suspected and radiographically confirmed CAP (1). It seems rational that in a patient with a high pretest probability for pneumonia, any biomarker (including PCT) that is not 100% accurate should not have a strong influence on treatment decisions. The advantage of using PCT for the management of patients with CAP, however, has been demonstrated for patients in whom a CAP diagnosis is unclear (e.g., patients with no infiltrate in chest X-ray) and for monitoring patients with CAP to decide whether to stop treatment early. Most trials that evaluated PCT for the management of CAP did not rely on the initial PCT level and instead focused on the kinetics of this blood marker to indicate that antibiotic treatment should be stopped early. The initial PCT level was found to be helpful in patients with a bronchitis-like illness and possible CAP but an ambiguous clinical presentation (2, 3). A recent meta-analysis of individual patient data that focused specifically on patients with respiratory infection and CAP who had participated in randomized trials showed that PCT is highly effective in reducing the duration of antibiotic treatment (4, 5). Specifically, the analysis included 6,708 patients from 26 eligible trials in 12 countries and found a 2.4-day reduction in antibiotic exposure (5.7 vs. 8.1 d [95% confidence interval (CI), −2.71 to −2.15]; $P < 0.0001$) and a reduction in antibiotic-related side effects (16% vs. 22%, adjusted odds ratio, 0.68 [95% CI, 0.57 to 0.82]; $P < 0.0001$). Importantly, when PCT was used to guide discontinuation of treatment, patients had significantly improved clinical outcomes (odds ratio for mortality, 0.83 [95% CI, 0.70–0.99]; $P = 0.037$).

Thus, there is strong clinical evidence that PCT is useful for evaluating patients with lower respiratory infection and ambiguous presentation and for stopping antibiotics early in patients with confirmed CAP. It is unfortunate that the updated guideline (1) focused on a clinical situation in which no biomarker would be expected to have a strong influence on treatment (i.e., patients with clinically suspected and radiographically confirmed CAP) and unfortunate that it did not include recommendations for using PCT in ambiguous clinical situations and for guiding treatment duration, both of which have a strong impact on antibiotic overuse and associated health risks. ■

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

Philipp Schuetz, M.D., M.P.H.*
*Kantonsspital Aarau*
*Aarau, Switzerland*

*Corresponding author (e-mail: schuetzph@gmail.com).

## References

1. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, *et al*. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019;200:e45–e67.
2. Neeser O, Branche A, Mueller B, Schuetz P. How to: implement procalcitonin testing in my practice. *Clin Microbiol Infect* 2019;25: 1226–1230.
3. Schuetz P, Beishuizen A, Broyles M, Ferrer R, Gavazzi G, Gluck EH, *et al*. Procalcitonin (PCT)-guided antibiotic stewardship: an international experts consensus on optimized clinical use. *Clin Chem Lab Med* 2019;57:1308–1318.
4. Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, *et al*. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. *Lancet Infect Dis* 2018;18:95–107.
5. Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, *et al*. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. *Cochrane Database Syst Rev* 2017;10: CD007498.





## Viewing the Community-acquired Pneumonia Guidelines through an Antibiotic Stewardship Lens

*To the Editor*:

We read with interest the article titled "Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America" (1). We congratulate the authors on their comprehensive review of the evidence. Although we understand that they are limited in their ability to establish recommendations based on the Grading of Recommendations Assessment, Development, and Evaluation system process, we believe it would be helpful for the practicing clinician to understand how to interpret the guidelines through an antibiotic stewardship (AS) lens. Below, we discuss three AS-guided recommendations that should be considered when interpreting the community-acquired pneumonia (CAP) guidelines.

### Fluoroquinolone Use

Fluoroquinolones (FQs) are recommended as a first-line option along with β-lactam plus macrolide combination therapy for ambulatory patients with CAP and comorbidities and for inpatients. The increased compliance issues regarding the use of two medications may drive clinicians to prescribe FQs, especially in the outpatient setting. The authors mention that adverse reactions to FQs are rare; however, FQ use is among the strongest risk factors for *Clostridioides difficile* infections (2), and the list of U.S. Food and Drug Administration black-box warnings associated with FQ use continues to grow.

### Inpatient Empiric Antimicrobial Therapy for Nonsevere CAP and No Risk Factors for Methicillin-Resistant *Staphylococcus aureus* or *Pseudomonas aeruginosa*

The guidelines recommend combination therapy with a β-lactam and a macrolide for all patients who receive a non-FQ regimen. Although one randomized trial failed to demonstrate noninferiority of β-lactam monotherapy versus β-lactam plus macrolide combination therapy in attainment of clinical stability



Author Contributions: V.F., E.M.S., and S.C.K. contributed to the conception and content of this letter.

