REVIEW

Strategies for Diagnosing and Treating Suspected Acute Bacterial Sinusitis

A Cost-effectiveness Analysis

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OBJECTIVE: **Symptoms suggestive of acute bacterial sinusitis are common. Available diagnostic and treatment options generate substantial costs with uncertain benefits. We assessed the cost-effectiveness of alternative management strategies to identify the optimal approach.**

DESIGN: **For such patients, we created a Markov model to examine four strategies: 1) no antibiotic treatment; 2) empirical antibiotic treatment; 3) clinical criteria-guided treatment; and 4) radiography-guided treatment. The model simulated a 14-day course of illness, included sinusitis prevalence, antibiotic side effects, sinusitis complications, direct and indirect costs, and symptom severity. Strategies costing less than $50,000 per quality-adjusted life year gained were considered "cost-effective."**

MEASUREMENTS AND MAIN RESULTS: **For mild or moderate disease, basing antibiotic treatment on clinical criteria was cost-effective in clinical settings where sinusitis prevalence is within the range of 15% to 93% or 3% to 63%, respectively. For severe disease, or to prevent sinusitis or antibiotic side effect symptoms, use of clinical criteria was cost-effective in settings with lower prevalence (below 51% or 44%, respectively); empirical antibiotics was cost-effective with higher prevalence. Sinus radiography-guided treatment was never cost-effective for initial treatment.**

CONCLUSIONS: **Use of a simple set of clinical criteria to guide treatment is a cost-effective strategy in most clinical settings. Empirical antibiotics are cost-effective in certain settings; however, their use results in many unnecessary prescriptions. If this resulted in increased antibiotic resistance, costs would substantially rise and efficacy would fall. Newer, expensive antibiotics are of limited value. Additional testing is not cost-effective. Further studies are needed to find an accurate, low-cost diagnostic test for acute bacterial sinusitis.**

KEY WORDS: **acute bacterial sinusitis; decision analysis; cost-effectiveness analysis; Markov model.**
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Symptoms suggestive of community-acquired, acute bacterial sinusitis occur commonly, resulting in millions of office visits and antibiotic prescriptions annually. In 1995, nonfederally employed physicians in office-based practices saw an estimated 3 million cases of acute sinusitis. The incidence of acute sinusitis has been increasing along with the use of more expensive broader-spectrum antibiotics.[1,2]

The high frequency of these symptoms translates into high costs for an individual's health, work time lost, and medical expenditures for evaluation, diagnostic testing, and treatment. However, given the high rate of spontaneous resolution,[3] the uncertain prevalence of bacterial infection among patients with symptoms suggestive of sinusitis, the need to weigh the benefits of antibiotic treatment against its cost and side effects, and the high cost and uncertain diagnostic accuracy of many diagnostic tests,[4] the management of these patients remains controversial,

To lower health care costs and to minimize the societal risk of antibiotic overuse while maintaining quality care, the cost and effectiveness of diagnostic and treatment strategies for acute bacterial sinusitis must be evaluated. No randomized clinical trial covering all these variables has been performed, and such a trial would be prohibitively expensive to conduct because of the large number of patients required. We therefore created a decision analytic model using the results of recent meta-analyses to estimate the cost-effectiveness of alternative diagnostic and treatment strategies for patients who present with symptoms suggestive of uncomplicated, community-acquired acute bacterial sinusitis.[3] We used a societal perspective and applied consensus recommendations on creating and reporting cost-effectiveness analyses.[5–8]

METHODS

We considered patients with suspected, uncomplicated, community-acquired, acute bacterial sinusitis who had had symptoms for less than 4 weeks and who had not

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had recurrent sinusitis (multiple closely-spaced episodes of acute sinusitis). Patients were not immunocompromised, did not have atopy, malignancy, cystic fibrosis, or a history of sinus trauma or surgery. Because few data exist for young children, patients included in the model were adults or teenagers with fully developed sinuses.

We compared the cost and effectiveness of four management strategies: 1) no patients given antibiotic treatment; 2) all patients given empirical amoxicillin treatment; 3) patients given amoxicillin based on the results of a set of clinical criteria[9]; and 4) patients given amoxicillin based on the results of sinus radiography (plain film x-ray).

We assumed that all patients were seen by a clinician at an office visit and were treated with prescription or over-the-counter medications, such as decongestants, for symptom relief. We did not consider treatment decisions for patients evaluated over the telephone because of insufficient data. Patients undergoing diagnostic testing with clinical criteria or with sinus radiography received either a 10-day course of amoxicillin, 250 mg 3 times a day or no antibiotic treatment, depending on the test outcome and the sensitivity and specificity of each test. Patients given amoxicillin could experience antibiotic side effects, such as rash, gastrointestinal distress, or vaginitis. Patients with acute bacterial sinusitis who did not receive antibiotics could develop a serious disease complication, such as meningitis or brain abscesses.

We used the results of meta-analyses of treatment options and diagnostic methods for acute bacterial sinusitis,[3,4] supplemented where necessary with data from representative individual studies and specialist opinions. For effectiveness, we estimated the number of symptom-free and quality-adjusted days for patients with mild, moderate, and severe sinus symptoms, from the patients' perspective. We used costs, rather than charges, and included both the costs to the health care payers and the societal costs of lost work days. Any strategy with a marginal cost-effectiveness less than the commonly cited threshold of $50,000 per quality-adjusted life year[10–14] or, equivalently, $137 per quality-adjusted day, was considered to be "cost-effective."

Decision Model

To compare the outcomes of hypothetically identical cohorts of patients with acute sinusitis symptoms who received each of the strategies, we developed a Markov or state-transition model[15] (Figure 1) with DecisionMaker 7.0 (Pratt Medical Group, Boston, Mass). The Markov model simulated the natural history of suspected sinusitis as a progression from one health state to another over a 14-day period. A 14-day limit was applied because treatment efficacy data beyond this time horizon are unavailable. All patients began the simulation with symptoms suggestive of acute sinusitis and no recent exposure to antibiotics. In the Markov simulation, during each day, patients may remain in the same state of health, experience serious complications from sinusitis, develop antibiotic side effects (if being treated), or have improvement in their symptoms. The likelihood of improvement depended on the time elapsed since the office visit. In a preliminary model, we assumed that minor side effects, such as vaginitis or gastritis, would lower quality of life and have a small additional cost but would not require a change of antibiotics. Because the minor side effects did not substantially affect the outcomes, the final model included only major side effects that necessitated a change in antibiotics to folate inhibitors (such as trimethoprim-sulfamethoxazole).

