PACE Pharmaceutical Assistance Contract for the Elderly

Alosa Health
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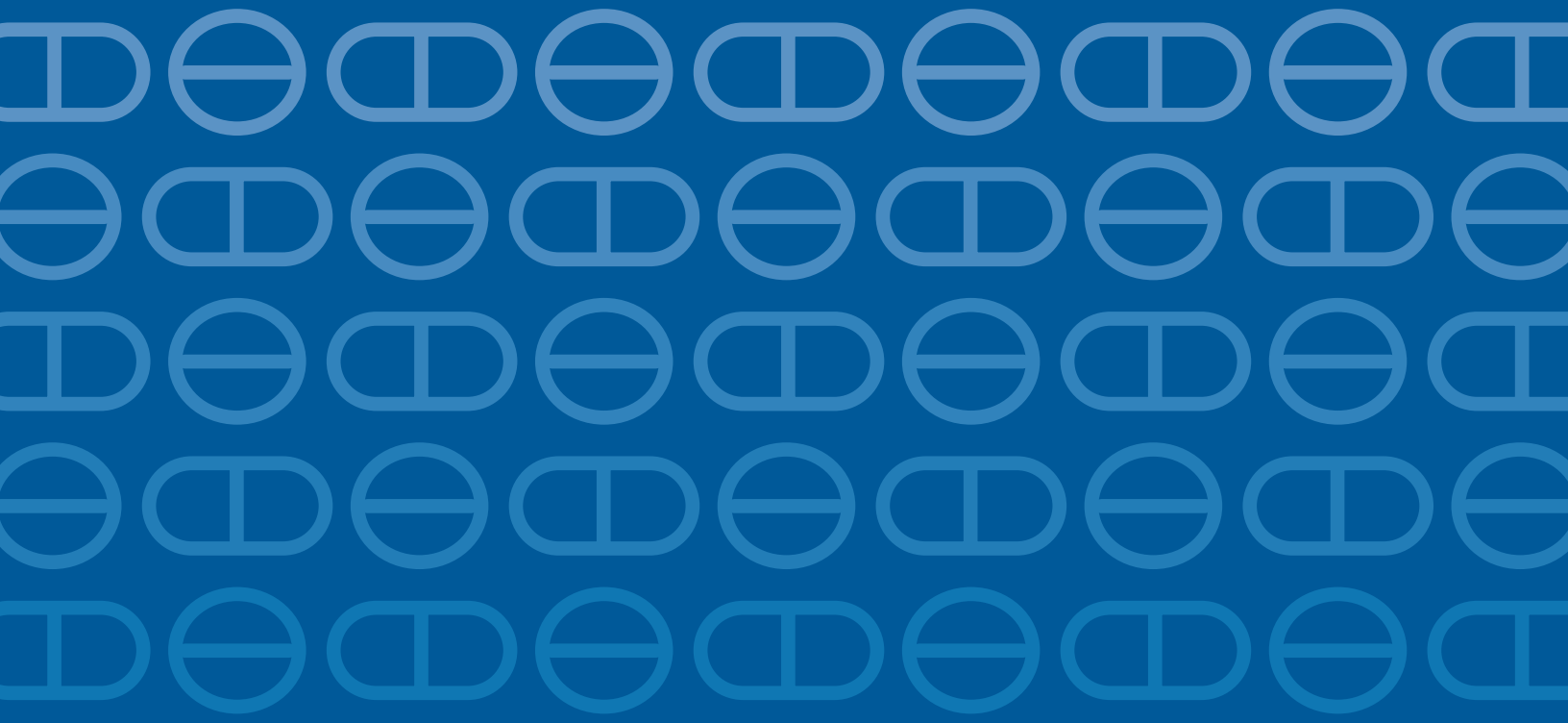
Clearing the air

Evidence-based management of respiratory infections in older adults



Clearing the air

Evidence-based management of respiratory infections in older adults

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These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition.

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Evidence-based management of respiratory infections in older adults

Activity Start Date: August 19, 2025
Activity Termination Date: August 18, 2028

This activity offers CE credit for:

1. Medicine (AMA)
2. Nurses (ANCC)
3. Other

All other attendees will receive a Certificate of Attendance

Activity Overview:

The goal of the educational program is to help practitioners diagnose and treat acute infections of the upper and lower respiratory system; understand the evidence regarding appropriate testing and treatment options; and improve the quality of prescribing and patient care.

The educational program includes a written evidence report (print monograph) and several non-CME/CE components:

1. Summary document of top 4-5 key messages
2. “Academic detailing” educational sessions in clinicians’ offices with trained outreach educators (pharmacists, nurses, physicians) who present the material interactively
3. Patient education information (brochure/tear off sheets)

This program synthesizes current clinical information on this topic into accessible, non-commercial, evidence-based educational material, which is taught interactively to providers by specially trained clinical educators.

Learning Objectives:

After completing this activity, participants will be able to:

- Describe ways to help prevent respiratory infections (e.g., vaccination, handwashing).
- Select appropriate tests to diagnose acute respiratory illnesses when needed.
- Implement communication strategies to speak with patients about the restricted role of antibiotics for many respiratory infections.
- Assess the risks and potential benefits of antiviral medications for viral infections.
- Identify respiratory illnesses that are either positively or probably of bacterial origin and select the best antibiotic for treatment.
- Employ effective symptom management strategies.

Financial Support:

There is no commercial support associated with this activity.

Target Audience:

The educational program is designed for primary care providers, including general internal medicine doctors, family practice physicians, nurse practitioners, physician assistants, nurses, and all other clinicians caring for patients who have acute respiratory infections.

Credit Information:

In support of improving patient care, this activity has been planned and implemented by CME Outfitters, LLC and Alosa Health. CME Outfitters, LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physicians: CME Outfitters, LLC, designates this enduring activity for a maximum of 1.25 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Nurses: This activity is designated for 1.25 nursing contact hours.

California Residents: This continuing nursing education activity was approved by the California Board of Registered Nursing. CME Outfitters LLC's provider number is CEP15510.

Disclosure Declaration

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This material is provided by Alosa Health, a nonprofit organization which accepts no funding from any pharmaceutical company. No commercial support has been received for this activity. All individuals including planners, authors, reviewers, academic detailers, staff, etc., who are in a position to control the content of this educational activity have reported no financial relationships related to the content of this activity.

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All identified Conflicts of Interest have been mitigated

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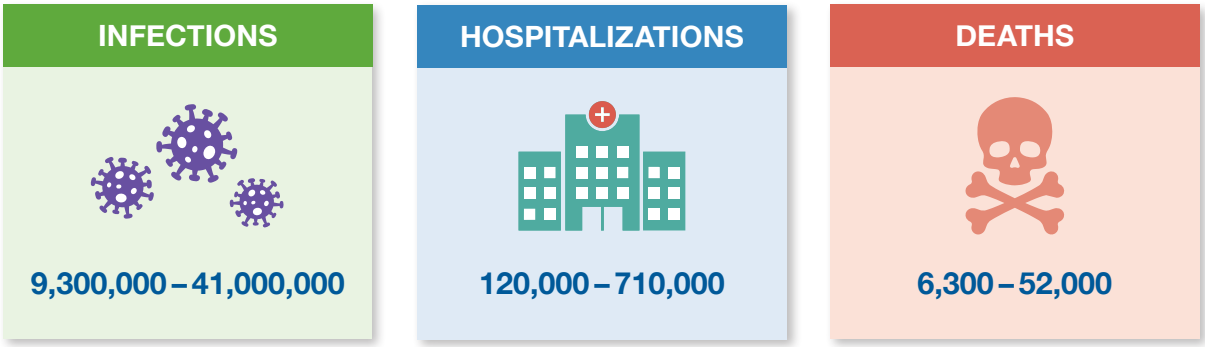
Introduction

Infections of the upper and lower respiratory tracts pose significant health risks to older adults, often leading to severe illness, hospitalization, and increased mortality.[1] Aging can weaken the immune system and impair lung function, making older individuals more vulnerable to these infections.[2] Additionally, older adults often have underlying health conditions that can increase the risk for severe respiratory infections.

Respiratory symptoms are among the most common complaints seen in primary care, with roughly 14 million adults aged ≥ 65 years visiting a clinician for upper respiratory symptoms in 2019.[3] Respiratory infections can also be deadly: older adults account for more than 80% of total pneumonia deaths.[4] Annual mortality from influenza ranges widely, from 6,300 to 52,000 between 2011 and 2024 (excluding the 2020/2021 season).[5] Between 2016 and 2023, there were 123,000 to 193,000 annual hospitalizations for people with respiratory syncytial virus (RSV), with the highest burden in adults 75 years or older.[6]

Figure 1: Annual mortality and morbidity ranges due to influenza, 2011 - 2024[5]*



Strategies for addressing respiratory infections must include prevention, effective treatment, and symptom management, while taking into account the unique vulnerabilities and characteristics of the older adult population. In addition, correct identification of viral vs. bacterial respiratory infections has implications at both the patient and population levels. Although viral upper respiratory infections (URIs) are far more common than bacterial infections and are usually self-limiting, viral URIs are associated with inappropriate use of antibiotics. A cohort study in nearly 6,136 adults with acute respiratory infections who were prescribed an antibiotic found that 41% of those prescriptions were not clinically indicated.[7] Antibiotics are not without risk, as they alter the microbiome, cause significant side effects in older adults, and potentially increase the prevalence of antibiotic-resistant pathogens.

This evidence document focuses on community-acquired respiratory infections of the upper and lower respiratory tract and summarizes the latest evidence for the diagnostic, treatment, and prevention options available to primary care clinicians.

Strategies when older patients seek care

When older patients come to a primary care clinician with a respiratory illness, their symptoms tend to cluster into three common acute respiratory syndromes:

- generalized viral illnesses (e.g., flu, COVID-19)
- community-acquired pneumonia
- sinusitis

The general approach when an older patient presents with symptoms such as cough, congestion, sore throat, fever, or body aches is to determine which of these syndromes is likely; this categorization will guide testing, symptom management, and treatment decisions. Many over-the-counter (OTC) products purporting to ease symptoms contain medications that may be ineffective or unsafe for older adults, hence it is important to focus on products or medications for which at least some data exist.

Testing is reserved for situations in which the results would plausibly change management, such as is the case for influenza and COVID-19 where antiviral medications are available and may be appropriate. Testing is not recommended for rhinoviruses, adenoviruses, parainfluenza virus, or human metapneumovirus. Testing typically involves antigen tests (i.e., immunoassays or "rapid tests") done at home or in the office. Rapid tests have high specificity (i.e., when positive for a target one can have high confidence in its accuracy), but low sensitivity (i.e., false negatives may be common). For this reason, in high risk patients with high clinical suspicion of infection, negative rapid tests should not be relied upon.[8] Nucleic acid amplification tests (PCR) are useful if antigen testing is negative and there is a clinical need to document a specific type of infection. PCR is slower but has both high specificity and high sensitivity. RSV testing is available OTC, but collected samples require mailing to a lab for analysis (PCR only), and the results do not generally affect treatment in an outpatient setting (where targeted antiviral treatment is generally not available).

Symptoms suggestive of a serious condition that would require more urgent care include:[8]

- fever >100.4°F
- hypoxemia (SpO2 <94% on room air)
- tachycardia
- hypotension
- exam signs of dehydration (poor oral intake, decreased urine output)

Older patients considered at higher risk for complications associated with a respiratory illness include those with lung disease, diabetes, chronic kidney disease, advanced liver disease, Class III obesity (i.e., body mass index (BMI) ≥40 kg/m^2), a compromised immune system (e.g., individuals with poorly controlled diabetes or HIV, or those taking corticosteroids, chemotherapy or other immunosuppressive therapies), or those with neurologic compromise (e.g., stroke).

