Clinical Practice Guidelines for the Diagnosis and Treatment of Respiratory Tract Infections

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Presentation Summary

Clinical practice guidelines can be indispensable tools for managed care organizations (MCOs) in providing cost-effective treatment of common conditions. Guidelines for acute respiratory tract infections, such as acute otitis media (AOM) and acute sinusitis, can assist clinicians in accurately diagnosing these conditions, in providing treatment rationales, and in reducing the costs associated with inappropriate antibiotic prescriptions. Barriers to the implementation of practice guidelines include negative attitudes clinicians may have about guidelines promoted by MCOs; patient/parent expectations for antibiotic treatment; lack of financial resources, information system resources, and support for implementation; and lack of commitment to patient and provider education on the part of MCOs. MCOs can facilitate the adoption and implementation of guidelines with a systematic approach that involves establishing a guideline review process, gaining the support of providers, selecting outcomes measures, collecting and analyzing outcomes data, and providing feedback to clinicians about the impact of changes in their practices. This systematic approach should be used as part of the process for the National Committee for Quality Assurance accreditation. Evidence-based clinical practice guidelines for AOM and sinusitis have been developed recently by national consortia of infectious disease experts. Adoption of these guidelines can assist in preventing the spread of resistant pathogens.

Clinical practice guidelines can help managed care organizations (MCOs) improve the quality of care they provide for patients with acute respiratory tract infections (RTIs), decrease the use of inappropriate and ineffective antibiotics, and reduce variations in care among health plan providers. The guidelines can assist clinicians in diagnosing and treating RTIs by providing specific treatment algorithms, suggesting alternative therapies for treatment failures, detailing appropriate diagnostic strategies, and providing recommendations for empiric therapy. Accurate diagnosis and appropriate treatment improve therapeutic outcomes by producing faster resolution of signs and symptoms, increased numbers of clinical cures, fewer relapses/recurrences, and by preventing sequelae and chronic infection.

Guidelines can also be used by clinicians to explain treatment choices to patients. Given this information, patients can take a more active role in their care. Health plan members who understand both the causes of their RTIs and appropriate treatment options are more likely to have better clinical outcomes and, therefore, fewer absences from work, fewer office visits, and fewer recurrences of infections. Such patients are also likely to be happier with their healthcare providers and plans. Guidelines can also help MCOs better manage treatment costs by decreasing the expenses associated with nonindicated antibiotics, treatment failures, recurrent infections, and chronic conditions.

Implementing clinical practice guidelines for RTIs can also help MCOs obtain accreditation from the National Committee for Quality Assurance (NCQA) by demonstrating that they meet certain quality improvement (QI) standards. One of these standards, QI 8, requires that MCOs adopt and disseminate scientifically sound practice guidelines for providing acute and chronic care services for diseases that are relevant to their enrolled membership.[1] Guidelines in treating other acute RTIs can help all MCOs meet this standard. Other appropriate standards are QI 10, which requires that MCOs identify opportunities for improvement in clinical care, and QI 11, which requires that MCOs act to improve quality by addressing these opportunities.[1] Analyzing and assessing antibiotic use and demonstrating improvement in appropriate utilization can satisfy these standards.

Obstacles to Adopting Guidelines

The primary obstacles to implementing successful practice guidelines are the clinicians, patients, and MCOs themselves. Clinician acceptance of and adherence to guidelines are critical in translating treatment recommendations into improved outcomes. However, a variety of barriers can undermine this process. These barriers include negative attitudes about guidelines in general or lack of knowledge of particular guidelines. Despite adequate knowledge and positive attitudes, external barriers (eg, time constraints, inadequate staff support, patient expectations and preferences, concern over increased liability, and direct-to-consumer advertising) can also affect a clinician's ability or desire to execute guideline recommendations.[2]

Patient expectations for antibiotics for uncomplicated viral RTIs are another major barrier to clinician adherence to guidelines. For example, 1 study reported that more than half of patients diagnosed with viral RTIs expected antibiotics, even though the agents would be of little clinical value.[3] In the same study, when clinicians believed patients wanted antibiotics, they were about 2 1/2 times more likely to prescribe them than when they believed patients did not expect them.[3]

