# Selective Testing for Streptococcal Pharyngitis in Adults

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Some physicians test for group A streptococcal pharyngitis in all patients who have a sore throat, while others use a variety of clinical strategies to select patients to be tested. Using published data on the accuracy of a clinical decision rule, this benefit-cost analysis compares the calculated outcomes of 21 different management strategies applied to 1,000 hypothetical adults with pharyngitis. Strategies that best accomplish one physician's treatment goals may perform poorly when evaluated in a different practice setting or using different goals. The best strategies are identified for different treatment objectives and for different assumptions about the benefits of treatment so each physician can choose a strategy consistent with his or her preferences.

while some physicians test for group A streptococcal pharyngitis in all patients who have a sore throat, surveys show that many physicians use clinical information to decide whom to test. <sup>1,2</sup> Among those who test only selected patients, there are wide variations in clinical strategies. The purpose of this study is to discover how various methods of selective testing affect the outcome in managing streptococcal pharyngitis. The analysis uses published data on the accuracy of a clinical decision rule for adults to show which of 21 different strategies are most effective, depending on the physician's treatment goals.

The ideal strategy for managing pharyngitis would provide antibiotic treatment for patients with acute group A streptococcal disease while sparing other patients the risk and expense of treatment. Throat cultures or rapid streptococcal antigen detection tests are often used to select patients for treatment, but they entail expense and are not perfectly accurate. The predictive values of laboratory tests for streptococcal pharyngitis are limited by the low prevalence of disease and by carriers, patients whose throat cultures are positive but in whom group A streptococci are not the pathogens for the disease. Because of the expense and potential errors of tests, a number of clinical

decision rules have been suggested for identifying groups of patients for whom the decision to treat can be made without using a laboratory test.<sup>4-7</sup> Each of these decision rules provides a method of using clinical information to group patients according to the probability of streptococcal disease.

The earliest clinical trials of decision rules for managing pharyngitis demonstrated that clinical information can be used to find patients whose pharyngitis is unlikely to be streptococcal. Some authors advocate withholding treatment from this group, as an "acceptably low" number of patients with streptococcal disease will be missed. 7-9 Others have suggested reducing the number of false-negative test results by giving presumptive antibiotic treatment to patients whose clinical presentation indicates a high probability of streptococcal disease. 5,10 A third recommendation is to combine strategies, withholding treatment from the low-probability group, treating the high-probability group, and testing only patients who have a moderate probability of streptococcal illness based on clinical findings. 6,11,12

Every treatment strategy is a compromise. If each patient with pharyngitis is given an antibiotic, every patient with streptococcal disease will be treated correctly. Most patients have nonstreptococcal disease, however, and will be treated inappropriately. At the opposite extreme, if an antibiotic is never used, all incorrect use of antibiotics will be eliminated, but every case of streptococcal illness will be untreated. Each strategy for selective testing results in a different compromise between the occurrence of these two kinds of errors. Consequently, the choice of the best

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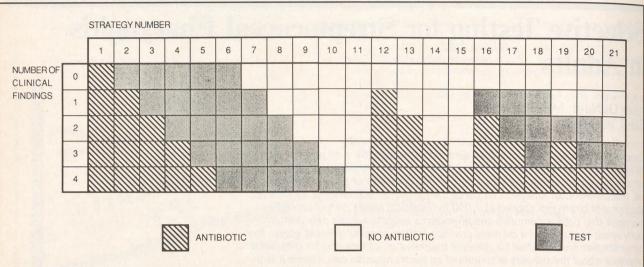


Figure 1. Twenty-one different strategies for managing patients with pharyngitis based on four clinical criteria: pharyngeal exudate, anterior cervical adenopathy, absence of cough, and history of fever

strategy depends on treatment priorities and on assumptions about streptococcal disease and its complications.

Tompkins et al<sup>13</sup> estimated the total costs of testing, treatment, and adverse outcomes for three nonselective strategies: treat everyone, treat no one, or test everyone. With inexpensive tests and a relatively high probability of rheumatic fever, the least expensive strategy is to treat no one if the positive culture rate is less than 5 percent. treat everyone if it is greater than 20 percent, and otherwise to test everyone. In a recent clinical trial, grouping patients using clinical data and selectively testing groups using these criteria would have incurred a lower total cost than testing everyone. 11 In a different analysis of clinical data where the cost of preventing a single case of rheumatic fever was estimated, Forsythe<sup>6</sup> recommended a similar selective testing strategy for adults. Pantell and Bergman<sup>14</sup> showed that the strategy with minimum total costs, including test and treatment costs, differs from the one that minimizes only adverse medical outcome costs. They recommended management based on clinical symptoms only if the positive or negative predictivity of a decision rule is greater than 0.9.