Since most acute respiratory infections are viral, it is best to avoid antibiotics, although these may be needed for confirmed or suspected bacterial infections or in the context of a chronic lung disease such as asthma or chronic obstructive pulmonary disease (COPD).

BOTTOM LINE: When an older patient presents with cough, shortness of breath, fever, sore throat, congestion, or body aches, determine which of three syndromes is most likely present (generalized viral infection, pneumonia, or sinusitis), and then proceed with appropriate testing and treatment.

Managing symptoms of respiratory infections

The discomfort of respiratory infections can be addressed with a variety of symptom-targeted treatment options. A vast range of prescription, OTC products, and “natural” or herbal remedies exist and are used by patients in their attempts to ease symptoms. The goal for primary care clinicians is to direct patients to treatments known to be effective and to steer them away from treatments with little or no evidence of benefit. This may not only benefit the patient clinically, but can help them avoid wasting money on products or services that range from useless to harmful.

Congestion

Nasal congestion is a common symptom in upper respiratory infections as well as other kinds of allergic and non-allergic rhinitis. Many physiological agents, such as histamine, interleukins, and cell adhesion molecules, participate in an inflammatory response in nasal passages, which results in venous engorgement, increased nasal secretions, and tissue swelling. Treatments for nasal congestion attempt to alleviate symptoms by altering selected pathways in this inflammatory response.

Antihistamines

Since antihistamines can reduce nasal inflammation via blockage of histamine receptors, they may help alleviate congestion associated with respiratory infections--although their side effect profiles warrant caution in older adults. First generation antihistamines (e.g., diphenhydramine) cross the blood-brain barrier, leading to cognitive side effects, while second generation antihistamines (e.g., cetirizine) have minimal activity across the blood-brain barrier.

A Cochrane review of 18 randomized trials comparing antihistamine monotherapy (including both first- and second-generation agents) to placebo in 4,342 participants suffering from the common cold found a short-term beneficial effect of antihistamines on severity of overall symptoms: 45% had a beneficial effect on day 1 or 2 with antihistamines versus 38% with placebo (OR 0.74; 95% CI: 0.60-0.92).[9] Over longer periods (3-10 days), however, no difference between antihistamines and placebo was reported. No clinically significant effects on specific symptoms (e.g., nasal obstruction, rhinorrhea, sneezing) were reported. A similar pattern of modest short-term benefit but non-significant longer-term benefit was found in a sub-analysis of overall symptoms limited to sedating antihistamines.

It can be helpful to caution older patients that many combination cold and flu products contain first generation antihistamines such as diphenhydramine and that they should carefully read all labels.

Table 1: Antihistamine safety

	1st generation antihistamines	2nd generation antihistamines
Medication names	diphenhydramine, chlorpheniramine, brompheniramine, doxylamine	loratadine, cetirizine, fexofenadine
Safety	Avoid in older adults	Safe in older adults
Side effects	Significant cognitive side effects since they cross blood-brain barrier: sedation, delirium Other effects: urinary retention, constipation	Minimal cognitive side effects

Nasal steroids

Intranasal steroid sprays are reasonable for clinicians to recommend to patients, with the caveat that most of the data supporting their use comes from studies evaluating their ability to reduce congestion in non-infectious rhinitis. Intranasal corticosteroids exert anti-inflammatory activity that may reduce symptoms of congestion from respiratory infections as well as from seasonal and perennial allergic rhinitis. Available intranasal corticosteroids include beclomethasone dipropionate, budesonide, ciclesonide, flunisolide, fluticasone furoate, fluticasone propionate, mometasone furoate, and triamcinolone acetonide.[10] A Cochrane review of 24 randomized placebo-controlled trials in patients with non-allergic rhinitis (total N=4,452) involving a range of intranasal corticosteroids, doses, and methods of administration found low-quality evidence that these agents may improve symptoms when measured up to 4 weeks.[11] Treatment was associated with an increased risk of nosebleeds, but no differences in the rates of other adverse effects were reported. Given the minimal risks, clinicians may recommend intranasal saline sprays as a second line adjunctive therapy.

Oxymetazoline

Oxymetazoline is a partial alpha-adrenergic receptor agonist that, when applied intranasally, induces nasal vasoconstriction and reduces nasal turbinate volume. A pooled analysis of two randomized trials (total N=128) comparing oxymetazoline 0.05% nasal spray vs. placebo in adult patients with acute rhinitis showed pronounced improvements in the oxymetazoline group in objectively-assessed nasal flow rates in the first hour after administration, which declined, but remained statistically significant, over 12 hours.[12] Adverse effects were characterized as “mild” and included burning sensation or sinus pain in two subjects, itchy nose/eyes in another subject, and chills/sweating in one subject.[12] Dosing is typically twice daily for no longer than three days to avoid rebound congestion.[13] If rebound congestion occurs, administration of intranasal steroids (e.g., fluticasone) may help improve symptoms.[14]

Phenylephrine

Although early trials suggested that oral phenylephrine (10 mg) was an effective decongestant,[15] more recent trials have failed to replicate those findings.[16] In 2023 the U.S. Food and Drug Administration’s Nonprescription Drugs Advisory Committee concluded unanimously that oral phenylephrine was ineffective as a nasal decongestant.[17] (The panel did not address the use of phenylephrine when

administered as a nasal spray.) Nonetheless, as an oral ingredient, phenylephrine is still present in more than 250 products representing approximately $1.8 billion in annual sales.[18]

When used in a nasal spray, the typical dose is 2-3 sprays every 4 hours for no longer than 3 days (to reduce the chances of rebound congestion upon cessation).[19] Side effects include temporary sinus burning/tingling, runny nose, and sneezing.

Pseudoephedrine

Pseudoephedrine primarily works by stimulating alpha-adrenergic receptors, leading to vasoconstriction in the nasal passages, which reduces swelling and mucus production. Because pseudoephedrine can be used as a precursor molecule in the illicit manufacture of methamphetamine, it is kept behind the pharmacy counter, and purchasers are required to show photo identification and sign a log. States can impose limits on the amount of pseudoephedrine a patient can buy in a given period of time. For example, Pennsylvania limits pseudoephedrine purchase to 3.6 grams contained in a product or combination of products per day, and 9 grams in a product or combination of products per 30-day period.[20] Some states (but not Pennsylvania) have also classified pseudoephedrine as a controlled substance, making it available only via prescription.

Because it stimulates the sympathetic nervous system, pseudoephedrine can slightly raise blood pressure; slightly increase heart and respiration rate; narrow peripheral blood vessels; induce bronchodilation, and increase blood glucose levels.[21] Clinically, effects on blood pressure (1-2 mmHg) and heart rate (2-3 beats per minute) are likely small, and effects can be mitigated by avoiding large doses or immediate release formulations. Caution is advised in individuals with coronary artery disease, as case reports of large doses of pseudoephedrine triggering acute coronary syndrome have been reported.[22]

Oral pseudoephedrine (single 60 mg dose) was evaluated in a double-blind randomized trial in 238 patients with nasal congestion associated with the common cold.[23] Nasal airway resistance (NAR) was measured objectively. Subjective participant reports using a visual analog scale were also assessed. A single dose pseudoephedrine was superior to placebo on both objective (P=0.006) and subjective measures (P=0.029). After multiple doses (i.e., over 3 days) objective measures of NAR were still statistically significantly better in the pseudoephedrine group (P<0.001), but subjective measures were not significantly different. Mean heart rate in the pseudoephedrine group was 2-4 beats per minute higher in the pseudoephedrine group, but no adverse effects associated with the intervention were reported.

The efficacy of pseudoephedrine was also evaluated in a randomized, placebo-controlled trial that compared pseudoephedrine 60 mg vs. oral phenylephrine 12 mg vs. placebo in 39 patients with grass allergies who were exposed to grass pollen in a controlled setting and self-reported symptoms.[24] Mean decreases in nasal congestion scores at 6 hours were 21.7% for pseudoephedrine (P < 0.01 vs. placebo), 7.1% for phenylephrine (P=0.56 vs. placebo) and 2.2% for placebo.

Saline nasal washes

Nasal irrigation with a sterile saline solution may help relieve congestion and help clear nasal blockages, although evidence to date is relatively weak. A Cochrane review of five randomized trials (3 in children, N=544, and 2 in adults, N=205) compared saline irrigation to routine care or other nose sprays.[25] Most results showed no difference between nasal saline treatment and control. However, one larger trial, conducted with children, did show a significant reduction in nasal secretion score (mean difference -0.31;

95% CI: -0.48 to -0.14) and nasal obstruction score (MD -0.33; 95% CI: -0.47 to -0.19) in the saline group. The study authors note, however, that a MD of -0.33 on a four-point symptom scale may have minimal clinical significance.

Since nasal irrigation is safe and may offer some symptom relief it is a reasonable option to suggest to patients. Patient education is important: The water used should be sterile (not tap water), and any syringes and containers for flushes should be cleaned with hot, soapy water and left to dry before using. Administration is typically 1-3 times daily.

OTC sterile saline nasal sprays or nasal saline gels are another option to alleviate symptoms of congestion or nasal dryness. They can be used throughout the day.

BOTTOM LINE: The best options to alleviate nasal congestion are products containing pseudoephedrine (instruct patients to bring ID and ask at the pharmacy counter) or oxymetazoline. Nasal saline irrigation, second-generation antihistamines, and nasal steroids may be viable alternative options. Avoid oral phenylephrine and first-generation antihistamines such as diphenhydramine.

Cough

Cough is a complex physiological response mechanistically related to many organs and systems, including the lungs, larynx, ear, medulla, diaphragm, expiratory muscles, and the nerves controlling and coordinating all these parts. Because cough can be an adaptive bodily response that helps clear the lungs and airways, it should be treated cautiously.[26] Explain to patients that cough is one way our bodies try to combat infection and that cough suppression is, therefore, sometimes not advised. In addition, acute cough, which may be indicative of respiratory infection, needs to be distinguished from a chronic cough that may have many drivers including COPD, asthma, or gastroesophageal reflux disease.

Patients with a chronic cough, however, will often describe a worsening or change in the nature of their cough with an acute illness. Therefore, determining the chronicity and character of a patient's cough is crucial for accurate diagnosis and management, especially in patients with underlying lung disease who may be at risk for severe clinical outcomes with interval respiratory illness. The acute cough associated with respiratory infections may be treated in a variety of ways, although evidence for the efficacy of such treatments is generally weak.

Codeine

Codeine exerts cough suppressant activity by binding to opioid receptors in brain stem regions responsible for triggering the cough reflex. Although some older trials of codeine for cough suppression appeared to show efficacy,[27] more recent double-blind trials have failed to demonstrate efficacy compared to placebo—hence this is no longer a recommended intervention for cough management.[28-30] In addition, the significant side effects of codeine (e.g., constipation, somnolence) and its potential for abuse as an opioid have contributed to recommendations that it not be used as a cough suppressant.[31] Codeine requires a prescription. Liquid formulations combined with other symptomatic medications are typically Schedule V.

Cough drops

Cough drops are OTC lozenges which may contain an array of products, including menthol, benzocaine, herbs, or honey. Partly due to the heterogeneity of active ingredients, there is little high-quality data to evaluate the effectiveness of cough drops, although some small, poorly controlled studies have found that some formulations may reduce cough.[19] In general, cough drops are reasonable for patients to try, with the best evidence for drops containing honey and some evidence for drops that contain menthol. Instructing patients to avoid drops with high amounts of sugar may be worthwhile.

