

Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention

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Background: Acute respiratory tract infection (ARTI) is the most common reason for antibiotic prescription in adults. Antibiotics are often inappropriately prescribed for patients with ARTI. This article presents best practices for antibiotic use in healthy adults (those without chronic lung disease or immunocompromising conditions) presenting with ARTI.

Methods: A narrative literature review of evidence about appropriate antibiotic use for ARTI in adults was conducted. The most recent clinical guidelines from professional societies were complemented by meta-analyses, systematic reviews, and randomized clinical trials. To identify evidence-based articles, the Cochrane Library, PubMed, MEDLINE, and EMBASE were searched through September 2015 using the following Medical Subject Headings terms: "acute bronchitis," "respiratory tract infection," "pharyngitis," "rhinosinusitis," and "the common cold."

High-Value Care Advice 1: Clinicians should not perform testing or initiate antibiotic therapy in patients with bronchitis unless pneumonia is suspected.

High-Value Care Advice 2: Clinicians should test patients with symptoms suggestive of group A streptococcal pharyngitis (for

example, persistent fevers, anterior cervical adenitis, and tonsillopharyngeal exudates or other appropriate combination of symptoms) by rapid antigen detection test and/or culture for group A Streptococcus. Clinicians should treat patients with antibiotics only if they have confirmed streptococcal pharyngitis.

High-Value Care Advice 3: Clinicians should reserve antibiotic treatment for acute rhinosinusitis for patients with persistent symptoms for more than 10 days, onset of severe symptoms or signs of high fever (>39 °C) and purulent nasal discharge or facial pain lasting for at least 3 consecutive days, or onset of worsening symptoms following a typical viral illness that lasted 5 days that was initially improving (double sickening).

High-Value Care Advice 4: Clinicians should not prescribe antibiotics for patients with the common cold.

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Acute respiratory tract infection (ARTI), which includes acute uncomplicated bronchitis, pharyngitis, rhinosinusitis, and the common cold, is the most common reason for acute outpatient physician office visits and antibiotic prescription in adults. Antibiotics are prescribed at more than 100 million adult ambulatory care visits annually, and 41% of these prescriptions are for respiratory conditions (1). Inappropriate antibiotic use for ARTI is an important contributor to antibiotic resistance, an urgent public health threat (2). In the United States, at least 2 million antibiotic-resistant illnesses and 23 000 deaths occur each year, at a cost to the U.S. economy of at least \$30 billion (2). Increased community use of antibiotics is highly correlated with emerging antibiotic-resistant infections. In places with greater prescribing of broad-spectrum antibiotics, specifically extended-spectrum cephalosporins and macrolides, rates of multidrug-resistant pneumococcal disease are higher (3).

Antibiotics are also responsible for the largest number of medication-related adverse events, implicated in 1 of every 5 visits to emergency departments

for adverse drug reactions (4). Adverse events range in severity from mild (for example, diarrhea and rash) to life-threatening (for example, Stevens-Johnson syndrome, anaphylaxis, or sudden cardiac death). Although data on adverse events after inappropriate antibiotic use are not available, an estimated 5% to 25% of patients who use antibiotics have adverse events, and about 1 in 1000 has a serious adverse event (2). *Clostridium difficile* diarrhea, which can be life-threatening and is usually a result of antibiotic treatment, causes nearly 500 000 infections and 29 300 deaths in the United States each year, leading to an estimated \$1 billion in extra medical costs (5).

See also:

- Summary for Patients 1
- Web-Only Supplement

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In 2009, direct antibiotic prescription costs totaled \$10.7 billion; 62% of these costs (\$6.5 billion) were attributed to antibiotic prescribing in the community setting, followed by \$3.6 billion in hospitals and \$527 million in nursing homes and long-term care facilities (6). An estimated 50% of antibiotic prescriptions may be unnecessary or inappropriate in the outpatient setting (7) (Unpublished data. Centers for Disease Control and Prevention), which equates to more than \$3 billion in excess costs. Over the past decade, antibiotic prescriptions have decreased by 18% among persons aged 5 years or older in the United States; however, prescriptions for broad-spectrum antibiotics (fluoroquinolones and macrolides) have increased by at least 4-fold (8). Reducing inappropriate antibiotic prescribing in the ambulatory setting is a public health priority.

This article by the American College of Physicians (ACP) and the Centers for Disease Control and Prevention presents available evidence on the appropriate prescribing of antibiotics for adult patients with ARTI. The high-value care advice is intended to amplify rather than replace messages from recent clinical guidelines on appropriate antibiotic prescribing (9-19) and serves as an update of the 2001 *Principles of Appropriate Antibiotic Use for Treatment of Acute Respiratory Tract Infections in Adults* (9) and a complement to the pediatric principles published in 2013 (20). The target audience for this article is all clinicians providing care to adults seeking ambulatory care for ARTI.

METHODS

We conducted a narrative review of evidence about appropriate antibiotic use for treatment of patients with ARTI syndromes, including acute uncomplicated bronchitis, pharyngitis, rhinosinusitis, and the common cold. We included current clinical guidelines from leading professional societies, such as the Infectious Diseases Society of America (IDSA). Clinical guideline recommendations were augmented with evidence-based meta-analyses, systematic reviews, and randomized clinical trials. To identify these evidence-based articles, we conducted literature searches in the Cochrane Library, PubMed, MEDLINE, and EMBASE through September 2015. We included only English-language articles and used the following Medical Subject Headings terms: "acute bronchitis," "respiratory tract infection," "pharyngitis," "rhinosinusitis," and "the common cold". The focus of the article was limited to healthy adults without chronic lung disease (such as cystic fibrosis, bronchiectasis, and chronic obstructive pulmonary disease) or immunocompromising conditions (congenital or acquired immunodeficiencies, HIV infection, chronic renal failure, nephrotic syndrome, leukemia, lymphoma, Hodgkin disease, generalized cancer, multiple myeloma, iatrogenic immunosuppression, or a history of solid organ transplantation). We present our findings for 4 ARTI syndromes and present a framework for antibiotic prescribing strategies for each (Table).

This article was reviewed and approved by the Centers for Disease Control and Prevention and by the ACP High Value Care Task Force, whose members are physicians trained in internal medicine and its subspecialties and which includes experts in evidence synthesis. The Task Force developed the high-value care advice statements, which are summarized in the Figure, based on the narrative review of the literature. At each conference call, all members of the High Value Care Task Force declared all financial and nonfinancial interests.

