

Reply to Burnham and Vazquez Guillamet

TO THE EDITOR—We thank Burnham et al for their interest in our findings [1, 2]. We agree that to expand the pool of infectious diseases/critical care medicine (ID/CCM) physicians, we will need to demonstrate to hospitals that it is worth investing in the training and hiring of these physicians. For this, Burnham et al suggest a cost-benefit analysis drawing analogies to the revelations of cost savings from hiring hospitalists that once fueled the expansion of that discipline.

In our study, we found that the existing pool of ID/CCM physicians is still relatively small; they practice varied combinations of CCM and inpatient and outpatient ID, and assume research, educational, administrative, and several other roles; they are interspersed with other physician types across myriad public and private healthcare systems. Prospective or even pre-/postemployment antibiotic-use outcomes and revenue assessments suggested by Burnham et al would be difficult to measure as hiring of most ID/CCM providers nationwide has occurred piecemeal and unannounced. Many intensive care units (ICUs) are now staffed on a shift basis with several intensivists including tele-ICU providers starting and stopping antibiotics on one patient. As such, it would not be feasible to selectively extract the net economic impact of this dually trained cohort on a given hospital, health system, or region. Initially, one would have to rely on qualitative measures rather than balance sheets to assess their usefulness—emphasizing an implied impact in areas such as infection control, antibiotic stewardship, management of sepsis and immunocompromised hosts, and high-containment pathogen preparedness and acknowledging the possibility of collateral cost savings that would accompany these enhancements.

Although we may be many steps away from being able to demonstrate the economic utility of ID/CCM physicians,

our first steps should focus on demonstrating that such training tracks can in fact be operationalized. As a pilot, centers with CCM only rather than pulmonary-CCM programs could be approached with proposals for establishing dual tracks with the ID division at their respective locations. This would simplify combining the ID and CCM clinical and research years and appeal more broadly to trainees than the current system, which requires most to pursue training separately. Success of the proposed pilot could be gauged from annual statistics of the nascent ID/CCM tracks on matching, graduation, and grants/awards as well as new job placements and associated salary packages.

Note

Potential conflicts of interest. Both authors: No reported conflicts. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Sameer S. Kadri and Naomi P. O'Grady

Critical Care Medicine Department, National Institutes of Health Clinical Center, Bethesda, Maryland

References

1. Kadri SS, Rhee C, Magda G, et al. Synergy, salary, and satisfaction: benefits of training in critical care medicine and infectious diseases gleaned from a national pilot survey of dually trained physicians. *Clin Infect Dis* 2016; 63:868–75.
2. Burnham JB, Vazquez Guillamet MC. How will we pay for the new infectious diseases/critical care medicine subspecialty? *Clin Infect Dis* 2017; 64:530.

Correspondence: S. S. Kadri, National Institutes of Health Clinical Center, Critical Care Medicine Department, 10 Center Drive, Bldg 10, #2C-145, Bethesda, MD 20892 (sameer.kadri@nih.gov).

Clinical Infectious Diseases® 2017;64(4):531
Published by Oxford University Press for the Infectious Diseases Society of America 2017. This work is written by (a) US Government employee(s) and is in the public domain in the US. DOI: 10.1093/cid/ciw790

Penicillin Allergy Testing: A Key Component of Antibiotic Stewardship

TO THE EDITOR—We read with great interest the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America guidelines

for implementing an antibiotic stewardship program [1]. The authors note in section XII that antibiotic stewardship programs should “promote [antibiotic] allergy assessments and penicillin skin testing when appropriate,” and determined that this merits a weak recommendation. We disagree and offer evidence that this merits a strong recommendation.

The GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) approach entails a clear separation between quality of evidence and strength of recommendation [2]. For instance, a strong recommendation exists for epinephrine in acute anaphylaxis despite low quality of evidence [3]. GRADE defines quality of evidence as “the extent to which our confidence in an estimate of the treatment effect is adequate to support a particular recommendation” [2]. Study design is important, but not the sole factor, in appraising quality of evidence. As noted in Figure 1, the strength of a recommendation also is contingent upon consideration of desirable and undesirable consequences of a management decision, patient values and preferences, resources, and cost.

There is a substantial morbidity associated with not performing penicillin allergy testing in patients with unconfirmed penicillin allergy. In the absence of diagnostic intervention, patients with self-reported penicillin allergy are at increased risk for untoward outcomes of care, including greater rates of exposure to non- β -lactams (eg, quinolones, carbapenems, vancomycin) that will encourage development of nosocomial resistant organisms [4]. Diagnostic intervention can remove this label in approximately 90% of such patients [5].

Performance of penicillin allergy testing in hospitalized patients with unconfirmed penicillin allergy fulfills criteria for a strong recommendation. Most patients with penicillin allergy would want to undergo penicillin skin

testing, informed healthcare providers would recommend this course of action, policymakers would be inclined to adopt this as policy, and further research would be very unlikely to change our confidence in the magnitude of effect associated with this intervention. The American Board of Internal Medicine Foundation's Choosing Wisely campaign recommended in 2014 that physicians "don't overuse non-beta lactam antibiotics in patients with a history of penicillin allergy, without an appropriate evaluation" [6].

