Management of Sore Throats in Children

A Cost-effectiveness Analysis

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Objective: To perform a cost-effectiveness analysis of treatment management strategies for children older than 3 years who present with signs or symptoms of pharyngitis.

Design: Decision model with 7 strategies, including neither testing for streptococcus nor treating with antibiotics; treating empirically with penicillin V; basing treatment on results of a throat culture (Culture); and basing treatment on results of enzyme immunoassay or optical immunoassay rapid tests, performed alone or in combination with throat cultures. In these 7 strategies, all tests are performed in a local reference laboratory. In a sensitivity analysis, we examined the cost-effectiveness of 4 strategies involving office-based testing. We obtained data on event probabilities and test characteristics from our hospital's clinical laboratory and the literature; costs for the analysis were based on resource use.

Results: At a baseline prevalence of 20.8% for streptococcal pharyngitis, the Culture strategy was the least expensive and most effective, with an average cost of $6.85 per patient. The outcome was sensitive to the prevalence of streptococcal pharyngitis, the rheumatic fever attack rate, the cost of the enzyme immunoassay test, and the cost of culturing and reporting culture results. The Culture strategy was also preferred if amoxicillin was substituted for oral penicillin. For office-based testing, Culture was the least costly strategy, but treatment based on results of the optical immunoassay test alone had an incremental cost-effectiveness ratio of $1.6 million per additional life saved.

Conclusion: In a setting with adherent patients, children with sore throats should generally get throat cultures in lieu of rapid streptococcus antigen tests.

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SORE THROATS are one of the most common presenting complaints of patients, accounting for nearly 18 million office visits in 1996.[1] Although the one to cause the most concern, group A β-hemolytic streptococcus (GABHS) is only one of many causes of sore throats, accounting for 15% to 30% of cases in recent reviews,[2-4] with significant geographic, seasonal, and age variation, especially in children.[5] When streptococcal pharyngitis is present, it is important to treat the patient with antibiotics to prevent acute rheumatic fever (ARF) in the host, prevent transmission, and perhaps decrease the duration of symptoms and prevent suppurative complications. Penicillin therapy—despite being the therapy of choice[6]—carries the risk of adverse reaction, including anaphylaxis, financial cost, and the potential of contributing to the emergence of resistant strains, so penicillin should not be prescribed indiscriminately.

Although there is general agreement that patients with streptococcal pharyngitis should receive antibiotic treatment, there continues to be wide variation in other facets of management.[7-10] Regarding testing for streptococcus, there is now a choice among several types of rapid antigen tests[11] with or without the standard throat culture, there is variation in culture technique regarding the type of atmosphere and identification method,[12] and there is a choice between performing the test in the physician's office or a laboratory.[4]

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There is also practice variation in the way tests are used to guide therapy.[7] According to the threshold model of clinical decision making,[13] testing and treatment decisions should be based on the probability of disease (here streptococcal pharyngitis) and the risks and benefits as-

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METHODS

THE DECISION MODEL

We constructed a decision analysis model to examine the short-term costs and cost-effectiveness associated with 7 strategies:

1. Neither test nor treat (Do Nothing).
2. Perform an enzyme immunoassay (EIA) rapid test. If results are positive, prescribe penicillin V—250 mg orally thrice daily for 10 days; if results are negative, do nothing (EIA Only).
3. Perform an EIA rapid test. If results are negative, obtain a culture; if findings of either test are positive, prescribe penicillin (EIA/Culture).
4. Perform an OIA rapid test. If results are positive, prescribe penicillin; if results are negative, do nothing (OIA Only).
5. Perform an OIA rapid test. If results are negative, obtain a culture; if findings of either test are positive, prescribe penicillin (OIA/Culture).
6. Obtain a culture. If results are positive, prescribe penicillin (Culture).
7. Treat empirically (Empiric Therapy).