ACUTE UNCOMPLICATED BRONCHITIS

Acute uncomplicated bronchitis is defined as a self-limited inflammation of the large airways (bronchi) with a cough lasting up to 6 weeks. The cough may or may not be productive (24) and is often accompanied by mild constitutional symptoms. Acute bronchitis is among the most common adult outpatient diagnoses, with about 100 million (10%) ambulatory care visits in the United States per year (8), more than 70% of which result in a prescription for antibiotics (25, 26). Acute bronchitis leads to more inappropriate antibiotic prescribing than any other ARTI syndrome in adults (8).

Determining the Likelihood of a Bacterial Infection

More than 90% of otherwise healthy patients presenting to their outpatient providers with an acute cough have a syndrome caused by a virus (Table) (10, 21, 22). Nonviral pathogens, such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*, are occasionally identified in patients with acute bronchitis (10), and *Bordetella pertussis* may be considered in situations where transmission in the community has been reported. However, determining whether a patient has a viral or nonviral cause can be difficult. The presence of purulent sputum or a change in its color (for example, green or yellow) does not signify bacterial infection; purulence is due to the presence of inflammatory cells or sloughed mucosal epithelial cells. Acute bronchitis must be distinguished from pneumonia. For healthy immunocompetent adults younger than 70 years, pneumonia is unlikely in the absence of all of the following clinical criteria: tachycardia (heart rate >100 beats/min), tachypnea (respiratory rate >24 breaths/min), fever (oral temperature >38 °C), and abnormal findings on a chest examination (rales, egophony, or tactile fremitus) (10, 27).

Appropriate Management Strategies

The most recent clinical guidelines for management of acute uncomplicated bronchitis recommended against routine antibiotic treatment in the absence of pneumonia (11). A systematic review of 15 randomized, controlled trials found limited evidence to support the use of antibiotics for acute bronchitis and a trend toward increased adverse events in patients treated with antibiotics (28). A randomized, placebo-controlled trial (not included in the Cochrane review) comparing ibuprofen, amoxicillin-clavulanic acid, and placebo

Table. Antibiotic Prescribing Strategies for Adult Patients With Acute Respiratory Tract Infection

Variable	Acute Bronchitis	Pharyngitis	Acute Rhinosinusitis	Common Cold
Case definition	Productive or nonproductive cough that lasts up to 6 wk, with mild constitutional symptoms	Sore throat (often worse with swallowing) with a usual duration of 1 wk, with possible associated constitutional symptoms	Nasal congestion, purulent nasal discharge, maxillary tooth pain, facial pain or pressure, fever, fatigue, cough, hyposmia or anosmia, ear pressure or fullness, headache, and halitosis Symptoms have a variable duration (1 to 33 d) and sometimes take longer to resolve completely	Mild upper respiratory viral illness with sneezing, rhinorrhea, sore throat, cough, low-grade fever, headache, and malaise that lasts up to 14 d
Causes	Most cases are caused by viruses: influenza, rhinovirus, adenovirus, human metapneumovirus, coronavirus, parainfluenza, and respiratory syncytial virus. Nonviral causes include <i>Mycoplasma pneumoniae</i> and <i>Chlamydophila pneumoniae</i> .	Most cases are caused by viruses. Nonviral causes occur in <15% of cases and include group A β -hemolytic streptococci (most commonly) and groups C and G streptococci. Rare causes include <i>Arcanobacterium haemolyticum</i> , <i>Fusobacterium necrophorum</i> , <i>Neisseria gonorrhoeae</i> , <i>Corynebacterium diphtheriae</i> , <i>Staphylococcus aureus</i> , <i>Francisella tularensis</i> , <i>Yersinia pestis</i> , <i>Yersinia enterocolitica</i> , and <i>Treponema pallidum</i> .	Most cases are caused by viruses, allergies, or irritants. Nonviral causes occur in <2% of cases and include <i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> , <i>Streptococcus pyogenes</i> , <i>Moraxella catarrhalis</i> , and anaerobic bacteria.	All causes are viral. Leading causes include rhinovirus (up to 50%); coronavirus (10% to 15%); influenza (5% to 15%); respiratory syncytial virus (5%); parainfluenza (5%); and, less commonly, adenovirus, enterovirus, human metapneumovirus, and probably other unknown viruses (20).
Benefits of using antibiotics	No benefit	If the patient has a streptococcal infection, antibiotics may shorten the duration of illness and prevent acute rheumatic fever or suppurative complications.	Limited benefit	No benefit
Harms of using antibiotics	Mild reactions: diarrhea and rash Severe reactions: Stevens-Johnson syndrome Severe infection: <i>Clostridium difficile</i> -associated diarrhea Life-threatening reactions: anaphylactic shock and sudden cardiac death	Mild reactions: diarrhea and rash Severe reactions: Stevens-Johnson syndrome Severe infection: <i>Clostridium difficile</i> -associated diarrhea Life-threatening reactions: anaphylactic shock and sudden cardiac death	Mild reactions: diarrhea and rash Severe reactions: Stevens-Johnson syndrome Severe infection: <i>Clostridium difficile</i> -associated diarrhea Life-threatening reactions: anaphylactic shock and sudden cardiac death	Mild reactions: diarrhea and rash Severe reactions: Stevens-Johnson syndrome Severe infection: <i>Clostridium difficile</i> -associated diarrhea Life-threatening reactions: anaphylactic shock and sudden cardiac death
Antibiotic prescribing strategy	In the absence of pneumonia, antibiotics are not indicated. Routine testing for nonviral causes is not recommended.	Prescribe antipyretics and analgesics. β -Lactam antibiotics are indicated with positive results on a streptococcal test.	Antibiotics may be prescribed if symptoms last >10 d, severe symptoms last for >3 consecutive days, or worsening symptoms last after 3 consecutive days.	Antibiotics should not be used.
Recommended antibiotic regimen Persons without penicillin allergy	Never indicated	1) Oral penicillin V, 250 mg 4 times daily or 500 mg twice daily for 10 d 2) Oral amoxicillin, 50 mg/kg of body weight (maximum, 1000 mg) once daily or 25 mg/kg (maximum, 500 mg) twice daily for 10 d 3) Intramuscular benzathine penicillin G, single dose of 1 200 000 U	1) Oral amoxicillin, 500 mg, and clavulanate, 125 mg, 3 times daily for 5 to 7 d 2) Oral amoxicillin, 875 mg, and clavulanate, 125 mg, twice daily for 5 to 7 d 3) Oral amoxicillin, 500 mg 3 times daily for 5 to 7 d	Never indicated

