

Antibiotic Usage for Respiratory Tract Infections in an Era of Rising Resistance and Increased Cost Pressure

Eugene Spiritus, MD

Presentation Summary

Pharmacoeconomic study models have a number of inherent problems that significantly limit their use within the medical community. They are frequently retrospective and thus have only limited relevance in a field in which resistance patterns are highly volatile. Moreover, the study models do little to consider the numerous economic perspectives involved, such as the patients themselves as well as society at large. Prescribing patterns profoundly affect overall

healthcare costs. As much as \$8.4 billion is spent on community-acquired pneumonia each year; 8% of that cost is for antibiotic therapies. Moreover, studies show that inappropriate prescribing for upper respiratory tract infections is the norm not the exception, with significant cost and health consequences. Also adding to costs is patient noncompliance, which could possibly be reduced with once-daily dosing regimens and widespread patient education about appropriate use of antibiotics.

No matter where one sits within the medical community, measuring quality in healthcare poses a number of challenges. In the past decade, with the rise in managed care and in issues of cost containment, pharmacoeconomics has entered the discussion when quality of care is considered. Because respiratory tract infections (RTIs) accounts for the most frequent number of antibiotics used in the outpatient setting as well as the greatest number of visits to primary care physicians, these infections lend themselves to a discussion of cost and quality.

Although many have attempted to define quality, it is apparent in many instances that volume has become an easy and frequently used marker for

this definition. For example, many centers of excellence have been initially selected on the basis of the number of procedures done under the presumption that “practice makes perfect.” For some economists value is defined as obtaining the best quality for the lowest cost. This is sometimes referred to as the cost/quality curve, which is predicated on the assumption that to achieve quality of care, some dollars must be spent. A good example might be the use of an antibiotic for the treatment of bacterial pneumonia. If managed care, physicians, or patients did not pay for the medication, the outcome of care and hence the quality might be adversely affected. On the other hand, if a clinician obtained daily

chest X rays and multiple laboratory tests that would not improve the outcome, we would make the assumption that value was not achieved. Defining the value point for a specific patient might be difficult, but with the advent of clinical pathways and guidelines we are better able to define acceptable levels of cost to achieve a quality outcome.

It is often not obvious that if more than necessary is spent in a given situation quality would not improve and may even decrease. Keeping patients in the hospital longer than necessary may expose them to nosocomial infections, pulmonary embolisms, or adverse reactions to an unnecessary test. The physician needs to understand the balance of cost and quality in patient care so that patients receive the best value for their healthcare dollar.

Pharmacoeconomic modeling is based on studies designed to compare the medical costs and health outcomes of new therapies with those of existing interventions. However, what generally drives the items being compared is the marketplace, with emphasis on market comparisons. Although market-driven studies may not be ideal, the reality is that the pharmaceutical industry has been the only industry willing to finance research on drug interventions. Managed care organizations, which clearly can benefit from pharmacoeconomic research, are struggling with financial issues that do not allow such research.

Limitations of Pharmacoeconomic Modeling

Historically, pharmacoeconomic studies were frequently conducted by reanalyzing data from clinical trials that were designed to measure efficacy and safety, such a process was far from ideal. Ideally, pharmacoeconomic analyses of antibiotic use should be conducted prospectively as controlled, double-blind, randomized tri-

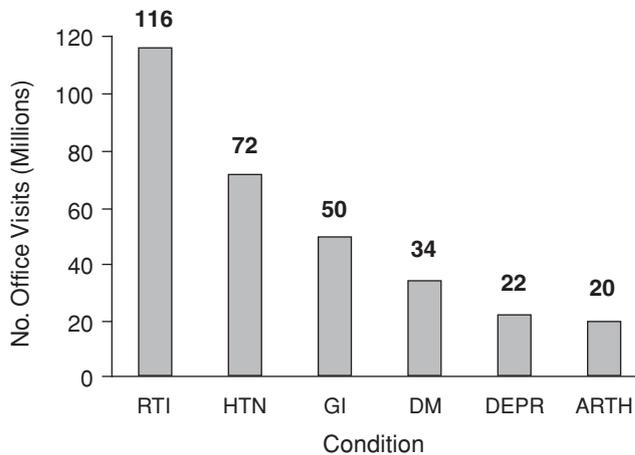
als, with pharmacoeconomic endpoints.¹ Because resistance patterns for the most common bacteria that cause RTIs have changed significantly during the past decade, earlier pharmacoeconomic studies may not represent today's reality.

Many decisions need to be made to define pharmacoeconomic studies in respiratory diseases. The first decision usually revolves around the selection of a comparator drug, followed by a decision concerning the cost analysis model to be used. In this environment, it is critical to understand who will be the end user of the information and from what perspective they will view the data. Economic consequences can be viewed from the perspective of society at large or from the payer, the public, the patient, the caregiver, or the employer. In the United States, there has been little standardization of pharmacoeconomic models, and the literature suggests that although cost/benefit analyses appear to generate more useful information than cost-effectiveness studies, the latter studies nonetheless are performed more frequently.

