Antibiotics: Neither Cost Effective nor 'Cough' Effective

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BACKGROUND. Clinicians often prescribe antibiotics to treat acute bronchitis despite scant evidence that this approach is effective at speeding symptom resolution. Because patients infected with bacteria but not treated with antibiotics may need to return in the future for therapy, however, this approach may be cost effective.

METHODS. To evaluate the cost of various treatment strategies to treat acute bronchitis, this study examined three different strategies including: (1) withholding antibiotics and treating only patients with persistent cough; (2) screening patients for *Mycoplasma pneumoniae* or *Chlamydia pneumoniae* and treating all patients with positive results with antibiotics; and (3) treating all patients with antibiotics. The cost analysis was approached from the patient's perspective. The main outcome measured was the cost per person in whom acute bronchitis was diagnosed.

RESULTS. Withholding antibiotics and treating only patients with a persistent cough was the most cost-effective strategy given the baseline assumptions. If the cost per patient visit was over $110, the cost of an initial course of antibiotics less than $2.72, or the prevalence of bacterial infection greater than 25%, then treatment of all patients was more cost effective. Assuming a screening test of 90% sensitivity and specificity, the screening strategy was only cost effective if the cost of the screening test was less than $2.35, or less than $3.80 if the test had no false-positive or false-negative results.

CONCLUSIONS. Under most circumstances, the most cost-effective strategy for treating acute bronchitis is to withhold antibiotics and treat only patients whose cough does not resolve.

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Acute bronchitis in otherwise healthy individuals is a self-limited condition most often caused by viruses. Yet physicians commonly prescribe antibiotics for this condition,[1] even though most controlled studies of antibiotics for acute bronchitis demonstrate little benefit[2] and despite advice from authoritative sources that antibiotics are not indicated for acute bronchitis.[3,4] Furthermore, growing concerns about increasing antimicrobial resistance presumably linked to antibiotic overuse indicate that reevaluation of the use of antibiotics and critical analysis of why these agents are prescribed may be warranted.[5,6]

While acute bronchitis is predominantly caused by viruses, a small number of cases have been linked to *Mycoplasma pneumoniae* or *Chlamydia pneumoniae* infection.[7-10] Many clinicians believe that other bacteria cause acute bronchitis, but there is no evidence to support this contention and no evidence that antibiotic treatment is useful even when the sputum appears purulent.[11,12] Even the evidence linking *M pneumoniae* and *C pneumoniae* to acute bronchitis suggests that these agents are not very common. Most studies have shown that 5% to 10% of persons with acute bronchitis have *M pneumoniae* infections[7-9] and that another undetermined number are infected with *C pneumoniae*.[10] In these cases, antibiotics may be effective. For example, King and co-workers[13] have shown that when *M pneumoniae* rates are high in a population, erythromycin is effective at reducing time lost from work, although it has little effect on the duration of cough.

In most circumstances, however, the prevalence of bacterial infections in acute bronchitis cases is low. In these situations, physicians may be prescribing antibiotics to match patients' expectations[14] or to avoid having the patient make a second visit because the cough has not cleared in the anticipated amount of time. Even though most patients with acute bronchitis may not benefit from antibiotics in this scenario, antibiotic prescibing could be cost effective if patients taking antibiotics avoid

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additional outpatient visits for unresolved symptoms. The aim of this study was to determine whether universal antibiotic treatment of acute bronchitis is a more cost-effective clinical strategy than selective treatment of patients with persistent cough, and to determine the conditions under which a screening test for *M pneumoniae* or *C pneumoniae* infection would be cost efficient.

METHODS

To evaluate the cost of antibiotic use in acute bronchitis, three strategies were selected (Figure). In strategy 1, antibiotics are not prescribed for patients unless their cough has not resolved in 30 days. Since the cough from acute bronchitis associated with viruses can persist up to 1 month,[15] 30 days was chosen to distinguish cases more likely to be due to bacteria from those due to viral disease, although there is little evidence to suggest that *M pneumoniae* or *C pneumoniae* is more common in patients with chronic coughs. In strategy 2, all patients with acute bronchitis are subjected to a screening test that identifies patients infected with *M pneumoniae* or *C pneumoniae*, or both, and only patients who test positive are treated. In the third strategy, all patients with acute bronchitis are treated with antibiotics.