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Table—Continued

Variable	Acute Bronchitis	Pharyngitis	Acute Rhinosinusitis	Common Cold
Persons with penicillin allergy	Never indicated	-	-	Never indicated
No history of type I hypersensitivity (anaphylaxis)	-	1) Oral cephalexin, 20 mg/kg twice daily (maximum, 500 mg/dose) for 10 d 2) Oral cefadroxil, 30 mg/kg once daily (maximum, 1 g) for 10 d	1) Oral doxycycline, 100 mg twice daily or 200 mg once daily for 5 to 7 d 2) Oral levofloxacin, 500 mg once daily for 5 to 7 d 3) Oral moxifloxacin, 400 mg once daily for 5 to 7 d	-
History of anaphylaxis	-	1) Oral clindamycin, 7 mg/kg 3 times daily (maximum, 300 mg/dose) for 10 d 2) Oral azithromycin, 12 mg/kg once daily (maximum, 500 mg) for 5 d 3) Oral clarithromycin, 7.5 mg/kg twice daily (maximum, 250 mg/dose) for 10 d	1) Oral doxycycline, 100 mg twice daily or 200 mg once daily for 5 to 7 d 2) Oral levofloxacin, 500 mg once daily for 5 to 7 d 3) Oral moxifloxacin, 400 mg once daily for 5 to 7 d	-
References	10, 11, 21, 22	12, 13	14-18	9, 19, 23

showed no significant differences in the number of days to cough resolution (24). Although macrolides (azithromycin) are frequently prescribed for patients with a cough, one study showed that patients with acute bronchitis treated with a macrolide had significantly more adverse events than those receiving placebo (29).

Patients may benefit from symptomatic relief with cough suppressants (dextromethorphan or codeine), expectorants (guaifenesin), first-generation antihistamines (diphenhydramine), decongestants (phenylephrine), and β -agonists (albuterol), although data to support specific therapies are limited. β -Agonists have not been shown to benefit patients without asthma or chronic obstructive lung disease (30), and symptomatic therapy has not been shown to shorten the duration of illness (30, 31). Over-the-counter symptomatic relief has a low incidence of minor adverse effects, including nausea, vomiting, headache, and drowsiness (32). Providers and patients must weigh the benefits and potential for adverse effects when considering symptomatic therapy.

High-Value Care Advice 1

Clinicians should not perform testing or initiate antibiotic therapy in patients with bronchitis unless pneumonia is suspected.

PHARYNGITIS

Pharyngitis is usually a benign, self-limited illness characterized by a sore throat that is worse with swallowing, with or without associated constitutional symptoms. It is a common outpatient condition, with about 12 million visits representing 1% to 2% of all ambulatory care visits in the United States annually (33). Although antibiotics are usually unnecessary, they are prescribed at most visits for pharyngitis (34).

Determining the Likelihood of a Bacterial Infection

Most pharyngitis cases have a viral origin; common causes include rhinovirus, coronavirus, adenovirus, herpes simplex virus, parainfluenza, enterovirus, Epstein-Barr virus, cytomegalovirus, and influenza (35). Patients with a sore throat and associated symptoms, including cough, nasal congestion, conjunctivitis, hoarseness, diarrhea, or oropharyngeal lesions (ulcers or vesicles), are more likely to have a viral illness and should not have further testing. Providers must rule out group A *Streptococcus*, the predominant bacterial pathogen, and exclude more serious infections (13). Patients with symptoms suggesting a bacterial cause should be tested for group A *Streptococcus* with a rapid antigen detection test, throat culture, or both. Suspicious symptoms include persistent fever, rigors, night sweats, tender lymph nodes, tonsillopharyngeal exudates, scarlatiniform rash, palatal petechiae, and swollen tonsils.

Clinical scoring criteria have been developed to help determine the likelihood of a bacterial cause. The most widely used are the modified Centor criteria, which include fever by history, tonsillar exudates, tender anterior cervical adenopathy, and absence of cough (36). Because the Centor criteria have a low positive predictive value for determining the presence of group A streptococcal infection, the IDSA suggests that they can be used to identify patients who have a low probability of group A streptococcal pharyngitis and do not warrant further testing (13). Patients who meet fewer than 3 Centor criteria do not need to be tested. Those who present with unusually severe signs and symptoms, such as difficulty swallowing, drooling, neck tenderness, or swelling, should be evaluated for rare throat infections (such as peritonsillar abscess, parapharyngeal abscess, epiglottitis, or Lemierre syndrome). Recent data suggest that *Fusobacterium necrophorum* is implicated in approximately 10% to 20% of endemic pharyngitis cases in adolescents (37,

Figure. Summary of the American College of Physicians and Centers for Disease and Control and Prevention advice for high-value care on appropriate antibiotic use for acute respiratory tract infection in adults.



SUMMARY OF THE AMERICAN COLLEGE OF PHYSICIANS AND CENTERS FOR DISEASE CONTROL AND PREVENTION ADVICE FOR HIGH-VALUE CARE ON APPROPRIATE ANTIBIOTIC USE FOR ACUTE RESPIRATORY TRACT INFECTION IN ADULTS