Using a different approach, Centor et al<sup>10,15</sup> weighed outcomes according to the preferences of healthy subjects and included the value to the patient of a shortened illness when treatment is started promptly. Excluding test and treatment costs and using a much lower risk of rheumatic fever than in other studies, they recommended treating patients who have a high clinical probability of disease and testing everyone else. The threshold they calculated

is a pretest probability of disease of 11 percent if testing with throat cultures and 47 percent if using rapid tests.

Thus, the physician has a number of recommendations to choose from, each based on a particular set of assumptions about his treatment goals. The purpose of the present study is to analyze the performance of a wide variety of clinical strategies judged against several different treatment objectives and different assumptions about the benefits of treatment. Because the actual cost of testing varies among practices and because of uncertainty in the risk of rheumatic fever, special attention is given to how these factors affect the conclusions.

#### **METHODS**

To compare the theoretical outcomes of different strategies for selective testing, the decision rule described by Centor et al<sup>4,5</sup> was chosen to divide adult patients into groups based on the presence or absence of four clinical criteria: pharyngeal exudate, tender and enlarged anterior cervical lymph nodes, absence of cough, and history of fever. Each of these findings is assigned a value of 1, resulting in a clinical score from 0 to 4 for each patient. Including the three nonselective strategies, there are 21 different ways of using this clinical score to specify a test threshold and a test-treatment threshold (Figure 1). For example, a physician who withholds antibiotic treatment from patients with a clinical score of 0 or 1, tests patients with a score

of 2, and treats with antibiotics patients with a score of 3 or 4 uses strategy number 19.

To evaluate the strategies shown in Figure 1 and to include the proper accounting of carriers, probability trees were used to calculate the outcomes for cohorts of 1,000 hypothetical adults with pharyngitis. For each strategy there are four outcomes: patients with acute streptococcal disease are correctly treated, patients with acute streptococcal disease are not treated, patients with nonstreptococcal disease have antibiotics correctly withheld, and patients with nonstreptococcal disease are incorrectly treated with antibiotics.

In the calculations, the baseline sensitivities of throat cultures and rapid antigen detection tests are 0.9.<sup>3</sup> Because false-positive results that are due to carriers are included in the probability trees, the test specificity is 1.0. Test errors and decision rule errors are assumed to be conditionally independent.

The published accuracy of the Centor et al<sup>4,5</sup> clinical decision rule was used: If a clinical score of 1 or more is considered positive, the sensitivity and specificity are 0.99 and 0.1, respectively. For a score of 2 or more, they are 0.86 and 0.42; for 3 or more, they are 0.60 and 0.75; and for a score of 4, they are 0.22 and 0.94.

The probabilities and costs used in the calculations are displayed in Table 1. The baseline values are those used by Pantell and Bergman, <sup>14</sup> with the costs increased by 15 percent based on comparisons with current diagnostic-related grouping allowances. The baseline prevalence and carrier rate for adults are 0.05. It is assumed that every patient is examined by the same physician, so the costs of the visit are not estimated when comparing strategies.

Recent studies have added to the evidence that early antibiotic treatment shortens the duration of symptoms by 24 to 48 hours. <sup>16,17</sup> As opinions on this point differ, <sup>11,18</sup> the analysis was performed both with and without this advantage. When assuming that streptococcal illness is shortened by treatment, the reduction is one day if treatment is delayed pending a culture result and two days if a rapid antigen detection test is used. When comparing the relative efficiencies of different strategies, it is not necessary to make assumptions about the total durations of illnesses.

Multiple two-way sensitivity analyses were performed to determine when the results are sensitive to assumptions.

## RESULTS

The best strategies for nine combinations of treatment objectives and assumptions about the benefit of early treatment are displayed in Table 2. Strategies in the first horizontal row minimize total costs to society. The three

TABLE 1. THE BASELINE PROBABILITIES AND COSTS USED IN THE ANALYSIS

	Probability × 10 <sup>5</sup>
Rheumatic fever	
Untreated streptococcal disease	300
Treated streptococcal disease	34
Allergic reaction	
Mild	170
Severe	8
	Dollars
Death	\$575,000
Rheumatic fever	19,200
Allergy	
Mild	30
Severe	1,470
One day of illness	40
Oral penicillin	6
Cost per test	5

best strategies from Figure 1 are listed, showing that total costs are minimized by testing no one regardless of whether treatment shortens the illness. This result is sensitive to the cost per test, and selective testing strategies become optimum when a test costs less than \$5 including labor. If treatment shortens the illness, selective testing using strategies 17, 19, 20, or 7 is best if a culture costs less than \$3 or if a rapid test costs less than \$4.50. All of the strategies in Table 2 remain optimum at all higher test costs.