In our base case analysis, all tests are performed in a local reference laboratory. A recent report by Gerber and colleagues[38] examined the accuracy of office-based testing and found that office-based OIA tests were more sensitive but less specific than office-based cultures. Based on these findings, the authors concluded that negative OIA test results may not always need to be confirmed with throat cultures. Thus, in a sensitivity analysis, we compared the expected cost and cost-effectiveness of 4 office-based strategies: Do Nothing, Empiric Therapy, OIA Only, and Culture.

In all models, patients with untreated streptococcal infection risk developing ARF, which could involve complications or be fatal, and suppurative complications. Treating the patient with penicillin reduces the risk of developing ARF and suppurative complications. However, with penicillin therapy, the patient risks developing a rash or anaphylaxis or both; anaphylaxis can be fatal. Patients sustaining a nonfatal reaction to penicillin are switched to erythromycin therapy per recently published guidelines.[6] All analyses were performed using a decision analysis software program (Decision Maker version 7.0; Pratt Medical Group, Boston, Mass).

ASSUMPTIONS

For the analyses, we made several simplifying assumptions. Because serum titers for streptococcal pharyngitis are rarely performed, the diagnosis of "definite" streptococcal pharyngitis is rarely confirmed. Therefore, performing the laboratory culture is generally regarded as the criterion standard—imperfect sensitivity and specificity notwithstanding.[12,39] Thus, in the base case analysis, we assumed the local reference laboratory throat culture (as opposed to the office-based culture) to be the criterion standard.

We further assumed that the effectiveness of penicillin therapy in reducing the risk of rheumatic fever and suppurative complications is not diminished by a 2-day delay in treatment.[6] Next, in accordance with recent studies,[40,41] we assumed that penicillin therapy has no benefit with regard to the duration of illness (this assumption could bias the analysis in favor of Do Nothing and any imperfect testing strategies).

We also made several assumptions regarding costs. First, per common practice in many physician's offices, we assumed that nurses, rather than physicians, would notify the patient of throat culture results, instruct the patient to take or forgo antibiotics, and call in prescriptions to the pharmacy as appropriate. Second, we did not consider the costs of transporting specimens—for the base case analysis, this simplification biases against the Do Nothing and Empiric Therapy strategies; for the office-based testing sensitivity analysis, such costs are not pertinent. Even when rapid tests were sent to the reference laboratory, we assumed the results would be available before the patient left the physician's office, eliminating notification costs; this assumption favors the rapid test strategies. Because we used a short time frame for the analysis, costs of secondary rheumatic fever prophylaxis were not considered (although such costs would be discounted, this assumption biases the analysis against the Empiric Therapy and Culture strategies).

Finally, in accordance with recent recommendations by an expert panel,[42] the base case analysis takes the societal perspective (excluding contagion) and does not consider costs such as the patient's parent missing work and the patient's loss of future productivity because of death or the development of long-term complications from rheumatic fever.

In a sensitivity analysis, we ascertained the cost-effectiveness of the 7 strategies from the perspective of a parent, including time costs for missing work. Here, we assumed a patient with streptococcal pharyngitis would require 24 hours of antibiotic therapy before returning to day care or school[43] and that a patient with undiagnosed streptococcal pharyngitis would miss day care or school for 1 day because of illness. We further assumed patients whose rapid test results were negative but whose culture results were positive would miss 2 days of day care or school. With the Culture strategy, all patients were assumed to miss 2 days of day care or school—those with positive culture results would start treatment 1 day later than patients with positive rapid test results, and those with negative culture results would stay home until notified of the results. Note that this parental perspective analysis assumes the parent is employed full-time and the child becomes ill during the work week. Thus, to the extent that the time costs represent an upper bound estimate, the analysis would be biased against the Culture strategy.

PROBABILITIES AND COSTS

Probabilities

We used the following probability estimates in our model, all of which were varied in sensitivity analyses to see whether changes in estimates affected the outcome (**Table 1**).

Prevalence of GABHS Infection. The prevalence of GABHS pharyngitis, defined as the proportion of throat cultures that grow GABHS, ranges from 15% to 30% in the literature.[2-4] At our children's hospital, routine practice is to obtain throat swabs from every patient with pharyngitis, and the prevalence of GABHS is 20.8% (S. Reising, PhD, oral communication, January 1996), which is the estimate used in our model.