The model estimated the number of symptom-free days associated with each strategy by summing the daily proportions of patients without symptoms. The model also calculated the number of quality-adjusted days associated with each strategy. Because the analyses had a time horizon of only 14 days, costs and utilities were not discounted.

Assumptions of the Model. We made the following assumptions in structuring the model:

1. Symptoms, once resolved, did not recur during the 14-day course;
2. The daily risk of antibiotic side effects remained constant during the 14-day course. Side effects persisted for 2 days, occurred only once per 14-day course, and required changing antibiotics, but did not alter the cure rate;
3. Antibiotic treatment of patients without true acute bacterial sinusitis did not alter the natural history of symptoms; and
4. Untreated patients with acute bacterial sinusitis could develop a severe disease complication, such as brain abscess, meningitis, or facial or orbital cellulitis. To bias our results in favor of empirical treatment, none of the antibiotic-treated patients experienced disease-related complications.

Data Summary

Tables 1 through 5 list the values used for the variables in the model, the range of values tested in the sensitivity analyses, and the data sources. Where available, data were compiled from applicable studies found in a systematic review of the literature from 1966 through May 1998. Where necessary, technical experts were consulted.[16] Sensitivity analyses were performed for all variables to determine the effect of the values used (Tables 1–3, 5).

Diagnostic Tests. *Clinical criteria.* For the clinical criteria strategy, we used the diagnostic approach taken in the only trial found that compared clinical findings to sinus puncture, the diagnostic gold standard for sinusitis.[9] This paper used a 4-item risk score based on factors

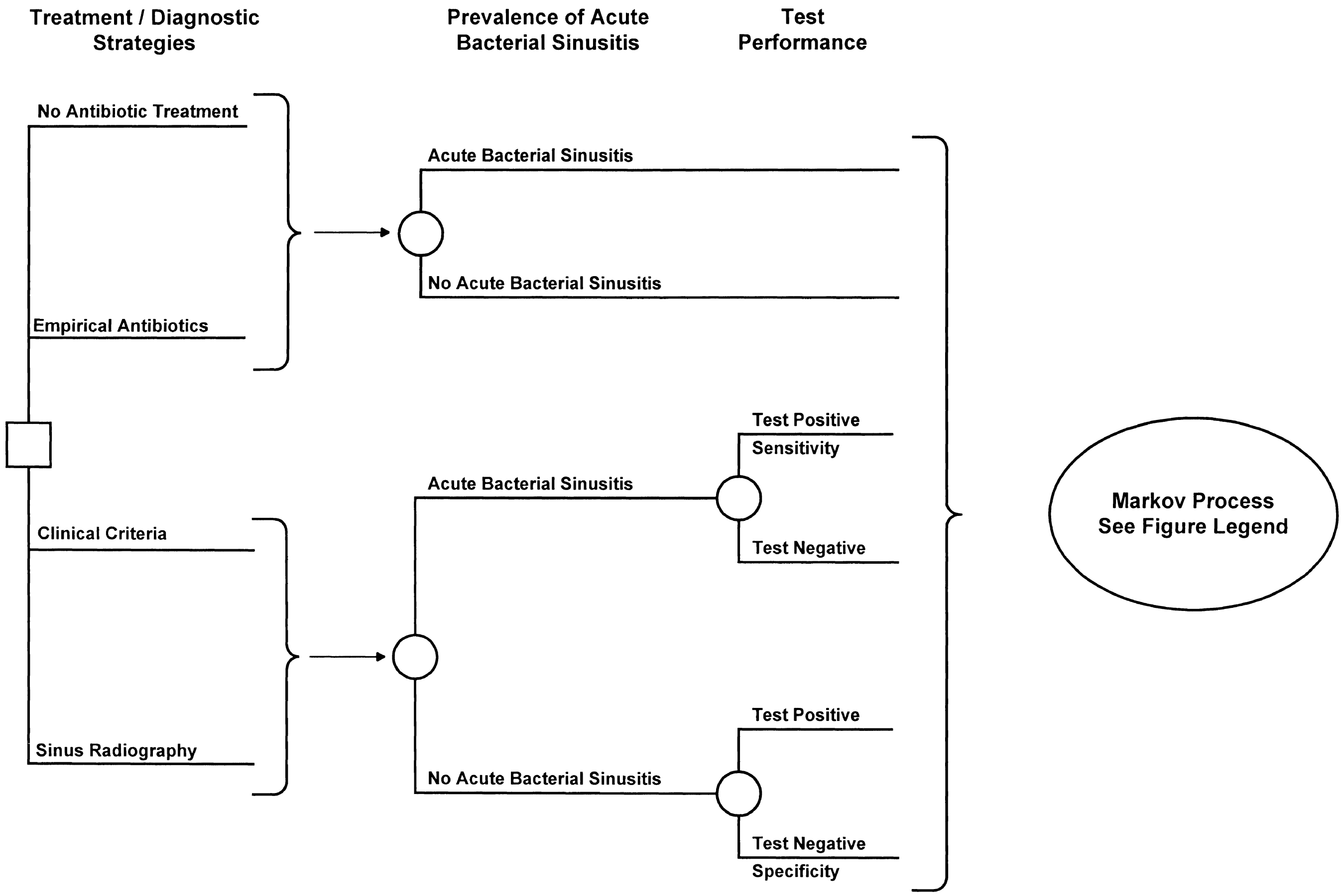

FIGURE 1. Markov decision model, showing each of the four treatment and diagnostic options on the first four branches. The square at the far left of the diagram represents a decision node, with each branch representing the clinical management choices. The brackets indicate that patients who received each of the strategies proceeded to the subtree to the right. The circles at the start of each subsequent branching indicate chance nodes representing the uncertainty surrounding possible subsequent outcomes indicated in the branches to the right. This diagram shows the portion of the decision tree modeling the management strategies, prevalence of sinusitis, and diagnostic test performance (sensitivity and specificity). The Markov process simulates 14 days during which patients may make various possible transitions: if they are sick, they may remain sick, become well, become sick with an antibiotic side effect, or develop a serious disease complication; if they are sick with a side effect, the side effect symptoms will last for 2 days, after which they may remain sick or become well without a side effect; if they are well, they may remain well or develop a side effect which will last for 2 days, after which they will return to the well state.

determined by patient history and physical examination done by a clinician: 1) purulent rhinorrhea with unilateral predominance; 2) local pain with unilateral predominance; 3) bilateral purulent rhinorrhea; or 4) pus in the nasal cavity. A positive test result, defined as the presence of 2 or more items, had a sensitivity of 96% and a specificity of 77% (Table 2).

