Challenges of Managed Care Organizations in Treating Respiratory Tract Infections in an Age of Antibiotic Resistance

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Presentation Summary

Managing respiratory tract infections (RTIs) presents many challenges to managed care organizations (MCOs). RTIs are among the most common illnesses treated by primary care clinicians; they seriously impact patient quality of life and are a leading cause of health-related absences from the workplace. The total direct costs of treating conditions such as acute otitis media, sinusitis, and acute exacerbations of chronic bronchitis are estimated to be $10.1 billion. The development of drug resistance has compounded these challenges by increasing treatment failures and costs and limiting treatment options. MCOs can meet these challenges by implementing clinical practice guidelines for acute respiratory infections, conducting focused studies of antibiotic use, and educating both healthcare clinicians and patients about appropriate antibiotic use.

According to a recent National Center for Health Statistics survey, approximately 240 million episodes of upper and lower respiratory tract infections (RTIs) occur annually in the United States.[1] RTIs, including the common cold, pharyngitis, sinusitis, otitis media, acute bronchitis and exacerbations of chronic bronchitis, influenza, and pneumonia, are the most common reasons for clinician office visits and the prescription of antibiotics.[1] The clinical and financial burdens of treating these common illnesses combined with the increasing rate of resistance to prescribed antibiotics present substantial challenges to managed care organizations (MCOs).

The Impact of RTIs

Acute otitis media (AOM) is the most commonly diagnosed bacterial infection in children.[2] By 7 years of age 75% of children have had 3 or more ear infections.[3] The number of office visits for AOM has risen steadily: from 10 million in 1975,[4] to nearly 25 million in 1990,[4] to almost 30 million in 1996.[2] This increase has been attributed to the growing use of day care for young children.[2,5]

Bacterial sinusitis, another common condition treated by clinicians, is reported to affect up to 20 million Americans[6]; and in the case of chronic sinusitis, it accounts for 12 million office-based visits annually.[7] Sinusitis is the fifth most common diagnosis for which an antibiotic is prescribed.[8]

Acute exacerbation of chronic bronchitis (AECB) is yet another common RTI. The National Center for Health Statistics estimated in 1994 that more than 14 million people had chronic bronchitis and sought treatment for 91% of their acute episodes. AECB accounts for 10 million outpatient office visits annually.[9]

Patient Quality of Life. Although acute RTIs are self-limiting and usually not considered serious conditions, they

can have a significant effect on health-related quality of life. Symptoms such as pain, discomfort, difficulty sleeping, and fatigue can all affect daily activities, performance at work or school, social interaction, psychological and emotional well-being, and overall quality of life. The costs of treating RTIs, especially recurrent episodes, also can affect patients financially, providing a further impact on their quality of life. Additionally, the negative impact of acute RTIs on patient quality of life may be prolonged. In a recent survey, researchers found that although symptoms of AECB often improve within 1 week of therapy, quality of life may not return to baseline for at least 2 months.[10] Conversely, it was noted that reducing the number of AECB-symptom days improved quality of life.[10]

Direct and Indirect Costs. The total annual direct medical costs of AOM (the costs of prescriptions plus office visits) for children younger than 5 years of age have been estimated at $4 billion.[11] Adding the costs of treating AOM in older children brings the total to more than $5 billion.[10] The estimated total cost of treating one complicated 3-month episode of AOM is $1331,[12] with treatment costs for recurrent episodes substantially higher. Sinusitis expenditures are estimated to be $3.5 bilion.[13] If the costs of treating comorbid diseases such as asthma, allergies, and AOM are included, the total costs of sinusitis are estimated to be $5.8 billion.[13] The average cost of a sinusitis episode also increases with treatment failures: from estimates of $304 for the first episode, to $667 for the second, to $1743 for the third.[14] The total treatment costs for AECB are estimated to be $1.6 billion, of which $1.5 billion are spent on hospitalizations.[9] The total direct costs of treating these conditions are estimated to be $10.1 billion.