Preferably, a randomized prospective trial of penicillin allergy testing would have been performed more than 10 years ago; however, it would be unethical to perform such a trial today. There is no equipoise on this issue. Penicillin allergy testing is safe in young children, pregnant women, emergency department patients, preoperative patients, and critically ill hospitalized patients [7]. The reference standard for penicillin allergy evaluation is an oral amoxicillin challenge. On this basis, the diagnostic utility of penicillin skin testing, prior to oral challenge, is well established and has been associated with a negative predictive value of 99.3% [5]. Penicillin allergy testing can favorably alter the antibiotics prescribed for skin test negative patients [8]. Patients with positive skin tests for whom no equally efficacious alternative antibiotic can be used are candidates for penicillin desensitization [9]. The remaining question is how much morbidity is prevented by penicillin allergy testing in specific situations, rather than whether penicillin allergy testing should be routinely performed.

Note

Potential conflicts of interest. E. M. has received research grants from ALK and serves on data and safety monitoring boards for BioMarin and Ultragenyx. D. A. K. has received research grants from the Vanberg Family Foundation and speaker honoraria from Genentech. He also serves on a data and safety monitoring board for Aimmune. M. C. C. has been a consultant for Sanofi, Genetic, Merck, Lytic Biopharma, Contractect, Arete Discoveries, and Bentham

Science and serves on the board of directors of the American Academy of Allergy, Asthma, and Immunology. D. M. L. has carried out clinical research with, has served as a consultant for, and/or has received honoraria from Genentech/Novartis, GlaxoSmithKline, AstraZeneca, Media, and Merck. The authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Eric Macy,¹ David A. Khan,²
Mariana C. Castells,³ and David M. Lang⁴

¹Department of Allergy, Kaiser Permanente San Diego Medical Center, California; ²Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas;

³Division of Rheumatology, Immunology and Allergy, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; and

⁴Department of Allergy and Clinical Immunology, Cleveland Clinic, Ohio

References

1. Barlam TF, Cosgrove SE, Abbo LM, et al. Executive summary: implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016; 62:1197–202.
2. Brozek JL, Akl EA, Alonso-Coello P, et al; GRADE Working Group. Grading quality of evidence and strength of recommendations in clinical practice guidelines. Part 1 of 3. An overview of the GRADE approach and grading quality of evidence about interventions. *Allergy* 2009; 64:669–77.
3. Lieberman P, Nicklas RA, Oppenheimer J, et al. The diagnosis and management of anaphylaxis practice parameter: 2010 update. *J Allergy Clin Immunol* 2010; 126:477–80.e1–42.
4. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. *J Allergy Clin Immunol* 2014; 133:790–6.
5. del Real GA, Rose ME, Ramirez-Atamoros MT, et al. Penicillin skin testing in patients with a history of beta-lactam allergy. *Ann Allergy Asthma Immunol* 2007; 98:355–9.
6. <http://www.choosingwisely.org/clinician-lists/american-academy-allergy-asthma-immunology-non-beta-lactam-antibiotics-penicillin-allergy>. Accessed 25 May 2016.
7. Macy E, Ngor EW. Safely diagnosing clinically significant penicillin allergy using only penicilloyl-polylysine, penicillin, and oral amoxicillin. *J Allergy Clin Immunol Pract* 2013; 1:258–63.
8. Nadarajah K, Green GR, Naglak M. Clinical outcomes of penicillin skin testing. *Ann Allergy Asthma Immunol* 2005; 95:541–5.
9. Castells M. Desensitization for drug allergy. *Curr Opin Allergy Clin Immunol* 2006; 6:476–81.

Correspondence: E. Macy, Department of Allergy, Kaiser Permanente, 7060 Clairemont Mesa Blvd., San Diego, CA 92111 (eric.m.macy@kp.org).

Clinical Infectious Diseases® 2017;64(4):531–2

© The Author 2016. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com. DOI: 10.1093/cid/ciw795

Reply to Macy et al

TO THE EDITOR—We appreciate the opportunity to respond to the comments of Macy et al regarding the use of penicillin allergy testing as a strategy for antibiotic stewardship [1]. The authors reference the discussion of penicillin skin testing in our recent guideline on implementing an antibiotic stewardship program [2]. They take issue with our assignment of a weak recommendation to the question, "should antibiotic stewardship programs (ASPs) facilitate initiatives to implement allergy assessments with the goal of improved use of first-line antibiotics?" Their central argument rests on the observation that patients with self-reported penicillin allergy often are not prescribed first-line therapy with beta-lactam agents and thus penicillin skin testing can improve their care by documenting the patient is not allergic. While we recognize that treatment with second-line non-beta-lactam antibiotic regimens because of incorrectly labeled penicillin allergy may impact patient outcomes [3], we believe that the authors misunderstand the goal of the guideline and the context in which we evaluated both the quality of the literature and the strength of the recommendation, in full accordance with the Grades of Recommendation, Assessment, Development, and Evaluation process [4].

The goals of this guideline were to examine different ASP implementation strategies and to evaluate the existing evidence to determine if a particular strategy is a productive use of ASP resources. We note in the section titled Process Overview that "the evidence was graded based on the effectiveness of the antibiotic stewardship intervention, not the underlying data that provided the groundwork for the intervention." Thus, we do not dispute the authors' discussion of skin testing but must reinforce that there is sparse literature examining it as a primary ASP strategy. Because most antibiotic stewards do not perform the skin testing themselves, there is delay and effort to coordinate the performance of the tests. We do not have good data to quantify how skin testing can improve prescribing or how