Finally, guidelines are sometimes distributed to providers by MCOs without support for implementation or evaluation of the impact of changes in provider prescribing behavior on outcomes. A systematic approach to establishing treatment guidelines is key to obtaining clinician adherence, changing patient expectations, and ultimately, improving antibiotic prescribing and treatment outcomes. Lack of resources and systems for data capture and analysis may also be a major barrier to guideline implementation. Most MCOs can capture pharmacy data on first-line and second-line prescriptions and link those data to provider practice patterns, but information systems are not always available to link prescribing to diagnosis through claims data and chart review. Personnel and staff resources are often not available to analyze data on provider performance and clinical outcomes. MCOs may also fail to involve providers in guideline development and review or may offer inadequate education to providers and patients.

Guideline Implementation Process

Successfully implementing clinical practice guidelines requires a vigorous, sustained, and systematic approach on the part of MCOs. As part of the NCQA accreditation process, MCOs must implement practice guidelines that are relevant, which means they must address acute diseases that affect a substantial member population. RTIs are relevant in all health plans. Baseline demographic and epidemiologic data can be used to determine and document relevance (eg, incidence, prevalence, morbidity, and mortality).

Guidelines may be developed by an MCO or adopted/modified from an outside source; however, they must be based on medical evidence that is

incorporated into the guidelines or documented as part of the development process. The guidelines should also be endorsed by independent organizations (eg, national health associations and public health organizations), reviewed at least every 2 years, and updated as needed. Furthermore, the clinicians implementing the guidelines should be involved in the review process.

To carry out new guidelines, healthcare providers need explicit instructions and timetables. New roles and expectations must be delineated and agreed upon. Educational materials and resources necessary to meet new responsibilities should be offered by MCOs, and processes for dealing with problems in implementation and evaluating outcomes must be established.

MCOs should offer healthcare providers medical evidence in support of the guidelines, including data from current clinical studies on antibiotic efficacy using pharmacokinetic/pharmacodynamic (PK/PD) breakpoints, regional surveillance data on resistant pathogens, and educational tools for dealing with patient expectations about antibiotics. Profiles of prescribing patterns and meaningful outcomes data on antibiotic use should be furnished to individual clinicians and primary care departments so that healthcare providers can evaluate prescribing decisions.

MCOs should select specific outcomes measures and collect relevant data. They should choose quantitative measures to assess current clinical outcomes (baselines) and changes resulting from use of the guidelines. Outcomes measures must be objective and based on current scientific knowledge and clinical experience, in addition to being explicit, clearly defined, and quantifiable (eg, number of children with acute otitis media [AOM] who received appropriate antibiotics). Performance goals or outcomes must be set for each measure (eg, percent increase in the use of first-line versus second-line agents). MCOs must determine that necessary information systems are in place to collect data, such as pharmacy and clinician encounter data, medical records, and administrative data.

Finally, outcomes should be compared with goals to determine if the guidelines make meaningful improvements in the quality of clinical care. Reasons for these outcomes should be assessed, as should potential barriers to improvement if the goals are not met. Actions should be undertaken to improve guidelines, clinical performance, and outcomes as indicated.

Centers for Disease Control and Prevention Guidelines for AOM

In 1996, the Centers for Disease Control and Prevention (CDC) convened a panel of experts in the management of AOM to develop treatment recommendations.[4] Participating in the panel were infectious disease specialists, pediatricians, family physicians, internists, academicians, and public health practitioners. The objectives of the panel were to determine if amoxicillin should remain as first-line therapy and to recommend appropriate second-line antibiotics. The CDC panel made the following recommendations.