Dextromethorphan

Dextromethorphan decreases the sensitivity of cough receptors in the brain and is typically given as an oral liquid. A systematic review and meta-analysis of evidence on dextromethorphan vs. placebo found six trials with modest effect sizes favoring dextromethorphan for cough severity (SMD 0.37; 95% CI: 0.19-0.56) and cough frequency (SMD 0.40; 95% CI: 0.18-0.85).[27] Although generally safe at recommended doses, dextromethorphan is subject to abuse, and doses ≥1,500 mg/day can induce a state of psychosis including delusions, hallucinations, and paranoia.[32] It is found in more than 140 OTC cough and cold preparations and has overtaken codeine as the most widely-used cough suppressant.[32]

Guaifenesin

Guaifenesin is an OTC expectorant/mucolytic that can help with cough and congestion. A Cochrane review found three trials (N=604) comparing guaifenesin to placebo, with one trial (N=239) showing a 75% reduction in cough compared to 31% with placebo, but the other two trials were inconclusive and possibly underpowered.[33] Side effects can include dizziness, headache, and gastrointestinal disturbance.[34] Guaifenesin is available as tablets, gels, or liquids and as either immediate release or sustained-release (12-hour) products. It also appears in formulations that may include cough suppressants such as dextromethorphan or decongestants such as pseudoephedrine.

Honey

A 2021 meta-analysis of eight clinical trials evaluating honey as a treatment for cough associated with upper respiratory infections found significant benefits for cough frequency (standard mean difference [SMD] -0.36; 95% CI: -050 to -0.21) and cough severity (SMD -0.44; 95% CI: -0.64 to -0.25).[35] Honey can be taken by the spoonful or mixed in water or tea, although part of its mechanism of action may be related to the way it coats the throat, which might be reduced by dilution. Typical doses are 1-2 tablespoons 1 to 3 times daily. Honey can be taken with other medications and has very few potential adverse effects, although it does contain 17 grams of carbohydrates per tablespoon.

Antitussives with only weak evidence for efficacy

Evidence is too weak to support any recommendations for the following antitussives: benzonatate; cromolyn; vitamin C; antihistamines; bronchodilators (except in patients with COPD); gabapentin; zinc; tea; steroids; humidified air/cool mist; eucalyptus/menthol rubs; and probiotics.

BOTTOM LINE: Honey is the best option for treating cough related to a respiratory infection (1-2 tablespoons 2-3 times daily). Guaifenesin and dextromethorphan are viable alternatives. Avoid codeine for cough.

Sore throat

Acute sore throat (i.e., symptoms <10 days) are usually caused by viruses, hence antibiotics are not indicated (see page 30 for a discussion of treatments for streptococcal pharyngitis). Acetaminophen and/or ibuprofen are recommended for relief of acute sore throat pain by the European Society for Clinical Microbiology and Infectious Diseases based on a systematic review and six randomized clinical trials comparing these agents to placebo.[36]

Honey may also help alleviate sore throat pain, although supportive evidence is weak. A trial in 200 patients with sore throat randomized participants to either a range of medications (including antibiotics and antiseptic gargles) or those medications plus 1 tablespoon of honey twice daily. In evaluations at 5, 10, and 15 days, authors reported faster relief of signs and symptoms of sore throat in the honey group, although no statistics were presented in the paper.[37]

A randomized trial in 165 patients with acute, uncomplicated sore throat compared a lozenge containing benzocaine with a placebo lozenge and found benzocaine significantly (i.e., P=0.0086) reduced pain on a patient-reported pain scale, with median time to pain relief of 20 minutes.[38] Throat sprays containing the local anesthetic phenol are available and may provide some relief, but evidence is weak.[39] Swallowing phenol spray may cause stomach upset.

Evidence for a range of other treatments for sore throat, including Chinese herbal remedies, probiotics, and acupuncture is inconsistent and weak.[36] Menthol-based lozenges may help relieve sore throat pain because it acts as a mild local anesthetic, temporarily reducing nerve activity and causing a numbing sensation in the throat. However, an industry-sponsored study of antiseptic lozenges found only a small reduction in sore throat pain (a 1-unit difference on a 10-point scale).[40]

BOTTOM LINE: Treat sore throat pain with acetaminophen or ibuprofen, and use honey as an adjuvant if desired. Remedies containing menthol or other analgesics may provide temporary relief as well.

Pain/myalgias/fever

Fever, body aches, headache, and painful sore throat are common symptoms of respiratory infections, hence many patients seek relief from OTC preparations. Evidence supports using acetaminophen[41] or nonsteroidal anti-inflammatory drugs (NSAIDs)[42] such as ibuprofen or naproxen to address these symptoms.

Recommended dosing tips for older adults:[43]

- acetaminophen 500–1000 mg every 6 hours (maximum daily dose 3,250 mg)
- ibuprofen 200–400 mg every 6-8 hours (maximum daily dose 1,200–2,400 mg)
- Reduce maximum daily dose of acetaminophen for patients with liver disease to 2,000 mg
- Ibuprofen and acetaminophen can be used together

Dehydration

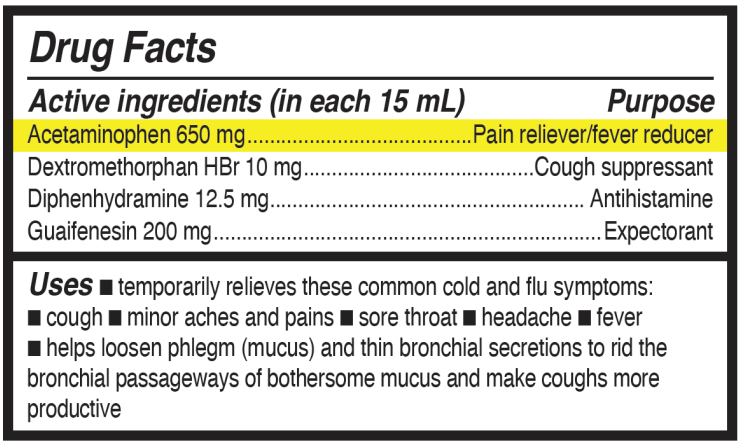
Dehydration in older people is an easily-overlooked variable in the overall health equation, particularly in those taking a diuretic. Dehydration has been associated with increased severity of illness, length of hospital stay, readmission, in-hospital mortality, and costs for health services.[44,45] Dehydration may also

impair cognition and increase risk of metabolic and renal disease, although evidence for this effect is weak.[44,45]

Reading OTC product labels

While many products address symptoms, the pharmacy aisle is overwhelming with the myriad of combination products available. Patients should understand what is in the combination product being purchased. In many cases, components could be ineffective (e.g., phenylephrine) or harmful (e.g., diphenhydramine or doxylamine). Counsel patients to read labels carefully, because many combination products contain acetaminophen or an NSAID as an active ingredient—so it is easy to overdo these agents.

Figure 2: Example drug facts on an OTC label



This is for educational purposes only and does not reflect any particular product.

Teaching tips for reading the label

- Avoid combinations with phenylephrine
- Avoid combinations with first generation antihistamines
  - diphenhydramine
  - doxylamine
  - chlorpheniramine
  - brompheniramine
- Look for the amount of acetaminophen or ibuprofen
- Watch out for liquids with alcohol content.

BOTTOM LINE: Acetaminophen and ibuprofen are reasonable choices for managing fever, pain, and myalgia in older adults with respiratory infections. Encourage product label review to avoid exceeding dosing limits.

Generalized viral illnesses

Syndromes caused by the common cold (i.e., infection with adenoviruses or rhinoviruses), influenza, COVID-19, and RSV can all present as generalized infections. It may be hard to differentiate between upper respiratory tract infections and community-acquired pneumonia (CAP). Typically, exposure, duration of symptoms, and respiratory effects can help differentiate the two syndromes.

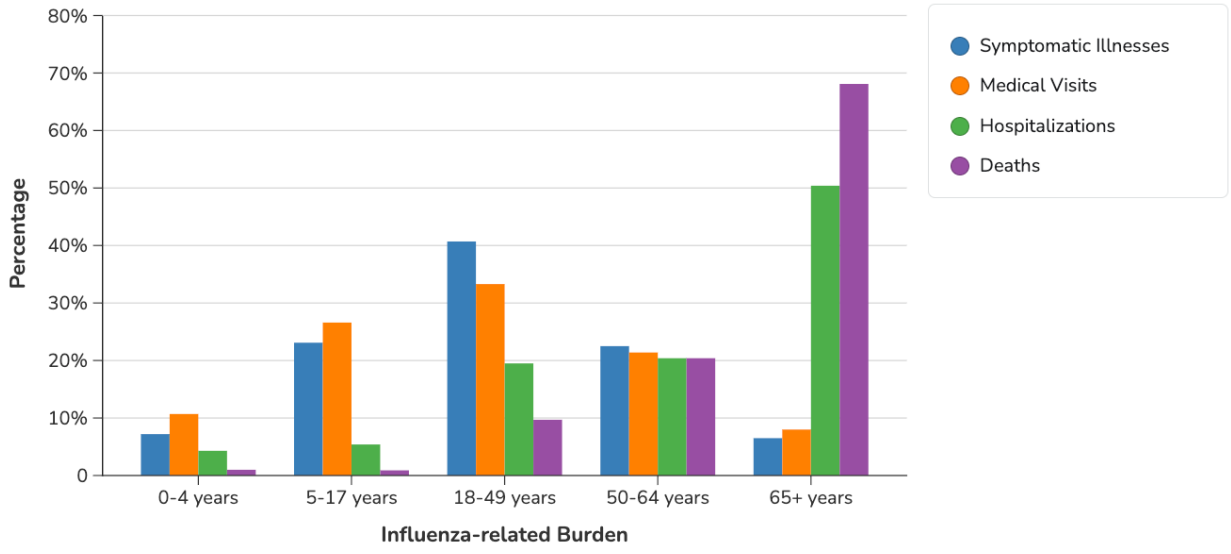
Influenza

The severity and extent of seasonal influenza outbreaks vary considerably from year to year. This variation is driven by the virulence of the circulating viruses, the effectiveness of the vaccines developed each year against those viruses, and the extent and timing of mass influenza vaccinations.

In the 2023-2024 influenza season, the Centers for Disease Control and Prevention (CDC) estimates that between 34 million and 63 million people in the U.S. became ill with the flu, between 380,000 and 790,000 people were hospitalized, and between 24,000 and 69,000 people died.[46] In Pennsylvania, roughly 4,300 people (mostly adults) are hospitalized weekly for influenza at the peak of an average influenza season.[47]

The morbidity and mortality burden falls heavily on older adults (i.e., age ≥ 65 years), as illustrated in Figure 3. Despite representing only 8% of medical visits for flu, adults over 65 represented 70% of influenza deaths.[48]

Figure 3: Influenza morbidity and mortality burden by age, 2022-2023[48]



Despite the proven efficacy of influenza vaccines and the risks of influenza, only 48.5% of adults in the U.S. received the flu vaccine in the 2023-2024 influenza season.[49] The rate of influenza vaccination varied by age, with nearly 74% of adults aged ≥ 65 years getting a flu shot, but only 37.5% of adults aged 18-49 years doing so.[49]

Clinical presentation

Influenza typically presents with fever, chills, and body aches, with both upper and lower respiratory symptoms. Gastrointestinal (GI) symptoms may be present in those infected with influenza A, but they are more common in those infected with influenza B. Both types of Influenza infection leave their hosts susceptible to post-viral pneumonia.

Testing

Recommended when the results of the test would inform or alter management of the disease, immunoassay (i.e., "rapid tests") have high specificity (i.e., when positive for a target one can have high confidence in its accuracy) but low sensitivity (i.e., false negatives may be common). Influenza antigen tests are now available OTC.

