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Summary for Clinicians: Clinical Practice Guideline for the Diagnosis and Treatment of Community-acquired Pneumonia



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Evidence-based guidelines for the management of community-acquired pneumonia (CAP) were updated in 2019 by a multidisciplinary panel of experts (1). A systematic review of the literature was performed. This summary is intended to provide the practicing clinician with key takeaway points. These guidelines focus on the management of CAP once the diagnosis is made, not on initial diagnostic criteria or prevention. The guidelines have different implications for patients, clinicians, and policymakers (Table 1). Clinicians should always consider unique individual clinical circumstances when managing patients with CAP.

Respiratory and Blood Cultures

• We recommend not obtaining sputum Gram stain and culture routinely in adults with CAP managed in the outpatient setting (strong recommendation, very low quality of evidence).

- We recommend obtaining pretreatment Gram stain and culture of respiratory secretions in adults with CAP managed in the hospital setting who:
- Are classified as severe CAP (see Table 1), especially if they are intubated (strong recommendation, very low quality of evidence); or
 - a. Are being empirically treated for methicillin-resistant Staphylococcus aureus (MRSA) or Pseudomonas aeruginosa (strong recommendation, very low quality of evidence); or
 - b. Were previously infected with MRSA or P. aeruginosa, especially those with prior respiratory tract infection (conditional recommendation, very low quality of evidence); or
 - c. Were hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days (conditional recommendation, very low quality of evidence).
- We recommend not obtaining blood cultures in adults with CAP managed in the outpatient setting (strong recommendation, very low quality of evidence).

- We suggest not routinely obtaining blood cultures in adults with CAP managed in the hospital setting (conditional recommendation, very low quality of evidence). We recommend obtaining pretreatment blood cultures in adults with CAP managed in the hospital setting who:
- 1. Are classified as severe CAP (see Table 1) (strong recommendation, very low quality of evidence); or
- 2.
 - a. Are being empirically treated for MRSA or P. aeruginosa (strong recommendation, very low quality of evidence); or
 - b. Were previously infected with MRSA or P. aeruginosa, especially those with prior respiratory tract infection (conditional recommendation, very low quality of evidence); or
 - c. Were hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days (conditional recommendation, very low quality of evidence).

The panel recognized that although obtaining adequate samples is difficult and lacks evidence of benefit, cultures also have the potential to identify resistant organisms or those with public health implications,

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Ann Am Thorac Soc Vol 17, No 2, pp 133–138, Feb 2020 Copyright © 2020 by the American Thoracic Society DOI: 10.1513/AnnalsATS.201909-704CME Internet address: www.atsjournals.org guide the tailoring of broad-spectrum regimens, and enhance clinicians' understanding of local microbiology. The panel noted the need for new diagnostic tests to improve identification of causative pathogens in CAP and to distinguish between infection and colonization.

Streptococcus pneumoniae and Legionella Urinary Antigens

- We suggest not routinely testing urine for pneumococcal antigen in adults with CAP (conditional recommendation, low quality of evidence), except in adults with severe CAP (conditional recommendation, low quality of evidence).
- We suggest not routinely testing urine for Legionella antigen in adults with CAP (conditional recommendation, low quality of evidence), except
- 1. in cases where indicated by epidemiological factors, such as association with a Legionella outbreak or recent travel (conditional recommendation, low quality of evidence); or
- 2. in adults with severe CAP (see Table 1) (conditional recommendation, low quality of evidence).
- We suggest testing for Legionella urinary antigen and collecting lower respiratory tract secretions for Legionella culture on selective media or Legionella nucleic acid amplification

testing in adults with severe CAP (conditional recommendation, low quality of evidence).

Randomized controlled trials have failed to demonstrate improved outcomes with strategies that used urinary antigens for pathogen-directed therapy (2), although some observational studies suggested a reduction in mortality in sicker patients. *Legionella* is increasing, and diagnosis may have important individual and public health implications, especially for sick patients. Thus, the panel recommended testing for patients with severe CAP, travel, or in the presence of local outbreaks.

Influenza Testing

• When influenza viruses are circulating in the community, we recommend testing for influenza with a rapid influenza molecular assay (i.e., influenza nucleic acid amplification test), which is preferred over a rapid influenza diagnostic test (i.e., antigen test) (strong recommendation, moderate quality of evidence).

Although no studies have evaluated the impact of influenza testing on outcomes in adults with CAP, the panel based this recommendation on recent influenza guidelines (3) and substantial literature demonstrating benefit in patients with an influenza-like illness. Rapid molecular testing is more accurate than antigen testing, is increasingly available, and has infection control as well as therapeutic implications.