The first consideration in selecting a first-line antibiotic for treating AOM is efficacy against *Streptococcus pneumoniae* because the pathogen causes approximately 30% to 40% of ear infections, whereas *Haemophilus influenzae* causes about 21% to 26%, and *Moraxella catarrhalis* about 10% to 15%.[5,6] The CDC recommended that amoxicillin be used as the first-line agent for treatment of drug-resistant *S pneumoniae* (DRSP) because, based on its PK/PD breakpoints, more than 90% of the strains remain susceptible to the antibiotic.[4]

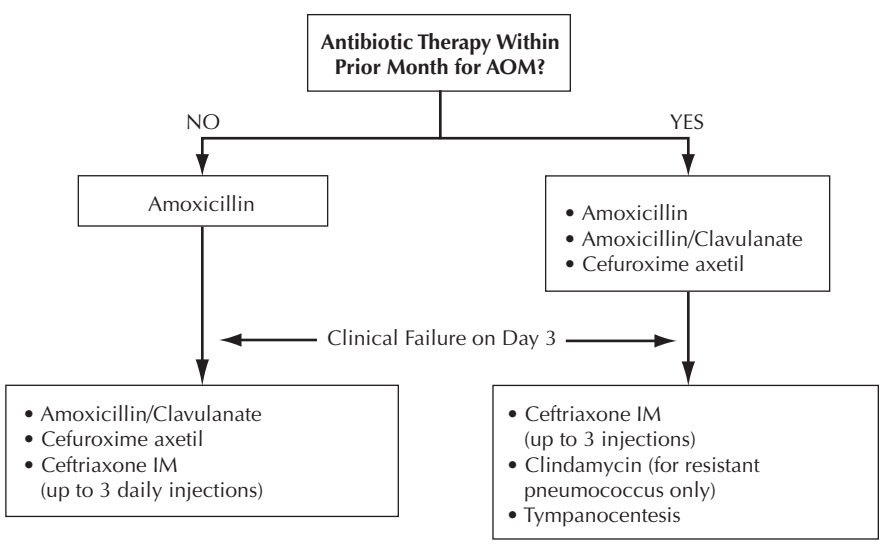
However, administration of recommended dosages of amoxicillin (40 to 45 mg/kg/day) may not eradicate DRSP in a proportion of cases.[4] Recent clinical information indicates that high-dose amoxicillin (80 to 90 mg/kg/day) may be sufficient to eliminate penicillin-

resistant strains.[4] Although the US Food and Drug Administration (FDA) has not approved high-dose amoxicillin and there has been no comparative trial of standard-dose versus high-dose amoxicillin, high-dose amoxicillin has been shown in an open-label, noncomparative, multicenter, double-tympanocentesis study in Israel to eradicate > 95% of *S pneumoniae* and β-lactamase-negative *H influenzae* by the fifth day of treatment.[7] Additionally, high-dose amoxicillin therapy has a long history of efficacy and safety, evidence of high middle ear fluid levels, and absence of substantial dose-related toxicity.

The use of an alternative first-line agent may be indicated in areas where resistance is high as a result of recent antimicrobial treatment (ie, in the past 4 weeks),[4,8] history of lack of response, presence of resistant organism (upon culturing), and day care attendance, which is associated with a high risk of infection with resistant organisms.[8]

In such cases, or in cases of treatment failure with amoxicillin, a second-line agent should be selected that is active against DRSP, β-lactamase-producing *H influenzae*, and *M catarrhalis*.[4] Because many FDA-approved drugs lack good evidence of effectiveness against DRSP, the CDC panel concluded that only 3 agents meet the criteria for second-line treatment: amoxicillin/clavulanate, cefuroxime axetil, and intramuscular (IM) ceftriaxone.[4] The group noted that many of the 16 agents approved for treatment of AOM lack evidence of efficacy against DRSP.[9] Although a single IM injection of ceftriaxone achieves very high middle ear fluid concentrations for at least several days,[9] clinical outcome is not improved compared with a 10-day course of amoxicillin/clavulanate.[10] To improve the effectiveness of ceftriaxone for some penicillin-resistant *S pneumoniae*, a series of 2 or 3 daily injections may be warranted. Although the newer

Figure 1. CDC Pediatric Treatment Algorithm: Initial



AOM = acute otitis media; CDC = Centers for Disease Control and Prevention; IM = intramuscular.
Source: Reference 4.

