# Determining the Cost of Gastroesophageal Reflux Disease: A Decision Analytic Model

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*Abstract*

***Objective:*** **To design a decision analytic model to help determine the costs associated with various treatment regimens for gastroesophageal reflux disease (GERD).**

***Study Design:*** **A decision analytic model incorporating Markov processes was developed to calculate clinical and direct economic outcomes for patients with GERD after 2 years of treatment.**

***Patients and Methods:*** **We used retrospective data in the Markov model to generate clinical and economic outcomes. The primary data sources were the 1993 MarketScan® claims database, the 1992 National Hospital Discharge Survey, and the clinical literature.**

***Results:*** **Patients with mild GERD (17.6% of patients) contributed 37.8% of costs, while those with moderate to severe disease (14.4% of patients) contributed 49.9% of costs. The remaining 12.3% of costs was spent on the 68% of patients with non-GERD diagnoses. The class of drugs with the highest acquisition cost—proton pump inhibitors—had the lowest total cost per case. The high level of efficacy of these drugs may explain this result. Sensitivity testing showed no evidence that our model's results depended heavily on any one probability or cost factor.**

***Conclusions:*** **This model showed that patients with moderate to severe GERD were the most expensive cases to treat and that proton pump inhibitors resulted in the lowest total cost per case. Further testing and manipulation of the model are required to gain a better understanding of the trade-offs involved in different options for GERD management.**

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Gastroesophageal reflux disease (GERD) is a common clinical problem seen in all segments of the US population. Heartburn, the primary symptom of GERD, occurs in 7% of Americans on a daily basis, 14% on a weekly basis, and 40% on a monthly basis.[1] Data from other sources support these estimates, noting that between 21% and 42% of the general population in the United States suffers symptoms of GERD at least monthly.[2-5] In a recently completed national survey, approximately 10% of respondents reported taking prescription medication for heartburn or acid regurgitation or having GERD symptoms at least twice a week.[6] Thus it is no surprise that a significant amount of money is spent on the diagnosis and treatment of GERD, unfortunately with variable results.

The approaches taken to diagnose and treat GERD vary widely. Using decision analysis, we can help clarify the uncertainty surrounding GERD diagnosis and treatment. With this objective in mind, we constructed a decision analytic model that illustrates the costs and outcomes associated with various GERD management options at the patient level.

## ··· METHODS ···

We used clinical decision analysis to model treatment costs. In this conceptual framework, a decision tree is created that displays clinical decision points and the events that follow from each clinical decision. The decision tree for the GERD cost-of-illness model is shown in Figure 1. The decision model begins with identification of the GERD population, both the diagnosed population (those who seek medical attention for their symptoms) and the undiagnosed population (those who do not seek medical attention for their symptoms). Persons who seek medical attention remain in the model, which branches through diagnostic and treatment states. This analysis assumes that patients entering the model have not previously received treatment for GERD.

Our cost-of-illness model takes the perspective of the payer and models the costs for paid claims over a 2-year period using Markov processes. Markov processes allow a model to incorporate time-dependent transition probabilities, which simplifies longitudinal calculation of the outcome variables of interest. We used reimbursed or paid charges for private insurance claims as our unit price. Although GERD often is a chronic problem for many patients, the duration of care can vary. We selected a 2-year model because most clinical studies are not designed to determine whether patients with GERD continue to receive successful or unsuccessful treatment for more than 2 years. This situation limits the precision of any estimates of probability of outcomes beyond that point.

