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Acute Exacerbation of Chronic Bronchitis: Disease-Specific Issues That Influence the Cost-Effectiveness of Antimicrobial Therapy

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ABSTRACT

Background: Acute exacerbation of chronic bronchitis (AECB) is a common condition, with substantial associated costs and morbidity. Research efforts have focused on innovations that will reduce the morbidity associated with AECB. Health care payers increasingly expect that the results of evidence-based economic evaluations will guide practitioners in their choice of cost-effective interventions.

Objectives: To provide a framework on which to base effective and efficient antimicrobial therapy for AECB, we present a concise clinical review of AECB, followed by an assessment of the available data on the economic impact of this disease. We then address several AECB-specific issues that must be considered in cost-effectiveness analyses of AECB antimicrobial interventions.

Methods: Published literature on the clinical and economic impact of AECB was identified using MEDLINE®, pre-MEDLINE®, HealthSTAR, CINAHL, Current Contents/All Editions, EMBASE, and International Pharmaceutical Abstracts databases. Other potential sources were identified by searching for references in retrieved articles, review articles, consensus statements, and articles written by selected authorities.

Results: In evaluating cost-effectiveness analyses of AECB antimicrobial therapy it is critical to (1) use the disease-free interval as an outcome measure, (2) evaluate the sequence of multiple therapies, (3) address the impact of both current and future antibiotic resistance, and (4) measure all appropriate AECB-associated costs, both direct and indirect.

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Conclusions: Incorporating these approaches in economic analyses of AECB antimicrobial therapy can help health care organizations make evidence-based decisions regarding the cost-effective management of AECB.

Key words: lung diseases, obstructive; chronic bronchitis; costs; cost analysis. (*Clin Ther.* 2001;23:499–512)

INTRODUCTION

Chronic bronchitis is defined as the presence of a mucus-producing cough that occurs most days of the month, for 3 months of the year, and for ≥ 2 successive years.¹ The Centers for Disease Control and Prevention estimate that >13 million individuals in the United States, or ~5% of the adult population, suffer from this condition, making it the seventh most common chronic disease in the United States.^{2,3} Individuals with chronic bronchitis typically experience several exacerbations of their disease each year. These unpredictable events, for which a cause is usually not easily identified, have been demonstrated to have a significant detrimental impact on the quality of life of affected individuals.⁴

Most individuals who experience an acute exacerbation of chronic bronchitis (AECB) seek treatment from a health care provider; each year >10 million visits for AECB occur in the United States.⁵ Ambulatory management usually leads to an eventual return to baseline clinical function without the need for further visits, medication, or diagnostic testing.⁶ However, for particularly severe episodes or those unusual cases for which outpatient care is unsuccessful, hospitalization is required. More than 500,000 hospital admissions in the United States are attributable to AECB each year.⁷

The epidemiology, associated morbidity, and broad range of medical services required make AECB a significant economic burden to the health care sector and society as a whole. The annual direct medical costs associated with the diagnosis and treatment of AECB have been estimated to be >\$1 billion.⁵ The accurate calculation of the total burden of chronic bronchitis is complicated since most financial projections tend to exclude non-medical direct costs (eg, family caregiving, travel) as well as indirect costs (eg, absenteeism, decreased productivity), both of which are likely to be considerable. Until these costs are adequately quantified, the aggregate financial burden of this disease will be substantially underestimated.

Significant resources have been directed toward developing interventions that will reduce the morbidity associated with chronic bronchitis. Much of the current research focuses on drugs that more effectively treat AECB and/or reduce the occurrence of acute events. The increasing awareness among health care payers of rising drug costs is requiring that new agents demonstrate that the additional clinical benefits gained justify the incremental expenditures incurred. There is an expectation among payers that the results of evidence-based economic evaluations will guide practitioners in their choice of cost-effective interventions.

Although published standards for economic evaluation exist,⁸ it is critical to address AECB-specific issues (Table I) before performing or interpreting cost-effectiveness analyses of interventions for AECB, particularly antimicrobial therapy. These AECB-specific issues include advances in basic and applied research, as well as the clinical aspects of AECB that differentiate chronic bronchitis from other

Table I. Acute exacerbation of chronic bronchitis (AECB)-specific issues that influence economic evaluations.