fluoroquinolones have demonstrated activity against DRSP, they are not approved for use in pediatric patients and should be reserved for possible use only in patients who have demonstrated resistance to other agents.[4] **Figure 1** and **Figure 2** illustrate a pediatric treatment algorithm based on the panel's recommendations.[4]

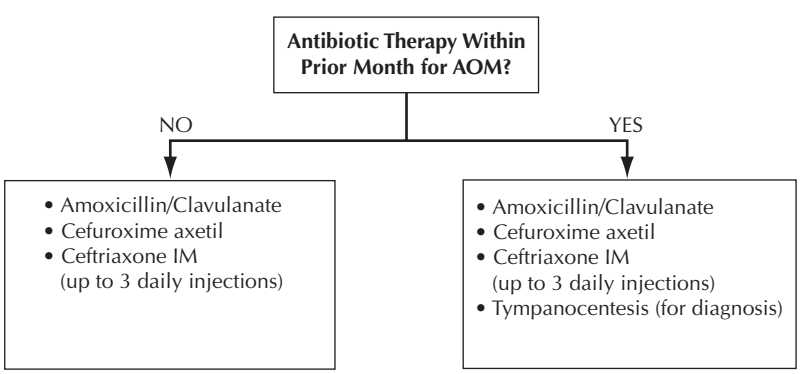
Sinus and Allergy Health Partnership Guidelines for Acute Sinusitis

The Sinus and Allergy Health Partnership is a collective coalition consisting of representatives from the American Academy of Otolaryngology–Head and Neck Surgery, the American Academy of Otolaryngic Allergy, the American Rhinology Society, the CDC, the FDA, and individuals from the fields of infectious diseases, pediatric infectious diseases, microbiology, and pharmacology. A consensus panel representing the partnership developed clinical practice guidelines for treating patients with acute bacterial sinusitis.

These sinusitis treatment guidelines apply to both adults and children and divide sinus disease into 2 categories of severity: mild and moderate. They do not address severe, life-threatening infection with or without complications.[11] Prior antibiotic use is considered the major risk factor associated with the development of infection as a result of antibiotic-resistant strains; therefore, treatment recommendations were also divided into 2 categories based on the patient's history of antibiotic use in the previous 4 to 6 weeks. Lack of response to therapy within 72 hours was an arbitrary time established to define treatment failures.[11] The panel also stratified the efficacy of antibiotics by PD profile against *S pneumoniae* and *H influenzae* and used this as the basis for making its treatment recommendations (**Table 1**).

First-line therapy for adult patients with mild disease and no antibiotic therapy during the previous 4 to 6 weeks should include amoxicillin (high dose), amoxicillin/clavulanate, cefpodoxime proxetil, or cefuroxime axetil. Cefprozil is associated with a 20% to 25% bacteriologic failure rate. Although trimethoprim/sulfamethox-

Figure 2. CDC Pediatric Treatment Algorithm: Clinical Failure on Days 10 to 28



AOM = acute otitis media; CDC = Centers for Disease Control and Prevention; IM = intramuscular.
Source: Reference 4.

zole (TMP/SMX), doxycycline, azithromycin, clarithromycin, or erythromycin may be considered for patients with β-lactam allergies, bacteriologic failure rates of 20% to 25% are possible.[11] Additionally, the use of TMP/SMX has been associated rarely with potentially fatal toxic epidermal necrolysis.[11]

In adults with mild disease and recent antibiotic treatment as well as those with moderate disease and no previous antibiotic therapy, first-line treatment may be initiated with amoxicillin/clavulanate, amoxicillin (high dose), cefpodoxime proxetil, or cefuroxime axetil. Gatifloxacin, levofloxacin, and moxifloxacin are indicated for patients who are β-lactam allergic or intolerant.

First-line treatment for adults with moderate disease and recent antibiotic use include amoxicillin/clavulanate, gatifloxacin, levofloxacin, moxifloxacin, or combination therapy with amoxicillin or clindamycin for gram-positive coverage and cefixime or cefpodoxime proxetil for gram-negative therapy. However, the safety and effectiveness of these combination therapies has not been documented clinically.