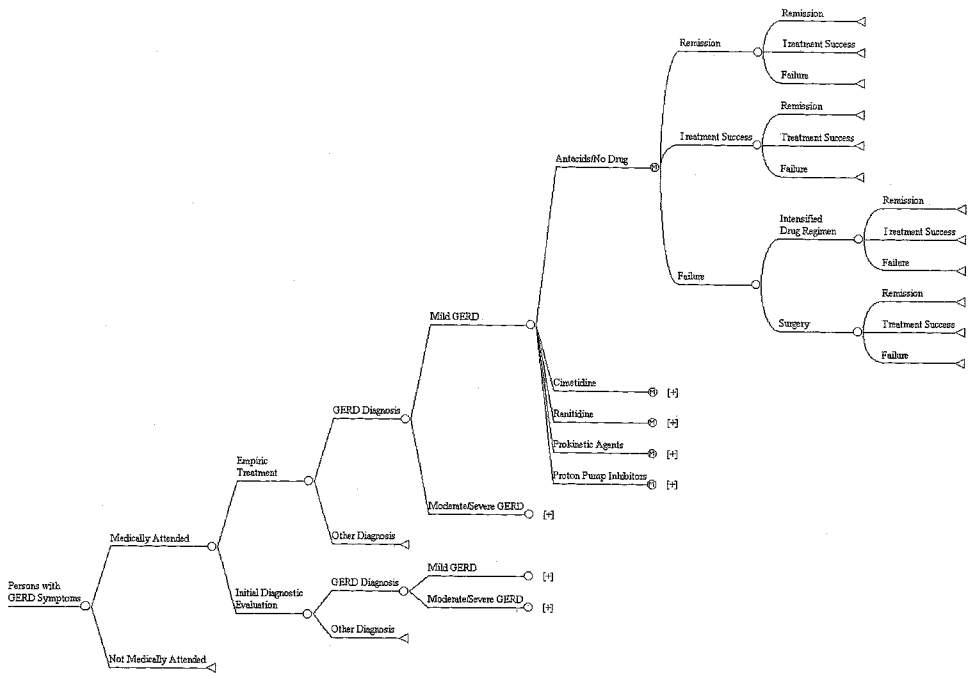
## Data Sources

The three primary data sources used in our decision analytic model were the MarketScan® claims database, the National Hospital Discharge Survey, and the clinical literature. The MEDSTAT Group's Market-Scan database[3] is the largest database of private sector healthcare claims in the United States. We currently track more than 7 million Americans covered by health insurance provided by a sample of large employers. MarketScan contains standardized patient-level clinical and financial information derived from medical claims data processed by more than 200 private health insurers and Blue Cross/Blue Shield plans.

We identified persons with at least one ICD-9-CM diagnosis of GERD in the outpatient setting from the 1993 MarketScan Medical and Drug databases. We also used these databases to summarize cost and utilization rates for physician visits, procedure codes, and hospital stays. These databases were particularly useful in deriving the volume and cost of diagnostic tests for patients with GERD symptoms. The National Hospital Discharge Survey (NHDS)[4] provides national statistics on the experience of the US population in short-stay non-Federal hospitals. Using the 1992 NHDS, we identified hospital stays with GERD listed as the first ICD-9-CM diagnosis or antireflux surgeries listed in any ICD-9-CM procedure field. We used this information to calculate age-specific hospitalization rates for GERD. Estimates of drug efficacy and failure were derived from the clinical literature.

We also used four minor data sources for our analysis. Data from IMS America's 1995 National Disease & Therapeutic Index Report were used to determine the distribution of specific types of drugs among patients

**Figure.** Decision Tree for Gastroesophageal Reflux Disease (GERD)



with GERD.[7] We also used data from the National Health Interview Survey (NHIS),[2] a continuous nationwide survey conducted through household interviews. Using ICD-9-CM diagnosis codes, as well as coded responses to a question about the occurrence of indigestion, we were able to obtain from 1993 NHIS data an annual prevalence rate for GERD and indigestion. The 1988 Gallup Organization National Survey: Heartburn Across America[5] provided information on the prevalence of GERD symptoms among the US adult population. Drug prices were culled from the 1997 edition of *Physicians GenRx: The Complete Drug Reference*.[8]

## Data Inputs

The model uses data inputs that were gathered from the most definitive sources available to the authors. The probability data inputs are shown in Table 1[2-5,7,9-14] and all of the cost data inputs are shown in Table 2.[3,8] The treatment outcome data inputs are presented in Table 3.[15-51] For the treatment outcome data, we defined efficacy as endoscopically verified lesion healing. Although most patients with GERD are managed on the basis of their symptoms, clinical trials primarily focus on lesion healing verified by endoscopic examination. Therefore, it was necessary to use lesion healing as the clinical endpoint in this analysis.

*Initial Presentation and Diagnosis Choice.* In our decision tree (Figure 1), patients with GERD are initially divided into two groups—those who seek medical attention and those who do not. The decision tree's next node models two clinical choices: empiric treatment or diagnostic evaluation. This node includes the probability and payments associated not only with the choice of empiric treatment or diagnostic evaluation but also with selection of a primary care physician or a specialist.

Each patient who seeks care will do so from either a primary care physician or a specialist (typically a gastroenterologist). When the physician first reviews the case, he or she makes a diagnostic assessment. Numerous tests are available to aid in the diagnosis of GERD, including endoscopy, 24-hour pH monitoring, acid perfusion testing, and esophageal manometry.[52] In most patients with probable GERD, physicians start empiric therapy rather than use diagnostic testing. (The cost and discomfort associated with diagnostic testing are possible explanations for the high level of empiric therapy.) If empiric therapy fails, diagnostic testing typically is performed.