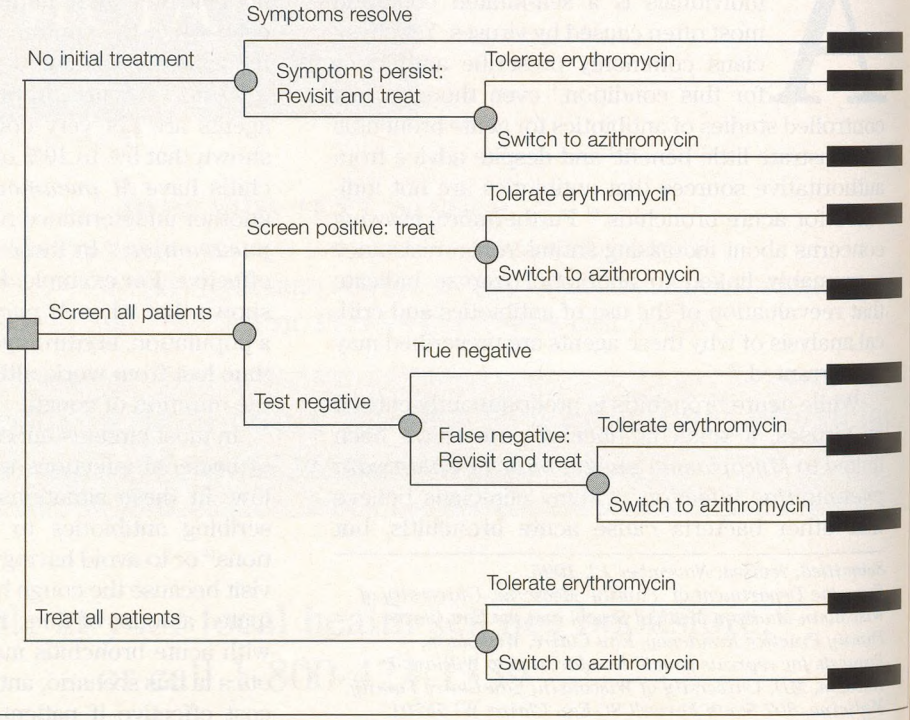
In all three strategies, erythromycin was chosen as the antibiotic of choice. The choice of erythromycin was based on the low cost of this agent and the sensitivities of presumed organisms. Previous studies suggest that between 0% and 9% of nonpregnant patients will not be able to tolerate erythromycin.[16] The decision model accounts for antibiotic intolerance by including a branch for the proportion of patients treated with erythromycin who will be switched to a second macrolide antibiotic, in this case, azithromycin. It was assumed that the intolerance to erythromycin could be communicated over the telephone and that no office visit would be required to change antibiotics.

For the strategy involving a screening test for *M pneumoniae* or *C pneumoniae*, the test was assumed to have a sensitivity of 90% and specificity of 90%. Although no commercial test is currently available that meets these high levels of specificity and sensitivity in the clinical setting, some screening tests are in development.[17] The primary purpose of including this strategy was to determine at what cost this test would be more cost effective than either of the other two strategies.

Office visits were presumed to occur for the initial diagnosis and treatment plan. For the strategy of withholding antibiotic treatment except for patients

FIGURE

A schematic representation of the three treatment strategies for acute bronchitis and the associated decision choices in the model. The terminus of each branch represents the cost of the options.



with prolonged cough, it was assumed that patients will have to make a second office visit for reexamination and to receive an antibiotic. Previous studies have shown a prevalence of *M pneumoniae* in up to 10% of some populations,[7-9] so initial analysis estimated that this proportion of patients would continue to cough beyond 30 days.

Because clinicians have reported that their motivation to prescribe antibiotics is based on patient expectations,[14] the analysis was conducted from the patient's perspective, ie, using charges likely to be assumed by the patient as the basis of comparison. Charges for services and medications were based on current problem-focused visit charges in the author's practice ($38) as well as the mean pharmacy charges for erythromycin 250 mg four times a day for 7 days ($10.56) and azithromycin 250 mg a day for 5 days ($33.37). The frequency of changing antibiotics because of intolerance to erythromycin was assumed to be 4.5%, which represents the midpoint in the range observed elsewhere. Since a screening test for *M pneumoniae* or *C pneumoniae* is not being marketed, current charges for this service are not available. To approximate a charge for a rapid diagnostic test for bacteria, clinic charges for a rapid group A streptococcal test in the author's clinic ($22.70) were used in the initial testing of this strategy.