Disease/Condition	Acute respiratory tract infection (ARTI)
Target Audience	Primary care providers, emergency medicine providers
Target Patient Population	Healthy adults
Intervention	Reduction in antibiotic prescriptions
Evidence That Using Antibiotics in Patients With ARTI Does Not Improve Outcomes	Multiple randomized clinical trials have shown that antibiotics are ineffective for most ARTIs. There is no benefit for patients with the common cold or acute uncomplicated bronchitis and limited benefit for patients diagnosed with bacterial rhinosinusitis.
Harms of Using Antibiotics	Annual direct costs are \$6.5 billion and annual indirect costs are >\$30 billion in the United States. Antibiotics are responsible for 1 of every 5 emergency department visits for drug-related complications. Complications occur in 5% to 25% of patients who use antibiotics. Antibiotic-associated diarrhea caused by <i>Clostridium difficile</i> is the most common serious complication, responsible for 29 300 deaths in the United States per year.
Approaches to Overcome Barriers to Evidence-Based Practice	Multidimensional approaches involving active clinician education work best to reduce antibiotic prescriptions, including physician and patient education, physician audit and feedback, delayed antibiotic prescriptions, health information technology, and financial or regulatory incentives.
Talking Points for Clinicians When Discussing the Use of Antibiotics in Patients With ARTI	The average adult has 2 to 3 episodes of ARTI per year. Symptoms usually resolve in 1 to 2 weeks, but cough can last up to 6 weeks. Symptomatic treatment tailored to patient preferences may provide relief. Antibiotics do not cure most ARTIs or reduce time to resolution of symptoms. Antibiotics cause many serious adverse effects and should be reserved for patients with confirmed group A streptococcal pharyngitis.
High-Value Care Advice	High-Value Care Advice 1: <i>Clinicians should not perform testing or initiate antibiotic therapy in patients with bronchitis unless pneumonia is suspected.</i> High-Value Care Advice 2: <i>Clinicians should test patients with symptoms suggestive of group A streptococcal pharyngitis (for example, persistent fevers, anterior cervical adenitis, and tonsillopharyngeal exudates or other appropriate combination of symptoms) by rapid antigen detection test and/or culture for group A Streptococcus. Clinicians should treat patients with antibiotics only if they have confirmed streptococcal pharyngitis.</i> High-Value Care Advice 3: <i>Clinicians should reserve antibiotic treatment for acute rhinosinusitis for patients with persistent symptoms for more than 10 days, onset of severe symptoms or signs of high fever (>39 °C) and purulent nasal discharge or facial pain lasting for at least 3 consecutive days, or onset of worsening symptoms following a typical viral illness that lasted 5 days that was initially improving (double sickening).</i> High-Value Care Advice 4: <i>Clinicians should not prescribe antibiotics for patients with the common cold.</i>

38). It has also been implicated as a cause of Lemierre syndrome (39), which is a rare and life-threatening condition. The role of *F necrophorum* in pharyngitis and subsequent development of Lemierre syndrome warrant further study. Routine testing for *F necrophorum* is not recommended, but clinicians should remain vigilant and suspect Lemierre syndrome in adolescent and young adult patients with severe pharyngitis. Urgent diagnosis and treatment of Lemierre syndrome is necessary to preclude complications and death. Other rare bacterial causes are listed in the Table. No rapid diagnostic tests for other bacterial causes of pharyngitis exist, and the risks and benefits associated with antibiotic treatment are unclear.

Appropriate Management Strategies

The 2012 IDSA clinical guidelines recommend antibiotic therapy only for patients with a positive streptococcal test result (13). Patients with confirmed acute group A streptococcal pharyngitis should be treated for a duration likely to eradicate group A *Streptococcus* from the pharynx (usually 10 days) with an appropriate narrow-spectrum antibiotic. Specific regimens are listed in the Table.

Even though most pharyngitis cases are caused by viruses, more than 60% of adults presenting with a sore throat receive an antibiotic prescription (34). For patients diagnosed with group A streptococcal infection,

antibiotics shorten the duration of sore throat by 1 to 2 days, but the benefit is modest and the number needed to treat to reduce symptoms is 6 after 3 days of treatment and 21 after 1 week of treatment (40). Evidence suggests that antibiotics may prevent complications from group A streptococcal infection, including acute rheumatic fever (which is more common in children and adolescents than adults), peritonsillar abscess, and further spread of group A *Streptococcus* in outbreaks (40). However, little evidence supports the prevention of acute glomerulonephritis (40). Antibiotics are not recommended for chronic group A *Streptococcus* carriers because they are unlikely to spread infection to close contacts and are at little or no risk for complications. Tonsillectomy solely to reduce the frequency of group A streptococcal pharyngitis in adults is not recommended (13).

Adult patients with sore throat should be offered analgesic therapy, such as aspirin, acetaminophen, nonsteroidal anti-inflammatory drugs, and throat lozenges, which can help reduce pain. Salt water, viscous lidocaine, and other mixtures are often used in clinical practice for topical pain relief, but there are few data examining these approaches. Patients can be assured that the typical course of a sore throat is less than 1 week and that antibiotics are usually not needed because they do little to alleviate symptoms and may have adverse effects (12, 13, 40).

High-Value Care Advice 2

Clinicians should test patients with symptoms suggestive of group A streptococcal pharyngitis (for example, persistent fevers, anterior cervical adenitis, and tonsillopharyngeal exudates or other appropriate combination of symptoms) by rapid antigen detection test and/or culture for group A Streptococcus. Clinicians should treat patients with antibiotics only if they have confirmed streptococcal pharyngitis.

ACUTE RHINOSINUSITIS

Acute rhinosinusitis is usually a self-limited illness resulting from a viral infection, allergy, or irritant that causes inflammation of the mucosal tissue in the nasal and paranasal sinus cavity. Clinical symptoms include nasal congestion and obstruction, purulent nasal discharge, maxillary tooth pain, facial pain or pressure, fever, fatigue, cough, hyposmia or anosmia, ear pressure or fullness, headache, and halitosis. Symptom duration ranges from 1 to 33 days, with most episodes resolving within a week (41). More than 4.3 million adults are diagnosed with sinusitis annually, and more than 80% of ambulatory care visits result in an antibiotic prescription, most commonly a macrolide (42). Most antibiotic prescriptions for this condition are unnecessary (43).

Determining the Likelihood of a Bacterial Infection

Acute rhinosinusitis is usually caused by a viral pathogen. Acute bacterial rhinosinusitis (ABRS) is considered to be a secondary infection resulting from obstruction of the sinus ostia that leads to impaired mu-

cosal clearance as a result of a viral upper respiratory tract infection (URI). Fewer than 2% of viral URIs are complicated by ABRS (14). The gold standard for diagnosis of bacterial sinusitis is sinus puncture with aspiration of purulent secretions, although it is rarely performed. Common bacteria isolated from sinus puncture are listed in the **Table**. Radiographic imaging has no role in ascertaining a bacterial cause (14, 44). Although radiologic findings, such as mucous membrane thickening or sinus fluid or opacity, have a sensitivity of 90% in detecting a bacterial cause, the specificity is only 61% (44). Imaging is not helpful in guiding treatment because viral and bacterial causes have similar radiologic features, and it would increase costs by at least 4-fold (44).