Test Characteristics of the EIA Rapid Test. At our children's hospital, the sensitivity of the EIA rapid test is 85.9% (S. Reising, PhD, oral communication, January 1996) and is comparable to previous studies in children.[11,12,44,45] The specificity of the EIA rapid test at our hospital is 94.3% and is similar to or perhaps slightly lower than the specificity reported elsewhere.[11,12,44,45] We used local estimates in the base case analysis but varied the estimates widely in sensitivity analyses.

Test Characteristics of the OIA Rapid Test. We used the test characteristics of the OIA rapid test as reported at our children's hospital, where the sensitivity is 80.8% and the specificity is 89.5% (S. Reising, PhD, oral communication, January 1996). These values are less favorable than the manufacturer's data (sensitivity of 98.9% and specificity of 98.4%) (K. DiSilvestro, written communication, August 1995) or those from previous studies[36,37]; thus, the values were varied in sensitivity analyses. For the office-based testing analysis, we used a sensitivity of 84% and a specificity of 93%, with a culture sensitivity of 78% and culture specificity of 99%, as reported by Gerber et al.[38]

Penicillin Reaction. The risk of the patient developing an allergic reaction to penicillin is 0.7% to 4.0%.[46-48] We set the probability of the patient developing a drug allergy from penicillin therapy at 1.5%. We set the risk of the patient developing an anaphylactic penicillin reaction at 1 per 10 000 and the case-fatality rate from such a reaction at 10%.[46-49]

Probability of ARF Following Untreated Streptococcal Pharyngitis. The probability of the patient developing ARF from untreated streptococcal pharyngitis depends primarily on whether there is an ongoing epidemic. In epidemic times, the risk of developing ARF can be as high as 3%[50,51]; in endemic times, the risk is probably considerably lower,[5,18,31,52] although a leading textbook of pediatrics disagrees.[53] For the base case analysis, we used a conservatively high estimate of 3% and varied the probability widely in a sensitivity analysis.

Morbidity and Mortality From ARF. For the morbidity and mortality from ARF, we used published estimates by Hillner and Centor[31]: 1% of cases are fatal and 10% result in nonfatal complications.

Effectiveness of Penicillin Therapy in Preventing ARF. Del Mar[41] summarized the controlled trials of penicillin therapy in preventing ARF and found that penicillin therapy reduced the risk of developing ARF by 75%. We used Del Mar's estimate as our baseline and varied the estimate in a sensitivity analysis.

Suppurative Complications Following Streptococcal Pharyngitis. Untreated streptococcal infection can result in peritonsillar or retropharyngeal abscesses, otitis media, sinusitis, and cervical adenitis; it can also result in life-threatening infections such as necrotizing fasciitis, malignant scarlet fever, bacteremia, and streptococcal toxic shock syndrome.[54-56] The risk of the patient developing one of the life-threatening infections is difficult to quantify,[54] whereas the risk of the patient developing peritonsillar abscess is 1% to 2%.[31-33] For this analysis, we focused on peritonsillar and retropharyngeal abscesses and used a risk of 1.25%, the average of 2 published estimates.[32,33]

Effectiveness of Penicillin Therapy in Preventing Suppurative Complications. Del Mar's review revealed only one study evaluating the effectiveness of penicillin in preventing peritonsillar abscess, in which the risk was reduced by 89%.[41,57] We used 89% as our baseline estimate.

Costs

Cost estimates in this analysis represent actual resource costs rather than charges[58] (Table 1). All costs were converted to 1995 US dollars using the medical care component of the consumer price index. Because of the short time frame for the analysis, we did not discount costs. As with probability estimates, we subjected all cost estimates to sensitivity analysis to see how changes in baseline values affected the results.

Tests. Costs of performing the EIA rapid test, the OIA rapid test, and the throat culture were obtained from internal data at Biostar (K. DiSilvestro, written communication, August 1995). The cost of the EIA rapid test, including the test itself and the requisite quality control, is $3.90. The analogous cost of the OIA rapid test is $6.50. The cost of pharyngeal culture, including materials, quality control, and labor, is $2.40.