RESULTS

The cost per case for treating patients with the three strategies is shown in Table 1. Given the assumptions regarding bacterial prevalence and screening test accuracy, using antibiotics only for patients with persistent cough is the favored strategy. This strategy resulted in a saving of $7.05 per patient over empiric antibiotic treatment of all patients and $18.64 over initial screening with antibiotics prescribed for those whose tests were positive.

To assess the effect of changes in the underlying assumptions in the analysis, sensitivity and threshold analyses were performed on all variables to determine the conditions under which each strategy would be favored. Univariable thresholds were calculated while holding other variables at the values of the initial set of assumptions. The analysis examined variation in the cost of office visits, screening test, and antibiotics; frequency of intolerance to erythromycin; and the sensitivity and specificity of the screening test.

TABLE 1

Average Cost per Case to Treat Bronchitis Using Differing Treatment Strategies

Strategy	Cost per Case,* $
Treat only patients with unresolved cough	43.01
Treat all patients	50.06
Screen all patients and treat those with positive results	61.65

*Based on the following assumptions: Cost per visit = $38; cost of first-line treatment of erythromycin = $10.56; frequency of erythromycin intolerance, 4.5%; cost of second-line treatment of azithromycin = $33.37; prevalence of *Mycoplasma* or *Chlamydia pneumoniae* = 10%; screening test cost = $22.70; and both sensitivity and specificity of screening test = 90%.

Results of the threshold analysis are shown in Table 2. Empiric antibiotic therapy was favored over selective treatment of those with a persistent cough only when the cost of a visit exceeded $110, the cost of a course of erythromycin was less than $2.72, or if the prevalence of bacterial infection exceeded 25% of the population. For the screening strategy to be the most cost effective, the cost of the screening test would have to drop below $2.35. If, however, the sensitivity and specificity of the test were improved to 100% (a best-case scenario), the screening strategy would be favored if the cost of the test was under $3.80.

While holding the prevalence of bacterial infection and costs for visits constant at baseline assumptions, variations in the frequency of intolerance to erythromycin and the cost of azithromycin did not alter the decision. When the frequency of intolerance to erythromycin or the cost of azithromycin was reduced to zero, the strategy to treat only patients with persistent coughs remained favored, although the difference in costs between this strategy and empiric antibiotic treatment was reduced. When erythromycin intolerance or azithromycin costs increased, the strategy to treat only those with persistent coughs was even more cost effective.

Finally, it was assumed that only patients infected with *M pneumoniae* or *C pneumoniae* would have coughs persisting beyond 30 days. If patients with viral acute bronchitis continued to cough as well, these patients might also be treated with antibiotics if their cough lasted more than 1 month. To evaluate the impact of this potential situation, an analysis was performed using increasing percentages of patients

TABLE 2

Sensitivity and Threshold Analysis: Under What Circumstances Would Alternative Strategies Be Most Cost Effective?

Strategy	Circumstances When Most Cost Effective
Treat all	Cost per visit > $110 Cost of erythromycin < $2.72 Prevalence of bacteria infection < 25%
Screen all and treat those with positive results	Test cost <$2.35 Test perfect* and cost <$9.40

* Sensitivity and specificity both equal 100%.

with chronic cough from viruses. Holding the prevalence of *M pneumoniae* at 10% and increasing the percentage of patients with a virus who cough for more than 30 days shows that withholding antibiotic treatment and treating at 30 days is still preferred unless more than 25% of the total patients continue to have a cough. If more than 25% of the initial population continues to cough, then initial treatment would be a better strategy. Of great importance, however, is that this strategy assumes that physicians will not prescribe a second antibiotic for the 90% of patients with viral causes who do not respond to the initial drug!