Inclusion of the disease-free interval
Evaluation of multiple therapies as prescribed in clinical practice (sequencing)
Impact of antibiotic resistance (current and future)
Measuring all appropriate AECB-associated costs

conditions from the provider's perspective. To provide a framework on which to base clinically relevant discussions regarding best clinical practices for AECB antimicrobial management, we present a concise review of the pathogenesis, natural history, and current treatment of AECB, followed by an assessment of the available data on the economic impact of this condition. In light of the available data, the potential impact of each of the disease-specific issues on the cost-effectiveness of AECB interventions will be explored in detail. Analyzing the clinical and economic implications of these issues is crucial to making evidence-based decisions regarding the cost-effective antimicrobial management of AECB.

METHODS

Published literature on the clinical and economic burden of AECB was identified. First, using various combinations of appropriate medical subjects headings and key words (eg, chronic bronchitis; treatment; lung diseases, obstructive; costs and cost analysis), a computerized search of the following databases was performed: MEDLINE®, Pre-MEDLINE®, HealthSTAR, CINAHL, Current Contents/All Editions, EMBASE, and International Pharmaceutical Abstracts. Several of these databases were also searched for articles written by selected authorities in the field

of chronic bronchitis. Other potential sources were identified by examining the references cited in retrieved articles, review articles, and consensus statements. Both peer-reviewed publications and reports published as theses or in abstract form were considered.

CLINICAL ASPECTS OF ACUTE EXACERBATION OF CHRONIC BRONCHITIS

Pathogenesis

Cigarette smoking is the most important cause of declining pulmonary function and the development of chronic bronchitis.⁹ The mucociliary system, a primary defense mechanism against inhaled particles, may be altered by cigarette smoke,¹⁰ thereby predisposing patients to secondary infection.¹¹ These secondary infections, which are usually due to a variety of viral and bacterial pathogens,^{3,12-21} are usually responsible for episodes of AECB. In general, bacteria account for up to 50% of exacerbations of chronic bronchitis (Table II).

Definition and Clinical Course

On average, a patient with chronic bronchitis experiences 1 to 4 exacerbations per year,^{22,23} with symptoms lasting ~2 weeks per episode.²³ Patients with an episode of AECB will usually have increasing symp-

toms of cough, dyspnea, and/or sputum production before they seek treatment from a health care provider. During the office visit, the provider must choose the type of therapy (eg, antimicrobial, bronchodilator, and/or systemic corticosteroid therapy) and the site for administration (inpatient vs outpatient). Deciding whether to treat a patient with an antimicrobial agent—and which agent to use—is often difficult and should depend on the etiology of the episode. However, because there is no rapid or reliable method to predict etiology based on patient history, physical examination, or routine laboratory test results, physicians must rely on epidemiologic data to predict the most likely pathogens (Table II). The majority of patients (~90%) will not require hospitalization for treatment of AECB.^{24–26} Patients with moderate to severe underlying disease, however, are likely to be hos-

pitalized more often than those with less severe disease.²⁷

The specific role of corticosteroids as adjunctive therapy for patients with AECB is not clear. Data are emerging, however, that corticosteroid therapy results in moderate improvement in clinical outcomes among patients with AECB.²⁸ However, most of the data on adjunctive treatments for AECB (eg, corticosteroids, bronchodilators) are observational, and the methods used to collect the data are often inconsistent or do not adjust for potential confounding factors.

Antimicrobial Therapy

Given the high costs associated with AECB and the theoretical, but unproven, potential for persistent bacterial infection to further deteriorate lung function,³ the use of effective antibiotic therapy in the

Table II. Infectious etiologies of acute exacerbation of chronic bronchitis.^{3,12–21}

Etiology	Estimated Range (%)
No infectious etiology identified	30–50
Viral pathogens	
Adenovirus	1–2
Influenza	5–25
Parainfluenza	3–30
Rhinovirus	5–20
Coronavirus	5–20
Respiratory syncytial virus	0–10
Herpes simplex	1–2
Bacterial pathogens	
<i>Streptococcus pneumoniae</i>	15–33
<i>Haemophilus influenzae</i>	30–50
<i>Moraxella catarrhalis</i>	5–20
<i>Staphylococcus aureus</i>	0–15
Enteric gram-negative bacilli	0–40
Atypical pathogens	
<i>Mycoplasma pneumoniae</i>	0–5
<i>Chlamydia pneumoniae</i>	5–20

treatment of bacterial AECB seems logical. Anthonisen et al²³ evaluated antibiotic efficacy in 173 patients with AECB. In this study, the antibiotic efficacy results were stratified based on the number of symptoms at baseline (increase in dyspnea, increase in sputum production, and/or change in sputum color). Patients with all 3 symptoms derived the greatest benefit from antibiotic therapy, whereas patients with only 1 symptom did not benefit from therapy.²³ A meta-analysis of 9 trials that randomly assigned patients with AECB to either antibiotic therapy or control found a statistically significant but clinically small benefit in patients treated with antibiotics.²⁹