Notifying Patients of Culture Results, Calling in Prescriptions. Because culture results take 2 days to be completed, we incorporated the cost of calling patients with notification of the results and instructions on whether to get penicillin at the pharmacy. We surveyed 2 pediatrician's offices and found that it takes an average of 2½ minutes for an office nurse to reach a patient and report the results. The estimated salary for an office nurse is $12 to $15 per hour (J. Weiland, RN, oral communication, March 1996). Using a salary of $15 per hour, the cost of notifying the patient is $0.63.

We also determined the time it takes an office nurse to call in a prescription to the pharmacy by timing calls to 155 patients. The mean time was 1.7 minutes, giving an estimated prescription call-in cost of $0.43.

Penicillin Therapy. The cost of penicillin therapy is based on a dose of 250 mg taken orally 3 times daily for 10 days.[6] The wholesale cost of penicillin V elixir at that dose is $3.78,[59] to which we added a pharmacy dispensing cost of $5.28,[60] for a total cost of $9.06.

Amoxicillin Therapy. Although penicillin is the recommended agent of choice, many pediatricians prescribe amoxicillin instead.[4] We did a sensitivity analysis that looked at using amoxicillin—250 mg orally 3 times a day for 10 days. The total for the acquisition and dispensing cost is $8.22.[59,60]

Penicillin Rash. In our analysis, treating a drug rash incurs the following costs:

- $1.25 in nursing time (5 minutes at $15 per hour, based on a survey of 3 pediatrician's offices);
- $24 in physician time (based on the resource-based relative value scale reimbursement rate in Ohio for *Physicians'*

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Current Procedural Terminology [*CPT*] code 99212[61]) for an office visit;

- $5.52 for a 2-day course of diphenhydramine—12.5 mg orally 4 times daily (wholesale acquisition plus dispensing cost)[59,60]; and
- $19.22 for a 10-day course of erythromycin ethylsuccinate—200 mg orally 4 times daily[6] (wholesale acquisition plus dispensing cost).[59,60]

Anaphylaxis. Based on a previous analysis, the cost of treating anaphylaxis was estimated to be $1500.[49]

Acute Rheumatic Fever. The cost of ARF was first estimated by Tompkins and colleagues[29] in a cost-minimization analysis published in 1977. Adjusting that cost to 1995 dollars, the cost would be $40 842 per case. That estimate, however, is probably far too high for this analysis because most cases of ARF are now treated on an outpatient basis and because that estimate includes the cost of premature death (not included in this analysis). A study[62] conducted in New Zealand found that the cost of treating uncomplicated ARF was US $13 650 and the cost of treating a complicated case was US $45 536. Because cost data from the 1970s or from New Zealand are likely not generalizable to current US costs, we obtained financial data from our hospital's financial accounting department for 34 consecutive cases of ARF (including 7 inpatients) seen in fiscal years 1994-1996.

The cost accounting system (HBOC, Atlanta, Ga) estimates all of the relevant costs except for physician fees. We estimated physician fees using resource-based relative value scale inpatient and outpatient reimbursement rates, as follows:

- For inpatients, we assigned an admission day cost of $97.83 (*CPT* code 99222), then $46.22 for each subsequent day (*CPT* code 99232), and then $52.00 for discharge day management (*CPT* code 99238). We also added $123.95 and $25.22 for a consultation (*CPT* codes 99254 and 99261, respectively).
- For outpatients, we added $87.16 for new patient visits (*CPT* code 99204) and $24 for established patient visits (*CPT* code 99212).

Including estimated physician costs, the mean variable cost per patient with ARF, rounded to the nearest $100, was $700. We used that estimate for our base case cost but examined costs as high as $20 000 in a sensitivity analysis.

Suppurative Complications. Costs for treating patients with peritonsillar or retropharyngeal abscess (n = 117) were estimated in a similar fashion—by adding any hospitalization costs to physician costs. Physician costs were estimated in the same way as estimated for ARF, except that new outpatients were assigned a lower cost of $43.17, representing a less complex *CPT* visit code (99202), and no inpatient consultation fees were added because most inpatients were hospitalized on the otolaryngology service. The mean variable cost for suppurative complications, including estimated physician fees, was $2000.