Strategies in the second row of Table 2 minimize the adverse medical outcome costs, ie, the costs of testing and treatment are excluded. These results are very sensitive to the consequences of incorrect treatment with antibiotics. As in previous calculations of adverse outcomes, 10,14,15 only a small penalty for incorrect treatment, the averaged \$0.17 per patient cost of allergic reactions, has been used. To represent a stronger preference for avoiding incorrect antibiotic use, the cost of the unnecessary antibiotic prescriptions was included in the analysis reported in the third horizontal row of Table 2. Unlike the results in the second row, these strategies are relatively insensitive to the specific cost penalty chosen, so sensitivity to the uncertain risk of an allergic reaction 10,15 is avoided. Most important, the results in row 3 may more accurately represent the preferences of some physicians regarding the unnecessary use of antibiotics.

It is important not to overlook other strategies that are approximately equal in effectiveness. The analysis shows that, because fewer than 20 percent of patients have clinical scores of 0 or 4, strategies that differ only in the management of these patients are almost equally efficient. Strategies 5, 6, and 7 illustrate this point, differing in cost

TABLE 2. THE MOST EFFICIENT STRATEGIES BY NUMBER FROM FIGURE 1 FOR DIFFERENT TREATMENT PRIORITIES, METHODS OF TESTING, AND ASSUMED BENEFITS OF TREATMENT

Costs Considered	If Antibiotic Does Not Shorten Illness	If Antibiotic Shortens Illness	
		Throat Culture	Rapid Test
Tests, antibiotics, and adverse outcomes	15	14	14
Adverse outcomes	3	1	2
Adverse outcomes and unnecessary antibiotics	7	5	6

by less than 0.2 percent. Consequently, any of them is a reasonable choice for minimizing the costs of adverse outcomes and incorrect antibiotic use, regardless of whether antibiotics shorten the illness and independent of the laboratory test used.

In Table 2 the best strategies under the assumption that treatment does not affect the duration of symptoms differ only slightly from the best strategies under the assumption that treatment shortens the illness. The most efficient overall approach (test most patients, treat most patients, or withhold treatment from most patients) is not affected by changing this assumption.

Assumptions were varied (sensitivity analysis) to determine whether they change the conclusions. The results are not sensitive to the carrier rate, which was varied from 0.5 to 2.0 times the prevalence. Based on published data for adults, the prevalence of acute disease was varied from 0.0 to 0.15. Over this range the best strategies varied from those in Table 2 in a predictable way: The fundamental management approach (eg, test most patients or treat most patients) does not change, but as prevalence increases, it becomes more efficient to treat an additional group of patients. For example, strategy 5 is replaced by 4, and strategy 15 is replaced by 14. As prevalence decreases, it is more efficient to delete one group from treatment, eg, strategy 5 is replaced by 6, and strategy 14 is replaced by 15.

A physician who knows the prevalence of disease at any given time could thus improve his efficiency by departing from the strategies in Table 2 accordingly. However, for two reasons, physicians generally have no convenient way to determine the exact prevalence of acute streptococcal disease: First, the fraction of tests that are positive depends on the clinical criteria used in selecting patients for testing. Second, the fraction of patients who are carriers can only be measured using acute and convalescent serum antibody titers. Fortunately, strategies that differ only in the management of a single clinical group of patients are almost equally effective over the range of commonly reported prevalence for adults, so it is not necessary to know the exact prevalence to choose an effective strategy.

Previous cost-benefit analyses differ in the assumed attack rate of rheumatic fever. 6,10,11,13-15 The question is how much of the observed decrease in the incidence of endemic rheumatic fever is due to a lower attack rate and how much is explained by improved access to treatment. The baseline rate of 0.003 is intermediate between previous estimates, which range from 0.0005 to 0.006. 10,13,14 Between these limits only strategies 3 and 15 of those in Table 2 depended on the attack rate. In those two cases it was more efficient to treat an additional group of patients if attack rates are higher and to delete one group from treatment for lower rates. When it was assumed that treatment shortens illness, the results did not vary with the attack rate of rheumatic fever.