Because ABRS lacks a simple and accurate diagnostic test, clinical guidelines recommend using clinical signs and symptoms to differentiate bacterial from viral causes (15). A bacterial cause is more likely when symptoms persist for more than 10 days without clinical improvement, symptoms are severe (fever $>39^{\circ}\text{C}$, purulent nasal discharge, or facial pain lasting for >3 consecutive days), or symptoms worsen after an initial period of improvement (double sickening) for more than 3 days. In addition, a patient with new-onset fever, headache, or increased nasal discharge after a typical viral URI that was initially improving is suspicious for a bacterial cause.

Appropriate Management Strategies

The 2012 IDSA clinical practice guidelines recommend empirical antibiotics as soon as a clinical diagnosis of ABRS is established on the basis of clinical criteria (15). Amoxicillin-clavulanate is the preferred agent, and doxycycline or a respiratory fluoroquinolone may be used as an alternative in patients with ABRS. The American Academy of Otolaryngology-Head and Neck Surgery emphasizes watchful waiting (without antibiotic therapy) as initial management for all patients with uncomplicated ABRS, regardless of severity (16). Some professional societies, including the American Academy of Allergy, Asthma & Immunology and the American Academy of Family Physicians, recommend amoxicillin as the preferred agent (17, 18). Although the IDSA recommendation is based on concern for antibiotic resistance, specifically ampicillin-resistant *Haemophilus influenzae* and *Moraxella catarrhalis*, no direct evidence suggests that amoxicillin-clavulanate is superior. Adjunctive therapy, such as intranasal saline irrigation or intranasal corticosteroids, has been shown to alleviate symptoms and potentially decrease antibiotic use (15). Patients who are seriously ill, who deteriorate clinically despite antibiotic therapy, or who have recurrent episodes should be referred to a specialist (for example, an otolaryngologist, infectious disease specialist, or allergist) (15).

Acute uncomplicated rhinosinusitis is a self-limited infection that usually resolves without antibiotics, even in patients with a bacterial cause. Most patients diagnosed with acute rhinosinusitis have more adverse effects than benefits from antibiotics (45). A meta-analysis

of adults with acute rhinosinusitis showed that the number needed to treat was 18 for 1 patient to be cured rapidly, but the number needed to harm from adverse effects from antibiotics was 8 (45).

Most patients with acute rhinosinusitis should be managed with supportive care (16); analgesics may be offered for pain, and antipyretics may be offered for fever. Additional therapies that may provide symptomatic relief include systemic or topical decongestants, saline nasal irrigation, mucolytics, intranasal corticosteroids, and antihistamines tailored to the patient's symptoms.

High-Value Care Advice 3

Clinicians should reserve antibiotic treatment for acute rhinosinusitis for patients with persistent symptoms for more than 10 days, onset of severe symptoms or signs of high fever (>39 °C) and purulent nasal discharge or facial pain lasting for at least 3 consecutive days, or onset of worsening symptoms following a typical viral illness that lasted 5 days that was initially improving (double sickening).

COMMON COLD (NONSPECIFIC UPPER RESPIRATORY INFECTION)

The common cold, a benign, self-limited illness, is the most common acute illness in the United States (19). It is a mild upper respiratory viral illness that may include some or all of the following symptoms: sneezing, rhinorrhea, sore throat, cough, low-grade fever, headache, and malaise. The symptoms are dependent on the host's inflammatory response to the particular viral infection (23). Complications of the common cold include acute bacterial sinusitis, asthma exacerbation, and otitis media; antibiotics play no role in preventing these complications (19, 46). There are about 37 million (3%) ambulatory care visits each year for the common cold, and roughly 30% result in an antibiotic prescription (47).

Causes

Multiple viruses have been associated with the common cold (Table). These viruses demonstrate seasonality and are spread through various routes of transmission: direct hand contact, contact with a contaminated environmental surface, or airborne droplets after an infected person sneezes or coughs (48). The most efficient means of transmission is direct hand contact; thus, the best method to reduce spread is appropriate handwashing.

Appropriate Management Strategies

Clinical guidelines state that symptomatic therapy is the appropriate management strategy for the common cold and that antibiotics should not be prescribed because they are not effective and lead to significantly increased risk for adverse effects (9, 19, 49). Patients seeking medical advice for the common cold should be advised that symptoms can last up to 2 weeks and should be advised to follow up with the clinician if symptoms worsen or exceed the expected time of re-

covery (9, 19, 49). They should also be apprised of the risks and benefits of symptomatic therapy and should be assured that antibiotics are not needed and may have adverse effects.

Symptomatic therapy is recommended for management of common cold symptoms. Although antihistamines have more adverse effects than benefits when used alone, 1 out of 4 patients treated with combination antihistamine-analgesic-decongestant products has significant symptom relief (50). Other symptomatic treatments that may offer relief include inhaled ipratropium bromide, inhaled cromolyn sodium, antitussives, and analgesics. Zinc supplements have been shown to reduce the duration of common cold symptoms in healthy persons if administered less than 24 hours after symptom onset; however, their potential benefits should be weighed against adverse reactions, such as nausea and bad taste (51, 52). No evidence supports the use of vitamins and herbal remedies, such as vitamin C or echinacea (53, 54).

High-Value Care Advice 4

Clinicians should not prescribe antibiotics for patients with the common cold.

DOES PRACTICE FOLLOW THE EVIDENCE?

Antibiotic prescribing for ARTI has decreased since the 1990s according to the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey, but the greatest reductions have been seen for ambulatory care visits for children (8, 55). This may be a result of the Centers for Disease Control and Prevention's "Get Smart: Know When Antibiotics Work" campaign and program, as well as efforts by state and local health departments to promote appropriate antibiotic use, especially among parents and providers who care for children (56–58). Furthermore, introduction of the pneumococcal conjugate vaccine for children has led to decreases in pneumococcal disease burden in both children and adults (59). Despite improvements, antibiotics are often prescribed for adults when they are not indicated, and broad-spectrum agents are prescribed at 61% of visits that lead to an antibiotic prescription even though a narrow-spectrum agent is usually preferred (1).

HOW CAN CLINICIANS PROMOTE APPROPRIATE ANTIBIOTIC PRESCRIPTION?