Originally Published in Press as DOI: 10.1164/rccm.201910-2026LE on December 4, 2019

on hospital Day 7, a clinical benefit of combination therapy was seen in patients with confirmed atypical pathogens or patients with Pneumonia Severity Index category IV pneumonia (3). Another cluster randomized trial that was not discussed in the guidelines demonstrated noninferiority of β-lactam monotherapy versus β-lactam plus macrolide combination therapy in 90-day mortality, favoring β-lactam monotherapy in non-ICU patients (4). A subsequently published meta-analysis that included observational data and results from the above-mentioned randomized trials found a mortality benefit from combination therapy only for severe CAP. Because atypical pathogens account for <5% of CAP in U.S. population studies (5) and combination therapy may only benefit patients with severe CAP, routine atypical coverage may not be necessary in outpatients or inpatients with nonsevere CAP; therefore, β-lactam monotherapy is recommended in CAP guidelines in other countries (6, 7).

### Antibiotic Recommendations and Influenza

The guidelines recommend antibiotics for both inpatients and outpatients with clinical and radiographic evidence of CAP who test positive for influenza, with a consideration to stop antibiotics within 72 hours if no bacterial pathogen is found and the patient achieves early clinical stability. This recommendation is likely to lead to increases in unnecessary antibiotic prescriptions for patients with influenza. In the outpatient setting, sputum cultures and chest X-rays are not routinely obtained; hence, providers may not know when to stop antibiotics. Additionally, the rate of bacterial complications of influenza is low (∼<2.5%) (8, 9). Antibiotics may not be necessary for most outpatients with influenza or those who are hospitalized but are not severely ill.

Guidelines regarding the use of antibiotics must balance treatment recommendations with AS considerations and specifically note when regimens are supported by clinical trials but may be suboptimal because of side effects or costs. Many providers regard the guidelines as strict recommendations rather than as a starting point for clinical decision-making. Thus, discussions about areas in which the available evidence is inconclusive should include the viewpoint of antibiotic stewards at the patient and population levels. We strongly encourage active engagement from AS on future guidelines to facilitate discussions about judicious prescribing of antibiotics and to inform practical interpretation and implementation of those guidelines. ■

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

**Acknowledgment:** The authors thank Dr. Sara E. Cosgrove for her review of this letter.

Valeria Fabre, M.D.*
*Johns Hopkins University School of Medicine*
*Baltimore, Maryland*

Emily S. Spivak, M.D., M.H.S.
*University of Utah School of Medicine*
*Salt Lake City, Utah*

Sara C. Keller, M.D., M.P.H., M.S.H.P.
*Johns Hopkins University School of Medicine*
*Baltimore, Maryland*

ORCID ID: 0000-0001-7374-9678 (V.F.).

*Corresponding author (e-mail: mfabre1@jhmi.edu).

### References

1. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, *et al*. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019;200:e45–e67.
2. McCusker ME, Harris AD, Perencevich E, Roghmann MC. Fluoroquinolone use and *Clostridium difficile*-associated diarrhea. *Emerg Infect Dis* 2003;9:730–733.
3. Garin N, Genné D, Carballo S, Chuard C, Eich G, Hugli O, *et al*. β-Lactam monotherapy vs β-lactam-macrolide combination treatment in moderately severe community-acquired pneumonia: a randomized noninferiority trial. *JAMA Intern Med* 2014;174:1894–1901.
4. Postma DF, van Werkhoven CH, van Elden LJ, Thijsen SF, Hoepelman AI, Kluytmans JA, *et al*.; CAP-START Study Group. Antibiotic treatment strategies for community-acquired pneumonia in adults. *N Engl J Med* 2015;372:1312–1323.
5. Jain S, Self WH, Wunderink RG; CDC EPIC Study Team. Community-acquired pneumonia requiring hospitalization. *N Engl J Med* 2015;373:2382.
6. Woodhead M, Blasi F, Ewig S, Garau J, Huchon G, Ieven M, *et al*.; Joint Taskforce of the European Respiratory Society and European Society for Clinical Microbiology and Infectious Diseases. Guidelines for the management of adult lower respiratory tract infections: full version. *Clin Microbiol Infect* 2011;17:E1–E59.
7. Wiersinga WJ, Bonten MJ, Boersma WG, Jonkers RE, Aleva RM, Kullberg BJ, *et al*. Management of community-acquired pneumonia in adults: 2016 guideline update from the Dutch Working Party on Antibiotic Policy (SWAB) and Dutch Association of Chest Physicians (NVALT). *Neth J Med* 2018;76:4–13.
8. Podewils LJ, Liedtke LA, McDonald LC, Hageman JC, Strausbaugh LJ, Fischer TK, *et al*.; Infectious Diseases Society of America Emerging Infections Network. A national survey of severe influenza-associated complications among children and adults, 2003-2004. *Clin Infect Dis* 2005;40:1693–1696.
9. Metersky ML, Masterton RG, Lode H, File TM Jr, Babinchak T. Epidemiology, microbiology, and treatment considerations for bacterial pneumonia complicating influenza. *Int J Infect Dis* 2012;16:e321–e331.





## Reply to Chahine, to Schuetz, and to Fabre *et al.*

*From the Authors*:

We appreciate the letters submitted in response to the recently published guidelines for the treatment of community-acquired pneumonia (CAP) in adults (1).



The authors are the cochairs of the official American Thoracic Society Document entitled, "Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America."

Originally Published in Press as DOI: 10.1164/rccm.201910-2000LE on December 4, 2019