Table 1. Event Probabilities

Variable	Base Case Value, %	Sensitivity Analysis Values, %
Sinusitis (prevalence)[19–21]	50	0 to 100
Antibiotic side effect (rate)[28–31]	5	20
Complication due to sinusitis (rate)[22–25]	1/10,000	1/1,000

Sinus radiography. Sinus radiography test performance data were derived from a meta-analysis of diagnostic methods.[4] For this analysis, we used the radiographic criteria for plain film x-rays that provided the highest sensitivity (90%) while allowing for a moderate specificity (61%), (Table 2) namely, "sinus opacity or fluid or mucous membrane thickening."

Prevalence. Prevalence estimates of acute bacterial sinusitis in various settings range from 38%[17] to 83%.[18] To be consistent with most studies, we used a baseline estimate of 50% prevalence.[19–21]

Complications. Because no published data were found for the rate of serious complications caused by acute bacterial sinusitis, we considered brain abscesses secondary to sinus infections to be a proxy for all severe disease

Table 2. Test Performance

Variable	Base Case Value	Sensitivity Analysis Range: Bias Against Test	Sensitivity Analysis Range: Bias Toward Test
Applied clinical criteria*[9]			
Sensitivity	0.96	0.60	1.00
Specificity	0.77	0.60	1.00
Sinus radiography[4]			
Sensitivity	0.90	—†	1.00
Specificity	0.61	—†	1.00

* *Two of four factors positive, determined by clinician in office setting: unilateral purulent rhinorrhea, unilateral pain, bilateral purulent rhinorrhea, nasal cavity pus.*
† *Low estimate of radiography diagnostic criteria not tested because test not cost-effective at base case values.*

complications. Using the figures of fewer than 5,000 hospital admissions in 1994 nationally for brain abscess,[22] 16% to 27% of all brain abscess caused by sinus infections,[23,24] and 5 to 20 million cases of acute bacterial sinusitis cases annually in the United States (including those who do not seek health care),[25] we derived a liberal disease complication rate of 1/10,000 cases.

Cure Rates of Sinusitis Symptoms Caused by Acute Bacterial Sinusitis. Amoxicillin and folate inhibitors (such as trimethoprim-sulfamethoxazole) are both as efficacious as the more costly, broad-spectrum antibiotics[3] in treating acute bacterial sinusitis. While concern exists that emerging bacterial resistance may decrease the effectiveness of amoxicillin and folate inhibitors, a recent meta-analysis involving antibiotic trials from 1970 to 1997 did not support this contention. In addition, higher doses of amoxicillin did not improve cure rates.[3] To estimate the daily likelihood of cure associated with amoxicillin or placebo, we fitted a Weibull function (a generalized form of the exponential function commonly used to estimate survival curves)[26] to each Kaplan-Meier curve from the only published study[27] that provided near-daily cure rate data (Figure 2 and Table 3). Trial results were consistent with those of the meta-analysis.

Table 3. Cure Rates

	Cure Rate of Symptoms Caused by Acute Bacterial Sinusitis, %: For Antibiotic[26]		Cure Rate of Symptoms Caused by Acute Bacterial Sinusitis, %: For No Antibiotic Treatment[26]	Cure Rate of Symptoms Caused by Other Diseases, %[16]
	Amoxicillin	Amoxicillin Resistance*	Symptomatic Treatment	Antibiotics Ineffective
Day 3	2	1	0	35
Day 7	24	14	5	61
Day 10	54	35	15	75
Day 14	87	68	41	84

* *Derived from lower 95% confidence intervals of Kaplan-Meier curve for amoxicillin. Used in sensitivity analysis.*

Cure Rates of Sinusitis Symptoms not Caused by Acute Bacterial Sinusitis. Otolaryngologists, internists, family practitioners, and pediatricians familiar with typical courses of patients with acute sinusitis symptoms not caused by bacterial infection estimated symptom relief in 50% at day 5 and 75% at day 10.[16] As above, we fit a Weibull curve to these estimates (Table 3).

Harm from Antibiotic Use. In the absence of specific published data regarding the occurrence of side effects with amoxicillin, we estimated that 5% of patients receiving amoxicillin would require an antibiotic change for severe drug allergies. This was consistent with reports of 1% to 10% incidence of side effects of penicillins[28] and of 5% of hospitalized patients having cutaneous or more severe drug reactions.[29–31]

No reliable data exist concerning either how antibiotic use directly affects resistance patterns or how antibiotic resistance affects patient outcomes in acute sinusitis. While future antibiotic resistance resulting from current antibiotic use is important to society, it is unlikely that it will result in any harm or additional costs to those patients taking the antibiotics. For these reasons, and because models that account for future antibiotic resistance have not been validated, costs and outcome utilities from resulting antibiotic resistance have not been included in the model.

Severity of Sinusitis Symptoms. Two separate approaches were used to evaluate the effectiveness of the treatment and diagnostic strategies. In the first we measured the total

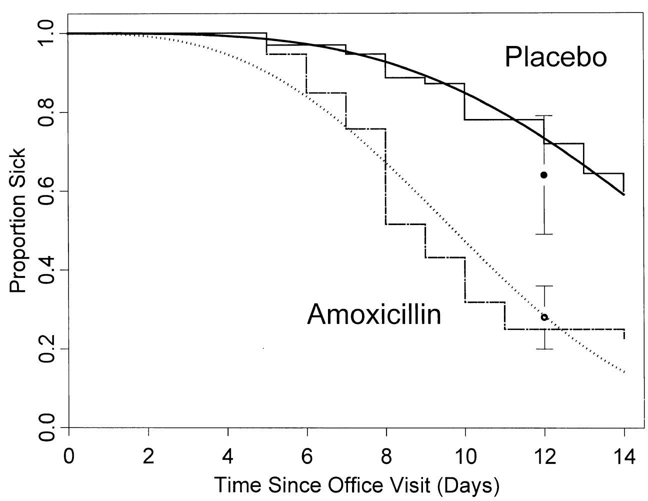

FIGURE 2. Kaplan-Meier curves and fitted Weibull curves for the placebo and amoxicillin arms of trial evaluating amoxicillin for the treatment of acute bacterial sinusitis.[26] Point estimates and 95% confidence intervals are shown at day 12 for treatment meta-analysis estimates of cure at days 10 to 14.[4]

number of days in the 14-day course that patients would be symptom-free. Each day that a patient was without symptoms from sinusitis or antibiotic side effects was given a value of 1, whereas all other days were given a value of 0. This scenario considered the total duration (over 14 days) of any symptom related to disease or treatment (Table 4).