Cost-effectiveness studies have significant limitations; they rarely take into consideration larger difficult-to-quantify issues such as quality of life, loss of productivity, and loss of the patient and caregiver income. In addition, there is significant variability in the incidence of resistance in different parts of the country. Because the driver of cost of care is usually days of hospitalization, the varying comfort level among physicians for treating outpatients may in fact skew the end results.

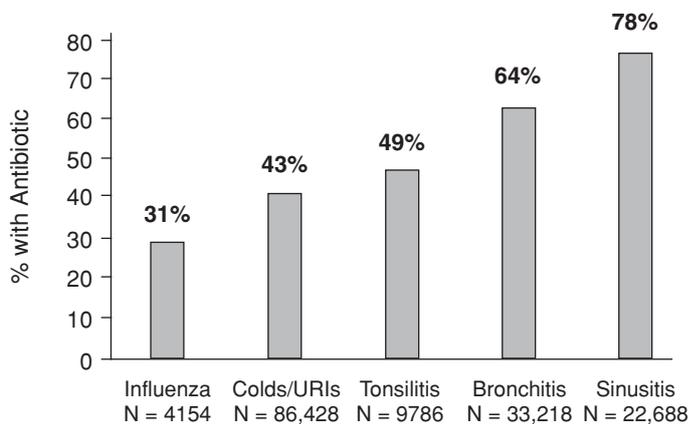
Widespread variations also exist for outcome definition and selection of measurement tools. Research surrounding RTIs frequently focuses on clinical cure or success yet ignores issues of morbidity and mortality. Other key outcome indices include length of hospital stay, quality of care, patient satisfaction, and quality of life,

Figure 1. Most Common Reasons for Physician Office Visits



HTN = hypertension; GI = gastrointestinal; DM = diabetes mellitus; DEPR = depression; ARTH = arthritis; RTI = respiratory tract infections. *In this figure, RTIs include bronchitis, sinusitis, pharyngitis, and pneumonia. Source: IMS American NDTI (National Disease Therapeutic Index), Apr 96-Mar 9.

Figure 2. Antibiotic Usage in RTIs: Percentage of Episodes with Antibiotic Prescriptions



URIs = upper respiratory infections. RTIs = respiratory tract infections. Source: Reference 3.

but no single standard of measurement exists.

Despite the availability of admittedly limited and flawed pharmacoeconomic evidence, in the United States few formulary decisions are based on pharmacoeconomic studies. Thus, the medical community must ask whether pharmacoeconomics is important in the treatment of RTIs.

Inappropriate Use and Economic Impact

Inappropriate use of antibiotic drugs has a profound impact on healthcare costs. RTIs account for as many as 120 million physician office visits a year, with hypertension a distant second (Figure 1). As many as 3 million to 4 million cases of pneumonia are diagnosed each year, resulting in at least 500,000 hospitalizations at a cost of \$8.4 billion a year. Another \$8.4 billion is spent treating community-acquired pneumonia.² Cost breakdown shows that 85% of those costs are medical, 7% nonantibiotic, and 8% antibiotic.

In a retrospective study based on a 150,000-member health plan, 31% of patients with a diagnosis of influenza were treated with an antibiotic and 43% of patients who were diagnosed with upper RTI received antibiotics (Figure 2).³ In the United Kingdom, a similar study⁴ examined 1089 patient visits to 115 general practitioners for lower RTIs. Although 75% of the patients received antibiotics, when physicians were asked to review the cases themselves, they believed that perhaps only one third of those cases in which a patient was given an antibiotic really warranted it. In almost two thirds of the cases, antibiotic prescribing was probably a gray zone. In one fifth of cases, an antibiotic was not needed. Factors influencing antibiotic prescribing were:

- Older age of physician, patient, or both
- Patient symptoms and signs

- Patient pressure
- MD work pressure

Drug utilization reviews suggest a consistent pattern of antibiotic overutilization for diseases not known to be caused by bacteria. Studies clearly illustrate the problem of overutilization, which is believed to be a cause in the development of resistant organisms. In addition to overutilization, there are the issues of inappropriate selection, premature discontinuation, failure to follow directions, and drug-drug interactions. All may play a role in appropriate use of antibiotics. A review of pharmacoeconomic studies reveals that many of these issues are not taken into account or addressed.

In most cases, the prevalence of bacterial infections in acute bronchitis is low, yet physicians may prescribe antibiotics to avoid additional office visits for persistent cough. To evaluate the ramifications of this practice, Hueston conducted a study evaluating this and other strategies for the management of acute bronchitis.⁵ The study examined costs associated with 3 different strategies: withholding antibiotics and treating only patients with persistent cough, screening patients for *Mycoplasma pneumoniae* or *Chlamydia pneumoniae* and then treating those testing positive with antibiotics, and treating all patients with antibiotics. The outcome measured was the cost-per-person for patients diagnosed with acute bronchitis.

