

# Correspondence

## Healthcare-Associated Pneumonia and Multidrug-Resistant Bacteria: Do We Have a Convincing Answer?

TO THE EDITOR—Classification of community-onset pneumonia is an important matter in which we are involved, having published pieces of evidence in the recent past [1, 2]. We have read with considerable interest the systematic review and meta-analysis of Chalmers and colleagues [3] as we are completing a work on the same issue. However, several methodological issues have to be addressed. First, it is very difficult to assess the main endpoint of this systematic review, because no studies have been specifically designed to identify microbiology patterns of community-acquired pneumonia and healthcare-associated pneumonia (HCAP). As a matter of fact, across all studies, causative pathogens have been identified only in a minority of cases. Just as important is the fact that invasive diagnostic procedures (eg, bronchoscopy) have been never systematically adopted to ascertain etiologies.

In their systematic review, Chalmers and colleagues do not show the flow diagram regarding selection of studies. Because the search string that was used had a massive recall (>16 000 bibliographic citations!), it would be valuable for the reader to understand how the selection process was conducted. In particular, an eligible paper we published was not included in the systematic review [4], as well as at least 4 additional studies published in 2013 (1 retrospective study and 3 retrospective studies [5–8]) for a total number of 2894 patients. Statistical analysis section, figure legends, and graphics do not disclose any information about the methods that were performed.

No information was given about random- or fixed-effect models.

Moreover, the authors used inverse analysis method. In this regard, we note that because low frequencies of causative pathogens were recognized, the Mantel-Haenszel method had to be avoided; in this case, the Peto 1-step odds ratio method had been found to be the least biased and most powerful method to use [9]. Some other issues are not clear or have not been considered. For example, the number needed to treat is usually calculated in meta-analyses analyzing interventional or randomized clinical studies, and, in any case, Altman [10] hardly recommended the use of confidence intervals. Furthermore, on the one hand, robust conclusions might be invalidated by pooling studies with different designs; on the other, excluding 1 study (to reduce statistical heterogeneity) or analyzing only 4 studies (because results were adjusted for age) possibly biased the conclusions.

We believe that data presented in the published systematic review do not definitively disclose whether or not the HCAP condition is a test for prediction of resistant bacteria etiology. We are not sure that HCAP itself is the most appropriate tool to segregate patients with multidrug-resistant etiology, but there is consistent evidence that a percentage of patients with community-onset pneumonia have a multidrug-resistant infection, and in the majority of cases these patients fulfill the HCAP definition. The changing etiology of infections in patients exposed to the healthcare setting have been clearly demonstrated in various types of infection (including bacteremia, endocarditis, spontaneous bacterial peritonitis, urinary

tract infections), but pneumonia remains an unresolved question due to the at least suboptimal quality of diagnostic microbiology investigations of published studies.

### Note

**Potential conflicts of interest.** All authors: No reported conflicts.

All 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.

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### References

- Venditti M, Falcone M, Corrao S, Licata G, Serra P; the Study Group of the Italian Society of Internal Medicine. Comparison of the outcomes of patients hospitalized with community-acquired, health care-associated, and hospital-acquired pneumonia. *Ann Intern Med* 2009; 150:19–2631.
- Falcone M, Corrao S, Licata G, Serra P, Venditti M; Italian Society of Internal Medicine (SIMI). Clinical impact of broad-spectrum empirical antibiotic therapy in patients with healthcare-associated pneumonia: a multi-center interventional study. *Intern Emerg Med* 2012; 7:523–31.
- Chalmers JD, Rother C, Salih W, Ewig S. Healthcare-associated pneumonia does not accurately identify potentially resistant pathogens: a systematic review and meta-analysis. *Clin Infect Dis* 2014; 58:330–9.
- Falcone M, Venditti M, Corrao S, Serra P; the Italian Society of Internal Medicine (SIMI) Study Group. Role of multidrug-resistant pathogens in health-care-associated pneumonia. *Lancet Infect Dis* 2011; 11:11–12.

5. Polverino E, Torres A, Menendez R, et al. Microbial aetiology of healthcare associated pneumonia in Spain: a prospective, multi-centre, case-control study. *Thorax* **2013**; 68:1007–14.
6. Maruyama T, Fujisawa T, Okuno M, et al. A new strategy for healthcare-associated pneumonia: a 2-year prospective multicenter cohort study using risk factors for multidrug-resistant pathogens to select initial empiric therapy. *Clin Infect Dis* **2013**; 57:1373–83.
7. Shindo Y, Ito R, Kobayashi D, et al. Risk factors for drug-resistant pathogens in community-acquired and healthcare-associated pneumonia. *Am J Respir Crit Care Med* **2013**; 188:985–95.
8. Jeong BH, Jeon EJ, Yoo H, et al. Comparison of severe healthcare-associated pneumonia with severe community-acquired pneumonia [published online ahead of print]. *Lung* **2013**.
9. Bradburn MJ, Deeks JJ, Berlin JA, Russell Localio A. Much ado about nothing: a comparison of the performance of meta-analytical methods with rare events. *Stat Med* **2007**; 26:53–77.
10. Altman DG. Confidence intervals for the number needed to treat. *BMJ* **1998**; 317:1309–12.

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**Clinical Infectious Diseases** 2014;58(8):1196–7

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DOI: 10.1093/cid/ciu033