In the second approach, we used quality-of-life adjustments based on the Quality of Well-being General Health Policy Model to account for differing degrees of severity of sinusitis symptoms.[32] In this approach, each day with symptoms had a lower value than a healthy day (Table 4). For example, a day spent with antibiotic side effects was given a value of 0.760. Thus, such a day was worth only 76% of a healthy day. I.e., people would be willing to give up 24% of a day, or 6 hours, to avoid a day with antibiotic side effects.

In separate scenarios, we calculated quality adjustments for three levels of symptom severity: mild, moderate, and severe (Table 4). These quality-of-life adjustments reflect clinical impairment from sinusitis and increase the benefit of antibiotic treatment for more severely ill patients. For patients with both sinusitis symptoms and antibiotic side effects, the quality-of-life adjustments for these two events were multiplied together. This may overstate the overall severity of illness of patients with both sinusitis and antibiotic side effects; however, it reflects clinical concern that antibiotic treatment may cause side effects.

Table 4. Outcome Utilities

Variable	Symptom-free Days	Sinusitis Severity* Severe	Moderate	Mild
Cure				
Without antibiotic side effects	1.0	1.0	1.0	1.0
With antibiotic side effects	0	0.760†	0.760†	0.760†
Sick				
Without antibiotic side effects	0	0.498‡	0.560§	0.769‖
With antibiotic side effects	0	0.378#	0.426**	0.584††
Serious complication due to sinusitis	0	0.387‡‡	0.387‡‡	0.387‡‡

** Utilities derived from Quality of Well-being General Health Policy Model (Utility = 1 + Symptom/Problem Complex weight + Mobility Scale weight + Physical Activity Scale weight + Social Activity Scale weight).[32]*
† 1− 0.24 (large rash).
‡ 1− 0.257 (cough, etc.) −0.062 (cannot drive) −0.077 (bed-bound) −0.106 (no major activity).
§ 1− 0.257 (cough, etc.) −0.062 (cannot drive) −0.060 (limited ambulation) −0.061 (limited activity).
‖ 1− 0.170 (sinus pain) −0 (no mobility limitation) −0 (no physical limitation) −0.061 (limited activity).
 # 0.760 (rash) × 0.498 (severe symptoms). Multiplication of symptoms biases model against use of antibiotics because of the concern for antibiotic adverse events.
*** 0.760 (rash) × 0.560 (moderate symptoms). See #.*
†† 0.760 (rash) × 0.769 (mild symptoms). See #.
‡‡ 1− 0.340 (altered mental status) −0.090 (hospitalized) −0.077 (bed-bound) −0.106 (no major activity).

Table 5. Costs

Variable	Base Case Value, $	Sensitivity Analysis Value, $
Antibiotic prescription	15*	100*
Sinus radiography	79†	See text
Clinical criteria	0‡	—§
Antibiotic side effect, per day		
No work loss	22.50‖	65‖
Work loss	80‖	122.50‖
Disease outcome (at end of 14-day course)		
Cure	0¶	—§
Sick (daily cost for work loss from sinusitis)		
Mild scenario	0#	—§
Moderate scenario	57.50**	—§
Symptom-free model or severe	115††	—§
Sick (persistent sinusitis after 14 days)		
No antibiotic treatment	55‡‡	140§§
Empirical amoxicillin	140§§	—§
Diagnostic test		
Negative → no antibiotics	55‡‡	140§§
Positive → antibiotics	140§§	—§
Serious disease complication	10,000‖‖	—§

** Antibiotic cost plus pharmacy handling cost.[33]*
† Median cost as of 1998 of radiologic examination, sinuses, paranasal, less than three view ($58) and radiologist's reading ($21).[35]
‡ Included in initial office visit. Therefore, no additional cost.
§ Value not varied in sensitivity analyses.
‖ 50% return for level 3 office visit (0.5 × $40),[35] treatment of side effect symptoms ($10)[33] and change antibiotics to folate inhibitor ($15, base)[33] or newer, more expensive antibiotic ($100).[33] With work loss, 1 day at median earnings ($115)[34] assumed. Not double-counted if workday lost due to sinusitis. Total cost divided between two days of symptoms.
¶ There is no additional cost to patients not receiving antibiotics or to being cured.
 # Assumed no work loss with mild symptoms.
*** Assumed half-day of work lost per day with moderate symptoms.*
†† Full day of work lost each day sick. Value derived from median weekly earnings, first quarter 2000 ($575/week).[34]
‡‡ Return office visit ($40) and amoxicillin or folate inhibitor ($15). For Symptom-free Day model, severe, and moderate symptom scenarios, we assumed work loss at $115/day, median earnings.[34] For mild symptom scenario, we assumed no work loss.
§§ Return office visit ($40) and new, expensive antibiotic ($100). Cost of work loss determined as in.‡‡
‖‖ Estimate of hospital costs, including intravenous antibiotics, surgery,[16] and work loss determined as in.‡‡

Costs. Table 5 presents the cost estimates and their sources. Because all patients were assumed to have an office visit and to use prescription or over-the-counter symptomatic therapies, no additional costs arose from the initial office visit. Antibiotic costs were based on wholesale drug costs[33] and pharmacy handling charges. The cost of

Table 6. Results for Clinical Outcomes and Antibiotic Prescriptions at Various Prevalence Rates