In the 1993 MarketScan data, 75% of GERD claims were submitted by primary care physicians, 12.7% by gastrointestinal or surgical specialists, and 4.6% by non-gastrointestinal or surgical specialists. Type of physician was unavailable for 7.8% of claims. Data from the National Disease & Therapeutic Index yielded similar estimates for physician visits for

**Table 1.** Probability Data Inputs

| Probability Data Input | Representative/Average Probability (%) | Range of Probabilities (%) |
|---|---|---|
| Symptomatic adults[2-5] | | |
| GERD symptoms | 30.0 | 21 - 42 |
| No GERD symptoms | 70.0 | 58 - 79 |
| Medically attended adults[2,5,14] | | |
| Average rate | 39.0 | – |
| Physician type[3,7] | | |
| Primary care | 65.0 | 50 - 80 |
| Specialist | 35.0 | 20 - 50 |
| Diagnostic choice[3,14] | | |
| Empiric treatment | 87.5 | 35 - 90 |
| Diagnostic testing | 12.5 | 10 - 65 |
| GERD diagnoses[2] | | |
| Average rate | 32.1 | 19 - 41 |
| GERD severity[9-14] | | |
| Mild GERD | 55.0 | 40 - 70 |
| Moderate/severe GERD | 45.0 | 30 - 60 |
| First-line treatment[7] | | |
| Visits without prescribed drugs | 5.8 | – |
| Visits with antacids | 6.2 | – |
| Visits with $H_2$-receptor antagonists | 40.1* | – |
| Visits with prokinetic agents | 18.9 | – |
| Visits with proton pump inhibitors | 29.0 | – |
| Second-line treatment[4] | | |
| Intensified drug regimen | 99.6 | – |
| Surgery | 0.4 | – |
| Transitional treatment[4] | | |
| Non-surgical medical stays | 2.4 | – |

GERD = gastroesophageal reflux disease.
*The model assumes that half of these visits are for cimetidine and half are for ranitidine

esophagitis, with 66% of visits made to primary care physicians and 34% made to specialists (primarily gastroenterologists). Based on these data, we estimate that primary care physicians account for 65% of patient visits for GERD and specialists account for 35% of these visits.

According to MarketScan data, slightly less than 10% of all claims have gastrointestinal procedure codes. When we consider only the first claims for patients with a GERD diagnosis, these procedure codes occur in only 12.5% of cases. Thus we estimate that only 12.5% of initial GERD diagnoses are made using gastrointestinal diagnostic testing and that 87.5% of patients with suspected GERD receive empiric treatment initially based on an unaided diagnosis by the physician. Note that the initial treatment strategy does not affect the availability of treatment choice.

*Diagnostic Outcome and Disease Severity.* The exact point at which the severity of the patient's disease enters into the model is difficult to determine. For example, the severity of symptoms probably contributes to the likelihood that patients seek medical attention for their illness. Illness severity probably also is considered before the physician decides on the best method of diagnosing the illness, although the actual severity of the illness can only be quantified after diagnostic tests or empiric treatment is implemented. We obtained the rate at which patients are diagnosed with GERD from the 1993 NHIS data. The NHIS estimate represents the proportion of potential patients with GERD who reported that they sought medical attention for and were suffering from GERD.

In our model, disease type and disease severity are established as two chance nodes that are made known only after the diagnostic process is completed. Among the options for diagnosis outcomes, we included the probability that a proportion of symptomatic patients will not be diagnosed with GERD and will be dropped from the decision tree. Among those diagnosed with GERD, the severity of the illness can be classified as either mild or moderate to severe. Mild GERD corresponds to grade I erosive esophagitis. Moderate to severe GERD corresponds to grades II to IV erosive esophagitis. In the clinical literature, estimates of the proportion of patients with moderate to severe GERD range from 30% to 60%.[9-13] The model takes the midpoint of this range. Thus 45% of the patients in our model are classified as having moderate to severe GERD and 55% as having mild GERD.