The utility of each outcome has been expressed as a cost in dollars. The relative sizes of the utilities, not the absolute amounts, determine the results. So, for example, when the strategies in Figure 1 were reevaluated using the different, independently chosen utilities and probabilities of Tompkins et al<sup>13</sup> (but using the test costs and rheumatic fever attack rate in Table 1), all of the strategies in Table 2 remained optimum.

### DISCUSSION

The strategies that minimize the costs of adverse medical outcomes and incorrect antibiotic use (strategies 5, 6, and 7) are the least sensitive to uncertainty in the rheumatic fever attack rate, and they are independent of test costs. A physician using these strategies would test most or all adults with pharyngitis regardless of whether he believes that treatment shortens the illness and regardless of the laboratory test he uses. Similar recommendations have recently been made by Centor et al, 10,15 based on test-treatment thresholds calculated from the preferences of healthy individuals.

Total costs, including testing and treatment, are minimized by a different approach (strategies 14 and 15). Depending on assumptions about the benefits of treatment, the total cost of testing everyone, ie, minimizing only the

adverse outcomes, is between \$2,000 and \$3,000 higher per 1,000 patients than the cost of strategy 14 or 15. In return for paying this premium, the benefits of testing each of the 1,000 patients are 15 fewer missed cases of streptococcal disease and 193 fewer patients who receive unnecessary antibiotics. By making these trade-offs explicit, this analysis can help each physician decide how hest to deliver cost-effective care in his or her own practice.

This analysis is restricted to adults. The clinical decision rule has been tested only on patients older than 12 years of age, 4,5 and previous studies have shown that decision rules developed for one age group are less accurate when applied to younger patients. Also, the prevalence and carrier rates among children are usually higher than the values used here for adults.

# SUMMARY

Twenty-one strategies for using a clinical decision rule have been analyzed. Every patient is given a score from 0 to 4 by assigning one point for each of the following clinical findings: pharyngeal exudate, tender and enlarged cervical lymph nodes, absence of cough, and a history of fever. 4.5 The results of the analysis can be summarized according to the physician's treatment goals:

To minimize total costs: If a culture costs more than \$3 or a rapid test costs more than \$4.50 including labor, an antibiotic is given to each patient with three or four clinical findings and is withheld from all others. For less-expensive tests, it is most efficient to test selectively patients with an intermediate number of clinical findings (eg, patients with a score of 2, or patients with scores of 1 and 2).

To minimize adverse outcome costs: If a rapid test is used, patients with a score of 0 are tested, and the remaining patients are treated presumptively with antibiotics. If throat cultures are preferred to rapid tests, treating every adult with pharyngitis is most efficient.

To minimize costs of adverse outcomes and unnecessary antibiotics: If rapid tests are used, all patients are tested. If throat cultures are employed, all patients are tested except those with all four clinical findings. This latter group is treated presumptively to reduce the total number of days spent waiting for culture results.

No single approach for managing streptococcal pharyngitis is clearly superior. Strategies that best accomplish one physician's treatment goals perform poorly when evaluated in a different practice setting or using different

goals. The benefits and costs of 21 different strategies have been analyzed so each physician can choose a strategy consistent with his or her preferences.

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# Commentary

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In the August issue Gehlbach<sup>1</sup> introduced this series of commentaries by noting the paradox: we physicians are obsessed with doing the right thing, but we tend to rebel whenever somebody introduces a more logical, more precise, or more rational tool for deciding what is right in common clinical settings. Why family physicians should be this way is no mystery. Either the new tool gives answers very similar to our old way of practice, or else it suggests markedly different behavior. If the former, we will declare that we do not need it. If the latter, we will either have to admit that we have been acting irrationally in the past, or else we will have to find some flaw with the new tool, and we often prefer to find flaws rather than to change.

This response is understandable but also unfortunate. I believe that decision-analytic tools, appropriately understood and applied, reinforce the inherent wisdom of the best, most experienced family physicians. And yet, if this wisdom is ever going to influence others—practitioners of other specialties, designers of new research studies, and new family physicians in training—it must be made explicit and subjected to rigorous scrutiny, which requires the vocabulary and the logic of formal, mathematical decision analysis. I will try to illustrate these applications by citing some important features of the present paper by DeNeef.