		Average Outcomes			Antibiotic Prescriptions	
	Average Cost, $*	Days Sick with Sinusitis (Patients Sick at Day 14, %)	Days with Side Effect (Patients with Side Effect, %)	Patients with Sinusitis Complications, %	Patients without Sinusitis Given Antibiotics, %	Patients with Sinusitis Not Given Antibiotics, %
Prevalence = 25%						
No antibiotic treatment	853	7.3 (23)	0 (0)	0.003	0	25
Clinical criteria	771	6.5 (14)	0.02 (1)	0.0001	17	1
Empirical treatment	784	6.5 (12)	0.10 (5)	0	75	0
Sinus radiography	859	6.8 (13)	0.02 (2)	0.0003	29	3
Prevalence = 50%						
No antibiotic treatment	1,053	9.0 (35)	0 (0)	0.005	0	50
Clinical criteria	883	7.4 (17)	0.03 (2)	0.0002	12	2
Empirical treatment	886	7.3 (12)	0.10 (5)	0	50	0
Sinus radiography	974	7.5 (15)	0.03 (3)	0.0005	20	5
Prevalence = 75%						
No antibiotic treatment	1,253	10.7 (47)	0 (0)	0.008	0	75
Clinical criteria	994	8.4 (19)	0.04 (3)	0.0003	6	3
Empirical treatment	988	8.2 (13)	0.10 (5)	0	25	0
Sinus radiography	1,090	8.5 (16)	0.03 (3)	0.0008	10	8

* *Costs include full work day lost for all days sick or with side effects and exclude initial office visit and any symptomatic drug treatments.*

radiography was derived from the median 1998 fee for a 2-view sinus radiograph and reading.[16] Applying clinical criteria as a decision tool incurred no additional cost. The cost of serious sinusitis complications was based on average hospital costs, including surgery and intravenous antibiotics.[16] Indirect costs were derived from first quarter 2000 median weekly earnings for full-time workers ($575).[34] Lost earnings for a work day were defined as one-fifth of the weekly earnings ($115). By treating lost weekend days as equivalent to work days, we partially accounted for other productivity losses and indirect costs due to illness. Indirect costs were greater for severe illness than for mild illness. Persistent symptoms at the end of 14 days incurred follow-up costs, depending on the original strategy and test outcome (Table 5).[35]

RESULTS

Clinical Effectiveness Profile

No antibiotic treatment yielded the most sick days and the worst cure rate, but avoided all antibiotic side effects. Empirical antibiotic treatment yielded the shortest duration of illness and the highest cure rate at the end of 2 weeks, but also led to the highest rate of antibiotic side effects (Table 6) with many unnecessary antibiotic courses. In general, the application of clinical criteria or sinus radiography yielded cure rates similar to those of empirical antibiotics while decreasing unnecessary antibiotics and side effects.

Cost and Effectiveness at 50% Disease Prevalence

To avoid any day with symptoms from disease or treatment, the differences in symptom duration for patients given empirical antibiotic treatment, clinical criteria–guided treatment, or radiography-guided treatment were minimal in a typical setting, where the prevalence of disease is 50% (Table 7), but all were superior to no antibiotic treatment because of the latter's lower cure rate. Costs were driven largely by symptom duration, as the indirect productivity costs were substantially greater than the direct medical costs of diagnosis and treatment. Clinical criteria–guided treatment had the lowest cost, by properly treating most patients with bacterial sinusitis while avoiding most unnecessary antibiotic treatment. Empirical antibiotic treatment was slightly more effective and was cost-effective at $74 to avoid one day of symptoms when compared to clinical criteria–guided treatment. Radiography-guided antibiotic treatment and symptomatic (no antibiotics) treatment were both less effective and more costly (due to the test expense and additional lost work days).

Symptom Severity

When considering quality-of-life adjustments for different intensities of symptoms (Table 7), patients with milder symptoms were less affected (closer to being healthy) than those with more severe symptoms. Thus, effective antibiotic treatment yielded a greater benefit in patients with more severe symptoms.

Table 7. Results: Marginal Cost-effectiveness (MCE) of Each Management Strategy for Any Symptom and Differing Sinusitis Symptom Severity at a Prevalence Rate of 50%

	Symptom-free Day Scenario*			Severe Symptom Scenario*			Moderate Symptom Scenario†			Mild Symptom Scenario‡		
Strategy	Cost, $	Symptom-free Days	MCE, $/Symptom-free Day	Cost, $	Quality-adjusted Days	MCE, $/Symptom-free Day	Cost, $	Quality-adjusted Days	MCE, $/Symptom-free Day	Cost, $	Quality-adjusted Days	MCE, $/Symptom-free Day
Clinical-criteria-guided antibiotic treatment	883	6.5	—	883	10.3	—	454	10.8	—	26	12.4	34‖
Empirical antibiotic treatment	886	6.6	74	886	10.3	152	462	10.8	421	38	12.4	22,800
Radiography-guided antibiotic treatment	974	6.4	Inferior§	974	10.3	Inferior§	541	10.8	Inferior§	107	12.4	Inferior§
No antibiotic treatment	1,053	5.0	Inferior§	1,053	9.7	Inferior§	536	10.2	Inferior§	20	12.2	—‖

* *Assumes full work day lost per day with symptoms. See text and Table 4.*
† *Assumes half work day lost per day with symptoms. See text and Table 4.*
‡ *Assumes no work days lost for days with symptoms. See text and Table 4.*
§ *A strategy is inferior (or "dominated") when it is both less effective and more costly than other strategies. It is therefore eliminated from consideration as a cost-effective strategy by strict dominance.*
‖ *For mild symptoms, no antibiotic treatment (symptomatic treatment only) was the least expensive. Use of clinical criteria was the next most expensive and was cost-effective in comparison to no antibiotic treatment.*

For mild symptoms, no antibiotic treatment had the lowest cost, but clinical criteria–guided treatment increased total costs by $6 and improved effectiveness at a marginal cost-effectiveness of $34 to avoid a day of symptoms. Empirical antibiotic treatment added $12, but was only minimally more effective, so the marginal cost-effectiveness ratio rose sharply to $22,800 to avoid a day of symptoms. Sinus radiography was inferior because it was both more costly and less effective than empirical antibiotic treatment.

For moderate and severe symptoms (that resulted in lost work days), clinical criteria–guided treatment was least costly. Empirical treatment was more costly and effective with marginal cost-effectiveness ratios ranging from $152 to $421 per day of symptoms avoided. Both symptomatic treatment and radiography-guided treatment were inferior with higher costs and lower effectiveness.

Disease Prevalence

With rising prevalence, strategies resulting in antibiotic treatment rapidly increased in overall benefit. Empirical treatment was most effective at all but the lowest prevalence rates because the benefits from antibiotic-treated bacterial sinusitis outweighed their side effects. With all strategies, costs rose with increasing prevalence because of increasing lost work days, antibiotic usage, or follow-up because of lower 14-day cure rates.