*Treatment Choice.* The goals of GERD treatment are usually to control symptoms, heal erosive esophagitis if

**Table 2.** Cost Data Inputs

| | Dose per Day | Cost per Day ($) | Cost per 8-Week (60-Day) Treatment ($) |
|---|---|---|---|
| Cost of drug treatment[8] | | | |
| Antacids | 8 tablets | 0.27 | 16 |
| $H_2$-receptor antagonists | | | |
| Cimetidine* | 800 mg | 2.95 | 177 |
| Ranitidine* | 300 mg | 3.36 | 201 |
| Prokinetic agents† | 40 mg | 2.44 | 147 |
| Proton pump inhibitors† | 20 mg | 3.63 | 218 |
| Combination therapy‡ | | | 379 |
| Intensified drug regimen§ | | | 198 |
| Cost of physician visit ($)[3] | | | |
| Primary care | | 50 | |
| Specialist | | 135 | |
| Cost of diagnostic tests ($)[3] | | | |
| No | | 0 | |
| Yes | | 314 | |
| Average diagnostic costs ($)[3] | | | |
| Empiric treatment | | 80 | |
| Diagnostic testing | | 394 | |
| Cost per inpatient stay ($)[3]‖ | | | |
| Surgery | | 17,386 | |
| Other medical stays | | 9398 | |

*Cost estimates for $H_2$-receptor antagonists assume that 50% of cimetidine prescriptions are filled with generic drugs and that no rantidine prescriptions are filled with generic drugs.
†Data for prokinetic agents refer to cisapride and data for proton pump inhibitors refer to omeprazole.
‡The cost figure for combination drug therapy was determined by multiplying the combined cost of cimetidine and prokinetic agents by 20%, the combined cost of ranitidine and prokinetic agents by 20%, the combined cost of cimetidine and proton pump inhibitors by 30%, and the combined cost of ranitidine and proton pump inhibitors by 30%.
§The cost figure for intensified drug therapy was derived by multiplying the cost of no drug treatment by 5%, antacids by 5%, cimetidine by 17%, prokinetic agents by 17%, proton pump inhibitors by 25%, and combination therapy by 14%.
‖The cost figure inflated 1993 dollars to 1995 dollars.

present, and prevent recurrence and complications.[53] Symptoms can be treated through lifestyle modification, drug therapy, and surgery. Many physicians support lifestyle modification, with antacids as needed, as first-line treatment, particularly for patients with mild GERD. Lifestyle modification may include losing weight, avoiding certain foods and medications, stopping smoking, avoiding alcohol, and elevating the head of the bed.[54] The options for drug therapy include not only several different classes of agents but also first-line versus intensified treatment regimens. $H_2$ receptor antagonists, such as cimetidine and ranitidine, and proton pump inhibitors, such as omeprazole, inhibit gastric acid output. Prokinetic agents, such as cisapride, alter the speed with which the stomach empties its contents. If these treatments fail, the remaining pharmacotherapeutic option is to try higher doses of conventional treatments or combination therapies.[55] Surgical treatment for GERD mainly consists of fundoplication.

Our GERD model divides all three types of therapy into first- or second-line treatment options, with first-line treatment including no drugs or monotherapy and second-line treatment including intensified pharmacotherapy and surgery. We identified the distribution of medications prescribed during physician visits for esophagitis.[7] We also determined the recommended dosages and expected payments for an 8-week course of treatment with each product, with differences between mild and moderate to severe GERD noted where possible. (The dosage and cost of a specific drug is the same whether the patient is undergoing initial treatment or maintenance treatment.) Drug payments in the model are aver-age wholesale prices for 1997.[8] In the absence of drug therapy, patients were treated with lifestyle modification and antacids. Given the lack of quantifiable data in this area and because these costs would be equivalent across all treatment options, we excluded estimates for lifestyle modification from this model.

Intensified drug therapy is a weighted average of the five first-line treatment options and combination therapy (ie, dual-drug therapy). Thus the drug cost and efficacy of intensified drug therapy would be the same for a patient who did not respond to antacids as it would be for a patient who did not respond to prokinetic agents. The cost of the intensified drug regimen is a weighted average of the costs associated with all five individual drugs and combination therapy (the cost calculation algorithms for combination drug therapy and the intensified drug regimen are shown at the bottom of Table 2). Efficacy for the intensified drug therapy was defined as the effectiveness of the most effective drug. Because of the difficulties surrounding accurate diagnosis and coding of GERD severity, we were not able to determine the distribution of different treatment options for mild versus moderate to severe GERD. The model assumes that GERD treatment benefits only patients with GERD.