Over the past 2 decades, many interventions have been shown to decrease inappropriate antibiotic use by targeting physicians, patients, or both, including education, physician audit and feedback, delayed prescribing strategies, financial incentives, and health information technologies. Concern over patient satisfaction scores may limit the success of these interventions given that patient pressure plays a role in antibiotic overprescribing (60). However, patient satisfaction depends more on the patient-centered quality of the encounter, such as the provider spending enough time

with the patient to explain the patient's illness, than on the receipt of an antibiotic prescription (61).

To increase patient satisfaction and decrease antibiotic prescriptions for ARTI, we offer the following evidence-based strategies. Clinicians can promote appropriate antibiotic use by labeling acute bronchitis as a "chest cold" or "viral upper respiratory infection" (62) and providing patient information sheets about appropriate antibiotic use and alternatives to antibiotics for managing symptoms (www.cdc.gov/getsmart) (63). A recent study showed an 85% decrease in antibiotic prescribing for ARTI and increased satisfaction ratings when providers gave advice on symptomatic therapy and explained why antibiotics were not needed for ARTI (64). A symptomatic prescription pad can be used to provide recommendations for management of symptoms, allowing patients to walk away with a plan of action (Supplement, available at www.annals.org). When it is unclear whether an antibiotic is needed, delayed or postdated antibiotic prescriptions (also known as the wait-and-see approach) offer the possibility of future antibiotic treatment if the condition does not improve. This approach has also been shown to increase patient satisfaction and decrease antibiotic use (65).

Reducing antibiotic prescriptions on a large scale will require a multidimensional approach. A community-level, randomized trial in Massachusetts showed that implementing a multichannel intervention that includes targeting physician behavior, small-group education, disseminating educational materials to the community, and providing provider prescribing feedback in various settings further decreases antibiotic prescription rates (66). A systematic review of 39 studies showed that multifaceted interventions that combine physician, patient, and public education in various settings are most effective (67). In addition to education, examples of provider-level interventions that have been shown to be effective include audit and feedback and clinical decision support (68, 69). Although it is everyone's responsibility to use antibiotics appropriately, providers have the power to control prescriptions. Reducing inappropriate antibiotic prescribing will improve quality of care, decrease health care costs, and preserve the effectiveness of antibiotics.

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References

- Shapiro DJ, Hicks LA, Pavia AT, Hersh AL. Antibiotic prescribing for adults in ambulatory care in the USA, 2007-09. *J Antimicrob Chemother.* 2014;69:234-40. [PMID: 23887867] doi:10.1093/jac/dkt301
- Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013. Atlanta, GA: Centers for Disease Control and Prevention; 2014. Accessed at www.cdc.gov/drug-resistance/threat-report-2013 on 25 September 2015.
- Hicks LA, Chien YW, Taylor TH Jr, Haber M, Klugman KP; Active Bacterial Core Surveillance (ABCs) Team. Outpatient antibiotic prescribing and nonsusceptible *Streptococcus pneumoniae* in the United States, 1996-2003. *Clin Infect Dis.* 2011;53:631-9. [PMID: 21890767] doi:10.1093/cid/cir443
- Shehab N, Patel PR, Srinivasan A, Budnitz DS. Emergency department visits for antibiotic-associated adverse events. *Clin Infect Dis.* 2008;47:735-43. [PMID: 18694344] doi:10.1086/591126
- Lessa FC, Mu Y, Bamberg WM, Beldavs ZG, Dumyati GK, Dunn JR, et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med.* 2015;372:825-34. [PMID: 25714160] doi:10.1056/NEJMoa1408913
- Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Danziger LH. A national evaluation of antibiotic expenditures by healthcare setting in the United States, 2009. *J Antimicrob Chemother.* 2013;68:715-8. [PMID: 23148204] doi:10.1093/jac/dks445
- Hicks LA, Taylor TH Jr, Hunkler RJ. U.S. outpatient antibiotic prescribing, 2010 [Letter]. *N Engl J Med.* 2013;368:1461-2. [PMID: 23574140] doi:10.1056/NEJMc1212055
- Grijalva CG, Nuorti JP, Griffin MR. Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *JAMA.* 2009;302:758-66. [PMID: 19690308] doi:10.1001/jama.2009.1163
- Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman JR, et al. Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults: background, specific aims, and methods. *Ann Intern Med.* 2001;134:479-86. [PMID: 11255524] doi:10.7326/0003-4819-134-6-200103200-00013
- Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman JR, et al; American Academy of Family Physicians. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: background. *Ann Intern Med.* 2001;134:521-9. [PMID: 11255532] doi:10.7326/0003-4819-134-6-200103200-00021
- Snow V, Mottur-Pilson C, Gonzales R; American Academy of Family Physicians. Principles of appropriate antibiotic use for treatment of acute bronchitis in adults. *Ann Intern Med.* 2001;134:518-20. [PMID: 11255531] doi:10.7326/0003-4819-134-6-200103200-00020
- Cooper RJ, Hoffman JR, Bartlett JG, Besser RE, Gonzales R, Hickner JM, et al; American Academy of Family Physicians. Principles of