Procalcitonin

• We recommend that empiric antibiotic therapy should be initiated in adults with clinically suspected and radiographically confirmed CAP regardless of initial serum procalcitonin level (strong recommendation, moderate quality of evidence).

A large proportion of pneumonia is viral, and several studies have suggested potential utility of procalcitonin to distinguish viral from bacterial infection. Although a higher procalcitonin level strongly correlates with identification of bacteria using current diagnostic tests, for patients with radiographically confirmed CAP, the sensitivity of procalcitonin to detect bacterial infection has varied widely (from 38–91%) (4). The panel thus concluded that no threshold of procalcitonin can safely be used to withhold antibacterial therapy.

Determining Inpatient versus Outpatient Treatment Location

• In addition to clinical judgement, we recommend that clinicians use a validated clinical prediction rule for prognosis, preferentially the Pneumonia Severity Index (PSI) (strong recommendation, moderate quality of evidence) over the CURB-65 (conditional recommendation, low quality of evidence) to determine the need for hospitalization in adults diagnosed with CAP.

Table 1. Implications of strong and conditional recommendations

	Strong Recommendation ("We Recommend")	Conditional Recommendation ("We Suggest")
For patients	The overwhelming majority of individuals in this situation would want the recommended course of action and only a small minority would not.	The majority of individuals in this situation would want the suggested course of action, but a sizable minority would not.
For clinicians	The overwhelming majority of individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for different patients, and each patient must be helped to arrive at a management decision consistent with her or his values and preferences. Decision aids may be useful to help individuals make decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.
For policymakers	The recommendation can be adapted as policy in most situations, including for use as a performance indicator.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

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Two multicenter, cluster-randomized trials have demonstrated that prognostication with the PSI safely reduces low-risk hospitalizations (5, 6). The CURB-65 (confusion, uremia [blood urea nitrogen \geq 20 mg/dL], respiratory rate \geq 30, blood pressure [systolic <90 mm Hg/diastolic $\leq 60 \text{ mm Hg}$], age $\geq 65 \text{ year}$) is simpler to use, but there is less quality evidence to support its utility, and it performs more poorly than PSI at identifying low-risk patients. The panel acknowledged a need to study the effectiveness of CURB and other prediction rules that use data from the electronic health record to reduce the burden of prognostication to guide the initial site of treatment.

Determining Inpatient Level of Care

• We recommend direct admission to an intensive care unit (ICU) for patients with hypotension requiring vasopressors or respiratory failure requiring mechanical ventilation (strong recommendation, low quality of evidence). For patients not requiring vasopressor or mechanical ventilator support, we suggest using the Infectious Diseases Society of America /American Thoracic Society (IDSA/ATS) 2007 minor severity criteria together with clinical judgment to guide the need for higher levels of treatment intensity (conditional recommendation, low quality of evidence).

Patients transferred to an ICU from a medical ward demonstrate a higher mortality than patients directly admitted to an ICU (7), highlighting the importance of early recognition of severe pneumonia beyond immediate need for ICU therapies. The 2007 IDSA/ATS SCAP (severe community-acquired pneumonia) criteria are sensitive in predicting ICU admission (8) and more easily obtainable than other severity scores.

Empiric Antibiotic Regimens

Outpatient Adults without Comorbidities

As several studies support the efficacy of single-agent amoxicillin for inpatients with CAP (9), the panel believed that this regimen could be safely generalized to outpatients with CAP, despite the lack of coverage for atypical pathogens. "Empiric Antibiotic Regimens" such as "Antibiotic recommendations" are summarized in Figure 1 and specified in Table 2. Doxycycline has activity against the most common CAP organisms. Because of increased *S. pneumoniae* resistance to macrolides, the use of macrolide monotherapy depends on local resistance patterns.

Outpatient Adults with Comorbidities

Patients with chronic heart, lung, liver, or renal disease, diabetes mellitus, alcoholism, malignancy, or asplenia are more vulnerable and may also have risk factors for antibiotic-resistant organisms. The recommended regimens cover resistant *S. pneumonia*, β -lactamase–producing *Haemophilus influenzae*, enteric gram negatives, *S. aureus*, and *Mycobacterium* and *Chlamydia pneumoniae*. Although the panel recognized adverse events associated with fluoroquinolones, numerous studies demonstrating efficacy justify their use for some patients.