Costs From the Parent's Perspective. For the analysis of costs from the parent's perspective, we assumed a copayment of $5 for office visits and $3 for prescriptions. For a working parent, the major germane costs are the time costs associated with missing work to care for the ill child (see "Assumptions" subsection of "Methods" section). We valued the time cost at $11.43 per hour, based on data from the Bureau of Labor Statistics.[63] For children who developed a rash, we estimated that the parent would miss half a day of work to take the child to the physician. Finally, we estimated that children with anaphylactic reactions would miss 2 days of day care or school and that children with ARF or suppurative complications would miss 5 days of day care or school.

sociated with testing and treatment. Several predictive models based on clinical findings are available to aid clinicians in assessing the probability that the patient has streptococcal pharyngitis.[14-27] Nevertheless, as Poses and coworkers[28] found, educational intervention decreases overestimation of the probability of streptococcal infection but does not change prescribing habits or practice variation.

Several analysts[18,29-35] have gone a step beyond developing predictive instruments by performing decision analyses and/or economic analyses of the management of sore throats. However, most of the previous analyses used data from adults and are not necessarily applicable to children, particularly in the office setting. Most were done before the advent of the rapid test, and none included the optical immunoassay (OIA) rapid test.[36-38] The cost data for the economic analyses were either old—from the 1970s—or incomplete. To reexamine the issue of how best to manage the treatment of children with sore throats in an office setting, we performed a cost-effectiveness analysis. The analysis applies to children older than 3 years who present with signs or symptoms of pharyngitis and who can be expected to adhere to the physician's management plan.

RESULTS

BASE CASE ANALYSIS

Under baseline assumptions, probabilities, and cost estimates, the Culture strategy has the lowest average cost per patient (**Table 2**). The Culture strategy is followed by EIA Only, Do Nothing, EIA/Culture, and Empiric Therapy. The OIA Only and OIA/Culture strategies are the most expensive. Culture also saves the greatest number of lives; by being less costly and more effective than the other 6 strategies, it is considered dominant from a cost-effectiveness standpoint.

SENSITIVITY ANALYSES (LABORATORY-BASED TESTING)

Prevalence of GABHS Infection

In the base case analysis, the estimated prevalence of GABHS infection was 20.8%. From a cost-minimization standpoint, if the prevalence is less than 11%, the Do Nothing strategy is the least expensive. If

Table 1. Input Data for GABHS Cost-effectiveness Analysis*

	Value in Base Case Analysis (Range in Sensitivity Analysis)
Prevalence of GABHS	0.208 (0-1.0)
EIA sensitivity	0.859 (0.5-1.0)
EIA specificity	0.943 (0.5-1.0)
OIA sensitivity	0.808 (0.5-1.0)
OIA specificity	0.895 (0.5-1.0)
Penicillin-induced rash	0.015 (0-0.1)
Anaphylaxis from penicillin	0.0001 (0-0.0005)
Anaphylaxis case-fatality	0.1 (0-1.0)
ARF following untreated pharyngitis	0.03 (0-0.05)
ARF case-fatality	0.01 (0-0.25)
ARF-associated morbidity	0.1 (0-0.2)
Effectiveness of penicillin vs ARF	0.75 (0-1.0)
Suppurative complications	0.0125 (0-0.05)
Effectiveness of penicillin vs suppurative complications	0.89 (0-1.0)
	Cost in Base Case Analysis, $ (Range in Sensitivity Analysis)†
EIA	3.90 (0-20)
OIA	6.50 (0-20)
Culture	2.40 (0-15)
Culture result notification	0.63 (0-24)
Calling in a prescription	0.43 (0-24)
Penicillin therapy	9.06 (0-20)
Amoxicillin therapy	8.22 (0-20)
Penicillin-induced rash‡	49.99 (25.99-73.99)
Anaphylaxis§	1500 (0-5000)
ARF§	700 (0-20 000)
Suppurative complications§	2000 (0-5000)

*GABHS indicates group A β-hemolytic streptococcal pharyngitis; EIA, enzyme immunoassay rapid test; OIA, optical immunoassay rapid test; and ARF, acute rheumatic fever.
†In 1995 US dollars.
‡Includes switch to erythromycin therapy (see text for details).
§Rounded to nearest $100.

the prevalence is greater than 66.8%, the physician should prescribe penicillin without testing. From a cost-effectiveness standpoint, for any prevalence between 11% and 66.8%, Culture is the dominant strategy.