Table 2: Addressing influenza antigen test results

Positive tests give high confidence for an influenza infection (specificity > 90%).

Negative tests can occur in up to 45% of patients who have influenza (sensitivity 55-85%). Retest if necessary, with a second antigen test or PCR, which is a definitive diagnostic test.[50]

Treatment

Empiric initiation of antiviral therapy may be appropriate even without testing if a patient is at high risk of complications, symptoms are consistent with influenza, and the antiviral can be given within 48 hours of symptom onset.[8] The neuraminidase inhibitors oseltamivir and zanamivir are available, as is the endonuclease inhibitor baloxavir (see Table 3). Amantadine and rimantadine have not been recommended since 2018 because of widespread resistance to these agents.[50]

Table 3: Dosing strategies for influenza antiviral medications[51-53]

	Baloxavir (Xofluza)	Oseltamivir (Tamiflu, generics)	Zanamivir (Relenza)
Mechanism	endonuclease inhibitor	neuraminidase inhibitor	neuraminidase inhibitor
Route	Oral	Oral	Inhaled
Dose	< 80 kg: 40 mg ≥ 80 kg: 80 mg	75 mg twice daily	10 mg twice daily
Usual duration	One time	5 days	5 days
Notes			Not recommended for patients with underlying airway disease

Neuraminidase inhibitors

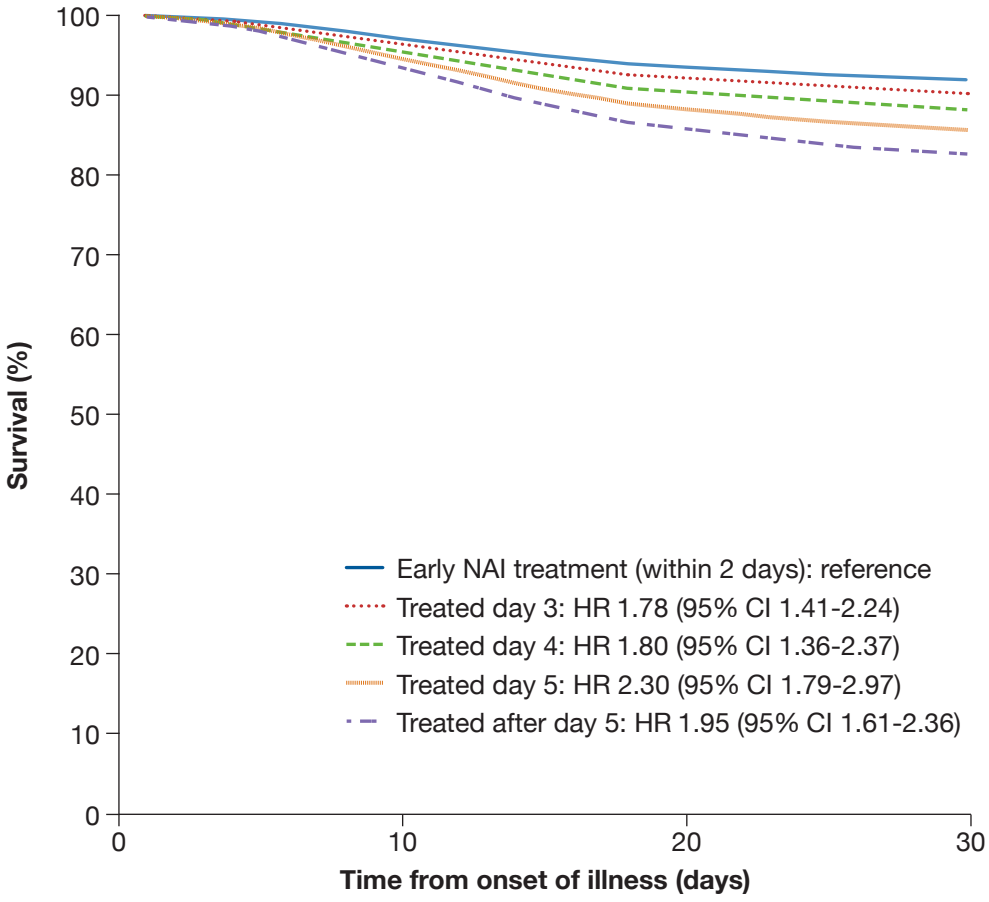
A Cochrane meta-analysis of eight placebo-controlled trials (N=3,954) of oseltamivir found a modest reduction in symptom duration (mean difference [MD] -16.76 hours; 95% CI: -25.1 to -8.42 hours).[54] A slightly larger meta-analysis (nine trials, N=4,328 patients) found that oseltamivir at 75 mg twice daily

shortened the time to alleviation of symptoms by 21% versus placebo recipients (time ratio 0.79; 95% CI: 0.74-0.85).[55] The median times to alleviation were 97.5 hours for oseltamivir and 122.7 hours for placebo groups (difference -25.2 hours; 95% CI: -36.2 to -16.0 hours). The oseltamivir subpopulation with lab-confirmed influenza also had fewer lower respiratory tract complications requiring antibiotics more than 48 hours after randomization (risk ratio [RR] 0.62; 95% CI: 0.49-0.79) and a trend toward fewer hospital admissions for any cause (RR 0.61; 95% CI: 0.36-1.03).

A meta-analysis of 13 trials of zanamivir vs. placebo (N=5,411) found similar modest reductions in symptom duration (MD -0.6 days; 95% CI: -0.81 to -0.39 days).[54]

The effectiveness of neuraminidase inhibitors is critically associated with how quickly they are initiated, as evidenced by mortality data from a meta-analysis of trial data in hospitalized patients in which a benefit was seen when the drug was started ≤ 2 days (OR 0.50; 95% CI: 0.37-0.67) but not when started >2 days after symptom onset (OR 1.20; 95% CI: 0.93-1.54) (Figure 4).[56]

Figure 4: Mortality benefit of neuraminidase inhibitors in hospitalized patients declines with increasing latency of initiation[56]



Commonly-reported adverse effects of neuraminidase inhibitors include nausea, headache, and diarrhea, although the rate of side effects resulting in treatment limitation or discontinuation in reported trials was not statistically significantly different from placebo.[56]

Baloxavir

Baloxavir is a polymerase inhibitor that has shown antiviral activity against influenza A and B viruses in vitro, including strains resistant to current antiviral agents.[57] A phase 3 trial compared baloxavir (40-80 mg) to either placebo or oseltamivir in 1,064 patients (aged 12-64 years) with acute uncomplicated influenza.[57] Median time to alleviation of symptoms was 53.7 hours (95% CI: 49.5 to 58.5 hours) with baloxavir, compared to 80.2 hours (95% CI: 72.6 to 87.1) with placebo (Figure 5). The time to alleviation of symptoms was similar with baloxavir and oseltamivir. Adverse events (mostly GI-related) were reported in 20.7% of baloxavir recipients, 24.6% of placebo recipients, and 24.8% of oseltamivir recipients (differences not statistically significant).

Figure 5: Alleviation of symptoms with baloxavir vs. placebo[58]

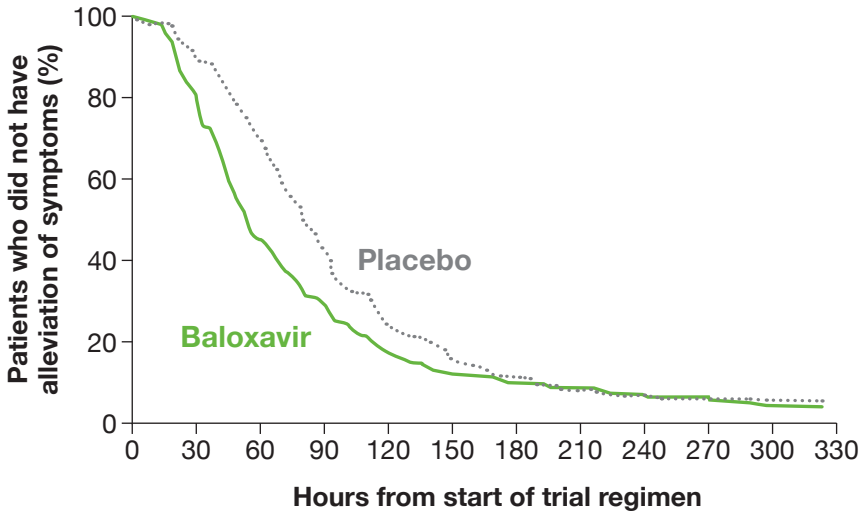


Table 4: Efficacy summary of antivirals for influenza[54-56,58,59]

Antiviral	Symptom improvement	Hospitalization	Mortality	Adverse effects
Baloxavir (Xofluza)	1 day reduction	**50% relative reduction** among high-risk patients	no reduction	nausea—more common in older adults (6%) than younger (1%)
Oseltamivir (Tamiflu, generics)	½ day reduction	**63% relative reduction** in patients with laboratory confirmed influenza	**may reduce mortality if started < 48 hours** for patients requiring hospitalization	nausea, vomiting, headache
Zanamivir (Relenza)	½ day reduction	no data	no reduction	

Green = effective

Corticosteroids

Corticosteroids should generally be used for influenza-associated acute exacerbations of COPD or asthma, but a meta-analysis of 15 studies in which corticosteroids were used as adjunctive treatments to antivirals in the inpatient setting found an almost 4-fold increased risk of mortality when the combination was used (OR 3.90; 95% CI: 2.31-6.60) compared to influenza treatment without corticosteroids.[60] Corticosteroids should not be used to treat influenza-associated symptoms in the outpatient setting.

Prevention

Antivirals approved to treat influenza can also be used to prevent infection in cases where a confirmed exposure to influenza exists. When used as influenza prophylaxis of close contacts in a study involving 10,064 residents of aged care facilities, oseltamivir was found to very significantly reduce the rate of influenza cases (RR 0.10; 95% CI: 0.08-0.12).[61] The efficacy of baloxavir for prophylaxis was evaluated in a randomized double-blind study of 752 household contacts of 545 index patients with confirmed influenza.[62] The rate of subsequent influenza in the close contacts was 1.9% in the baloxavir group vs. 13.6% in the placebo group (adjusted RR 0.14; 95% CI: 0.06-0.30).

Encourage prophylaxis in high-risk patients, particularly if they cannot be vaccinated. Discuss prophylaxis with all vaccinated high-risk patients and those who have contact with such patients. Start prophylaxis within 48 hours of exposure.[62,63] Annual vaccination with high dose or adjuvant formulations is recommended for patients aged ≥65 years. Ideally, vaccination should occur in September or October, but the vaccine can be given at any time during the influenza season.

BOTTOM LINE: neuraminidase inhibitors or baloxavir when started within 48 hours of symptom onset can modestly reduce time to symptom resolution in patients with influenza. Oseltamivir can significantly reduce the risk of developing bacterial pneumonia. Adjunctive use of corticosteroids, while recommended for patients with COPD or asthma exacerbations, likely increases mortality risk in inpatient settings among those without comorbid conditions and plays no role in the outpatient setting.

COVID-19

Although the SARS-CoV-2 (i.e., COVID-19) public health emergency ended in 2023, the virus is still circulating and people continue to die from it. The CDC reported more than 900 deaths every week from COVID-19 in the U.S. during January 2025, and even in May 2025, roughly 100 people a week were dying of a COVID-19-associated illness.[64] The virus continues to evolve, with more than a dozen variants (e.g., Omicron subtypes) currently being monitored by the CDC.[65]

As with other infectious diseases, older adults are at higher risk for COVID-19-related severe illness or death, hence vaccination in this population remains a public health priority. Nationwide about 91% of the ≥65 population have had at least one COVID-19 vaccine (89.3% in Pennsylvania).[66] However, only 38% nationwide are up to date with current COVID-19 vaccine recommendations (42% in Pennsylvania), a gap that leaves older adults at high risk for COVID-19-related negative outcomes.