Adults Hospitalized with Nonsevere CAP

Fluoroquinolone monotherapy demonstrates similar clinical outcomes to combination regimens with a β -lactam and other agents in patients with nonsevere CAP (10). The panel suggested that β -lactam monotherapy not be routinely used, because several studies indicated worse outcomes.

Adults Hospitalized with Severe CAP

The safety of fluoroquinolone monotherapy has not been established in severe CAP. Nonrandomized studies suggest macrolidecontaining therapies including a β -lactam are associated with improved mortality compared with other regimens. Thus, the panel strongly recommended combination of a β -lactam with a macrolide, doxycycline, or respiratory fluoroquinolone; however, the evidence was low quality.

Assessing Risk for MRSA and *P. aeruginosa*

• We recommend abandoning use of the prior categorization of healthcareassociated pneumonia (HCAP) to guide selection of extended antibiotic coverage in adults with CAP (strong recommendation, moderate quality of evidence).

- We recommend clinicians only cover empirically for MRSA or P. aeruginosa in adults with CAP if locally validated risk factors for either pathogen are present (strong recommendation, moderate quality of evidence).
- If clinicians are currently covering empirically for MRSA or P. aeruginosa in adults with CAP on the basis of published risk factors but do not have local etiological data, we recommend continuing empiric coverage while obtaining culture data to establish if these pathogens are present to justify continued treatment for these pathogens after the first few days of empiric treatment (strong recommendation, low quality of evidence).

HCAP criteria do not accurately predict resistant organisms. The panel encouraged clinicians to pursue local validation of risk factors using local microbiology to test their generalizability whenever feasible. The panel also stressed that patients who receive extended-spectrum antibiotics should be cultured and deescalated if resistant organisms are not identified. The single published factor most strongly associated with resistant pathogens is prior isolation of these organisms in cultures, particularly from the respiratory tract, within the last year, whereas recent hospitalization and exposure to parenteral antibiotics in the preceding 90 days are weakly associated (11). Given the high negative predictive value of rapid MRSA nasal testing and its increasingly rapid turnaround time, the panel suggested that a negative polymerase chain reaction (PCR) may be sufficient to withhold or deescalate therapy, especially in nonsevere CAP. The positive predictive value of nasal testing is low, but a positive PCR was believed to warrant empiric MRSA coverage until culture data are resulted.

Anaerobic Coverage for Suspected Aspiration Pneumonia

• We suggest not routinely adding anaerobic coverage for suspected aspiration pneumonia unless lung abscess or empyema is suspected (conditional recommendation, very low quality of evidence).