Antibiotic therapy fails to significantly improve symptoms in ~20% of patients with AECB.^{10,12} Patient characteristics that predict treatment failure include advanced age, >4 chest infections during the preceding 12 months, significant impairment of baseline lung function, poor performance status, and comorbid conditions.^{10,22,30–32} In patients at increased risk for treatment failure, newer and potentially more expensive antimicrobial agents could be justified for early therapy since these novel agents may be cost-effective when their use prevents more costly outcomes such as hospitalization.³³ Several stratification schemes have consequently been proposed for managing patients with AECB.^{10,32,34,35}

Results from several recent studies, including decision analyses using computerized modeling^{36–38} and a prospective evaluation,^{39,40} support the use of different AECB antimicrobial agents based on patient stratification. In patients with certain risk factors (eg, moderate to severe chronic bronchitis, frequent exacerbations, comorbid conditions), the use of

newer, broad-spectrum antibiotics led to better clinical outcomes and lower overall health care expenditures despite higher initial drug acquisition costs.^{36–40}

Factors in Antibiotic Choice

Factors other than a patient's clinical characteristics may affect antibiotic use in patients with AECB. Studies in patients with acute respiratory tract infection (eg, acute bronchitis without underlying lung disease) have shown that patients often demand antibiotic therapy^{41,42} possibly because they are unaware that antibiotics are not effective against viral infections.⁴³ Moreover, patients often expect to receive an antibiotic prescription during the office visit, especially if they improved with antibiotics during a prior episode.⁴¹ These expectations have been enhanced by the proliferation of direct-to-consumer advertising of antibiotics.⁴⁴

In addition, managed care and the increasing cost-consciousness in medical care has affected the way physicians prescribe antibiotics. Although formularies designed to constrain pharmaceutical costs limit the use of certain expensive antibiotics, the drive to shorten and prevent both outpatient and inpatient visits encourages the use of broad-spectrum antibiotics to ensure that the patient's infection will be adequately treated.⁴⁴ Other factors affecting antibiotic choice include presumed efficacy, safety, duration of therapy, and dosing.

Thus, review of the clinical aspects of AECB suggests that (1) the etiology of a specific AECB episode is difficult to determine, (2) patients at high risk for treatment failure or early recurrence of AECB can be identified using clinical history, and (3) individualizing treatment decisions in patients with AECB may prove cost-effective.

ECONOMIC ASPECTS OF ACUTE EXACERBATION OF CHRONIC BRONCHITIS

To accurately calculate the total economic burden of AECB, it is necessary to account for all disease-related expenditures over an appropriate time course.⁸ Measuring resource use from the societal perspective entails collection of (1) direct medical costs (value of all services and other medical resources consumed in the management of the disease); (2) direct nonmedical costs (value of all services and other nonmedical resources consumed in the management of the disease); and (3) indirect costs (value of lost productivity and premature death related to the disease). The societal perspective presents a significant challenge to investigators in that patient-level data from a variety of sources (eg, insurance company, patient's family, caregiver's employer) are required. Because of the difficulties in data collection, most of the economic data available for AECB address only direct medical costs.

Direct Medical Costs

The direct medical costs of AECB include those incurred from outpatient care, hospitalizations, emergency room visits, and drug costs. Published studies evaluating the economic impact of AECB have concluded that the direct medical expenditures attributable to AECB⁵ (and chronic obstructive pulmonary disease [COPD]²⁵) are substantial. Using Medicare claims and other national databases, Niederman and colleagues⁵ estimated the annual cost of AECB in the United States at \$1.6 billion. Using broader inclusion criteria not limited to patients with AECB (ie, using all patients with chronic bronchitis as a primary

or secondary diagnosis), Wilson et al²⁵ estimated the cost of chronic bronchitis in the United States at \$12 billion per year. In both studies, the majority of expenditures were associated with hospitalization, physician visits, and medications.^{5,25}