Clinical presentation

Patients ill with COVID-19 can present with a diverse constellation of symptoms, including some that are not generally seen with other viral respiratory infections, such as altered sense of taste. COVID-19 has also been associated with long-lasting syndromes (i.e., “long COVID”) which are poorly understood.

Testing

Although routine during the pandemic, testing of asymptomatic people is no longer recommended unless a risk of transmitting the virus to at-risk individuals exists. Testing of symptomatic patients is recommended for high-risk patients or for low- or moderate-risk patients if the result will influence prescribing choices or need for further diagnostic testing.

Table 5: Addressing COVID-19 antigen test results

Positive tests give high confidence that COVID-19 is present (specificity > 90%).

Negative tests can occur in up to 40% of patients who have COVID-19 (sensitivity 60-85%). Retest, if necessary, with an antigen test or PCR, which is a more definitive diagnostic test.[50]

Treatment

Antiviral medications can be a component of COVID-19 treatment, particularly for individuals at high risk of developing severe illness. As with antivirals for influenza, antivirals for COVID-19 are most effective when started as soon as possible after a positive test and within 5 days of symptom onset.

Table 6: Antiviral medications for COVID-19

	Nirmatrelvir-ritonavir (Paxlovid)	Molnupiravir (Lagevrio)
Mechanism	Nirmatrelvir: SARS-CoV-2 main protease inhibitor; Ritonavir: CYP3A inhibitor	nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis
Route	Oral	Oral
Dose	300 mg nirmatrelvir (two 150 mg tablets) 100 mg ritonavir Taken twice daily	800 mg (four 200 mg capsules) Taken twice daily
Usual duration	5 days	5 days
Notes	FDA approved	Emergency use authorization

Nirmatrelvir-ritonavir

A 2022 trial randomized 2246 COVID-19-symptomatic unvaccinated, non-hospitalized adults at high risk for progression to severe disease to nirmatrelvir-ritonavir or placebo.[67] By day 28 the incidence of COVID-19-related hospitalization or death was 6.32% lower in the nirmatrelvir-ritonavir group vs. the placebo group (95% CI: −9.04% to −3.59%). The absolute incidence of COVID-19-related hospitalization or death

by day 28 was 0.77% (3 of 389 patients) in the nirmatrelvir-ritonavir group, with 0 deaths, compared with 7.01% (27 of 385 patients) in the placebo group, with 7 deaths.

A 2024 randomized controlled trial (RCT) in 1,288 patients with COVID-19 (vaccinated and non-vaccinated), however, found less convincing evidence of symptom alleviation for nirmatrelvir-ritonavir. The median time to sustained symptom alleviation was 12 days in the nirmatrelvir–ritonavir group and 13 days in the placebo group, (P=0.60).[68] Similar non-significant results were reported in the high-risk subgroup (vaccinated participants with at least one risk factor for severe illness). Adverse events were more common in the nirmatrelvir/ritonavir group (7.8%) than in the placebo group (3.8%).[68] This difference was largely attributed to dysgeusia (4.5% vs. 0.2%) and diarrhea (1.3% vs. 0.2%), which were the only treatment-related adverse events reported in at least 1% of the treatment group.

A meta-analysis of 11 observational studies of nirmatrelvir-ritonavir in patients with COVID-19 at higher risk of developing severe disease (regardless of vaccination status) showed a 59% reduced risk of death (OR 0.4; 95% CI: 0.35-0.52) and a 53% reduction in the risk of hospital admission (OR 0.47; 95% CI: 0.36-0.60).[69] A subgroup analysis by vaccination status found that the risk of mortality or hospitalization was reduced by 47% in vaccinated patients (OR 0.53; 95% CI: 0.39–0.72) vs. 58% in unvaccinated patients (OR 0.42; 95%CI: 0.24–0.73).[69] Commonly-reported side effects include a bitter or metallic taste in the mouth and diarrhea, with less-common side effects that include nausea, vomiting, and headache.[70]

Because the ritonavir component inhibits metabolism of nirmatrelvir, it can also affect the metabolism of other therapeutic drugs (specifically via inhibition of CYP3A liver enzymes), which may require suspension or dose reductions of a wide range of medications including antiarrhythmics, statins, immunosuppressants, and antipsychotics.[71] It is essential that a full interaction check for drug/drug interactions be undertaken for any patient for whom you are considering prescribing nirmatrelvir/ritonavir. In addition, dose reductions or avoidance may be necessary in patients with chronic kidney disease. (An interactive COVID-19 drug interaction checker is available at: COVID-19-druginteractions.org/checker).

Molnupiravir

The COVID-19 antiviral molnupiravir is FDA-authorized for emergency use in patients at high risk for progression to severe symptoms and/or for whom alternative treatment options are not accessible or clinically appropriate.[72]

As with nirmatrelvir-ritonavir, the efficacy of molnupiravir was dependent on vaccination status, with no effect seen in vaccinated patients,[73] but a significant effect observed in unvaccinated patients. A phase 3 trial with 1,433 non-hospitalized, unvaccinated adults with mild-to-moderate COVID-19 and at least one risk factor for severe illness found a decreased risk of hospitalization for any cause or death through day 29: 6.8% in the molnupiravir group vs. 9.7% in the control group (95% CI for percentage difference: -5.9% to -0.1%).[74]

A meta-analysis of molnupiravir found a non-significant 31% decreased risk for hospitalization using an 800 mg dose (8 studies, RR 0.69; 95% CI: 0.47-1.01), and a barely significant decreased risk for death (4 studies, RR 0.35; 95% CI: 0.12-0.99).[75] The side effect profile of molnupiravir was similar to placebo in this meta-analysis. No drug-drug interactions have been identified.[76]

Table 7: Treatment options for COVID-19 vs. placebo[67,68,73,74]

Antiviral	Symptom resolution	Hospitalization or death		Adverse effects	Drug-drug interactions
		Vaccinated*	Unvaccinated†		
Molnupiravir (Lagevrio)	2 day reduction	no reduction	**31% relative reduction**	no difference	—
Nirmatrelvir-ritonavir (Paxlovid)	no reduction	no reduction	**88% relative reduction**	changes in taste, nausea, vomiting, diarrhea	⚠ **many** *(see COVID-19 interactions checker above)*

Green = effective; Red = warning.

*Vaccinated patients refers to patients current with recommended COVID-19 vaccines. †Unvaccinated patients are not current with recommendations, even if they have received one or more vaccines in the past.

Corticosteroids

Adjunctive corticosteroids should be used in patients with COPD or asthma who experience COVID-19-associated exacerbations, but should be avoided in cases of uncomplicated COVID-19 in the outpatient setting. Some benefit has been shown for corticosteroid therapy, however, in hospitalized patients. In a meta-analysis of 22 studies evaluating the effectiveness of adjunctive corticosteroid use in hospitalized patients, the overall pooled estimate (observational studies and RCTs) showed a significant reduced mortality in the corticosteroid group (OR 0.72; 95%CI: 0.57-0.87).[77]

Prophylaxis

Neither nirmatrelvir-ritonavir[78] nor molnupiravir[79] have been shown to be effective as prophylaxis against COVID-19.

Prevention

Continued immunization with updated vaccines is recommended because immunity from natural COVID-19 infection wanes over time and because COVID-19 viral spike proteins continue to evolve in ways that lead to reduced efficacy of previously administered vaccines.[80]

BOTTOM LINE: Vaccination status impacts the role of nirmatrelvir-ritonavir or molnupiravir, with reductions in morbidity and mortality in patients not current with recommended COVID-19 vaccines. Molnupiravir can be used in patients where drug-drug interactions limit nirmatrelvir-ritonavir use.

Respiratory syncytial virus

RSV is a relatively common seasonal virus that typically causes mild cold-like symptoms from which most people recover in a week or two.[81] In infants and older adults, however, symptoms can become severe or life-threatening. Every year in the U.S., 60,000 to 160,000 older adults are estimated to be hospitalized with RSV infection, and 6,000 to 10,000 older adults are estimated to die from RSV-related complications.[82]

Clinical presentation

Patients with RSV present with flu-like illness, with wheezing as a prominent feature because RSV causes small airway inflammation/bronchiolitis. The airway obstruction can result in hypercapnia. No effective targeted antivirals for RSV are yet available for outpatient use. No rapid tests are available, although PCR testing is available. PCR testing is generally reserved for high-risk patients (i.e., those with severe immunosuppression) or patients for whom the result would influence antibiotic prescription or further diagnostic testing.

Treatment

Because effective RSV-targeted antivirals do not exist, symptom management and prevention are critical. (The antiviral ribavirin has not been shown to be effective against RSV in the outpatient setting, although it may have value for treating patients with hematological malignancies who are hospitalized with RSV.[83])

Prevention

Three RSV vaccines are FDA-approved in the U.S. based on convincing evidence from clinical trials:

- Arexvy
- Abrysvo
- mRESVIA

Arexvy was evaluated in a double-blind RCT among 24,966 adults age ≥60 years given either a single dose of the vaccine or a placebo.[84] In this study, efficacy against RSV-related lower respiratory tract disease was 82.6% and efficacy against severe RSV-related lower respiratory tract disease was 94.1%.

Abrysvo was tested in an RCT that randomized 34,284 adults age ≥60 years to either a single dose of the vaccine or placebo prior to RSV season.[85] Efficacy against RSV-related lower respiratory tract disease was 66.7% (11 cases in vaccine group vs. 33 in placebo group), and efficacy against RSV-related acute respiratory illness was 62.1% (22 cases in vaccine group vs. 58 in placebo group).

The efficacy of the mRESVIA vaccine was assessed in 35,541 adults age ≥60 years who received either the vaccine or placebo with a median follow-up of 112 days.[86] Efficacy against RSV-associated lower respiratory tract disease with at least two signs or symptoms was 83.7% (95% CI: 66%-92.2%) representing 9 events in the vaccine group vs. 55 events in the control group.

The Advisory Committee on Immunization Practices (ACIP) recommends RSV vaccination using any of the available agents, citing as rationale rising rates of RSV-associated hospitalizations in adults, with a steep rise at age 75 (repeat vaccination in previously vaccinated individuals is not currently recommended).[87] The recommended dosing:

- one dose for anyone age 75 and older
- one dose for adults aged 60-74 years at moderate risk for RSV disease (see below)
- one dose for adults aged 50 years at high risk for RSV disease (i.e., frank immunocompromise)

Adults with the following conditions are considered at high risk for RSV because of documented associations between the conditions and higher incidences of RSV-associated hospitalizations:

- immune system compromise*
- frailty*
- advanced age*
- residence in nursing home or long-term care facility*
- prior hospitalization for RSV*
- lung disease
- cardiovascular disease
- obesity
- diabetes mellitus
- neurologic or neuromuscular conditions
- kidney disease
- liver disease
- hematologic disorder

* These groups were either excluded or had minimal representation in clinical trials testing the RSV vaccines.

RSV vaccines should ideally be given prior to RSV season (i.e., in the fall), although they can be given at any time. The vaccines can be co-administered with other vaccines, such as influenza vaccine. Contraindications to RSV vaccination are current moderate or severe acute illness (with or without fever) or a history of severe allergic reaction to any component of the vaccine.

BOTTOM LINE: with no effective treatments for RSV available, the goals of care are symptom management and prevention using one of the three currently-available vaccines.