The indirect costs of decreased functioning, lost productivity, and absences from the workplace raise the total costs of RTIs substantially, costs usually borne by patients. For example, it has been estimated that 90% of the total costs of treating an episode of AOM can be attributed to indirect costs, primarily for parental or caregiver time away from work.[12] Sinusitis was responsible for an estimated 13 million lost work days and an estimated 59 million restricted-activity days in 1994.[13]

Table. Prevalence and Economic Impact of Respiratory Tract Infections

	AOM	Sinusitis	AECB
Prevalence	Most common bacterial disease in children	Affects 20 million people per year	14 million people have chronic bronchitis
Office visits (per year)	≈30 million	12 million*	≈10 million
Number of prescriptions (per year)	24 million	13 million	>13 million
Costs (total per year)	>$5 billion	$3.5 billion	$1.6 billion

*Chronic condition.
AECB = acute exacerbation of chronic bronchitis; AOM = acute otitis media.
Source: References 2, 6, 8-10, 13, 15, 21.

Respiratory problems, such as sinusitis and bronchitis, have been reported to be the second most common reason for disability-related lost work time.[15] A summary of the prevalence and economic impact of 3 of the most common RTIs is shown in the **Table**.

Antibiotic Prescribing. The use of antibiotics in outpatient facilities has increased dramatically over the past 20 years; these drugs are now the second largest category of drugs prescribed by clinicians.[16] Antibiotic use increased by 28% from 1980 to 1992,[8] and by nearly 140% from 1992 to 1998, with 261 million prescriptions written in 1998.[16]

Many antibiotic prescriptions are written for patients with RTIs. RTIs account for approximately 67% of all antibiotic use in adults and 87% of use in children.[16] Yet as many as half of these prescriptions may be unnecessary.[17]

Antibiotic-Resistant Pathogens

Emergence. In a study of prescribing habits, Gonzales et al[18] found that the antibiotic prescribing rate was 51% for colds, 52% for upper RTIs, and 66% for bronchitis. Yet antibiotics are ineffective for more than 90% of all colds, upper RTIs, and acute bronchitis because the pathogen is usually viral.[18] This overexposure of patients to antibiotics may be 1 factor leading to drug resistance, particularly in children.

Patient noncompliance with antibiotic regimens may also contribute to resistance. Patients may stop taking an antibiotic before the end of the prescribed course of treatment because of improvement in symptoms, frequent dosing regimens, or unpleasant side effects. This practice results in ineffective antibiotic concentrations (subtherapeutic dosing), which encourages the proliferation of resistant pathogens. In addition, patients may self-diagnose an RTI as bacterial in origin and take a short course of leftover antibiotics, which also leads to subtherapeutic dosing.

Consequences of Antibiotic Resistance. The consequences of the increased prevalence of resistant bacterial strains are both immediate and long term. Short-term consequences include antibiotic treatment failures, additional courses of antibiotics (usually with broader-spectrum agents), and unresolved respiratory infections, all of which can lead to disease sequelae and chronicity. For example, inadequately treated AOM can result in persistence of middle ear effusion, suppurative complications, the need for surgical implantation of tubes, long-term hearing loss, decreased perception of language, impaired speech development, and learning deficiencies.

Other examples include recurrences of bacterial sinusitis, which can result in permanent damage to nasal mucosa leading to chronic disease, which may require surgery. Treatment failures in AECB may further decrease pulmonary function. Repeated exacerbations can significantly compromise lung function, leading to acute respiratory failure, prolonged hospital stays, mechanical ventilation, and even death.

As more pathogens become resistant to antimicrobial agents, fewer therapeutic options are available and broader-spectrum agents must be used. In the past 20 years, prescriptions for expensive broad-spectrum drugs, such as macrolides and brand-name cephalosporins, have increased dramatically, whereas prescriptions for less expensive, narrower-spectrum drugs, such as penicillins, have decreased.[8]

As existing antibiotics become increasingly less effective against targeted pathogens, the chances of widespread epidemics (ie, pandemics) of infectious diseases may become greater. Additionally, the elderly, young, seriously ill, and individuals residing in institutions are

particularly vulnerable to infections caused by resistant pathogens.