There are relatively few studies of the efficacy of antibiotic therapies for children with acute sinusitis. Considerations for therapy are derived in part from antibiotic trials in children with AOM. For pediatric patients with mild disease and no recent antibiotic treat-

Table 1. Expected Clinical Efficacy Rates of Antibiotics in Acute Bacterial Rhinosinusitis in Adults and Children

Efficacy Rate	Adults	Children
>90%	Amoxicillin/clavulanate Gatifloxacin Levofloxacin Moxifloxacin	Amoxicillin/clavulanate Amoxicillin (high dose)*
80% to 90%	Amoxicillin (high dose)* Cefpodoxime proxetil Cefixime (based on *Haemophilus influenzae* and *Moraxella catarrhalis* coverage only) Cefuroxime axetil TMP/SMX	Cefpodoxime proxetil Cefixime (based on *Haemophilus influenzae* and *Moraxella catarrhalis* coverage only) Cefuroxime axetil Clindamycin (based on gram-positive coverage) Azithromycin Clarithromycin Erythromycin TMP/SMX
70% to 80%	Clindamycin (based on gram-positive coverage only) Cefprozil Azithromycin Clarithromycin Erythromycin	Cefprozil
50% to 70%†	Cefaclor Loracarbef	Cefaclor Loracarbef

TMP/SMX = trimethoprim/sulfamethoxazole.
*High-dose amoxicillin is not yet approved by the Food and Drug Administration.
†50% to 60% effective for adults and 60% to 70% effective for children.
Source: Sinus and Allergy Health Partnership. Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. *Otolaryngol Head Neck Surg* 2000;123(suppl):S1-S32. Adapted with permission.

ment, first-line agents that may be used include amoxicillin/clavulanate, amoxicillin (high dose), cefpodoxime proxetil, or cefuroxime axetil. Azithromycin, clarithromycin, erythromycin, and TMP/SMX are recommended if the patient has a history of type 1 hypersensitivity reaction to β-lactams. As with adults, TMP/SMX has been reported rarely to be associated with a significant risk of potentially fatal toxic epidermal necrolysis.[11]

Treatment for children with mild disease and recent antibiotic use or moder-

Table 2. Sinus and Allergy Health Partnership: Agents Recommended for Treatment of ABRS

Population	Mild Disease	Moderate Disease
Adults If no antibiotics in past 4 to 6 weeks	Amoxicillin (high dose)* Amoxicillin/clavulanate Cefpodoxime proxetil Cefuroxime axetil Alternatives† — limited effectiveness, bacterial failure rates 20% to 25%: Cefprozil Clarithromycin TMP/SMX Doxycycline Azithromycin Erythromycin	Amoxicillin (high dose)* Amoxicillin/clavulanate Cefpodoxime proxetil Cefuroxime axetil Alternatives†: Gatifloxacin Levofloxacin Moxifloxacin
Adults If antibiotics in past 4 to 6 weeks	Amoxicillin (high dose)* Amoxicillin/clavulanate Cefpodoxime proxetil Cefuroxime axetil Alternatives†: Gatifloxacin Levofloxacin Moxifloxacin	Amoxicillin/clavulanate Gatifloxacin Levofloxacin Moxifloxacin Combination therapy: Gram-positive coverage (amoxicillin or clindamycin) + gram-negative coverage (cefixime or cefpodoxime proxetil)
Children If no antibiotics in past 4 to 6 weeks	Amoxicillin (high dose)* Amoxicillin/clavulanate Cefpodoxime proxetil Cefuroxime axetil Alternatives† — limited effectiveness, bacterial failure rates 20% to 25%: TMP/SMX Azithromycin Clarithromycin Erythromycin	Amoxicillin (high dose)* Amoxicillin/clavulanate Cefpodoxime proxetil Cefuroxime axetil
Children If antibiotics in past 4 to 6 weeks	Amoxicillin (high dose)* Amoxicillin/clavulanate Cefpodoxime proxetil Cefuroxime axetil	Amoxicillin/clavulanate Combination therapy: Gram-positive coverage (amoxicillin or clindamycin) + gram-negative coverage (cefixime or cefpodoxime proxetil)

