuming a 5% real discount rate.

We calculate two cost measures, the 5-year cost per patient treated and the cost per member per month. The 5-year cost per patient treated is the sum of costs for all management strategies divided by the total number of patients with active disease. The cost per member per month is the total direct cost per month for all management strategies divided by the total number of covered lives in the model.

Table 2 presents the direct and indirect cost inputs to the decision-analysis model. Direct costs for physician procedures and facility use are estimated, against 1994 Medicare payment amounts (ie, relative value units for physician costs, ambulatory surgical-center rates for outpatient-facility costs, and diagnosis-related groups (DRGs) for inpatient-facility costs). A direct cost figure for the serology test was not available through Medicare; therefore, the model uses a cost estimate provided by SmithKline Beecham Clinical Laboratories.

Direct costs for pharmaceuticals are assigned according to the lowest average wholesale price (AWP) as reported in the August 1994 *Update of the Red Book*.[28] If an AWP was not available in the August Update, we abstracted pricing information from the 1994 *Red Book*.[29] In addition, a $5 dispensing fee was included in the cost of each prescription. For patients receiving maintenance therapy, the model assumes that four prescriptions are filled each year, thus, $20 in dispensing fees.

Indirect costs are measured related to productivity lost due to morbidity. The model assumes that patients lose 8 hours of productivity when they experience a PUD, GERD, or functional dyspepsia event. Additionally, the model assigns a productivity loss of 2 hours to a physician visit, 4 hours to an upper-GI series, and 8 hours to an outpatient endoscopy. If the patient requires surgery, the model assumes a 3-week productivity loss (120 hours). The model uses the minimum hourly wage in the United States to estimate the cost of productivity loss in the model.

Side effects associated with the eradication of *H pylori* can influence economic costs in two ways: directly, through expenditures on drugs and medical care to treat the side effects themselves, and indirectly, by lowering patient compliance with treatment regimens. We assume that the direct costs attributable to common adverse reactions to antibiotics such as diarrhea, nausea/vomiting, and rashes are not significant enough to include in the model. We account for the indirect impact of side effects via the

antimicrobial/antisecretory therapy eradication rates, which include individuals who have discontinued treatment due to side effects, as treatment failures. Additionally, the model does not include costs that may accrue from rare antibiotic side effects such as pseudomembranous colitis due to their low incidence. The model also does not include any costs associated with complications from endoscopy, such as perforation, infection, or cardiopulmonary incidents.

In addition to costs, we model two outcome measures: time (months) with active dyspepsia per patient treated and the percentage of gastric cancers that are diagnosed early—that is, upon initial presentation of symptoms. To compare costs and outcomes among the management approaches, we also calculate a cost-effectiveness ratio, namely, cost per month of active dyspepsia avoided. This ratio is calculated by dividing the difference in costs by the difference in effectiveness (ie, $\Delta C/\Delta E$).

··· RESULTS ···

Results for each management alternative, including the 5-year cost per patient treated; the direct cost per member per month; the time with active dyspepsia; and the percentage of gastric cancers diagnosed early, are presented in Table 3. On the basis of both costs and outcomes, serology is always preferred to both empiric acute antisecretory therapy with endoscopy on recurrence (ie, lower cost and better outcomes) and empiric acute antisecretory therapy with serology on recurrence (ie, same costs and better outcomes). By contrast, endoscopy and upper GI series are associated with higher costs than serology but with fewer months of active dyspepsia and a higher percentage of cancers diagnosed early.

If insurers or health plans are willing to pay an additional 6% or 17% in costs, they will achieve a 19% or 36% improvement in outcomes using an upper-GI series or endoscopy. We also calculate the incremental cost of avoiding a month with active dyspepsia, compared with a serology baseline: use of endoscopy incurs a cost of $252 and use of an upper-GI series incurs $181 per month of active dyspepsia avoided.

Sensitivity Analyses

To test the strength of our model results, we investigated the sensitivity of our model to reasonable variation in key parameters. While cost per patient treated varied, our sensitivity analyses confirmed that serologic testing followed by appropriate drug therapy is the least costly management option in most cases.