After first-line treatment is selected, the model does not allow patients to switch to other drug choices (except to an intensified drug regimen). Although incorporating drug switching into the model would have more accurately reflected clinical practice, it also would have made the model considerably more complex and increased the number of branches on the decision tree exponentially. To keep the decision tree to a manageable level, we decided to omit drug switching from the model.

**Table 3.** Treatment Outcome Data Inputs

| Treatment Options | Probability of Treatment Success (%) | Probability of Remission (%) | Proportion in the Nondrug Cohort (%) |
|---|---|---|---|
| Mild GERD | | | |
| Antacids/no drug[14] | 30 | 68 | 30 |
| $H_2$-receptor antagonists[15-19] | 72 | 81 | 71 |
| Prokinetic agents[15 16 20-24] | 60 | 83 | 69 |
| Proton pump inhibitors[15 17 25-28] | 87 | 90 | 72 |
| Intensified drug regimen | 87 | 90 | 72 |
| Surgery[29-34] | – | 90 | – |
| Moderate/Severe GERD | | | |
| Antacids/no drug[14] | 30* | 68* | 30* |
| $H_2$-receptor antagonists[15 16 35-46] | 50 | 67 | 48 |
| Prokinetic agents[15 21-24] | 40 | 66 | 60 |
| Proton pump inhibitors[15 17 25 27 35-37 39-41 43 45-51] | 73 | 90 | 57 |
| Intensified drug regimen | 73 | 90 | 60 |
| Surgery[29-34] | – | 90 | – |

*Estimates from mild results; actual estimates not available.

## Estimation of Clinical and Direct Economic Outcomes

*Clinical Outcomes.* The outcomes specified in the model include both clinical outcomes and the direct economic expenses associated with those

outcomes. We established three outcome states to which any patient could belong. The first outcome ("treatment success") represents successful treatment with one of the treatment options described above to prevent recurrence of symptoms. The second outcome ("failure") represents the inability of the treatment to improve symptoms; this outcome might occur in patients who did not respond to a given treatment, did not comply with treatment, had severe adverse effects, or were lost to follow-up. The third outcome ("remission") represents complete remission of symptoms without the need for further treatment.

The paths from any given state imply certain clinical transitions. For example, from the treatment success state, patients might show signs of remission, continue treatment with success, or no longer respond to treatment and require a modified treatment approach. From the failure state, patients might be switched to an intensified drug regimen, which might succeed or fail, or undergo surgery, from which remission is possible. From the remission state, patients might remain symptom-free indefinitely or relapse back to requiring treatment. The model does not allow patients to transition from remission to failure. Instead, all patients in the remission state would first resume their previously successful treatment, which might succeed again or fail.

In this model, each Markov cycle lasts for 8 weeks. (The model equates 8 weeks with 2 months or 60 days). Thus, in a 2-year model, each patient undergoes an initial 8-week course of treatment and then can transition between outcome states 11 times. The probabilities associated with these clinical outcomes represent the efficacy (defined as endoscopically verified lesion healing) of medication and surgery.

Using MEDLINE, we searched the English-language medical literature for data on the effectiveness of initial treatment and the likelihood of remission with each treatment option. All data on the efficacy of disease treatments came from randomized, controlled trials, with the exception of efficacy estimates for antacids and lifestyle modification, which were based on expert opinion.[14] Because of gaps in the literature for some treatment options, we used data from some studies that included patients with grade I or grade II disease to generate estimates for mild GERD. Because we found only marginal differences in efficacy between 8 and 12 weeks, we included study periods from 8 to 12 weeks. We also considered data from a long-term study, which charted remission rates for several drug treatments over 1 year, in calculating the remission rates used in our model. Efficacy data from studies using dosage levels different from the recommended dosage for a specific medication were used only if there was no demonstrated dose-response relationship between the medication and its efficacy in treating GERD. Thus almost all of the efficacy data used in the model reflect the recommended dosage levels as described in *Physicians GenRx*.[8]

We used several criteria to exclude articles of questionable usefulness. Studies were excluded if: (1) the initial healing period or remission follow-up period lasted for less than 8 weeks; (2) there was no way to identify remission rates at 8 weeks after lesion healing; (3) the sample size was less than 25 for a relevant group (eg, patients with mild GERD treated with an $H_2$-receptor antagonist); and (4) the study population was the same as that in another clinical trial included in our decision analytic model.