ARF Attack Rate

In the base case analysis, we assumed the risk of developing ARF in untreated patients with streptococcal pharyngitis to be 3%. If the prevalence is less than 0.51%, the Do Nothing strategy is the least expensive. At a prevalence of 0.3%, one tenth of our baseline risk estimate, the incremental cost-effectiveness of Culture relative to Do Nothing is $88 246 per additional life saved. At a prevalence of 0.03%, one one-hundreth of our baseline risk estimate, Do Nothing is the dominant strategy.

Risk of Suppurative Complications

In the base case analysis, the risk of developing a suppurative complication from untreated streptococcal pharyngitis was 1.25%. If the actual risk were less than 0.52%, the Do Nothing strategy would be the least

Table 2. Cost-effectiveness of Pharyngitis Management Strategies*

Strategy†	Expected Cost, $‡	Incremental Cost-effectiveness
Base Case Analysis		
Culture	6.85	. . .
EIA Only	8.91	Dominated
Do Nothing	9.57	Dominated
EIA/Culture	10.45	Dominated
Empiric Therapy	11.62	Dominated
OIA Only	12.18	Dominated
OIA/Culture	13.35	Dominated
Office-Based Strategies		
Culture	8.20	. . .
Do Nothing	9.57	Dominated
Empiric Therapy	11.62	Eliminated by extended dominance
OIA Only	11.72	$1.6 million/additional life saved§

*EIA indicates enzyme immunoassay rapid test; OIA, optical immunoassay rapid test; Dominated, strategy is more costly and less effective; and Eliminated by extended dominance, strategy has a worse incremental cost-effectiveness ratio than the next cheapest strategy (OIA Only).
†For explanation of strategies, see "The Decision Model" subsection in the "Methods" section.
‡In 1995 US dollars.
§Relative to Culture.

expensive, but the Culture strategy would be the most effective.

Cost of Culture

In the base case analysis, the cost of obtaining a throat culture was estimated to be $2.40. At a cost of culture greater than $4.46, the EIA Only strategy would be the least expensive, but the Culture strategy would be the most effective.

Cost of Follow-up

We estimated the cost of reporting culture results to patients to be $0.63. If the cost is greater than $2.68, then EIA Only would be the least expensive strategy and Culture would be the most effective. If the cost of calling in a prescription exceeds $10.32 (baseline estimate = $0.43), then the EIA Only strategy would be the least expensive, with Culture remaining the most effective.

Cost of the EIA Rapid Test

In the baseline estimate, the cost of the EIA rapid test was $3.90. If the cost is less than $1.84, EIA Only would be the least expensive strategy and Culture would be the most effective.

Cost of the OIA Rapid Test

In the baseline estimate, the cost of performing an OIA test was $6.50. The cost would have to be less than $1.17 for the OIA Only strategy to be the least expensive.

Cost of Treating ARF

In the base case analysis, the cost of treating ARF was estimated at $700 per patient. At any cost greater than $119, Culture is the dominant strategy.

Cost of Treating Suppurative Complications

At costs of treating suppurative complications below $825 per patient (baseline cost = $2000), the Do Nothing strategy is the least expensive, and Culture is the most effective.

Amoxicillin Rather Than Penicillin

If amoxicillin is used for treatment instead of penicillin, Culture is the least expensive strategy as long as the prevalence of GABHS infection is 10.6% to 63.9%. At the baseline prevalence of GABHS infection (20.8%), Culture dominates even if the probability of developing a rash from amoxicillin therapy is 10%.