Role of antibiotics in respiratory infections

Many patients lack a good understanding of how viruses and bacteria differ, why antibiotics are not effective against viruses, and the fact that most community respiratory infections are viral rather than bacterial. As such, patients may ask for—or even demand—antibiotics for their condition even though they are inappropriate. Clinicians can help educate patients by calmly explaining the realities of viral vs. bacterial infections and the proper role of antibiotics. They can explain, for example, that getting an antibiotic when the infection is caused by a virus does not shorten the time of illness and that using an antibiotic when it isn't needed may make it work less well when it is needed. Clinicians can remind patients that antibiotics may only be appropriate for bacterial community acquired pneumonia, bacterial sinusitis that worsens after 10 days, and strep throat.

Risks of antibiotics

It may also be valuable to explain, using patient-friendly language, the potential risks of antibiotics, which include:

- Increased risk of side effects in older adults[84,85]
- Drug interactions with other necessary medications
- Changes in the microbiome
- Risk of antimicrobial resistance in the community and in the patient

Table 8: Potential adverse effects of antibiotics[88,89]

Antibiotic class	Common adverse reactions	Adverse reactions more likely in older adults
ß-lactams • Penicillins • Cephalosporins	Hypersensitivity reactions, GI intolerance, *C. difficile* infection	Nephrotoxicity, neurotoxicity, *C. difficile* infection (broad-spectrum penicillins, 3rd/4th generation cephalosporins)
Fluoroquinolones • Levofloxacin, moxifloxacin	Tendinopathy, *C. difficile* infection, cardiotoxicity	Tendinopathy, retinal tears, aortic aneurysms, neurotoxicity, *C. difficile* infection, hepatotoxicity, arrhythmia, hypoglycemia (especially if taking insulin or sulfonylureas)
Macrolides • Azithromycin, clarithromycin	GI intolerance, hepatotoxicity, cardiotoxicity, ototoxicity	Ototoxicity, neurotoxicity, arrhythmia

High dose fluoroquinolones are typically recommended for respiratory infections. In older adults these doses can increase the risk of adverse effects. Careful consideration to frailty, sarcopenia, and renal function can help determine whether a reduced dose may be preferred.

Drug interactions

Table 9: Drug interactions of antibiotics commonly used for respiratory infections[88]

Antibiotic class	Interacting drug and effect
ß-lactams • Penicillins • Cephalosporins	Amoxicillin and allopurinol: rash
Fluoroquinolones • Levofloxacin, moxifloxacin	Iron, magnesium, zinc, aluminum, antacids, sucralfate: decrease absorption of fluoroquinolone
Macrolides • Azithromycin, clarithromycin	Azithromycin and aluminum or magnesium: decreased azithromycin absorption Clarithromycin and calcium channel blockers: increased concentration of clarithromycin Clarithromycin and statins, digoxin, warfarin, direct-acting oral anticoagulants, cyclosporin, theophylline: increased concentration of interacting drug

As valuable as they are, antibiotics can entail important side effects, in particular disruption of the gut microbial community and reduction of microbiota diversity. Probiotics have been explored as either prophylaxis or treatment of antibiotic-associated symptoms. Probiotics are found in a range of fermented foods (e.g., yogurt, kefir, sauerkraut, kombucha, miso) as well as in supplements.

Current evidence has not addressed if probiotics can restore the gut microbiome to its pre-antibiotic state.[90] Some studies have shown that probiotics administered with antibiotics can lead to microbiota changes, but this may not mean microbiome restoration. Further, the current lack of knowledge about the composition of a healthy microbiome and how that microbiome adapts to antibiotic-associated changes makes it difficult to interpret results of studies evaluating the efficacy of probiotics to mitigate antibiotic harms.

A Cochrane review of 19 studies evaluating the effect of a range of probiotics (as either prophylaxis or treatment) on the incidence of antibiotic-associated diarrhea (AAD) in children found a reduced rate of AAD in the probiotic group (12% vs. 19% in the control group, RR 0.61; 95% CI: 0.49 -0.77).[91] However, with the limited age range and wide variety of probiotic regimens included, it is difficult to know how to use this information in the treatment of adults.

Penicillin allergy

For some syndromes, a penicillin or cephalosporin may be the best treatment option. For patients with either a known or suspected allergy to penicillin, it can be helpful to ask about the specific offending medication, reaction, and timeframe. Patients lose antibody mediated reactions over time, with fewer than 1% of patients maintaining their penicillin sensitivity after 20 years.[92] An estimated 90 to 95% of patients with a documented penicillin allergy can tolerate a penicillin rechallenge.[92]

The PEN-FAST tool can be used to identify low-risk penicillin allergies that do not require formal allergy testing.[93] A PEN-FAST score of less than 3 is associated with a low-risk penicillin allergy in the outpatient setting.

Table 10: PEN-FAST tool to identify risk of true penicillin allergy[93]

PEN	Penicillin allergy reported by patient	YES
F	Five years or less since reaction	2 points
A	Anaphylaxis or angioedema	2 points
S	Severe cutaneous reaction	2 points
T	Treatment required for reaction	1 point

Table 11: Interpretation of PEN-FAST score

Score	Interpretation	Risk of penicillin allergy
0	**Very low risk** of positive penicillin allergy test	< 1%
1-2	**Low risk** of positive penicillin allergy test	5%
3	**Moderate risk** of positive penicillin allergy test	20%
4-5	**High risk** of positive penicillin allergy test	50%

Cephalosporins, especially 3rd generation options like cefdinir or cefpodoxime, share little cross-reactivity (<1%) with penicillins. Unless the patient has had a life-threatening reaction to penicillin, these cephalosporins can likely be safely prescribed.

Community-acquired pneumonia

Community-acquired pneumonia (CAP) is pneumonia that develops in people who have not recently been hospitalized or spent time in other healthcare facilities, such as nursing homes or rehabilitation centers. CAP can be caused by a wide range of microorganisms, including bacteria (most commonly *Streptococcus pneumoniae*), viruses, and fungi. Pneumonia is a leading cause of morbidity and mortality (i.e., roughly 1.4 million emergency department visits and 41,000 deaths annually).[94] Pneumonia mortality is significantly higher among older adults compared to younger cohorts.

Clinical presentation and testing

CAP is a lower respiratory infection affecting the distal airways. Patients present with fever, chills, dyspnea, cough, and/or pleuritic chest pain. A chest x-ray that shows infiltrate or consolidation can solidify the diagnosis. Note that lower respiratory viral infections can also be considered CAP.

Several validated triage tools are available to assess CAP severity and guide decisions about whether to treat the patient in an outpatient or inpatient setting, with the Pneumonia Severity Index (PSI) having the most robust evidence base.[95] The PSI incorporates demographic, comorbid, physical, and laboratory findings to stratify patients into five risk classes. It can help identify low-risk patients suitable for outpatient

care and high-risk patients who may benefit from hospitalization or intensive care. Also available are various versions of the CURB assessment, which factors in measures of confusion, urea, respiratory rate, and blood pressure.

A prospective study following 3,181 patients with CAP assessing the discriminatory power of the CURB, CURB-65, and PSI tools found that the PSI has higher accuracy for predicting 30-day mortality than either of the CURB scores.[96]

Chest x-ray can be a critical part of CAP diagnosis when clinical signs and symptoms are insufficient.

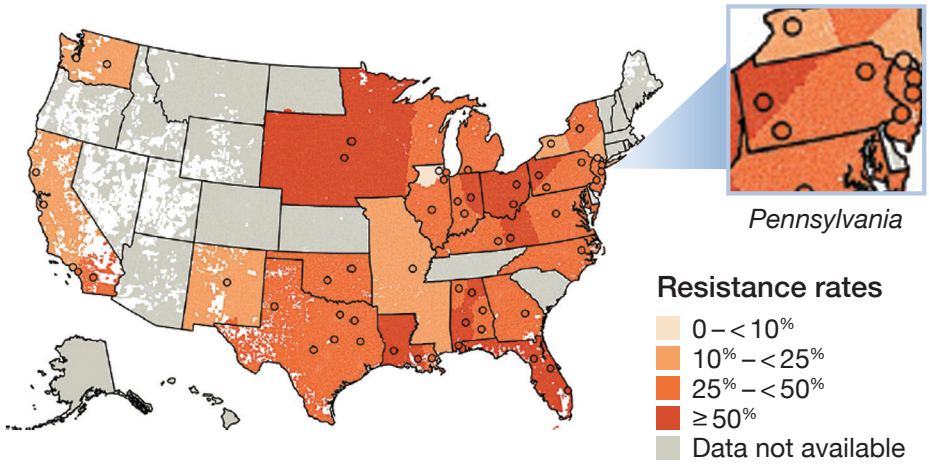
CT scans are typically reserved for hospitalized patients or patients with underlying lung disease and/or distorted anatomy. Sputum culture is not recommended because data have not shown that microbiologic diagnosis improves outcomes in ambulatory patients,[97] and because results seldom change management decisions. Similarly, blood cultures are not recommended because yield is very low in ambulatory patients and results rarely lead to a change in therapy.[98]

Assessing serum procalcitonin levels is not recommended because the reported sensitivity of procalcitonin to detect bacterial infection ranges widely, from 38% to 91%.[99] Additional tests with limited utility include urine antigen tests for bacterial infections, PCR for atypical bacterial infections, and blood cultures.

Treatment

When antibiotics are needed, choose the appropriate regimen based on the patient's age and location. Monotherapy, for example, may be appropriate for younger patients, but dual therapy providing coverage for both "typical" and "atypical" pathogens is usually recommended in patients aged ≥ 65 years. Choice is also driven by local patterns of antibiotic resistance, which can vary significantly by region.[100] For example, azithromycin monotherapy is not recommended anywhere that pneumococcal resistance exceeds 25%, which includes all of the state of Pennsylvania (Figure 6).[100] Azithromycin can still be used, however, as part of a dual-agent regimen to treat CAP where it is added to cover atypical bacteria.

Figure 6: *Streptococcus pneumoniae* resistance to azithromycin



Patients aged ≥65 years, or those with moderate CAP disease and/or risk factors, should be treated with **dual** therapy (i.e., a beta-lactam plus an atypical agent) or respiratory fluoroquinolone (although respiratory fluoroquinolones are associated with a higher risk of side effects than beta-lactam/atypical dual therapy).

Table 12: Outpatient treatment of CAP with oral medications[99]

Patient factors	Antibiotic		
No comorbidities or risk factors for resistant infections*	amoxicillin 1000 mg three times daily ***OR*** doxycycline 100 mg twice daily		
With comorbidities - First-line treatment	**Beta lactam** amoxicillin 500 mg – clavulanate 125 mg three times daily ***OR*** amoxicillin 875 or 2000 mg – clavulanate 125 mg twice daily ***OR*** cefpodoxime 200 mg twice daily ***OR*** cefuroxime 500 mg twice daily	**AND**	**Atypical agent** azithromycin 500 mg x 1 day, then 250 mg daily ** ***OR*** clarithromycin 500 mg twice daily ***OR*** clarithromycin ER 1000 mg daily ***OR*** doxycycline 100 mg twice daily
With comorbidities - Alternative treatments	levofloxacin 750 mg daily ***OR*** moxifloxacin 400 mg daily		

* recent respiratory infection or hospitalization with receipt of parenteral antibiotics in prior 90 days.
** resistance patterns do not apply to atypical coverage with azithromycin

Duration of treatment should generally be shorter than the previously-recommended 7-10 days. A 5-day course of antibiotics is generally sufficient, or 3 days using a macrolide such as azithromycin.[101]

Corticosteroids

Adjunctive use of corticosteroids is recommended for patients with COPD or asthma, but a mortality benefit in CAP has only been shown in patients with severe infections.[102,103]

Prevention

Two types of pneumococcal vaccines are available in the U.S.: conjugate vaccines, which chemically link (i.e., conjugate) the bacterial polysaccharide to a protein to enhance immune response, and the older polysaccharide vaccines, which react directly with the polysaccharides on the bacterial surfaces.[104] The vaccines cover varying numbers of bacterial serotypes:

Pneumococcal Conjugate Vaccines (PCVs)

- PCV15 (Vaxneuvance) covering 15 serotypes
- PCV20 (Prevnar 20) covering 20 serotypes
- PCV21 (Capvaxive) covering 21 serotypes

Pneumococcal Polysaccharide Vaccine (PPSV)

- PPSV23 (Pneumovax 23) covering 23 serotypes

The CDC recommends a pneumococcal vaccine for all adults aged ≥50 years (see Table 13 for specific options, based on prior vaccination status). Vaccination is also recommended for adults aged 19-49 with qualifying conditions (e.g., lung disease, diabetes, immunosuppression).