Using data from the identified studies, we calculated a best estimate of treatment success or failure for each treatment probability node. The best estimate of each treatment option's success or failure was derived by weighting the efficacy and failure rates of each study by its sample size to calculate a weighted average across studies. For each treatment option, we determined the range of success and failure rates by taking the highest and lowest rates among all of the studies. These ranges were used in sensitivity analyses.

We also used the clinical literature to estimate the proportion of successfully treated patients who might remain symptom-free if no medications were prescribed ("nondrug" cohort) and those likely require continued treatment to remain symptom-free ("drug" cohort). For each treatment option, we calculated the proportion of patients in the nondrug and drug cohorts.

*Direct Economic Outcomes.* The total costs represented in our model include costs accumulated along the decision tree and those associated with each Markov cycle. These costs represent expenditures for inpatient and outpatient care and drug therapy. Total direct costs in our model were calculated as follows: total direct costs = diagnosis costs + initial treatment costs + costs associated with treatment success + costs associated with failure + costs associated with remission.

Using 1993 MarketScan claims data inflated to 1995 dollars, we estimated the cost of physician visits and diagnostic testing. The costs incurred during the Markov process require further explanation. Costs can occur when patients enter each outcome state, during the time spent in each outcome state (incremental or stage costs), and during the transition between outcome states (transition costs). For example, the cost of treatment success is represented initially only by the cost of the maintenance drug therapy. However, even

if treatment remains successful, physician visits should occur at least once every 6 months. Thus the cost of treatment success includes the drug costs for each Markov cycle, plus a physician visit cost in one of every three bimonthly cycles. The cost of remission has no initial or transition costs.

The cost of failure is the most complex cost structure. The cost of beginning the Markov cycle in an outcome state of failure includes the same physician and diagnostic testing costs incurred in earlier nodes, since these costs occur despite the initial choice of empiric treatment or diagnostic testing. The incremental costs of remaining in a state of failure include additional physician visit costs in every bimonthly cycle. (The model assumes that symptomatic patients always return to their physician while asymptomatic patients do not.) Within each failure cycle, the treatment stage (intensified drug treatment versus surgery) is also associated with additional expenditures. Lastly, the transition costs for ending a treatment success cycle in a state of failure include the costs for a proportion of patients whose symptoms of failure are serious enough to require hospitalization. In the 1992 NHDS, patients with GERD who did not respond to treatment were hospitalized at a rate of 16.2 per 100 cases. Although the reason for hospitalization in 1.9 of these cases was GERD surgery, the reason for hospitalization in the remaining 14.3 cases was a need for medical care. Patients hospitalized for medical care reasons may have had severe symptoms or symptoms such as dysphagia and odynophagia that might have been signs of long-standing disease or predictive of diseases more severe than GERD (eg, stricture, adenocarcinoma, or Barrett's esophagus). From 1993 MarketScan data inflated to 1995 dollars, we calculated that the average cost of medical hospital stays for GERD is $9,398 per stay. Using the NHDS data, we assume that 14.3% of patients each year (or 2.4% per bimonthly cycle) will incur these expenses during the transition from a state of treatment success to failure or from intensified treatment to a state of failure.

### Sensitivity Analyses

Sensitivity testing is a key element in determining the quality of a decision analytic model. Sensitivity testing of a model's results demonstrates whether the model is robust (ie, not heavily dependent on any one probability or cost factor). We performed repeated one-parameter sensitivity analyses to assess the robustness of our model. The data in Tables 1 and 2 provided most of the information used in the sensitivity analyses. Three additional sensitivity analyses included decreasing compliance and efficacy by 10% to 20%, decreasing $H_2$-receptor antagonist costs by 25% to 75% (to reflect over-the-counter usage), and reducing the cost (or length) of non-surgical medical stays.

## ··· RESULTS ···

The expected outcome status for patients at the end of the 2-year study period, given their initial treatment regimen, is shown in Table 4. For example, for all patients with mild GERD who are started on a prokinetic agent, 73.8% would be in a symptom-free state of remission after 2 years, 21.9% would continue to be treated successfully, and 4.3% would be in a state of failure.

In general, our results reflect the relatively greater efficacy that can be expected with proton pump inhibitors, particularly among patients with moderate to severe GERD. Among patients with mild GERD, the use of antacids or no drug therapy stands alone in not maintaining a state of remission. Furthermore, $H_2$-receptor antagonists and prokinetic agents appear to provide slightly less opportunity for remission but no substantially greater chance of ending the 2-year period in a state of failure.