Challenges of Treating RTIs

Successfully managing acute RTIs as antibiotic resistance increases presents a number of clinical and financial challenges for MCOs:

- Clinical burden (inpatient and outpatient visits) increases with the rising incidence of RTIs and treatment failures.
- Treatment failures are associated with higher costs (eg, additional office visits, medications, diagnostic tests, hospitalizations, mechanical ventilation), increased use of second-line antibiotics (ie, broad-spectrum antibiotics), and therapy for chronic diseases (eg, sinus surgery, tympanocentesis).
- Treatment of RTIs is becoming more complex and many antibiotics are available for treating them. Clinicians must take into account the likely pathogens and an agent's potential efficacy in eradicating drug-resistant pathogens. Clinicians must also be aware of local and/or general resistance patterns.
- Patients expect and demand antibiotics for RTIs, especially for their children. In 1 study it was reported that 56% of patients diagnosed with viral upper RTIs expected an antibiotic and that these expectations influence clinician prescribing practices.[19]
- Patients are increasingly dissatisfied owing to a lack of understanding of the reasons for not receiving antibiotic prescriptions, treatment failures, and recurrent acute infections.
- Employers expect that MCOs will help reduce employee absences and lost productivity through health plan initiatives.

MCOs can meet these challenges by developing and implementing clinical practice guidelines for treating acute RTIs that will reduce inappropriate use of antibiotics, and by educating clinicians and patients.

Implementing Clinical Practice Guidelines for RTIs. The key to consistent and cost-effective diagnosis and treatment strategies for common acute RTIs is the implementation of clinical practice guidelines for AOM, sinusitis, and AECB.

Treatment guidelines for RTIs should be evidence based (ie, rely on properly controlled clinical trials) and must clearly take into account the prevalence of resistant bacterial strains in the region. They must clearly define the indications for antibiotics and include diagnostic strategies (eg, tympanocentesis for treatment failures in AOM) and alternative treatments (eg, combining amoxicillin with clavulanate and longer courses of therapy) for clinical failures that may result from resistant strains. Treatment algorithms should be incorporated into the guidelines to assist clinicians in selecting the most appropriate antibiotic and adjunctive therapies.

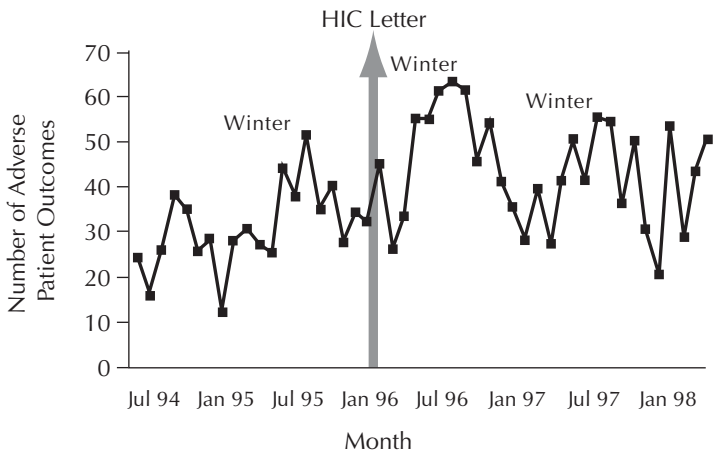
Paramount to the success of clinical guidelines is choosing appropriate antibiotics for inclusion in formularies. Antibiotics are often selected on the basis of drug acquisition costs rather than the overall effectiveness of the antibiotic therapy. A more rational pharmacoeconomic approach would include consideration of the prevalence of resistant pathogens, medical costs of treatment failures (eg, management of adverse drug events, additional provider visits, diagnostic tests), and the indirect costs of impaired quality of life, days lost from work, or restricted-activity days.