Table 13: CDC recommendations for pneumococcal vaccinations in adults ≥50 years[105]

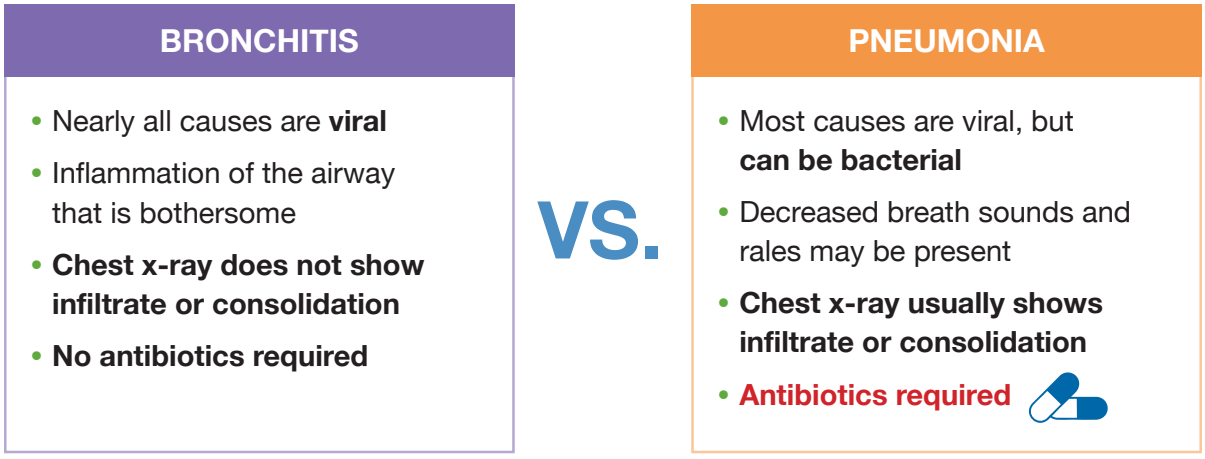
Prior vaccines	Option A	Option B
None*	PCV20 or PCV21	PCV15 → ≥1 year† → PPSV23†
PCV15 only at any age	≥1 year† → PPSV23†	NO OPTION B
PCV15 & **PPSV23** OR **PCV20** OR **PCV21** at any age	**No vaccines** recommended; schedule is complete.	
PPSV23 only at any age	≥1 year → PCV20 or PCV21	≥1 year → PCV15
PCV13 only at any age	≥1 year → PCV20 or PCV21	NO OPTION B
PCV13 at any age & **PPSV23** at <65 yrs	≥5 years → PCV20 or PCV21	

Because of the complex nature of pneumococcal vaccination decisions, it can be helpful to use a dedicated application such as PneumoRecs VaxAdvisor, which is available for use on smartphones.

Pneumonia vs. bronchitis

Patients presenting with a lower respiratory tract infection and cough pose the diagnostic challenge of determining whether they have bronchitis (almost always viral) or pneumonia. Chest x-ray is the preferred tool for making this determination, with infiltrate or consolidation confirmatory for pneumonia (Figure 7).

Figure 7: Differentiating bronchitis and pneumonia



Treatment

Symptomatic relief is the focus for patients with viral bronchitis. See the previous section on symptom management for recommendations for relieving cough and congestion.

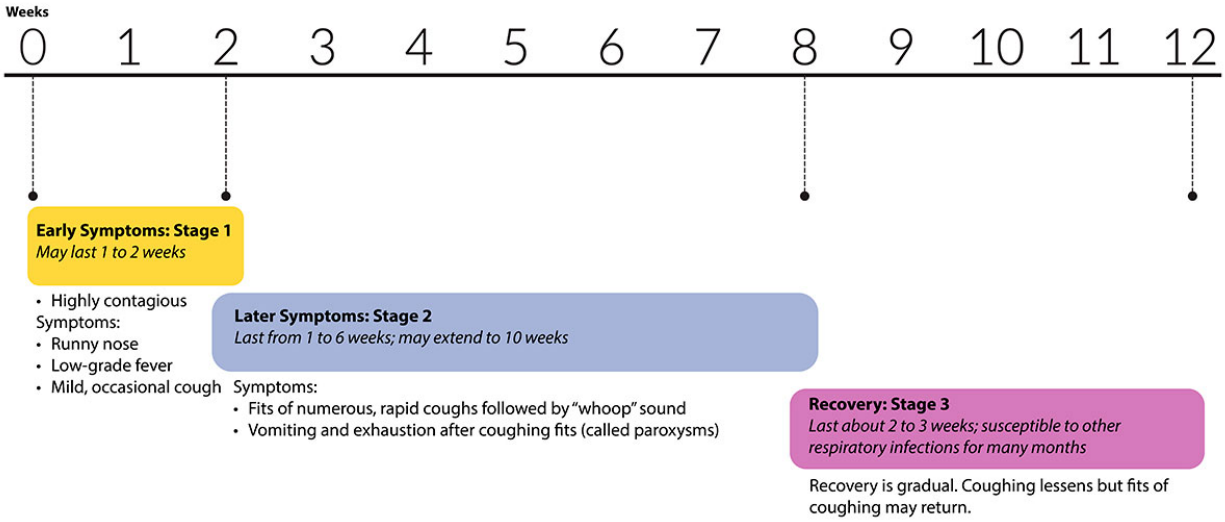
Pertussis

The incidence of pertussis has been increasing since the 1980s, with a dip during the COVID-19 pandemic and a return to pre-pandemic levels in recent years.[106,107] In 2024 the Pennsylvania Department of Health issued a health alert after increasing outbreaks of pertussis.[108] Infants, children, and young adults have the greatest incidence of pertussis, although cases can occur in older adults.

Clinical presentation and testing

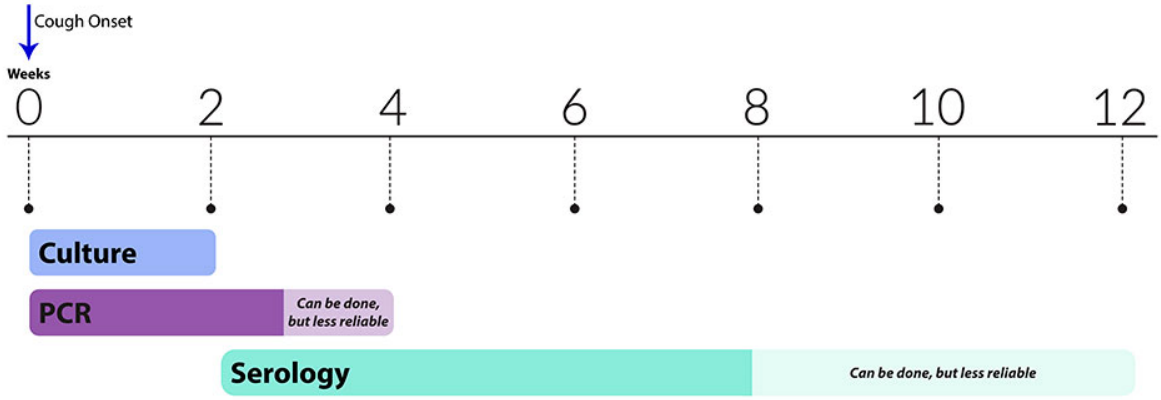
While whooping cough begins like any other respiratory infection, the cough may worsen over time. The whoop sound may be absent in older adults. It can present as paroxysms of coughing, post-tussive vomiting, or apnea.

Figure 8: Pertussis disease course[109]



The best testing option depends on time since symptom onset and availability. In general, PCR is one of the best, most accessible ways to identify pertussis. Culture has been considered the 'gold standard,' but it can take many days to get a result. Serologic testing can be useful later in the disease, but available serologic testing can vary in accuracy. It can be useful to consult with local experts if there is uncertainty about test quality.

Figure 9: Optimal timing for pertussis diagnostic testing[110]



Treatment

Antibiotics reduce pertussis illness duration and severity and decrease infectivity. Earlier treatment can result in less severe illness; CDC recommends to treat only if it can be started in the first three weeks of symptoms.[111] Azithromycin is preferred due to its shorter course and side effect profile.

Table 14: Antibiotics for pertussis[111,112]

Antibiotic	Dose and duration
Azithromycin	500 mg for 3 days 500 mg on day 1, then 250 mg on days 2 to 5
Clarithromycin	500 mg twice daily for 7 days
Erythromycin	500 mg four times daily for 14 days
Trimethoprim - sulfamethoxazole	160 mg – 800 mg twice daily for 14 days

Prevention

Chemoprophylaxis for pertussis is recommended for household contacts, people who are at high risk for severe illness, or those who have a close contact at risk of severe illness. It should be given within 21 days of exposure. Azithromycin, at the same dose as treatment, is the preferred medication. Vaccination should not be used to prevent infection after exposure.[111]

Vaccination remains an effective way to prevent pertussis. Following childhood vaccination, ACIP recommends a boosting dose of Tdap for all individuals age ≥11 years.[113] If a pertussis vaccine is due, adults should receive it at least 2 weeks before meeting infants. If a patient's vaccine history is unknown, Tdap is preferred over Td to assure adequate protection against both pertussis and tetanus. ACIP currently recommends Tdap vaccination in women at each pregnancy to reduce risk to infants.

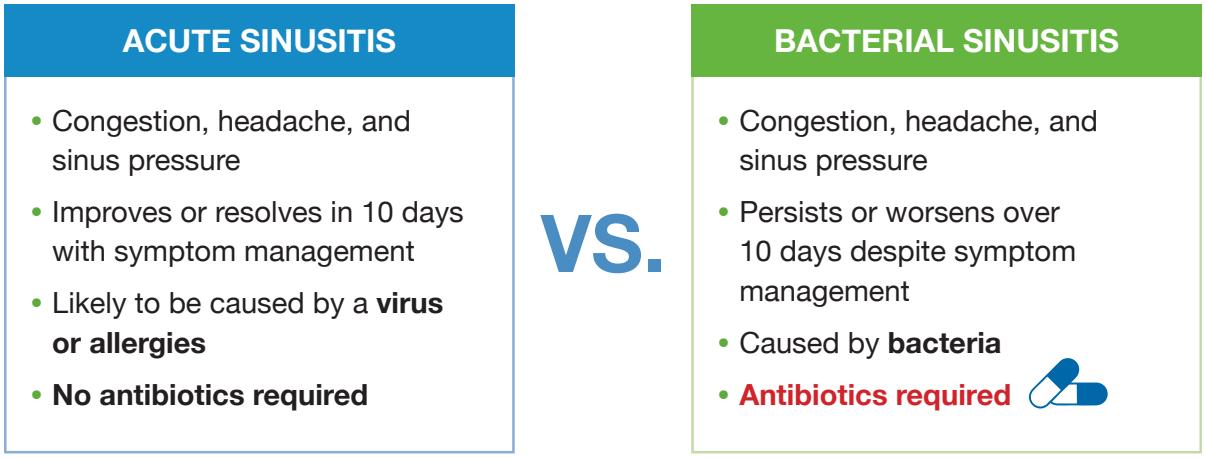
BOTTOM LINE: Dual therapy with a beta-lactam and an atypical agent is first-line treatment for adults aged ≥65 years with CAP, or adults younger than 65 with moderate disease or risk factors. Respiratory fluoroquinolones provide effective treatment but have a significant adverse effect profile. Shorter treatment durations (i.e., 5 days generally, or 3 days for azithromycin) are safe and

effective. Pneumococcal vaccination is recommended for patients aged ≥50 years and other select populations. A persistent cough, especially in fits, should trigger suspicion of a pertussis diagnosis.