**Table 4.** Distribution of Patients Across Outcomes at 2 Years

| | Percent of Patients Ending Model in Each Outcome State | | |
|---|---|---|---|
| **Initial Treatment Options** | **Success** | **Remission** | **Failure** |
| Mild GERD | | | |
| Antacids/no drug[14] | 49.8 | 31.9 | 18.3 |
| $H_2$-receptor antagonists | 23.5 | 71.3 | 5.1 |
| Prokinetic agents | 21.9 | 73.8 | 4.3 |
| Proton pump inhibitors | 13.2 | 85.3 | 1.5 |
| Moderate/Severe GERD | | | |
| Antacids/no drug | 48.1 | 30.8 | 21.1 |
| $H_2$-receptor antagonists | 41.1 | 40.3 | 18.6 |
| Prokinetic agents | 38.0 | 44.4 | 17.7 |
| Proton pump inhibitors | 16.0 | 81.8 | 2.2 |

GERD = gastroesophageal reflux disease.

These results are similar to those reported in a 1-year treatment follow-up study.[15]

Table 5 summarizes the cost outcomes that can be expected from current GERD treatments. These data show the outcome status at the end of the 2-year study period based on the patient's initial treatment regimen. In general, we found that drug price differences can be overshadowed by differences in treatment efficacy. For patients with mild GERD, the least costly treatment choice—antacids or no drugs—has the highest cost per case, given the low (30%) efficacy of antacid therapy. Conversely, proton pump inhibitors—the drug class with the highest acquisition cost ($218 per bimonthly cycle)—has the lowest cost per case. The reduced need for diagnostic testing and hospitalizations associated with products with higher efficacy are likely key reasons for proton pump inhibitors having the lowest cost per case.

Because the healthcare payer cannot select which patient populations to treat, evidence of probability and cost differences individually within the population does not fully address the costs of GERD. By linking together the costs and probabilities, we can see how each direct healthcare dollar is spent on the full subset of patients who seek medical attention for GERD symptoms. The data in Table 6 make clear the imbalance between the percent of weighted payments and the percent of weighted patients who seek care for GERD symptoms. For example, patients not diagnosed with GERD make up a large proportion of the expected patient population (68%) but account for a considerably smaller proportion of the expected total costs for GERD (12.3%). Conversely, patients with mild GERD contribute just over twice their relative size toward the total expected costs (17.6% of patients contribute to 37.8% of costs). The largest proportion of healthcare costs (49.9%) is spent on a fairly small segment (14.4%) of the GERD population—patients with moderate to severe GERD.

In general, sensitivity testing provided no evidence that our model's results depended heavily on any one probability or cost factor. The most important (although still small) changes that our sensitivity ranges produced were related to three factors. First, every 10% change in the distribution of the severity of GERD (between mild and moderate to severe) resulted in a 4% to 5% change in total costs. Thus, if the distribution between mild and moderate to severe disease was 65:35 rather than 55:45, the total costs for all medically attended patients with GERD symptoms would be $635 per medically attended patient rather than $663 per patient. Second, every 10% change in the probability of empiric treatment versus diagnostic testing changed total costs by 4% to 5%. Third, for every 10% decrease in patient compliance, the costs of treatment increased by 5% to 6% because of the simultaneous decrease in treatment efficacy

**Table 5.** Total Direct Healthcare Costs* Across Outcomes at 2 Years

| Initial Treatment Options | Total Payments per Patient by Final Treatment State | | | |
|---|---|---|---|---|
| | Total Payments ($) | Success ($) | Remission ($) | Failure ($) |
| Mild GERD | | | | |
| Antacids/no drug | 2040 | 1501 | 719 | 5815 |
| $H_2$-receptor antagonists | | | | |
| Cimetidine | 1324 | 1750 | 649 | 8843 |
| Ranitidine | 1758 | 2184 | 1004 | 10392 |
| Prokinetic agents | 1500 | 2099 | 756 | 11,224 |
| Proton pump inhibitors | 938 | 1858 | 591 | 12,567 |
| Moderate/Severe GERD | | | | |
| Antacids/no drug | 2263 | 1484 | 819 | 6148 |
| $H_2$-receptor antagonists | | | | |
| Cimetidine | 2559 | 2008 | 1104 | 6937 |
| Ranitidine | 3175 | 2533 | 1600 | 8007 |
| Prokinetic agents | 2774 | 2165 | 1296 | 7768 |
| Proton pump inhibitors | 1200 | 2295 | 613 | 15,085 |

*Represents average costs between the 87.5% of patients diagnosed empirically and the 12.5% of patients diagnosed through testing.

rates. These cost increases would occur despite the lower maintenance drug costs resulting from noncompliance. Products with greater efficacy may encourage patients to comply with the treatment regimen (because they know the treatment is working).