Figure 3 shows the effect of prevalence of acute bacterial sinusitis on the optimal management of patients in whom the sinusitis symptoms have different quality-of-life effects. For example, to avoid any symptom, no antibiotics is preferred for prevalence levels below 1%, and empirical antibiotics is preferred for prevalence levels above 44%. Clinical criteria is optimal for all other prevalence levels.

Regardless of the severity of symptoms, no antibiotics is preferred for low prevalence levels of acute bacterial sinusitis and empirical antibiotics is optimal for high prevalence levels. Clinical criteria is best suited for patients with intermediate probabilities. As the severity of symptoms increases, the threshold at which clinical criteria or empirical antibiotic treatment should be used becomes lower because patients with more severe symptoms from bacterial sinusitis obtain greater benefit from antibiotic treatment.

Sequential Application of Clinical Criteria and Sinus Radiography

In a variation of the model, we tested the strategy of applying clinical criteria, treating those patients with a negative test symptomatically, and ordering a sinus radiograph to determine treatment for those with a positive test. Due to the high cost of the radiograph and its relatively poor specificity, this sequential testing strategy remained more expensive than either clinical criteria alone or empirical antibiotic treatment at all levels of sinusitis prevalence.

Sensitivity Analyses

We performed sensitivity analyses to examine the effect of varying the values chosen for each variable used in the analysis (Tables 1–3, and 5). Variation in variables not

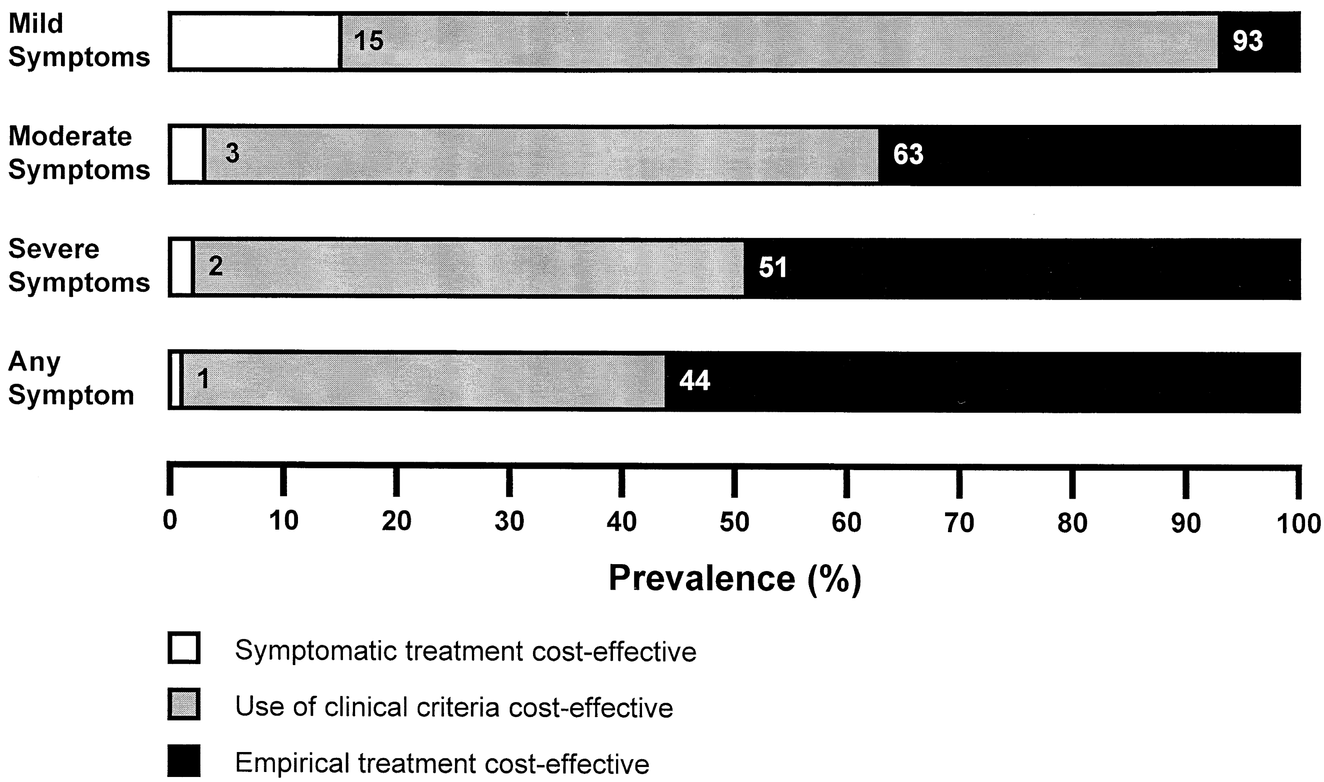

FIGURE 3. Optimal management strategies depending on symptom severity and prevalence of acute bacterial sinusitis in four groups of patients: 1) considering any symptom (sinusitis or antibiotic-related), 2) quality of life adjusted for severe sinusitis symptoms, 3) quality of life adjusted for moderate sinusitis symptoms, and 4) quality of life adjusted for mild sinusitis symptoms. Optimal strategies are effective and cost-saving, or cost-effective, at less than $137 per day (equivalent to $50,000 per quality-adjusted life year). White bars at left indicate prevalence levels for which no antibiotics is the favored strategy. Gray bars in the middle indicate prevalence levels for which use of clinical criteria is favored. Black bars at right indicate prevalence levels for which empirical antibiotics is favored. The numbers within the bars indicate the exact threshold at which the optimal strategy changes.

discussed below did not alter the results and are not presented (but are available from the authors).

Bacterial Resistance. To simulate increased bacterial resistance to amoxicillin, we decreased the efficacy of the antibiotic compared to placebo (Table 3). Thus all strategies were more costly and less effective. Empirical antibiotic treatment was cost-effective for levels of bacterial sinusitis prevalence above 59%, and no antibiotic treatment was optimal for prevalence levels below 4%. Clinical criteria was cost-effective for all other prevalence levels including the base case 50%.