Acute sinusitis

Acute sinusitis is an infection of the paranasal sinuses, usually following a viral URI. While most cases of acute sinusitis are viral, a subset is caused by bacteria, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis.* Bacterial sinusitis is diagnosed when symptoms persist or worsen, generally after 10 days. Differentiating bacterial sinusitis from allergies can be aided by looking for yearly or seasonal patterns in symptom onset.

Figure 10: Comparison of acute vs. bacterial sinusitis



Bacterial sinusitis symptoms can include:

- nasal congestion and obstruction
- thick yellow or green nasal discharge (purulent)
- facial pain, pressure, or tenderness (often worse when bending forward)
- headache
- toothache (especially upper teeth)
- reduced sense of smell
- cough (often worse at night)
- fever and fatigue (sometimes present)
- bad breath

Red flags for invasive/necrotizing infection include signs of extension to the orbit (pain in extraocular muscles, double vision), cranial nerve palsies, or severe uncontrolled diabetes.

Diagnosis of bacterial sinusitis is clinical. No testing is generally needed unless the patient has complicated disease or a possible invasive fungal infection.

Treatment

First line treatment for bacterial sinusitis in older adults is amoxicillin monotherapy.[114,115] Alternate therapies are doxycycline, levofloxacin, or moxifloxacin. A meta-analysis of 17 RCTs comparing an antibiotic to placebo (amoxicillin used in 10 of 23 treatment groups) found a higher rate of cure or improvement with antibiotics (OR1.64; 95% CI: 1.35-2.00).[116] Amoxicillin monotherapy is favored, due to similar or better outcomes and lower adverse effects. A retrospective cohort study in 89,627 adults with acute sinusitis comparing amoxicillin monotherapy to amoxicillin-clavulanate found no significant differences in rates of infectious complications (OR 0.78; 95% CI: 0.57-1.07), hospitalizations (OR 0.92; 95% CI: 0.81-1.04), or sinusitis-related return visits (OR 0.96; 95% CI: 0.88-1.04).[117] Gastrointestinal-related adverse events were lower with amoxicillin monotherapy (0.5%) relative to amoxicillin-clavulanate (0.7%) (OR 0.67; 95% CI: 0.53-0.86).

Table 15: Oral antibiotic treatment of bacterial sinusitis[114]

Tier recommendation	Antibiotic regimen
First-line therapy	Amoxicillin 2000 mg twice daily ***OR*** Amoxicillin 500 mg and clavulanate 125 mg three times daily ***OR*** Amoxicillin 875 mg and clavulanate 125 mg twice daily
Second-line therapy	Amoxicillin 2000 mg and clavulanate 125 mg twice daily ***OR*** Doxycycline 100 mg twice daily ***OR***
ß-lactam allergy	Levofloxacin 500 mg daily Moxifloxacin 400 mg daily

Most professional societies recommend a treatment duration of 5-7 days for uncomplicated disease in adults, although a meta-analysis of a 3-7 day course vs. 6-10 day course found no differences in clinical success, microbiologic efficacy, or adverse events.[118]

BOTTOM LINE: Early presentation of acute sinusitis is likely viral and requires symptomatic management. Bacterial sinusitis persists for at least 10 days and requires antibiotics. First line treatment in adults is amoxicillin with or without clavulanate for 5-7 days.

Streptococcal pharyngitis

Although pharyngeal infection with group A streptococcus (GAS) is more commonly seen in children and young adults, older adults can acquire it as well, with potentially severe consequences, particularly for those living in long-term care facilities (LTCFs). The incidence of invasive GAS rises with age, from 8.3 cases per 100,000 population in adults aged 50-64 years to 15.2 cases per 100,000 in adults aged ≥85 years.[119] Compared to age-matched community-dwelling adults, those in LTCFs have a 3- to 8-fold higher incidence of invasive GAS infection and are 1.5 times more likely to die from those infections.[120]

Since sore throat is a common reason for patient visits to primary care clinicians, and since roughly 80% of these cases are caused by viral infections, it is important to determine the etiology of the pharyngitis.

Distinguishing bacterial from viral pharyngitis

Patients with bacterial pharyngitis generally do not have rhinorrhea, cough, or conjunctivitis. Symptoms suggestive of bacterial pharyngitis include:

- sudden onset
- fever (especially >38°C/100.4°F)
- tonsillar exudates (white or yellow patches on tonsils)
- tender anterior cervical lymphadenopathy
- history of exposure to strep throat

Testing for streptococcus

When clear viral symptoms are present and consistent with history and clinical examination, no testing for GAS is necessary and antibiotics are contraindicated.[121] If bacterial infection is suspected, testing is recommended. Rapid strep tests have specificity >90%, and such testing can help determine if antibiotics are needed. Antibiotics can reduce the risk of downstream complications like rheumatic fever or glomerulonephritis. Negative tests are possible, however, even in the setting of a bacterial infection (sensitivity 60-85%). In these cases, exposure to someone with known strep can help determine whether antibiotic treatment is appropriate. Throat culture is reserved for patients whose symptoms do not improve over time or who do not respond to antibiotics.

Treatment

GAS remains exquisitely susceptible to penicillin.[122] First line oral treatment is, therefore, penicillin V, penicillin K, or amoxicillin. Intramuscular benzathine penicillin G could be used for patients who have difficulty swallowing pills. Alternative therapies for those who are not penicillin allergic are cefadroxil or cephalexin. Cefdinir or cefpodoxime are alternatives for those with non-anaphylactic penicillin allergies (Table 16).

Early treatment is critical for avoiding post-streptococcal sequelae such as peritonsillar or retropharyngeal abscesses or streptococcal invasive diseases. The recommended course of treatment is 10 days because data from studies comparing short vs. longer courses show clear benefits of the longer course when analyses are limited to patients treated with penicillin.[123] Avoid clindamycin and azithromycin due to high resistance patterns; resistance to erythromycin has been increasing as well.[122]

Table 16: Antibiotic options for treating streptococcal pharyngitis[124]

First-line treatment	Penicillin V or K (oral tablet/liquid) 250 mg four times daily OR penicillin V or K (oral tablet/liquid) 500 mg twice daily OR amoxicillin 1000 mg daily (immediate release) OR amoxicillin 500 mg twice daily OR benzathine penicillin 1.2 million units intramuscularly once
Patients with a penicillin allergy (e.g., rash)	cefadroxil 1000 mg daily OR cephalexin 500 mg twice daily OR cefdinir 300 mg twice daily115 x 5 days OR cefdinir 600 mg daily x 5 days OR cefpodoxime 100 mg twice daily x 5 days
Patients with IgE mediated penicillin reaction (e.g., anaphylaxis)	clindamycin 300 mg three times daily OR azithromycin 500 mg daily x 5 days* OR clarithromycin 250 mg twice daily*

* resistance rates could preclude use in some locations

Duration of treatment is generally 10 days (5 days for cefdinir, cefpodoxime, and azithromycin).

BOTTOM LINE: first line treatment for streptococcal pharyngitis is an oral penicillin analogue for 10 days.

Preventing infection and transmission

In the spirit of "an ounce of prevention is worth a pound of cure," all patients should be encouraged to follow best practices for infection prevention, which includes:

- Appropriate masking (see details below)
- Hand hygiene (washing for at least 20 seconds with soap or using alcohol-based disinfectants). Note that alcohol-based disinfectants are not effective against norovirus or *C. difficile*.
- Getting adequate sleep (i.e., at least 7 hours each night)[125]
- Gargling with water (one trial reported that gargling 3 times daily reduced incidence of colds over 90 days).[126]

Masking

If you come into contact with individuals who have symptoms of upper respiratory infections, wearing a mask can help reduce transmission. In controlled settings evaluating efficacy, respiratory (N95) masks are best. Surgical masks are also effective and are superior to cloth masks, which vary in quality.[127] This hierarchy is due to the high filtration rate of respiratory masks, leading to their ability to prevent both

droplet (large particle) and aerosol (suspended small particle) transmission. This leads to protection from a wider spectrum of viral pathogens.

While respiratory masks likely confer greater protection than surgical or cloth masks in healthcare settings, they may be more uncomfortable to wear.[128] Masks likely also confer benefit in higher risk settings among asymptomatic individuals (crowds), although evidence is less strong. In reality, results from controlled experiments have been inconsistently replicated in large, randomized trials due to inconsistent adherence and other methodological challenges.[129,130] Nevertheless, the compelling benefits of masks in high-risk settings support their use by individuals who can tolerate them.

Vaccination

Vaccination remains a powerful tool for preventing respiratory infections in older adults. Follow CDC recommendations for immunizations, including:

- Influenza: annually
- COVID-19: at least annually
- RSV: one dose for all adults ≥75, and in high-risk patients ≥60
- Pneumococcal: at least one dose; more if risk factors
- Pertussis (with Tdap): every 10 years

Chemoprophylaxis

As noted earlier, prophylactic use of the antivirals oseltamivir and baloxavir in close contacts can help prevent influenza in household or nursing home settings.[61]

Over-the-counter options

Supplementation or taking large doses of vitamins C, D, and E have not been proven effective for common cold prophylaxis.[43] The efficacy of zinc supplements (mostly in the form of lozenges) to prevent the common cold or upper respiratory infections was evaluated in a Cochrane meta-analysis of placebo-controlled trials.[131] In an analysis of 9 trials (N=1,449) zinc did not reduce the risk of developing a cold (RR) 0.93; 95% CI: 0.85 to 1.01). An analysis of 8 trials (N=972) assessing zinc for treatment of the common cold, found a modest reduction in the mean duration of the cold in days (MD -2.37 days; 95% CI: -4.21 to -0.53 days).[131]

Putting it all together

Respiratory infections are common, and can increase morbidity and mortality in older adults. Key points of this evidence document:

- Diagnostic testing should be used when it helps guide treatment decisions (including decisions about isolation and/or prophylaxis of close contacts).
- Timely initiation of antivirals for influenza and COVID-19 can help reduce severe disease, particularly in patients who are not current with vaccinations.
- Antibiotics are not without risk and require close counseling with patients about the risks and possible benefit of antibiotics when bacterial infection is suspected.
- Penicillin antibiotics are first line treatment options for streptococcal pharyngitis and community-acquired pneumonia.
- Clarify penicillin allergy when appropriate because many patients may not actually be allergic.
- Prevent infections with vaccination.
- Counsel patients about the best OTC options to manage symptoms, avoiding oral phenylephrine and diphenhydramine as well as combination products that can contain potentially harmful medications for older adults.

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These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition.

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