For laboratory-based testing, the outcome was not sensitive to wide changes in each of the following variables: sensitivity of the EIA rapid test, specificity of the EIA rapid test, sensitivity of the OIA rapid test, specificity of the OIA rapid test, risk of adverse reaction to penicillin (rash or anaphylaxis), risk of complications from ARF, mortality from ARF, and effectiveness of penicillin therapy in preventing ARF and suppurative complications. The outcome was also not sensitive to the cost of penicillin, diphenhydramine, and erythromycin therapy, and to the cost of penicillin reactions.

Office-Based Testing

Among the 4 office-based strategies, Culture is the least expensive at $8.20 per patient, followed by Do Nothing ($9.57), Empiric Therapy ($11.62), and OIA Only ($11.72). Because of imperfect sensitivity and specificity, office-based culturing is not the most effective strategy in terms of lives saved. The incremental cost-effectiveness of OIA Only relative to Culture is $1.6 million per additional life saved.

Parent's Perspective

From a parent's perspective, the 2 least expensive strategies are Do Nothing ($23.13) and Empiric Therapy ($23.75). The 2 EIA strategies are several dollars more expensive, followed by the 2 OIA strategies, which are Dominated. The most expensive strategy is Culture ($184.54), owing to 2 days of missed work.

COMMENT

By nature of its high incidence, pharyngitis is a major health and economic issue, yet there is no agreement on how to care for children with sore throats. Despite the advent of new diagnostic tests with reasonably good sensitivities and specificities and short turn-around times, our analysis suggests that, in an office setting with adherent patients and with tests performed in a local reference laboratory, from the societal perspective, antibiotic therapy guided by the traditional throat culture is the least costly and most effective strategy. When tests are performed in an office laboratory, culturing is the least expensive strategy, with OIA testing marginally more effective. Given children's long life expectancies, at an incremental cost-effectiveness ratio of $1.6 million per additional life saved, office-based OIA testing is an economically reasonable alternative to office-based culturing. By comparison, screening newborns for sickle cell disease costs $3100 to $450 billion (in 1987 dollars) more per life saved than not screening, depending on the population screened.[49]

Several other decision and economic analyses of caring for patients with pharyngitis have been reported.[18,29-35] Two analyses pertained specifically to children. Dippel and coworkers[33] published a decision analysis for teenagers with acute pharyngitis. They considered 5 strategies: (1) symptomatic treatment only; (2) empiric therapy with penicillin; (3) testing with a rapid agglutination test; (4) culturing and awaiting culture results before treating; and (5) culturing and initiating treatment while awaiting culture results, then discontinuing therapy if results are negative. Outcomes were expressed as quality-adjusted days of life lost. Testing with a rapid agglutination test was favored, but only by a matter of a few quality-adjusted minutes. In essence, the decision was a toss-up. Economic costs were not considered.

Lieu et al[32] performed a cost-effectiveness analysis of the management of pharyngitis in children seen in an emergency department. They considered 4 strategies: (1) culture; (2) perform a rapid test (latex agglutination) only (Rapid Test Only); (3) perform a rapid test; if results are negative, culture (Rapid Test/Culture); and (4) treat empirically. Differences from most previous models were the addition of a Rapid Test/Culture strategy, an assumed high loss to follow-up rate (43% of patients with positive culture results were assumed to go untreated), and less than perfect sensitivity of culture and effectiveness of treatment in preventing ARF. Results showed that the Culture strategy yielded the fewest penicillin reactions per case of ARF prevented. The Treat Empirically strategy had the lowest cost per disease or complication prevented. The Rapid Test Only strategy had the lowest cost per patient ($0.06 lower than Treat Empirically). The incremental cost-effectiveness of Rapid Test/Culture vs Culture was $6475 per additional case of rheumatic fever prevented or $3885 per additional case of suppurative complications prevented. Their recommendation was to perform the rapid test followed by a culture if the test results were negative.