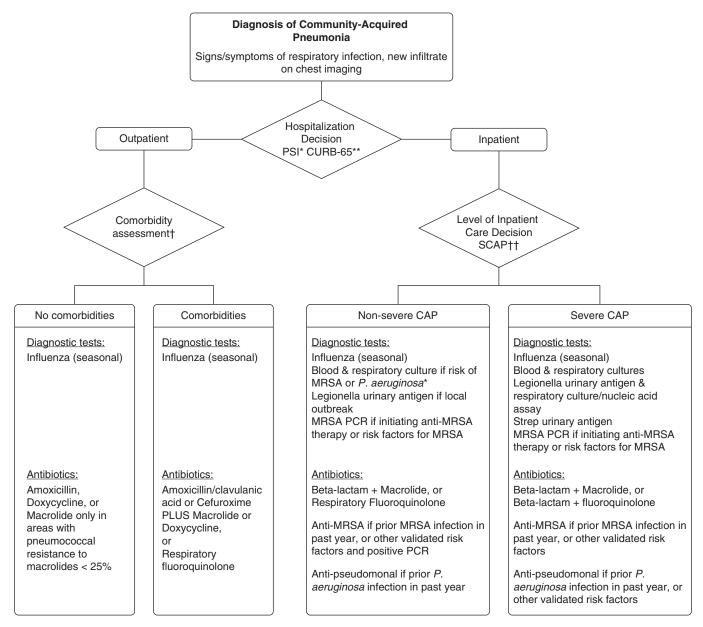


Figure 1. Management pathway for community-acquired pneumonia (CAP). Risk assessment definitions: *PSI: Pneumonia Severity Index using 20 patient characteristics (https://www.mdcalc.com/psi-port-score-pneumonia-severity-index-cap). Preferred over CURB-65. **CURB-65: confusion, uremia (blood urea nitrogen > 19 mg/dL), respiratory rate \ge 30 breaths/min, blood pressure > 90 mm Hg, age > 65. https://www.mdcalc.com/curb-65-score-pneumonia-severity. [†]Comorbidities: chronic heart, lung, liver or renal disease; diabetes mellitus, alcoholism, malignancy; or asplenia. ^{††}SCAP: severe community-acquired pneumonia definition. Severe CAP = \ge 1 major criteria, or \ge 3 minor criteria. Major: septic shock with need for vasopressors, respiratory failure requiring mechanical ventilation. Minor: respiratory rate \ge 30 breaths/min; Pa₀₂/Fl₀₂ ratio \le 250; multilobar infiltrates; confusion/disorientation; uremia (blood urea nitrogen \ge 20 mg/dL); leukopenia (white blood cell count < 4,000 cells/mm³); thrombocytopenia (platelet count < 100,000/mm³); hypothermia (temperature < 36C); hypotension requiring aggressive fluid resuscitation. CURB-65 = confusion, uremia (blood urea nitrogen \ge 20 mg/dL), respiratory rate \ge 30 mm Hg, age \ge 65 year; MRSA = methicillin-resistant *Staphylococcus aureus; P. aeruginosa = Pseudomonas aeruginosa*; PCR = polymerase chain reaction; PSI = Pneumonia Severity Index; SCAP = severe community-acquired pneumonia criteria.

Studies of aspiration pneumonia from the 1970s frequently isolated anaerobic bacteria trans-tracheal respiratory cultures among late-presenting patients, often with pulmonary abscesses. More recent studies have suggested that anaerobic bacteria are uncommon in traditionally defined aspiration pneumonia (12).

Corticosteroids and CAP

• We recommend not routinely using corticosteroids in adults with nonsevere

CAP (strong recommendation, high quality of evidence).

• We suggest not routinely using corticosteroids in adults with severe CAP (conditional recommendation, moderate quality of evidence).

Table 2. Recommended antibiotic regimens and dosing

Healthy outpatient adults with no comorbidities or risk factors for MRSA or P. aeruginosa:

Amoxicillin 1 g three times daily (strong recommendation, Moderate quality of evidence), or doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence), or a macrolide (azithromycin 500 mg on first day then 250 mg daily or clarithromycin 500 mg twice daily or clarithromycin extended release 1,000 mg daily) only in areas with >25% pneumococcal resistance to macrolides (conditional recommendation, moderate quality of evidence).

Outpatient adults with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia (in no particular order of preference):

Combination therapy: amoxicillin/clavulanate 500 mg/125 mg three times daily, or amoxicillin/clavulanate 875 mg/125 mg twice daily, or 2,000 mg/125 mg twice daily, or a cephalosporin (cefpodoxime 200 mg twice daily or cefuroxime 500 mg twice daily); AND macrolide (azithromycin 500 mg daily, clarithromycin [500 mg twice daily or extended release 1,000 mg once daily]) (strong recommendation, moderate quality of evidence for combination therapy), or doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence for combination therapy);

OR

Monotherapy: respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily, or gemifloxacin 320 mg daily) (strong recommendation, moderate quality of evidence).

Inpatient adults with nonsevere CAP without risk factors for MRSA or *P. aeruginosa*:

Combination therapy: a β-lactam (ampicillin 1 sulbactam 1.5–3 g every 6 h, cefotaxime 1–2 g every 8 h, ceftriaxone 1–2 g daily, or ceftaroline 600 mg every 12 h) and a macrolide (azithromycin 500 mg daily or clarithromycin 500 mg twice daily) (strong recommendation, high quality of evidence), or Monotherapy: a respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily) (strong recommendation, high quality of evidence).

A third option for adults hospitalized with CAP who have contraindications to both macrolides and fluoroquinolones: combination therapy with a β-lactam (ampicillin 1 sulbactam, cefotaxime, ceftaroline, or ceftriaxone, doses as above) and doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence).

Adults hospitalized with severe CAP: (specific agents and doses are the same as above):

A β-lactam plus a macrolide (strong recommendation, moderate quality of evidence); or a β-lactam plus a respiratory fluoroquinolone (strong recommendation, low quality of evidence).

Empiric treatment options for MRSA:

Vancomycin (15 mg/kg every 12 h, adjust based on levels) or linezolid (600 mg every 12 h).

Empiric treatment options for P. aeruginosa:

Piperacillin-tazobactam (4.5 g every 6 h), cefepime (2 g every 8 h), ceftazidime (2 g every 8 h), aztreonam (2 g every 8 h), meropenem (1 g every 8 h), or imipenem (500 mg every 6 h).