Contrast the method of the wise community practitioner with the more academic, biomedically oriented, diagnosis-driven mode of thinking most commonly taught in medical school and in residency—the mode we can call for short the "rule-out mode." Today, thoughtful medical critics are finding a lot of things wrong with the rule-out mode, not the least of which is that it is expensive out of proportion to the benefits it brings the patient.<sup>2</sup> The work of DeNeef particularly emphasizes two deficiencies of the rule-out mode—it tends to ignore both the actual frequency of disease in the population and the goal that the medical strategy seeks to optimize.

Even without knowing precise data, the wise community practitioner has always tempered both diagnosis and treatment with an understanding of how common a particular condition is in the given population. The rule-out mode allows no room for frequency or probability data. It says that one must somehow track down every possible

differential diagnosis, and that one cannot treat until one has first established the diagnosis. (Of course, when it says, "established the diagnosis," it means that a test has come back positive; the problem of false-positive and false-negative test results is another feature of the real world beyond its grasp.) Yet someone with a good grasp of the relative frequency of various conditions in community practice can readily identify recommendations growing out of the rule-out mode that are irrational or impractical.<sup>3</sup>

DeNeef makes it clear that one cannot decide upon the rational approach to diagnosing and treating streptococcal pharyngitis until one knows how common it is in the community. Centor further emphasizes the differential impact on rational strategy of the frequency of streptococcal pharyngitis and other data, such as the frequency of acute rheumatic fever. 4,5 Many of us were taught in medical school that the main reason one treats streptococcal pharyngitis is to prevent rheumatic fever. But analyses by Centor and colleagues<sup>4,5</sup> show that doubling or tripling the true incidence of rheumatic fever makes almost no difference in determining the rational strategy. while changing the frequency of streptococcal pharyngitis by a few percentage points will make a profound difference. (A wise community practitioner will conclude from this that the ideal strategy will therefore vary on a seasonal basis.)

DeNeef further makes clear that we will not know the rational approach to streptococcal pharyngitis until we define clearly what we want to accomplish. This apparently obvious and trivial point is a major break with the rule-out mode. According to the rule-out mode, the goal is diagnosis and treatment. What diagnosis and treatment are for is assumed to be self-evident. But when one looks more carefully at the rule-out mode and its practical consequences, the goal is either much more obscure than was thought, or when the goal does become obvious, it no longer seems very attractive. For instance, the rule-out mode, as commonly used, seems to imply that the goal is to avoid even the slightest chance that one will mislabel a case of serious disease as a case of minor disease; avoiding that catastrophe is worth labeling dozens of individuals as possibly having major disease when they do not, and subjecting several of those to iatrogenic harm as a result of overzealous testing or treatment. Others have shown how different the care of the elderly patient will be depending on whether the goal is to establish a firm diagnosis or to restore function.<sup>6</sup>

Now, demanding that we make our goals explicit rubs most readers the wrong way. We much prefer the sort of article that tells us the right answer to a clinical problem; we resent the author who makes us think by laving out several options and then instructing us to reflect upon our values and goals. But the "right-answer" thinking promotes the soothing but misleading lullaby of the rule-out mode—that trade-offs do not exist and that clinicians can both have and eat their cake. The most important and true sentence in DeNeef's article is, "Every treatment strategy is a compromise." We cannot, in this imperfect world, minimize adverse outcomes, minimize unnecessary use of antibiotics, and keep costs down all at the same time. The more standard article that concludes, "Here is the rational approach to treating such-and-such disease," comforts us with its neat take-home message, but only at the expense of hiding the true compromises that have been made.

It is at this point, I think, that DeNeef's work has one of its most interesting implications, which the author himself does not develop. He assumes here that the clinician's values will determine which strategy is most rational; but, since DeNeef's treatment options in fact reduce to nicely encapsulated bits of advice, which lend themselves easily to being printed on a form or flow sheet that can be inserted in the chart, why not let the patient decide which goal he wishes to optimize?

We have seen how difficult it is for physicians to educate ourselves about the inevitability of compromise and

trade-offs. But we do not have the leisure to focus all our education efforts within the profession. If the public at large is ever to grapple with the realities of a national policy for financing health care (and, as a more minor point but closer to home, cease suing physicians whenever a bad outcome occurs), then our patients will have to begin to understand how tradeoffs are unavoidable and how labeling goals explicitly is the first step toward making rational decisions. What better place to start this essential educational process, for both physician and patient, than with such a common office problem as streptococcal pharyngitis?

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