Newer, More Expensive Antibiotics. Use of newer, more costly antibiotics has not been shown to be more effective than amoxicillin in treating acute bacterial sinusitis.[3] However, if we assumed these antibiotics were 23% more effective than amoxicillin (the maximum benefit from the meta-analysis), use of clinical criteria or empirical treatment resulted in an additional half-day of symptom relief. The cost of using clinical criteria was unchanged because the higher initial cost of treatment was fully offset by the lower cost of follow-up care. However, empirical treatment cost an additional $31 and was not cost-effective at $510 per day of symptoms avoided (equivalent to $186,000 per quality-adjusted life year). Empirical treatment was cost-effective only when bacterial sinusitis prevalence exceeded 80%.

Clinical Criteria Test Performance. We used the only set of published clinical criteria that were compared to the gold standard of sinus puncture. Because no validation study exists, we determined the sensitivity and specificity levels at which a hypothetical set of clinical criteria would be cost-effective. Clinical criteria remained optimal for sensitivities above 93% and specificities above 72%. As the sensitivity of clinical criteria was reduced (e.g., from 95% to 90%), while specificity was unchanged, empirical antibiotic treatment became cost-effective at lower levels of sinusitis prevalence (e.g., from about 55% to 40%). Altering test specificity alone (or the false positive rate) had little impact on overall cost-effectiveness.

Sinus Radiography Test Performance. Sinus radiography was not cost-effective. Its cost was high compared to both treatment and follow-up care. Even if radiography were a perfect test (with 100% sensitivity and specificity), it was still not cost-effective at $883 per additional symptom-free day compared to clinical criteria for a disease prevalence of 50%. Even if perfectly discriminating, a sinus radiograph would be cost-effective only if it cost less than $19, including radiologist's fee.

DISCUSSION

Amoxicillin and folate inhibitors, such as trimethoprim-sulfamethoxazole, are effective in treating uncomplicated, community-acquired, acute bacterial sinusitis. However, given their costs, their risks of side effects, and the potential harm to society of increasing bacterial resistance from antibiotic overuse, antibiotics should be given only to those patients for whom they will be useful. We thus compared various management strategies for patients with acute sinusitis symptoms to determine the most efficient and cost-effective approaches.

Our analyses highlight the impact of disease prevalence and symptom severity on cost-effectiveness and the need to consider these factors in clinical decisions for both diagnosis and treatment of patients with sinusitis symptoms. The best strategy for diagnosing and treating acute sinusitis depends in part on the prevalence of the bacterial sinusitis (or the likelihood that a given patient actually has the disease).

In our model, only when the underlying likelihood of acute bacterial sinusitis among patients is extremely low (below 1% to 15%) is withholding antibiotic treatment for all patients optimal (Figure 3). In most clinical settings, however, the prevalence of acute bacterial sinusitis exceeds 15%, so applying the set of clinical criteria tested to determine antibiotic treatment should be both effective and cost-effective.

In a limited set of clinical circumstances, empirical antibiotics is cost-effective: 1) for patients with severe or possibly moderate symptoms; 2) solely to minimize symptom-days; or 3) for patients with mild symptoms in clinical settings with extremely high prevalence.

Currently, very few sets of clinical criteria have been investigated for acute sinusitis. We considered criteria from the only study that used the gold standard test for bacterial sinusitis.[9] Further studies are clearly needed. Nonetheless, our analysis suggests that any potential set of clinical criteria should have high sensitivity (>93%) and at least moderate specificity (>72%).

Because of its relatively high cost, sinus radiography for the initial management of uncomplicated, community-acquired, acute bacterial sinusitis would cost thousands of dollars for each additional healthy day gained, making it more expensive than other management strategies. At a cost below $19 total, it would, however, be cost-effective. Even if radiography were used only in those with negative clinical criteria, radiography would remain expensive. These findings hold true for any additional diagnostic tests, including computed tomography and ultrasonography.

Empirical treatment of all patients results in antibiotic overuse leading to increased bacterial resistance and perhaps reduced future effectiveness and increased drug costs. However, more studies substantiating and clarifying the link between individual antibiotic use and emerging community resistance are needed.

While the risks and costs of antibiotic overuse may be potentially high, withholding antibiotics also can increase risks and costs because of serious sinusitis complications. Our analysis explicitly examined this trade-off. For example, in the approximately 3 million patients seen annually for acute sinusitis symptoms, 50% have bacterial sinusitis, so treating all such patients empirically would prevent 150 serious complications but would entail 1.5 million unnecessary antibiotic prescriptions at an additional cost of $36 million. Thus, $240,000 would be spent per patient to avoid one serious complication. Further studies and guidelines for rational use of antibiotics for acute sinusitis could help to optimize benefits and minimize risks.

Although the decision analysis was limited by its reliance in some cases on a paucity of published data, our findings were robust over a wide range of sensitivity analyses and were internally consistent. Analysis of this and earlier versions of the model indicated that the overall findings were stable using various estimates of quality-of-life adjustments. Our decision analysis, however, applies only to older teenagers and adults because of insufficient prevalence, diagnostic testing, and treatment data in pediatric populations. Further studies are needed to arrive at better estimates of acute bacterial sinusitis prevalence in various settings, the efficacy of specific symptomatic treatments, the rate of disease complications, the effect on cure rate of increasing bacterial antibiotic resistance, and the effect on clinical methods of diagnosing disease.

It should be noted that our analysis applies only to patients with suspected community-acquired maxillary sinusitis symptoms. Patients with potentially more serious disease, such as frontal or sphenoid sinusitis, those with concurrent medical conditions such as immunocompromise, and those with evidence of more severe illness clearly should be treated more aggressively than implied by this analysis.

CONCLUSIONS

- In most primary care settings, the evidence supports using clinical criteria to guide antibiotic treatment of otherwise healthy patients with mild to moderate symptoms suspicious for community-acquired, acute bacterial maxillary sinusitis.
- Empirical antibiotic treatment of patients may be cost-effective: 1) if the goal is to minimize

symptom-days; 2) if patients have severe symptoms and bacterial sinusitis prevalence exceeds 51%; 3) if patients have moderate symptoms and bacterial sinusitis prevalence exceeds 63%; and 4) if patients have mild symptoms and bacterial sinusitis prevalence exceeds 93%. However, many patients would receive antibiotics unnecessarily.