- appropriate antibiotic use for acute pharyngitis in adults: background. *Ann Intern Med.* 2001;134:509-17. [PMID: 11255530] doi:10.7326/0003-4819-134-6-200103200-00019
13. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2012;55:1279-82. [PMID: 23091044] doi:10.1093/cid/cis847
 14. Hickner JM, Bartlett JG, Besser RE, Gonzales R, Hoffman JR, Sande MA; American Academy of Family Physicians. Principles of appropriate antibiotic use for acute rhinosinusitis in adults: background. *Ann Intern Med.* 2001;134:498-505. [PMID: 11255528] doi:10.7326/0003-4819-134-6-200103200-00017
 15. Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJ, Hicks LA, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis.* 2012;54:e72-e112. [PMID: 22438350] doi:10.1093/cid/cir1043
 16. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok Kumar K, Kramper M, et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg.* 2015;152:S1-S39. [PMID: 25832968] doi:10.1177/0194599815572097
 17. Slavin RG, Spector SL, Bernstein IL, Kaliner MA, Kennedy DW, Virant FS, et al; American Academy of Allergy, Asthma and Immunology. The diagnosis and management of sinusitis: a practice parameter update. *J Allergy Clin Immunol.* 2005;116:S13-47. [PMID: 16416688]
 18. Aring AM, Chan MM. Acute rhinosinusitis in adults. *Am Fam Physician.* 2011;83:1057-63. [PMID: 21534518]
 19. Gonzales R, Bartlett JG, Besser RE, Hickner JM, Hoffman JR, Sande MA; American Academy of Family Physicians. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults: background. *Ann Intern Med.* 2001;134:490-4. [PMID: 11255526] doi:10.7326/0003-4819-134-6-200103200-00015
 20. Hersh AL, Jackson MA, Hicks LA; American Academy of Pediatrics Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics.* 2013;132:1146-54. [PMID: 24249823] doi:10.1542/peds.2013-3260
 21. Boivin G, Abed Y, Pelletier G, Ruel L, Moisan D, Côté S, et al. Virological features and clinical manifestations associated with human metapneumovirus: a new paramyxovirus responsible for acute respiratory-tract infections in all age groups. *J Infect Dis.* 2002;186:1330-4. [PMID: 12402203]
 22. Mosser AG, Vrtis R, Burchell L, Lee WM, Dick CR, Weisshaar E, et al. Quantitative and qualitative analysis of rhinovirus infection in bronchial tissues. *Am J Respir Crit Care Med.* 2005;171:645-51. [PMID: 15591468]
 23. Heikkinen T, Järvinen A. The common cold. *Lancet.* 2003;361:51-9. [PMID: 12517470]
 24. Llor C, Moragas A, Bayona C, Morros R, Pera H, Plana-Ripoll O, et al. Efficacy of anti-inflammatory or antibiotic treatment in patients with non-complicated acute bronchitis and discoloured sputum: randomised placebo controlled trial. *BMJ.* 2013;347:f5762. [PMID: 24097128] doi:10.1136/bmj.f5762
 25. Gonzales R, Aderer T, McCulloch CE, Maselli JH, Bloom FJ Jr, Graf TR, et al. A cluster randomized trial of decision support strategies for reducing antibiotic use in acute bronchitis. *JAMA Intern Med.* 2013;173:267-73. [PMID: 23319069] doi:10.1001/jamainternmed.2013.1589
 26. Barnett ML, Linder JA. Antibiotic prescribing for adults with acute bronchitis in the United States, 1996–2010. *JAMA.* 2014;311:2020-2. [PMID: 24846041] doi:10.1001/jama.2013.286141
 27. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA.* 1997;278:901-4. [PMID: 9302241]
 28. Smith SM, Fahey T, Smucny J, Becker LA. Antibiotics for acute bronchitis. *Cochrane Database Syst Rev.* 2014;3:CD000245. [PMID: 24585130] doi:10.1002/14651858.CD000245.pub3
 29. King DE, Williams WC, Bishop L, Shechter A. Effectiveness of erythromycin in the treatment of acute bronchitis. *J Fam Pract.* 1996;42:601-5. [PMID: 8656171]
 30. Becker LA, Hom J, Villasis-Keever M, van der Wouden JC. Beta2-agonists for acute cough or a clinical diagnosis of acute bronchitis. *Cochrane Database Syst Rev.* 2015;9:CD001726. [PMID: 26333656] doi:10.1002/14651858.CD001726.pub5
 31. Chang CC, Cheng AC, Chang AB. Over-the-counter (OTC) medications to reduce cough as an adjunct to antibiotics for acute pneumonia in children and adults. *Cochrane Database Syst Rev.* 2012;2:CD006088. [PMID: 22336815] doi:10.1002/14651858.CD006088.pub3
 32. Smith SM, Schroeder K, Fahey T. Over-the-counter (OTC) medications for acute cough in children and adults in community settings. *Cochrane Database Syst Rev.* 2014;11:CD001831. [PMID: 25420096] doi:10.1002/14651858.CD001831.pub5
 33. Schappert SM, Rechtsteiner EA. Ambulatory medical care utilization estimates for 2006. *Natl Health Stat Report.* 2008;1-29. [PMID: 18958997]
 34. Barnett ML, Linder JA. Antibiotic prescribing to adults with sore throat in the United States, 1997–2010. *JAMA Intern Med.* 2014;174:138-40. [PMID: 24091806] doi:10.1001/jamainternmed.2013.11673
 35. Alcaide ML, Bisno AL. Pharyngitis and epiglottitis. *Infect Dis Clin North Am.* 2007;21:449-69, vii. [PMID: 17561078]
 36. Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making.* 1981;1:239-46. [PMID: 6763125]
 37. Price SL, Hardy S, Gale P, Basten GP. Prevalence of *Fusobacterium necrophorum* in persistent sore throat samples. *Br J Biomed Sci.* 2011;68:209-10. [PMID: 22263437]
 38. Centor RM, Atkinson TP, Ratliff AE, Xiao L, Crabb DM, Estrada CA, et al. The clinical presentation of *Fusobacterium*-positive and streptococcal-positive pharyngitis in a university health clinic: a cross-sectional study. *Ann Intern Med.* 2015;162:241-7. [PMID: 25686164] doi:10.7326/M14-1305
 39. Hagelskjaer Kristensen L, Prag J. Lemierre's syndrome and other disseminated *Fusobacterium necrophorum* infections in Denmark: a prospective epidemiological and clinical survey. *Eur J Clin Microbiol Infect Dis.* 2008;27:779-89. [PMID: 18330604] doi:10.1007/s10096-008-0496-4
 40. Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. *Cochrane Database Syst Rev.* 2013;11:CD000023. [PMID: 24190439] doi:10.1002/14651858.CD000023.pub4
 41. Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Nicklas RA, et al; American Academy of Allergy, Asthma and Immunology (AAAAI). Rhinosinusitis: establishing definitions for clinical research and patient care. *J Allergy Clin Immunol.* 2004;114:155-212. [PMID: 15577865]
 42. Fairlie T, Shapiro DJ, Hersh AL, Hicks LA. National trends in visit rates and antibiotic prescribing for adults with acute sinusitis [Letter]. *Arch Intern Med.* 2012;172:1513-4. [PMID: 23007315] doi:10.1001/archinternmed.2012.4089
 43. Garbutt JM, Banister C, Spitznagel E, Piccirillo JF. Amoxicillin for acute rhinosinusitis: a randomized controlled trial. *JAMA.* 2012;307:685-92. [PMID: 22337680] doi:10.1001/jama.2012.138
 44. Benninger MS, Sedory Holzer SE, Lau J. Diagnosis and treatment of uncomplicated acute bacterial rhinosinusitis: summary of the Agency for Health Care Policy and Research evidence-based report. *Otolaryngol Head Neck Surg.* 2000;122:1-7. [PMID: 10629474]
 45. Lemiengre MB, van Driel ML, Merenstein D, Young J, De Sutter AI. Antibiotics for clinically diagnosed acute rhinosinusitis in adults. *Cochrane Database Syst Rev.* 2012;10:CD006089. [PMID: 23076918] doi:10.1002/14651858.CD006089.pub4
 46. Kenealy T, Arroll B. Antibiotics for the common cold and acute purulent rhinitis. *Cochrane Database Syst Rev.* 2013;6:CD000247. [PMID: 23733381] doi:10.1002/14651858.CD000247.pub3
 47. Schappert SM, Burt CW. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 2001–02. *Vital Health Stat 13.* 2006;1-66. [PMID: 16471269]