Age-Representative Groups. Because the prevalence of PUD, GERD, gastric cancer, and functional dyspepsia varies with the age of a patient cohort, we calculated costs and outcomes for a patient cohort at age 40, age 55, and age 75.[8,30,31] Although costs and time with active dyspepsia varied across these simulations, the fundamental results did not change. Serology was always preferred to empiric acute antisecretory therapy with endoscopy on recurrence (ie, lower costs and better outcomes) and empiric acute antisecretory therapy with serology on recurrence (ie, similar costs and better outcomes). Endoscopy and upper-GI series had the best outcomes with the fewest months spent with active dyspepsia and the greatest percentage of cancers diagnosed early. The additional cost to avoid a month of active dyspepsia ranged from $168 to $288 in the different age cohorts for upper-GI series and endoscopy respectively.

Table 3. Results: Costs and Outcomes

Treatment Strategy	Five-Year Cost per Patient Treated ($)	Cost per Member per Month ($)	Time with Active Dyspepsia per Patient Treated (mo)	Cancers Diagnosed Early (%)
Endoscopy	1,950	1.62	2.0	98
Upper-GI Series	1,770	1.46	2.5	96
Serology	1,670	1.37	3.1	0
Empiric Acute Antisecretory Therapy, Serology on Relapse	1,670	1.36	4.2	0
Empiric Acute Antisecretory Therapy, Endoscopy on Relapse	1,750	1.43	3.2	0

GI = gastrointestinal.

Varied Endoscopy Price. Although our baseline cost assumption for endoscopy of $623 was derived from 1994 Medicare payment regulation, managed care organizations and physician groups may face a lower marginal cost; we, therefore, ran our model using endoscopy costs of $200 and $400. Because all of our management strategies involve the use of endoscopy upon recurrence, all approaches experience a decrease in the cost per patient treated when the price of endoscopy is decreased. At a price of $365, endoscopy would always be preferred to upper-GI series, because of better outcomes and lower costs, assuming the price of upper-GI series stays constant at Medicare levels. Serology always remains the lowest cost-management strategy.

Disregard of Indirect Costs. To simulate the perspective of a healthcare payer responsible for direct medical costs but not for lost wages, we eliminated indirect costs from the model. When only direct costs are included, we find that costs decrease by approximately 6.1%. Serologic testing and empiric acute antisecretory therapy with serology on recurrence were still the lowest cost management strategies at $1,560 per patient treated.

Compared with serology, the cost per month of active dyspepsia avoided did not change significantly: $258 for endoscopy and $182 for upper-GI series.

Varied Sensitivity and Specificity of Endoscopy in Diagnosing H pylori. Because the sensitivity and specificity of endoscopy in diagnosing *H pylori* varies, depending on the test used, such as histology versus a CLO test (for *Campylobacter*-like organisms), we replaced our baseline assumption of endoscopy with histology with the cost, sensitivity, and specificity of endoscopy with CLO test. The results from this sensitivity analysis suggest that while costs and outcomes vary slightly, the relationship of the results remains constant: serology and empiric acute antisecretory therapy with serology on recurrence were the least expensive strategies, but the best outcomes were achieved by the endoscopy and upper GI series management strategies. The cost per month of dyspepsia avoided did not change significantly ($247 for endoscopy and $175 for upper-GI series).

Varied Sensitivity of Endoscopy and Upper-GI Series in Diagnosing PUD, GERD, and Cancer. To measure the effect of the sensitivity of endoscopy and upper-GI series on our results, we increased by five percentage points and decreased by five percentage points the sensitivity of these tests in diagnosing PUD, GERD, and cancer. Neither alteration changed the relationship of the results as to costs per patient treated or time with active dyspepsia. However, the percentage of cancers diagnosed early by endoscopy and upper-GI series, did increase to 100 when we increased the sensitivities of the tests. The additional cost per month of active dyspepsia avoided, through use of endoscopy or upper-GI series, ranged from $168 to $258.

Prescription of Antibiotics without Testing for H pylori. Similar to studies on the most appropriate approach to treatment of PUD, we also modeled the costs and outcomes associated with empiric antimicrobial/antisecretory therapy. Under this management strategy, patients with dyspepsia visit the physician and are prescribed combination antimicrobial/antisecretory therapy without a diagnosis of dyspepsia or *H pylori.* The model predicts a cost of $1,620 per patient treated and an outcome of 3.1 months with active dyspepsia over the 5-year time frame. In other words, if physicians are willing to empirically prescribe antibiotics to all patients with dyspepsia, this option would be preferred to: (1) serologic testing and empiric acute therapy in terms of costs and outcomes and (2) endoscopy and upper-GI series regarding costs but not outcomes. Compared with empiric antimicrobial/ antisecretory therapy, the incremental cost of avoiding a month of active dyspepsia for endoscopy is $298; the cost per month avoided by upper-GI series is $270. Although the cost per patient treated with empiric antimicrobial/antisecretory agents is lower than those reported for all of the other management strategies considered above including serology, there is a risk that such an approach would increase the population's resistance to antibiotic therapy over time. Because quantifying the costs of resistance to antibiotic therapy is beyond the scope of our analysis, we offer this strategy only as a sensitivity analysis.