Hospitalization

Hospitalization for AECB (defined by *International Classification of Diseases, Ninth Revision* [ICD-9] codes 491.20 and 491.21) is the largest contributor to direct medical costs. Using data from Medicare claims and other inpatient databases, Niederman et al⁵ estimated the average cost for an AECB hospitalization to be \$5516. Wilson and colleagues²⁵ calculated a similar average hospitalization cost (\$5413) for all causes of bronchitis (ICD-9 codes 490 and 491). Although the average cost per hospitalization was roughly equivalent in the 2 studies, the broader inclusion criteria used by Wilson et al²⁵ led to an estimate of annual discharges that was ~4 times that reported by Niederman et al⁵ (1.17 million vs 280,000).

To update these findings, we derived the average cost of hospitalization for AECB (ICD-9 491.21) and for acute and chronic bronchitis (ICD-9 490, 491) from 2 additional sources using 1998–1999 data: the University HealthSystem Consortium (UHC) Clinical Database (>100 US academic hospitals) and the University of Michigan Health System (Table III). As in the published analyses, no appreciable difference was detected between the 2 databases in the average cost per hospitalization for AECB and for acute and chronic bronchitis. The 10% increase in mean costs (inflation adjusted) compared with the costs obtained by Niederman et al⁵ and Wilson et al²⁵ may be

Table III. Costs of inpatient hospitalization for bronchitis and acute exacerbation of chronic bronchitis (AECB).

	No. of Patients	Average Length of Stay (d)	Average Cost
AECB (ICD-9 code 491.21)			
University of Michigan	101	3.98	\$6285
University HealthSystem Consortium	12,379	5.22	\$6625
All acute and chronic bronchitis (ICD-9 codes 490 and 491)			
University of Michigan	154	3.86	\$6287
University HealthSystem Consortium	13,904	5.07	\$6524

ICD-9 = *International Classification of Diseases, Ninth Revision.*

attributable to the greater severity of illness often seen in patients admitted to academic medical centers.

Outpatient Services

Although ambulatory management for AECB is the norm, published data suggest that outpatient services (physician visits, diagnostic testing, and emergency services) contribute significantly less to AECB costs than do inpatient stays. Niederman et al⁵ estimated the average cost per visit to be \$74 for a physician office visit, \$159 for a hospital outpatient clinic visit, and \$76 for an emergency department visit.

Outpatient Medications

Several studies have shown outpatient prescription medications to be an important component of AECB total costs.^{5,24,37} The contribution of outpatient prescriptions to aggregate AECB expenditures is inversely related to the severity of illness because of the significant economic impact of disease-related hospitalizations.

Thus, studies that focus on primary care practices with less severely ill populations would be expected to have a greater proportion of AECB costs attributable to outpatient medications compared with specialty-based studies that enroll more severely ill patients who are more likely to be hospitalized.

The relationship of disease severity to rate of outpatient drug contribution has been illustrated in a study by van Barlingen et al,³⁶ which reported that outpatient drug costs varied inversely with severity of AECB. The contribution of drug costs to the total cost of AECB ranged from 7% (severe exacerbation) to 17% (mild exacerbation). The critical role of hospitalization in decreasing the outpatient drug cost contribution can be seen in the study of Destache et al.²⁴ In an AECB patient cohort in which 76% of patients were eventually hospitalized, the outpatient pharmacy costs per AECB episode ranged from 1% to 8% of total treatment costs (the variation explained by the antibiotic used to treat the AECB exacerbation).²⁴

Two population-based studies^{25,39} have demonstrated that outpatient prescription

costs can be a significant component of total AECB expenditures if hospitalization is rare. Wilson and colleagues,²⁵ using expert opinion, literature review, and wholesale drug prices, estimated the total cost of medication for treatment of chronic bronchitis at \$4.37 billion, or 37% of all direct medical costs.²⁵ Grossman et al³⁹ estimated that the total cost of both antibiotics and concomitant medications used for each episode of AECB accounted for 33% of total costs.

Direct Nonmedical Costs

Costs associated with nursing home care, paid and unpaid home health care, and family out-of-pocket expenditures for non-medical expenses (eg, travel, day care) are likely to contribute significantly to the total cost of AECB, but data are scarce. Niederman et al⁵ estimated that nursing home care accounts for 1% to 2% of total AECB treatment costs. Grossman and colleagues³⁹ estimated out-of-pocket expenses for patients and caregivers to be ~4% of total AECB costs, or ~\$85 per episode.