The potentially detrimental impact of treatment recommendations based solely on drug cost was demonstrated in a recent study in Australia.[20] The Australian Health Insurance Commission recommended that the top prescribers of amoxicillin/clavulanate use other antibiotics (eg, cephalosporins,

macrolides). Investigators subsequently reviewed patient records for AOM, sinusitis, and lower RTIs in 4 large general practices over a 4-year period. They found that total antibiotic prescribing remained stable but there was a substantial decline in the number of amoxicillin/clavulanate and amoxicillin prescriptions, accompanied by a rise in cephalosporin and macrolide prescriptions. While reviewing patient adverse outcomes both prior to and after changes in prescribing, researchers found a significant increase in the number and rate of adverse patient outcomes (eg, hospitalizations, diagnostic tests, referrals to specialists) (**Figure 1**) and an associated increase in costs of these outcomes (**Figure 2**).[20] This study demonstrated that a policy initiative aimed at decreasing prescription costs changed drug prescribing habits while resulting in ultimately higher treatment costs.

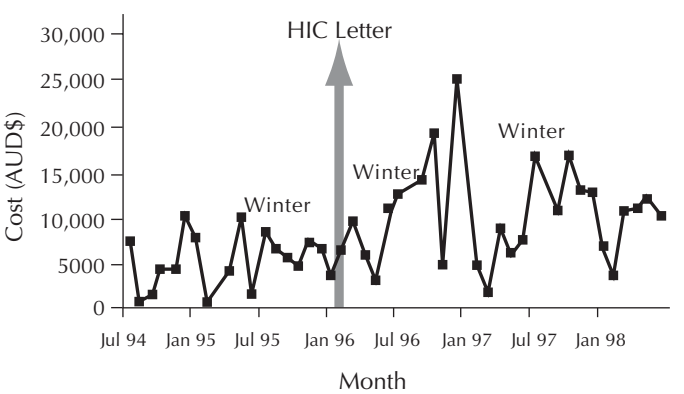
Reducing Inappropriate Use of Antibiotics. Overall, unnecessary use as well as utilization of second-line agents are 2 of the primary goals of treatment guidelines in order to prevent or delay the appearance of widespread antibiotic resistance. Another approach MCOs can use to improve antibiotic use is to conduct a focused antibiotic utilization study. Pharmacists can promote the appropriate use of antimicrobials with such a study and help contain the costs of antimicrobial therapy. Pharmacy claims data can help identify high prescribers of all classes of antibiotics, evaluate the use of first-line agents versus second-line agents, and even determine to what degree antibiotics are prescribed without a physician

Figure 1. Adverse Patient Outcomes per Month



These adverse patient outcomes were identified in the medical record notes. Each outcome was validated by review of all notes by trained staff.
HIC = Health Insurance Commission.
Source: Beilby J, Marley J, Walker D, et al. Effectiveness of antibiotic prescribing and patient outcomes in a community setting: The Australian experience [abstract]. *Clin Infect Dis* 1999;29:1055. Posters presented at: 37th Annual Meeting of the Infectious Diseases Society of America; November 18-21, 1999; Philadelphia, Pennsylvania. Reprinted with permission.

Figure 2. Adverse Patient Outcomes Cost per Month (Weighted by Relative Costs)



Cost was determined at AUD$56 (Australian dollars) for a referral, AUD$16 for a pathology test, AUD$133 for radiology, AUD$2095 for hospitalizations, and AUD$115 for all other tests. These adverse patient outcomes were identified in the medical record notes. Each outcome was validated by review of all notes by trained staff.
HIC = Health Insurance Commission.
Source: Beilby J, Marley J, Walker D, et al. Effectiveness of antibiotic prescribing and patient outcomes in a community setting: The Australian experience [abstract]. *Clin Infect Dis* 1999;29:1055. Posters presented at: 37th Annual Meeting of the Infectious Diseases Society of America; November 18-21, 1999; Philadelphia, Pennsylvania. Reprinted with permission.

visit. The information collected on prescriptions can be used to profile prescribing habits of primary care departments and individual clinicians. These profiles can form the basis for discussions at department meetings and face-to-face sessions between pharmacists and high-prescribing clinicians aimed at encouraging more cost-effective prescribing.

Educating Clinicians and Patients. Clinicians need to be kept informed about the problem of inappropriate use of antibiotics, resistance (local and national), diagnosis and treatment of RTIs, new approaches to determining efficacy of antimicrobials (eg, pharmacokinetic/pharmacodynamic breakpoints), and new recommendations for treatment. Patients need to be educated about the normal presentation of an uncomplicated RTI, the differences between viral and bacterial infections, the role of antibiotics in treating bacterial infections, the problem of resistance as it relates to compliance with antibiotic regimens, and the consequences of noncompliance and self-medication.