- In deciding whether to treat, the very small risk of serious disease complications must be weighed against the real risk of antibiotic side effects and the potential effect of increasing antibiotic resistance by prescribing antibiotics. Lowered antibiotic efficacy, as a result of increased antibiotic resistance, can substantially increase the cost while decreasing the benefit of using both clinical criteria to determine treatment and of treating patients empirically with antibiotics.
- Using newer, expensive antibiotics as initial treatment adds to costs without substantially improving outcomes compared to initially using amoxicillin or folate inhibitors, such as trimethoprim-sulfamethoxazole. Even if the newer antibiotics were more effective than amoxicillin, they would be cost-effective only at bacterial sinusitis prevalence levels above 80%.
- The use of additional costly tests, such as radiography, computerized tomography, or ultrasonography, is not cost-effective as part of an initial work-up of suspected uncomplicated, community-acquired acute sinusitis.
- Further studies are needed to find an accurate, low-cost diagnostic test for acute bacterial sinusitis.

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REFERENCES

1. National Ambulatory Medical Care Survey. National Center for Health Statistics. Series 13. 1990: CD-ROM.
2. McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. JAMA. 1995; 273:214–9.
3. de Ferranti SD, Ioannidis JP, Lau J, Anninger W, Barza M. Are amoxycillin and folate inhibitors as effective as other antibiotics for acute sinusitis? A meta-analysis. BMJ. 1998;317:632–7.
4. Engels EA, Terrin N, Barza M, Lau J. Meta-analysis of diagnostic tests for acute sinusitis. J Clin Epi. 2000;53:852–62.
5. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. JAMA. 1996;276:1253–8.
6. Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analyses. Panel on Cost-Effectiveness in Health and Medicine. JAMA. 1996;276:1339–41.
7. Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine. JAMA. 1996;276: 1172–7.
8. Canadian Coordinating Office for Health Technology Assessment. Guidelines for economic evaluation of pharmaceuticals: Canada. 1st edition. Ottawa: CCOHTA, 1994.
9. Berg O, Carenfelt C. Analysis of symptoms and clinical signs in the maxillary sinus empyema. Acta Otolaryngol. 1988;105:343–9.
10. Lee TT, Solomon NA, Heidenreich PA, Oehlert J, Garber AM. Cost-effectiveness of screening for carotid stenosis in asymptomatic persons. Ann Intern Med. 1997;126:337–46.
11. Owens DK, Sanders GD, Harris RA, et al. Cost-effectiveness of implantable cardioverter defibrillators relative to amiodarone for prevention of sudden cardiac death. Ann Intern Med. 1997;126: 1–12.
12. Hamel MD, Phillips RS, Davis RB, et al. Outcomes and cost-effectiveness of initiating dialysis and continuing aggressive care in seriously ill hospitalized adults. Ann Intern Med. 1997;127: 195–202.
13. Hunink MG, Wong JB, Donaldson MC, Meyerovitz MF, de Vries J, Harrington DP. Revascularization for femoropopliteal disease. A decision and cost-effectiveness analysis. JAMA. 1995;274:165–71.
14. Nease RFJ, Owens DK. A method for estimating the cost-effectiveness of incorporating patient preferences into practice guidelines. Med Decis Making. 1994;14:382–92.
15. Beck JR, Pauker SG. The Markov model of medical prognosis. Med Decis Making. 1983;3:419–58.
16. Diagnosis and treatment of acute bacterial sinusitis. AHCPR Publication No. 99–E017. 1998. Rockville, MD, Agency for Health Care Policy and Research.
17. Williams JW Jr., Simel DL, Roberts L, Samsa GP. Clinical evaluation for sinusitis. Making the diagnosis by history and physical examination. Ann Intern Med. 1992;117:705–10.
18. Savolainen S, Pietola M, Kiukaanniemi H, Lappalainen E, Salminen M, Mikkonen P. An ultrasound device in the diagnosis of acute maxillary sinusitis. Acta Otolaryngol Suppl. 1997;529: 148–52.
19. Kuusela T, Kurri J, Sirola R. Ultrasound in the diagnosis of paranasal sinusitis of conscripts: comparison of results of ultrasonography, roentgen examination, and puncture and irrigation. Ann Med Milit Fenn. 1982;57:138–41.
20. Laine K, Määttä T, Varonen H, Mäkelä M. Diagnosing acute maxillary sinusitis in primary care: a comparison of ultrasound, clinical examination and radiography. Rhinology. 1998;36:2–6.
21. van Buchem FL, Peeters MF, Beaumont J, Knottnerus JA. Acute maxillary sinusitis in general practice: the relation between clinical picture and objective findings. Eur J Gen Pract. 1995;1: 155–60.
22. National Hospital Discharge Survey. National Center for Health Statistics. Series 13. 1994: CD-ROM.
23. Bradley PJ, Shaw MD. Three decades of brain abscess in Merseyside. J R Coll Surg Edinb. 1983;28:233–8.
24. Small M, Dale BA. Intracranial suppuration 1968–1982—a 15 year review. Clin Otolaryngol. 1984;9:315–21.
25. Gwaltney JMJ. Acute community-acquired sinusitis. Clin Infect Dis. 1996;23:1209–23.
26. Kalbfleisch J, Prentice R. The statistical analysis of failure time data. New York: John Wiley & Sons; 1980:Chapter 2.
27. Lindbaek M, Hjortdahl P, Johnsen UL. Randomised, double blind, placebo controlled trial of penicillin V and amoxycillin in treatment of acute sinus infections in adults. BMJ. 1996;313: 325–9.
28. Lin RY. A perspective on penicillin allergy. Arch Intern Med. 1992; 152:930–7.

29. Bigby M, Jick S, Jick H, Arndt K. Drug induced cutaneous reactions: a report from the Boston Collaborative Drug Surveillance Program on 15,438 consecutive inpatients. JAMA. 1986;256: 3358–63.
30. Caldwell J, Cluff L. Adverse reactions to antimicrobial agents. JAMA. 1974;230:77–80.
31. Saxon A, Beall G, Rohr A, Adelman D. UCLA conference: Immediate hypersensitivity reactions to beta-lactam antibiotics. Ann Intern Med. 1987;107:204–15.
32. Kaplan RM, Anderson JP. A general health policy model: Update and applications. Health Services Research 1988;23:203–235.
33. Cardinale V, ed. Drug Topics Red Book. Oradell, NJ: Medical Economics Company; 1997.
34. Usual weekly earnings of wage and salary workers. First quarter 2000. Bureau of Labor Statistics. Available at: http://www.bls.gov/news.relese/wkyeng.nr0.htm. Accessed 6/16/2000.
35. Wasserman Y. Physicians' Fee Reference 1998. West Allis, Wisconsin: DMD Medical Publishers, Ltd.; 1998.