DISCUSSION

This analysis suggests that even when considering the cost of multiple visits for acute bronchitis, the strategy used by most physicians who deal with acute bronchitis, ie, to prescribe antibiotics, is not as cost effective as withholding antibiotics from all patients except those with a persistent cough. Patients still may expect or demand therapy with antibiotics, but physicians and patients should be aware that this strategy increases health care costs. If physicians are using a low-cost antibiotic such as erythromycin, routine antibiotic prescribing for acute bronchitis increases the cost per episode by about 16%.

While higher costs are associated with empiric antibiotic use for acute bronchitis, this analysis cannot determine whether patients are willing to pay this extra cost for a small chance of quicker relief from their cough or to avoid the inconvenience of having to return to the physician if their cough persists. More extensive evaluation of what patients are willing to pay for these benefits, given different probabilities that their bronchitis is a bacterial infection, would be useful to determine patient preferences.

So why do physicians prescribe antibiotics for an equivocal indication such as acute bronchitis? As noted earlier, evidence suggests that physicians may prescribe antibiotics because of an expectation that the patient wants an antibiotic.[14] Evidence from the treatment of upper respiratory infections, however, suggests that even patients who came into an encounter with the expectation of an antibiotic and did not have one prescribed are satisfied with their care, providing that their physician explains the rationale behind the medical decision-making.[18] In many cases, alternative therapies may be more effective than antibiotics, and patients could be offered these. For example, there is preliminary evidence that beta-agonist inhalers can reduce the symptom duration in acute bronchitis.[19-21] Consequently, patients may be more likely to derive some benefit from the use of these agents as opposed to antibiotics. Based on data from a large Medicaid database, however, physicians continue to prescribe antibiotics four times more often than bronchodilators for acute bronchitis.[1] If meeting patient expectations is the primary concern for prescribing a drug in cases of acute bronchitis, physicians might consider prescribing a beta-agonist, which has some supported success in the literature, as opposed to an antibiotic, which has little demonstrated effectiveness.

While this analysis offers some guidance regarding the cost of different strategies for antibiotic use in acute bronchitis, there are limitations that should be taken into account. First, this analysis did not calculate any cost of lost productivity. If the subset of patients with acute bronchitis of bacterial cause are able to return to work earlier, resulting in reductions in lost wages and lost productivity, then initial antibiotic therapy of all patients could be justified. However, other than King and co-workers,[13] whose population was enhanced by patients who had positive results from a sputum screening test for *M pneumoniae*, no previous studies using several types of antibiotics have shown that treated patients return to work any earlier than those treated with placebo.

Second, the analysis did not assume that physi-

cians performed extensive laboratory or radiological evaluations of patients with acute bronchitis. If laboratory testing or radiography is used more often when physicians are not going to prescribe antibiotics, then the difference in costs between strategies will be reduced or eliminated. Furthermore, the potential effects of misdiagnosis (eg, misclassification of a patient with pneumonia as having acute bronchitis) were not investigated in this model.

Finally, some evidence suggests that adult-onset asthma is associated with *C pneumoniae* infection[10] and that treatment with appropriate antibiotics can significantly improve asthma symptoms in these patients.[22] If earlier treatment results in a reduced risk of future asthma, then universal treatment may have an additional benefit over delayed treatment by reducing future costs for asthma care. It must be emphasized, though, that the causal link between *C pneumoniae* infection and asthma has yet to be firmly established, and that no evidence exists suggesting that earlier treatment reduces the risk of future development of asthma. Evidence from other studies shows a link between bronchitis and subsequent development of asthma,[23] suggesting that patients who develop bronchospasm with respiratory infections may be those already at greater risk for asthma regardless of the causative agent.

CONCLUSIONS

This study suggests that empiric antibiotic use for the treatment of acute bronchitis is not cost effective. It is possible that some clinical clues would be useful in identifying patients who might be more likely to respond to antibiotics, but so far, clinical factors such as the appearance of the sputum or historical factors such as smoking have not predicted an improved response to antibiotics. Further work at identifying patients more likely to respond to antibiotics would be helpful. In the interim, reserving antibiotics for patients with chronic cough is the least costly strategy in most community settings. For some patients, however, the trade-off in higher costs for a theoretical chance of more rapid improvement may be worth the extra expense.

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