The investigator found that withholding antibiotics and only treating patients with persistent cough was the most cost-effective strategy. The study confirms the fact that adding an antibiotic raises the cost of care by approximately 15%. Laboratory screening unfortunately still remains cost prohibitive, and there are still issues of false positive and false negative results. Clearly, enough literature suggests we must become more selec-

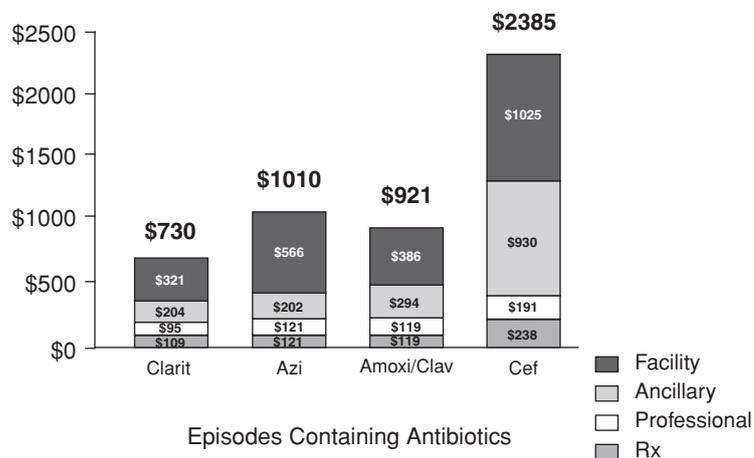
tive in treating patients with antibiotics if we are to practice cost-effective medicine and perhaps decrease the incidence of bacterial resistance.

Cost-Effectiveness Studies of Antibiotics

The cost effectiveness of a variety of antibiotic agents has been examined.⁶ A comparative review of those findings reveals that antibiotics comprise only 15% of the total cost of treating most RTIs.⁷ Moreover, the cost of care increases in patients with recurrent disease and comorbid conditions. Regardless of the disease state under investigation, costs are predominantly driven by those patients who fail outpatient care and require hospitalization.

In general, drug acquisition costs account for 15% of the total cost of care for the majority of illnesses. That percentage is less when considering hospitalized patients. For antibiotic agents in particular, drug costs account for only 1.5% of total hospital care.⁸ The major drivers of cost for

Figure 3. Factors that Drive Total Cost of Care of RTIs



Amox = amoxicillin; Azi = azithromycin; Cef = cefuroxime; Clari = clarithromycin; Clav = clavulanate; RTIs = respiratory tract infections.

treating RTIs, inpatient or outpatient, are facility fees and ancillary fees such as laboratory and radiology. The results from a study on costs for bronchitis treatment illustrate this trend (Figure 3).

Macrolides—Clinical Outcomes and Tolerance

A study presented at the Fourth International Congress on Azalides, Macrolides, and Streptogramins in 1998 looked at patients treated with erythromycin, clarithromycin, and azithromycin for bronchitis.⁹ The study indicated that 38% of patients treated with erythromycin withdrew because of side effects, but only 8% of the other 2 arms withdrew. The clinical success was similar in the clarithromycin and the azithromycin groups (Table); however, 40% of the azithromycin group requested a refill on the fourth or fifth day.

Patient Compliance Issues

In 1982 a review article by Peck and King¹⁰ raised a question: Do patients actually follow the advice of their physicians? The cited articles, going back to the 1960s, suggest that only 22% of prescriptions were taken

properly and that for 31% of the prescriptions, misuse of the drug may pose a serious threat. Through the years, numerous studies have suggested that approximately 20% to 30% of prescriptions written are never filled.

Davies et al¹¹ reported that 30% to 35% of patients who are given drugs fail to follow recommendations. Stimson¹² reported that 19% to 72% of patients did not follow instructions when given antibiotics. Blackwell¹³ reviewed 50 studies reporting complete noncompliance in a range from 25% to 50% of all outpatients. Throughout the studies, investigators suggest that patient compliance could be vastly improved by drug packaging with specific dosing instructions. Moreover, physician/patient interaction was noted as a key driver of compliance⁸: Patient compliance directly correlated with the amount of time providers spent advising patients about how to use the drug and explaining its clinical value.

Summary

It is universally agreed that the overuse of antibiotic agents is creating more pathogen resistance with significant potential health consequences. Studies that attempt to evaluate the economic consequences of overuse of antibiotics are scarce; many are based on flawed models that provide data of limited use within the actual clinical setting. Available data do suggest that prescribing antibiotics at the first medical visit does not reduce overall cost of care. Moreover, the efficacy of antibiotic therapies can be greatly enhanced through appropriate educational outreach.

Table. Clinical Outcomes for Macrolides*

| Treatment | Cure Rate |
|---|-----------|
| Erythromycin 333 mg tid 10 days | 70% |
| Azithromycin 500 mg day 1, 250 mg qd 4 days | 80% |
| Clarithromycin 250 mg bid 7 days | 85% |

bid = twice a day; tid = 3 times a day; qd = every day.

Source: Weiss ICMAS 1998;278:3-1-904.

*Results of a prospective trial on bronchitis:120 patients, randomized into 3 treatment arms.

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