Indirect Costs

The indirect cost burden of AECB includes lost labor time and productivity for both patients and caregivers. Grossman et al³⁹ found that time lost from work varied from \$197 to \$427 per episode of AECB depending on the antibiotic used; indirect costs relative to direct costs varied from 10% to 32%. We examined data for another chronic respiratory condition—COPD—to obtain a rough estimate of the proportion of indirect costs relative to direct medical costs. Sullivan et al⁴⁵ estimated indirect costs for COPD to be \$9.2 billion, almost two thirds of direct medical costs. Further

studies are needed to clarify the amount of indirect expenditures relative to direct costs in AECB.

In summary, the economic impact of AECB is substantial to the patient, the health care system, and society. Although the direct medical cost data analyses performed to date have been rather sophisticated, further work is necessary to better quantify the direct nonmedical and indirect costs of AECB. If clinical research and cost-effectiveness analyses are to truly guide clinically important decisions, the use of patient and employer resources during episodes of AECB must be clarified further.

DISEASE-SPECIFIC FACTORS THAT AFFECT COST-EFFECTIVENESS ANALYSIS

Given the substantial clinical and economic consequences of AECB, the development of clinically relevant, evidence-based recommendations to guide cost-effective antimicrobial management becomes paramount. Determining the most economically efficient antimicrobial treatment in specific patient populations is not straightforward. Several unique disease-specific analytical issues exist that must be considered when determining a cost-effective antimicrobial therapy for patients with AECB (Table I). Economic studies should explicitly discuss and, when appropriate, incorporate these considerations in the analyses.

Disease-Free Interval

The use of the disease-free interval (DFI), or infection-free interval, as an outcome measure of an AECB treatment has been debated in the AECB literature.⁴⁶ The commonly used definition of DFI is

“the length of time in days between the end of therapy and the beginning of the next AECB episode.”⁴⁶ Currently, the standard outcome used in clinical trials of AECB interventions is symptomatic cure of the index exacerbation. Clinical improvement should be the primary outcome of any analysis of AECB therapy; however, since chronic bronchitis is associated with multiple relapses, an evaluation that focuses exclusively on a single exacerbation may be shortsighted.

Published trials have concluded that giving patients certain antibiotics may prolong the time period between AECB episodes.^{47,48} The scientific rationale behind the DFI lies in the level of bacterial eradication achieved by the antibiotic. If the number of bacteria colonizing the lower airways is decreased substantially, then it can be hypothesized that a recurrent symptomatic episode will be delayed. Thus, the advantage of a treatment that will significantly delay a future exacerbation, independent of the cure rate of the index episode, is obvious. If the DFI differs significantly among available therapies, the effects on clinical outcomes and resource use would be substantial given the recurrent nature of AECB.⁴⁶ Thus, an antibiotic could prove to be beneficial not only based on its success or failure rates during the incident AECB episode, but also on its effect on the DFI.

To incorporate DFI as an outcome, current AECB decision-analytic models^{36–38,49} need to be expanded to allow clinical follow-up to be extended from the end of the incident exacerbation (cure, fail, death) to an end point based on chronology (based on months or years). Several aspects of the clinical course must be recorded to accurately estimate the impact of the DFI. Specifically, any clinical

predictors that may affect the probability of a subsequent AECB must be captured and stored. These include antibiotics used in the incident exacerbation, comorbid conditions, and severity of the exacerbation itself. Thus, a comprehensive evaluation of AECB that includes the DFI as an outcome measure will better assist decision-makers in determining the cost-effectiveness of specific therapies compared with evaluations that assess single episodes of AECB.

Evaluation of Antimicrobial Therapies Over the Course of Disease

To constrain health care expenditures, clinical practice guidelines for AECB treatment often recommend initially using less expensive, but less effective treatments and reserving more effective and more expensive regimens for treatment failures. Because patients with AECB may fail initial therapy or experience relapses after initial therapy is prescribed, the clinical and economic consequences of antibiotic therapy depend on subsequent diagnostic and treatment decisions that occur over the entire natural course of the disease. Given the recurring nature of chronic bronchitis, evaluation of treatments as they are prescribed during the course of disease, instead of a single exacerbation, will likely yield more accurate cost-effectiveness data.