Our model was far less sensitive to other factors, including some factors widely thought to have a significant effect on the cost of managing GERD. A 50% decrease in the likelihood of a non-surgical hospital stay (or in the cost of a non-surgical hospital stay) lowered costs by only 7% to 8%. Similarly, the cost of managing GERD would not change significantly if the cost of $H_2$-receptor antagonist therapy was transferred from payer to patient. By transferring 25% of patients using these products from prescription to over-the-counter therapy (resulting in a reduction in drug costs of 25%), healthcare payers would decrease their pharmacy costs by only 4%. Even transferring 75% percent of patients from prescription to over-the-counter treatment would decrease drug costs by only 12%.

Our model also has several limitations. First, we did not project results beyond 2 years, even though GERD typically is managed for longer periods of time. This time limitation resulted from the lack of data on disease prevalence over time and limited efficacy data beyond 2 years. However, data in our model indicate that limited changes in outcome occur after the first year, supporting the appropriateness of the 2-year time limit. Second, owing to the type of data produced by clinical trials, we defined efficacy in terms of lesion healing verified by endoscopic examination rather than self-reported symptom improvement, which is the primary treatment indicator used by physicians. Third, the model does not allow for drug switching after the initial drug treatment is selected (with the exception of switching to intensified drug therapy). Although these limitations make the model less realistic from a clinical standpoint, we had to incorporate them because of the lack of certain data and the need to simplify the model's complexity. Nevertheless, the model proved to be quite robust, since none of the sensitivity analyses produced sizable changes in overall treatment costs.

## ··· CONCLUSION ···

Of the 21% to 42% of adults in the United States with symptoms of GERD, approximately 39% seek medical attention for their symptoms, making diagnosis and treatment of this disease a sizable and costly undertaking. Because we have a limited ability to identify patients who might benefit from specific treatment options, payers and patients alike may be incurring a substantial amount of unnecessary medical costs.

From our model, we determined that patients with mild GERD (17.6% of all medically tested patients) contribute 37.8% of costs, while those with moderate to severe GERD (14.4% of patients) contribute 49.9% of costs. This finding is important because it shows that a fairly small group of patients—those with moderate to severe GERD—is responsible for half of the costs associated with treating GERD. The remaining 12.3% of costs is spent on the 68% of patients with diagnoses other than GERD. We also found that proton pump inhibitors, the class of drugs with the highest acquisition cost, had the lowest total cost per case. The high level of efficacy of these drugs may explain this result.

The most important implication of these findings for payers is that they need to assess costs in their entirety. Looking only at one cost center—inpatient costs, outpatient costs,

**Table 6.** Total Weighted Healthcare Costs over 2 Years by Clinical Status (Medically Attended Patients with Suspected Gastroesophageal Reflux Disease [GERD])

| Clinical Status | Weighted Payments per Patient (%) | Percent of Weighted Payments (%) | Percent of Weighted Patients (%) |
|---|---|---|---|
| Mild GERD | | | |
| Empiric treatment | 213 | 32 1 | 15.4 |
| Initial diagnostic evaluation | 38 | 5 7 | 2.2 |
| Moderate/Severe GERD | | | |
| Empiric treatment | 284 | 42 9 | 12.6 |
| Initial diagnostic evaluation | 46 | 7 0 | 1.8 |
| Other Diagnosis | | | |
| No initial diagnostic evaluation | 48 | 7.2 | 59.5 |
| Initial diagnostic evaluation | 34 | 5.1 | 8.5 |
| Weighted average, all medically attended patients with suspected GERD | 663 | 100.0 | 100.0 |

*Estimates from mild results; actual estimates not available

testing costs, or pharmaceutical costs—may lead to decisions that do not maximize the efficient use of payer resources. In addition, it is important to look at costs from a longitudinal standpoint. If only short-term costs are analyzed, the long-term economic ramifications of different treatment options may not be revealed. For example, less efficacious treatment options may look cost-effective in the short run, but may lead to significantly higher costs in the long run through, for example, a greater need for inpatient care.

Perhaps the greatest value of any model comes from subsequent testing and manipulation. Thus we caution that the results presented here do not cover the broad range of results that can be obtained from our model. We encourage further evaluation and testing to fully capitalize on our model as a research and planning tool.

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