Unlike the analysis of Lieu and coworkers,[32] which pertained to inner-city emergency department populations with a high loss to follow-up rate, the current analysis pertains to an office population with complete follow-up[64] and includes the OIA rapid test. In our base case analysis, the Empiric Therapy strategy was preferred to at least 2 of the rapid test strategies in nearly all circumstances. Thus, one can infer from the analysis that if loss to follow-up is a concern, Empiric Therapy—perhaps with penicillin G benzathine given intramuscularly—could be the preferred strategy overall.[65,66] This argument is bolstered when one realizes that although the turnaround time for the rapid tests is short, it may take much longer to get results if transportation time to the laboratory is an issue. Under these circumstances, a patient may not be able to wait in the physician's office for results, and the advantage of the rapid test is lost (there would be an added notification cost as well). Under one scenario in which there is no notification cost for the rapid test and the notification cost for reporting culture results is several times higher than our baseline estimate—as may be the case if a physician calls the patient or if the patient is hard to reach—the EIA Only strategy is the least expensive.

The previous decision and economic analyses have several limitations. Most were conducted before the advent of the rapid test, and none included the OIA rapid test. The cost data for the economic analyses are either old, are based on very few patients, pertain to adults, or reflect charges rather than costs.[58]

The current analysis also has certain limitations. First, the analysis assumes that patients would adhere to the physician's management plan. In such settings, Pantell and Berwick[67] also advocate Culture over other strategies.

Second, we did not include the costs of long-term complications and of secondary antibiotic prophylaxis for patients with rheumatic fever. Such costs, if included, would have to be discounted to present value, mitigating their impact. Even so, excluding those costs biases the analysis against the Culture and Empiric Therapy strategies, the 2 strategies most likely to avoid such costs. But while the cost of rheumatic fever may have been underestimated, any underestimate would likely be offset by our ARF attack rate, which represents an upper bound of many published estimates. Furthermore, our sensitivity analyses show that Culture is the dominant strategy at essentially any cost of rheumatic fever and is relatively cost-effective even at much lower attack rates.

Third, the analyses favoring Culture did not model time costs. The issue of time costs highlights the need to keep in mind the perspective of the analysis. From a parent's perspective, the rapid streptococcal tests provide timely information that may enable the child to return to day care or school 1 or 2 days sooner than if they had to await a culture result. However, the rapid test results are sometimes erroneous. For example, using the baseline prevalence of GABHS of 20.8%, OIA sensitivity of 80.8%, and OIA specificity of 89.5%, the negative predictive value of the OIA rapid test is 94.7%. This means that 5.3% of children with negative results from an OIA rapid test actually have streptococcal pharyngitis and might be sent back to day care or school before receiving treatment, thereby exposing other children, which is an adverse outcome from the societal perspective. Also, there is concern that if a physician treats streptococcal pharyngitis too early in its course (before an antibody response can be mounted), the risk of relapse increases.[4,68,69] Our analysis incorporated neither a benefit nor a penalty for early therapy per se (any benefit of early therapy would favor the Empiric Therapy strategy, particularly from the parent's perspective).

Our analysis did not examine antibiotic regimens other than penicillin, amoxicillin, and erythromycin for patients allergic to penicillin.[70] Although shorter courses of some of the newer agents have been tried, a recent expert panel[71] did not endorse them. Finally, we did not consider a strategy of caring for patients over the telephone exclusively. In other words, this analysis assumed that all children with sore throats would be seen at least once in the physician's office. Without such a requirement, Empiric Therapy would be the least costly strategy, but it is not clear that such a strategy would be acceptable to pediatricians or family physicians; furthermore, indiscriminate use of antibiotics could hasten the advent of resistant strains, greatly complicating and compromising the care of future patients.

In practice, the treatment of patients with sore throats is often driven by the wishes of the patient[72] (in this analysis, the parent). A parent may pressure the physician into performing a rapid streptococcal test to "know" whether the child has streptococcal pharyngitis so that if the test results are negative, the parent could send the patient back to day care or school a day earlier. But Froehlich and Welch[73] recently demonstrated that physicians can reduce unnecessary testing without compromising patient satisfaction.

We conclude that, in most cases, a physician should obtain a throat culture from adherent children with sore throats.

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