Analyses that compare antibiotics directly (first-line antibiotic vs second-line antibiotic) may not reflect actual clinical practice, since available alternatives are often used in sequence (ie, if the first-line antibiotic fails, then a second-line antibiotic is used). The most cost-effective first-line antibiotic agent for AECB, consequently, does not depend entirely on the

differences in bronchitis cure rates and treatment costs at the time of use, but also on the variation in patients' symptomatic response and resultant likelihood of future bronchitis-related health care expenditures. Economic analyses of AECB should consider the recurring nature of the condition and account for several treatment changes over an appropriate time period.

Impact of Bacterial Resistance

One important cost that differentiates antimicrobial agents from other pharmaceutical classes is the potential for organisms to develop resistance to specific drugs. Prospective surveillance programs have quantified the resistance of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* (bacteria commonly implicated in AECB) to many antibiotics. Doern et al⁵⁰ reported data from 845 *S pneumoniae* isolates from 27 medical centers in the United States and 202 isolates from 7 institutions in Canada. Although resistance rates varied widely, 56% of overall isolates were susceptible to penicillin, whereas 28% demonstrated intermediate resistance and 16% demonstrated high-level resistance.⁵⁰ Resistance has also been observed among the common gram-negative respiratory isolates such as *H influenzae* and *M catarrhalis*.⁵⁰

Although the in vitro data indicate significant levels of resistance, the in vivo impact of antibiotic resistance in patients with bronchitis remains unclear.⁵¹ Studies have not clearly demonstrated that patients infected with resistant strains have worse outcomes than similar patients infected with susceptible strains. If patients infected with resistant organisms do have a worse prognosis, the ability to select an effective antibiotic on initial presentation would be critical.

Decelerating the rate of antibiotic resistance is particularly problematic because the development of future resistance correlates with current antibiotic use.⁵² A report from the Canadian Bacterial Surveillance Network found that the prevalence of *S pneumoniae* with reduced susceptibility to fluoroquinolones increased from 0 in 1993 to 1.7% by 1998 as the use of fluoroquinolones increased during this period.⁵³ Limiting the excessive use of antibiotics has successfully reduced resistance.⁵⁴ As broad-spectrum agents are more frequently used empirically for patients with AECB, physicians must recognize the tradeoff between initiating effective therapy now and the resultant likelihood of future resistance. However, methods to stop this cycle remain elusive.

Evidence-based, economic analyses that consider the societal perspective may help clarify the tradeoff between optimizing care for an individual patient today and ensuring effective therapy in the future for patients with AECB. Thus, further studies that incorporate clinical effectiveness, future resistance patterns, and economic impact to determine the optimal treatment for AECB are clearly needed.

Measuring Appropriate Disease-Associated Costs

As discussed, the financial impact of AECB on patients, the health care system, and society is substantial. Although direct medical cost data for this disease are now available, data quantifying the additional AECB-related expenditures not paid for by third-party payers are scant. If clinical research and cost-effectiveness analyses are to truly guide clinically relevant decisions, a sizable investment to clarify AECB-associated resource use is war-

ranted. Recommendations based exclusively on direct medical costs may lead clinicians to choose interventions that, while benefiting health plans, actually lead to increased costs for patients, their families, and employers. Specifically, substantial clinical benefits may be foregone if the use of a better therapy is restricted based on high acquisition price alone while concomitantly underestimating all the potential benefits (eg, failure to include decreased absenteeism).

CONCLUSIONS

Interventions that can slow or prevent the development of chronic bronchitis, decrease the number of AECB episodes, and keep patients from requiring medical care services will play an important role in the clinical management of this disease. Given the clinical and economic impact of AECB, and the emergence of antimicrobial strains that are resistant to commonly available drugs, the importance of effective and cost-effective antimicrobial therapies has never been greater.

Although establishing the benefits of antimicrobial therapy for patients with AECB has been problematic, their use in most patients has become standard. Thus, selecting the most cost-effective initial therapy is crucial for both the symptomatic patient and for society, given the widespread concern over emerging antibiotic resistance. Although cost-effectiveness analyses may help determine the optimal initial therapy, the AECB-specific issues discussed in this article must be explicitly considered in any economic evaluation so that informed decisions regarding antimicrobial therapy for AECB can be made.

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