Selection Bias in Andes et al

To the Editor—We read with great interest the article by Andes et al published in Clinical Infectious Diseases on 15 April 2012 [1] and would like to make the following comments.

Andes et al conducted an individual patient–level quantitative review of 7 randomized trials including 1915 patients for the treatment of candidemia and invasive candidiasis; and concluded that “two treatment-related factors were associated with improved survival and greater clinical success: use of an echinocandin and removal of the CVC.” Mortality using an echinocandin was 27% compared with 36% when other antifungal drugs were used. We believe that this conclusion is not sustainable in the presented form as the study suffers from a selection bias, which consequently has influenced the results for the following reasons.

First, the 7 trials included are heterogeneous in design as only 3 of them compare the use of an echinocandin with other antifungal drugs. Of the remaining 4 trials, 3 did not include the use of echinocandins and 1 compared the use of 2 different echinocandin classes.

Second, as correctly mentioned by the authors in the discussion, the 7 studies took place between 1989 and 2006, covering a total of 17 years, with the echinocandin trials being conducted between 1997 and 2006. Advances in recent years demonstrate an increase in survival after fungal infection. Changes that have contributed to improved outcomes include high degree of suspicion, improved imaging studies, and the use of indirect biomarkers and biopsies as is the case with invasive aspergillosis, and not just antifungal therapy [2].

This selection bias could have been avoided, if only the 3 studies comparing echinocandins with other antifungals (amphotericin deoxycholate, liposomal amphotericin, and fluconazole), including a total of 1000 patients, were compared [3–5]. However, in that case conclusions would have been different, as the mortality rate of patients who received candinas in these 3 studies (23% [115 of 500 patients]) was similar to that of patients who received other antifungal treatment (24.2% [121 of 500 patients]).

Note

Potential conflicts of interest. J. M. C. has served as a speaker for Pfizer, Astellas, and MSD. O. N. and J. P. report no potential 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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