Definition of abbreviations: CAP community-acquired pneumonia; MRSA = methicillin-resistant Staphylococcus aureus; P. aeruginosa = Pseudomonas aeruginosa.

- We suggest not routinely using corticosteroids in adults with severe influenza pneumonia (conditional recommendation, low quality of evidence).
- We endorse the Surviving Sepsis Campaign recommendations on the use of corticosteroids in patients with CAP and refractory septic shock.

Prospective studies have failed to consistently show clinical benefit (mortality or organ failure) of corticosteroid use in patients with nonsevere CAP; there are limited data on the use of corticosteroids in patients with severe CAP. A meta-analysis of retrospective studies of influenza pneumonia suggests increased mortality in patients who receive corticosteroids (13). The panel does endorse the use of corticosteroids in patients with refractory septic shock with CAP, as per the Surviving Sepsis Campaign recommendations (14).

Influenza-Positive CAP and Antiviral Therapy

- We recommend that antiinfluenza treatment, such as oseltamivir, be prescribed for adults with CAP who test positive for influenza in the inpatient setting, independent of duration of illness before diagnosis (strong recommendation, moderate quality of evidence).
- We suggest that antiinfluenza treatment be prescribed for adults with CAP who test positive for influenza in the outpatient setting, independent of duration of illness before diagnosis (conditional recommendation, low quality of evidence).

Treatment of inpatients with influenzapositive CAP within 48 hours of symptom onset or hospitalization results in the best outcomes, but benefit is observed even when antiinfluenza therapy is started later (15, 16). Evidence is more limited for patients infected with influenza in the outpatient setting but suggests better time to symptom resolution and prevention of hospitalization. These recommendations are consistent with the recent IDSA Influenza Clinical Practice Guideline (3).

Influenza-Positive CAP and Antibacterial Therapy

• Antibacterial treatment is recommended to be initially prescribed for adults with CAP who test positive for influenza in both the inpatient and outpatient settings (strong recommendation, low quality of evidence).

Bacterial coinfections, including *S. aureus*, *S. pneumoniae*, *H. influenzae*, and others, contribute to as much as 30% of deaths in patients with influenza virus infection (17) and are difficult to exclude with current diagnostic capabilities. Antibiotic coverage for MRSA will be based on diagnostic testing and patient's risk factors. Discontinuation of antibiotics should be considered in patients with early clinical stability and no evidence of bacterial pathogens.

Duration of Antibiotics Treatment

• We recommend that the duration of antibiotic therapy should be guided by a validated measure of clinical stability (resolution of vital sign abnormalities [heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature], ability to eat, and normal mentation), and antibiotic therapy should be continued until the patient achieves stability and for no less than a total of 5 days (strong recommendation, moderate quality of evidence).

Antibiotics are to be continued until clinical stability, measured by the resolution of vital sign abnormalities, ability to eat, and normal mentation. Most studies support a total duration of 5 days for most patients except for suspected or proven MRSA or *P. aeruginosa*, when it should be 7 days (18). Failure to achieve clinical stability within 5 days of treatment requires consideration for resistant pathogens, complications of pneumonia such as empyema or lung abscess that may necessitate alternative management or duration, or alternative diagnoses.

Chest Imaging after CAP

• In adults with CAP whose symptoms have resolved within 5 to 7 days, we suggest not routinely obtaining follow-up chest imaging (conditional recommendation, low quality of evidence).

The clinical yield of follow-up chest imaging after pneumonia was deemed low, with abnormal chest findings from repeat imaging after pneumonia ranging from 0.2% to 5%. Many of these new abnormalities are lung malignancies and in current and previous smokers, for whom follow-up with lung cancer screening is indicated.

Conclusions and Future Directions

In this guideline update, several key changes to evidence-based practice for pneumonia

were made, including abandoning HCAP criteria to determine risk for resistant organisms, increasing the use of respiratory cultures, reducing the use of urinary antigen tests, preference of the PSI to guide hospitalization decisions, and avoiding macrolide monotherapy in areas of resistance. However, much of the foundation of pneumonia care remains the same: timely and appropriate diagnosis, treatment, and site-of-care remain the cornerstones of care, and although new diagnostic tests and biomarkers suggest the potential for more personalized and informed approaches to pneumonia care in the future, the antibiotic choice remains empiric, largely with agents that have been used for decades. The guideline authors noted low quality of evidence for many of the recommendations and emphasized the importance of clinical judgment and continued research to better inform best practice in the future.

Author disclosures are available with the text of this article at www.atsjournals.org.

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