Conclusion

MCOs can improve the quality and cost effectiveness of the care they provide for upper and lower RTIs by implementing clinical practice guidelines. The primary goals of these guidelines are to decrease the use of antibiotics for viral infections and inappropriate antibiotic selection for bacterial infections, which will ultimately prevent the further development of resistance. Treatment guidelines should be based on clinical evidence and local prevalence of resistant strains and include diagnostic strategies and alternative antibiotic recommendations for treatment failures. Recommendations for first-line and second-line antibiotics should be based on the appropriateness and cost effectiveness of antibiotic therapy rather than the initial cost of the antibiotics alone.

··· REFERENCES ···

1. Gonzales R. Antibiotic resistance and prescribing practices [editorial]. *Hosp Pract (Off Ed)* 1998;33:11-12.

2. Chartrand SA, Pong A. Acute otitis media in the 1990s: The impact of antibiotic resistance. *Pediatr Ann* 1998;27:86-95.

3. Teele DW, Klein JO, Rosner B, and the Greater Boston Otitis Media Study Group. Epidemiology of otitis media during the first seven years of life in children in greater Boston: A prospective, cohort study. *J Infect Dis* 1989;160:83-94.

4. Schappert SM. Office visits for otitis media: United States, 1975-90. *Adv Data* 1992; 214: 1-18.

5. Uhari M, Mäntysaari K, Niemelä M. A meta-analytic review of the risk factors for acute otitis media. *Clin Infect Dis* 1996;22:1079-1083.

6. Gwaltney JW Jr. Acute community-acquired sinusitis. *Clin Infect Dis* 1996;23:1209-1225.

7. National Committee for Health Statistics: Fastats A to Z. Chronic sinusitis. Available at: http://www.cdc.gov/nchs/fastats/sinuses.htm. Accessed June 26, 2000.

8. McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1995;273:214-219.

9. Niederman MS, McCombs JS, Unger AN, Kumar A, Popovian R. Treatment cost of acute exacerbations of chronic bronchitis. *Clin Ther* 1999;21:576-591.

10. Grossman RF. Acute exacerbations of chronic bronchitis: Pharmacoeconomics. *Infect Med* 1999;16(suppl A):41-52.

11. Gates GA. Cost-effectiveness considerations in otitis media treatment. *Otolaryngol Head Neck Surg* 1996;114:525-530.

12. Alsarraf R, Jung CJ, Perkins J, et al. Measuring the indirect and direct costs of acute otitis media. *Arch Otolaryngol Head Neck Surg* 1999;125:12-18.

13. Ray NF, Baraniuk JN, Thamer M, et al. Healthcare expenditures for sinusitis in 1996: Contributions of asthma, rhinitis, and other airway disorders. *J Allergy Clin Immunol* 1999;103:408-414.

14. Ober NS. Respiratory tract infections: Consider the total cost of care. *Drug Benefit Trends* 1998;10:23-29.

15. Winslow R. Aetna program aims to get workers on disability back on job more quickly. *Wall Street Journal* September 9, 1999:A3.

16. Jacobs MR. Emergence of antibiotic resistance in upper and lower respiratory tract infections. *Am J Manag Care* 1999;5(suppl): S651-S661.

17. Faryna A, Wergowske GL, Goldenberg K. Impact of therapeutic guidelines on antibiotic use by residents in primary care clinics. *J Gen Intern Med* 1987;2:102-107.

18. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care clinicians. *JAMA* 1997;278:901-904.

19. Hamm RM, Hicks RJ, Bemben DA. Antibiotics and respiratory infections: Are patients more satisfied when expectations are met? *J Fam Pract* 1996;43:56-62.

20. Beilby J, Marley J, Walker D, et al. Effectiveness of antibiotic prescribing and patient outcomes in a community setting: The Australian experience [abstract]. *Clin Infect Dis* 1999;29:1055.

21. *Physician's Drug and Diagnosis Audit.* Newton, PA: Scott-Levin PMSI Inc; 1998.