48. Turner RB. Epidemiology, pathogenesis, and treatment of the common cold. *Ann Allergy Asthma Immunol.* 1997;78:531-9. [PMID: 9207716]
49. Tan T, Little P, Stokes T; Guideline Development Group. Antibiotic prescribing for self limiting respiratory tract infections in primary care: summary of NICE guidance. *BMJ.* 2008;337:a437. [PMID: 18650239] doi:10.1136/bmj.a437
50. De Sutter AI, van Driel ML, Kumar AA, Lesslar O, Skrt A. Oral antihistamine-decongestant-analgesic combinations for the common cold. *Cochrane Database Syst Rev.* 2012;2:CD004976. [PMID: 22336807] doi:10.1002/14651858.CD004976.pub3
51. Singh M, Das RR. WITHDRAWN: Zinc for the common cold. *Cochrane Database Syst Rev.* 2015;4:CD001364. [PMID: 25924708] doi:10.1002/14651858.CD001364.pub5
52. Das RR, Singh M. Oral zinc for the common cold. *JAMA.* 2014;311:1440-1. [PMID: 24715076] doi:10.1001/jama.2014.1404
53. Hemilä H, Chalker E. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev.* 2013;1:CD000980. [PMID: 23440782] doi:10.1002/14651858.CD000980.pub4
54. Karsch-Völk M, Barrett B, Kiefer D, Bauer R, Ardjomand-Woelkart K, Linde K. Echinacea for preventing and treating the common cold. *Cochrane Database Syst Rev.* 2014;2:CD000530. [PMID: 24554461] doi:10.1002/14651858.CD000530.pub3
55. Centers for Disease Control and Prevention (CDC). Office-related antibiotic prescribing for persons aged ≤ 14 years—United States, 1993-1994 to 2007-2008. *MMWR Morb Mortal Wkly Rep.* 2011;60:1153-6. [PMID: 21881545]
56. Centers for Disease Control and Prevention. Get Smart: Know When Antibiotics Work. Atlanta, GA: Centers for Disease Control and Prevention; 2015. Accessed at www.cdc.gov/getsmart/community/index.html on 25 September 2015.
57. Gonzales R, Corbett KK, Wong S, Glazner JE, Deas A, Leeman-Castillo B, et al. "Get smart Colorado": impact of a mass media campaign to improve community antibiotic use. *Med Care.* 2008;46:597-605. [PMID: 18520314] doi:10.1097/MLR.0b013e3181653d2e
58. Weissman J, Besser RE. Promoting appropriate antibiotic use for pediatric patients: a social ecological framework. *Semin Pediatr Infect Dis.* 2004;15:41-51. [PMID: 15175994]
59. Nuorti JP, Whitney CG; Centers for Disease Control and Prevention (CDC). Prevention of pneumococcal disease among infants and children—use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine—recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2010;59:1-18. [PMID: 21150868]
60. Scott JG, Cohen D, DiCicco-Bloom B, Orzano AJ, Jaen CR, Crabtree BF. Antibiotic use in acute respiratory infections and the ways patients pressure physicians for a prescription. *J Fam Pract.* 2001;50:853-8. [PMID: 11674887]
61. Gonzales R, Steiner JF, Maselli J, Lum A, Barrett PH Jr. Impact of reducing antibiotic prescribing for acute bronchitis on patient satisfaction. *Eff Clin Pract.* 2001;4:105-11. [PMID: 11434073]
62. Phillips TG, Hickner J. Calling acute bronchitis a chest cold may improve patient satisfaction with appropriate antibiotic use. *J Am Board Fam Pract.* 2005;18:459-63. [PMID: 16322409]
63. Macfarlane J, Holmes W, Gard P, Thornhill D, Macfarlane R, Hubbard R. Reducing antibiotic use for acute bronchitis in primary care: blinded, randomised controlled trial of patient information leaflet. *BMJ.* 2002;324:91-4. [PMID: 11786454]
64. Mangione-Smith R, Zhou C, Robinson JD, Taylor JA, Elliott MN, Heritage J. Communication practices and antibiotic use for acute respiratory tract infections in children. *Ann Fam Med.* 2015;13:221-7. [PMID: 25964399] doi:10.1370/afm.1785
65. Mangione-Smith R, McGlynn EA, Elliott MN, McDonald L, Franz CE, Kravitz RL. Parent expectations for antibiotics, physician-parent communication, and satisfaction. *Arch Pediatr Adolesc Med.* 2001;155:800-6. [PMID: 11434847]
66. Finkelstein JA, Huang SS, Kleinman K, Rifas-Shiman SL, Stille CJ, Daniel J, et al. Impact of a 16-community trial to promote judicious antibiotic use in Massachusetts. *Pediatrics.* 2008;121:e15-23. [PMID: 18166533] doi:10.1542/peds.2007-0819
67. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database Syst Rev.* 2005:CD003539. [PMID: 16235325]
68. Mainous AG 3rd, Hueston WJ, Love MM, Evans ME, Finger R. An evaluation of statewide strategies to reduce antibiotic overuse. *Fam Med.* 2000;32:22-9. [PMID: 10645510]
69. Linder JA, Schnipper JL, Tsurikova R, Yu T, Volk LA, Melnikas AJ, et al. Documentation-based clinical decision support to improve antibiotic prescribing for acute respiratory infections in primary care: a cluster randomised controlled trial. *Inform Prim Care.* 2009;17:231-40. [PMID: 20359401]

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