··· DISCUSSION ···

Serology is always preferred to empiric antisecretory therapy regarding both costs and outcomes for the management of dyspepsia. Compared with endoscopy and upper-GI series, serology is less expensive, but is associated with more time with active dyspepsia and far fewer early detections of cancer. Physicians and patients in managed care plans must consider whether a 19% improvement in outcomes with upper-GI series or a 36% improvement in outcomes with endoscopy is worth an additional 9 cents or 25 cents per member per month respectively.

We ran a series of sensitivity analyses to test the strength of our conclusions and found that while our empiric results will change modestly when varying the model parameters, our fundamental conclusions are

robust to such changes. Serology remains the lowest cost option, even with dramatic changes in the age distribution of the cohort and the price of endoscopy. When the price of endoscopy drops to $365, primary endoscopic diagnosis is preferred to an upper-GI series for both cost and outcomes. Modest variation in the sensitivity and specificity of diagnostic tests for *H pylori* also did not significantly affect the results, although new formulations and approaches should be examined as they emerge.

Our fundamental conclusions change, however, if physicians are willing to use antibiotics without testing for *H pylori*. Costs per patient treated were lower for the empiric antimicrobial/antisecretory approach than for any other management alternative. As discussed above, however, our model does not attempt to assess the costs that might be generated by contributing to the presence of antibiotic-resistant bacteria.

Our study differs significantly from two recent clinical economic evaluations of dyspepsia. Silverstein and colleagues use a decision-analysis paradigm to compare the costs of two of our five dyspepsia-management strategies—endoscopy and empiric therapy—and conclude that the optimal management strategy is a toss-up between endoscopy and empiric therapy.[30] In addition to modeling only two management alternatives, the result of this study is highly dependent on assumptions related to the cost of gastric cancer. In the absence of any recently published studies on the cost of gastric cancer, Silverstein's group assumes a cost of $10,000 for early detection and treatment of gastric cancer, and $100,000 for late detection and treatment.

Although use of such a cost assumption would change our results such that endoscopy becomes the least expensive option, due to a lack of evidence in the literature on the cost of a delay in cancer detection, we present results without the costs of cancer treatment.

Our study also differs substantially from that of Silverstein and colleagues in the model time frame and the outcome measures calculated. We believe that our 5-year time frame is more appropriate than the 1-year frame they use, particularly in modeling the costs of long-term maintenance therapy for GERD and functional dyspepsia. Although life expectancy used by Silverstein is an important outcome measure, attribution of differences in this case is highly difficult; time spent with active dyspepsia and the percentage of gastric cancers detected early will also be important and more easily measured by managed care organizations in determining the preferred approach to the diagnosis and treatment of dyspepsia.

The second published study, written by Bytzer and fellow investigators, reports the cost and effectiveness of dyspepsia-management strategies, based on a clinical trial. The authors evaluate costs only for two of our six management strategies (endoscopy and empiric therapy with endoscopy upon recurrence) over a 1-year time frame.[32] Bytzer's group also differ in their approach to management of dyspepsia-related conditions; for example, patients suspected of having functional dyspepsia were not treated with antisecretory therapy. Other clinical economic studies related to GI management deal exclusively with peptic ulcer disease.[33-36]

Our model shows that important cost and outcome differences are associated with various options available to physicians for the management of dyspepsia. Serology offers a simple and inexpensive way to improve the accuracy of diagnosis and is always preferred to empiric antisecretory therapy. However, better outcomes can be obtained at a cost. For example, initial diagnosis using endoscopy increases costs by 17% but results in a 36% reduction in time spent with active dyspepsia and in the early detection of 96% of gastric cancers.

These results may present a dilemma for physicians, many of whom are increasingly under the scrutiny of managed care guidelines or utilization review. Although additional research on these outcomes is needed before a true cost-benefit analysis can be performed, such as data on cancer costs with and without a delay in detection and more information on the costs of empiric antibiotic treatment, our results provide managed care plans, physicians, and patients with additional information on costs and outcomes that is needed to guide the development of best practice protocols for the management of dyspepsia.

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