ABRS = acute bacterial rhinosinusitis; TMP/SMX = trimethoprim/sulfamethoxazole.
*High-dose amoxicillin is not yet approved by the Food and Drug Administration.
†For beta-lactam allergic patients.
Source: Sinus and Allergy Health Partnership. Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. *Otolaryngol Head Neck Surg* 2000;123(suppl):S1-S32. Adapted with permission.

ate disease and no recent antibiotic use may be initiated with amoxicillin/clavulanate, amoxicillin (high dose), cefpodoxime proxetil, or cefuroxime axetil. If *S pneumoniae* has been identified as the pathogen, clindamycin may be appropriate if the organism is resistant to amoxicillin. Azithromycin, clarithromycin, erythromycin, or TMP/SMX are recommended if the patient is β-lactam allergic. However, azithromycin and clarithromycin have been reported to fail in the prevention of streptococcal bacteremia, therefore, prescribing these antibiotics may not be advisable.[12] **Table 2** summarizes the Sinus and Allergy Health Partnership Guidelines for the treatment of acute bacterial rhinosinusitis in children and adults.

American Thoracic Society Treatment Recommendations for Acute Exacerbations of Chronic Bronchitis

An agent selected for treatment of acute exacerbations of chronic bronchitis (AECB) must be effective against β-lactamase-producing *H influenzae* and *M catarrhalis*, most DRSP, and *Staphylococcus aureus*. The following recommendations are based on the 1987 guidelines for the treatment of AECB developed by the American Thoracic Society. They have been updated to reflect current resistance patterns and recent PK/PD data. New guidelines are expected to be published this year.

Because amoxicillin is safe and relatively well tolerated, it is often the drug of choice for uncomplicated RTIs. However, the activity of amoxicillin is limited by β-lactamase production in *H influenzae, M catarrhalis, S aureus*, and gram-negative oral anaerobic species.

Doxycycline, a tetracycline, is also recommended as first-line therapy in patients 8 years of age and older. It is active against *S pneumoniae* and *M catarrhalis* but has poor activity against *H influenzae*.[13] It is appropriate as an alternative for penicillin-allergic patients. Because tetracyclines may cause permanent discoloration of the teeth in children younger than 8 years of age, this agent is not recommended for younger pediatric patients.

Agents that are recommended for second-line therapy or for use in patients with recent antibiotic therapy and in areas where the prevalence of resistant pathogens is high include amoxicillin/clavulanate, macrolides, cefdinir, and fluoroquinolones.

Recommendations for patients with complicated AECB include amoxicillin/clavulanate, azithromycin, cefdinir, clarithromycin, and fluoroquinolones. These patients include those older than 65 years of age or those who have moderate-to-severe chronic bronchitis, chronic bronchitis for more than 10 years, comorbidities (eg, congestive heart failure, renal failure, hepatic failure, cancer, diabetes mellitus, and compromised immune systems), ≥ 4 exacerbations per year, or individuals on chronic oxygen therapy.

Conclusion

Following the recommendations outlined in the treatment guidelines developed by the CDC, the Sinus and Allergy Health Partnership, and the American Thoracic Society will help clinicians decrease the use of inappropriate first-line antibiotics, improve clinical outcomes, and consequently, help prevent further development of resistance, especially to broad-spectrum agents that currently are effective against all predominant strains of respiratory pathogens. These guidelines can also be used by clinicians to educate patients about the role of antibiotics in bacterial and viral infections and the threat that antibiotic resistance poses for future treatment. Practice guidelines can help MCOs improve the overall quality of care for RTIs, enhance member/patient satisfaction with care, and contain the rising costs associated with RTIs. However, the success of these guidelines requires that MCOs commit financial resources, staff, and information

systems to the implementation and evaluation of their outcomes and that MCOs support the guidelines with sustained provider and patient education programs.

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