Rifampin plus Metronidazole for *Clostridium difficile* Infection

*To the Editor*—In their thorough joint Society for Healthcare Epidemiology of America—Infectious Diseases Society of America clinical practice guidelines for *Clostridium difficile* infection (CDI), Cohen et al.


Potential conflicts of interest. D.M.D. reports no conflicts of interest relevant to this article.

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Reply to Drekonja

*To the Editor*—We thank Dr Drekonja1 for his letter, which accurately describes the study of Lagrotteria et al.2 that reported increased mortality in the metronidazole plus rifampin arm of a randomized study of the treatment of *Clostridium difficile* infection (CDI) with metronidazole versus metronidazole plus rifampin. We note that the excess mortality in this study arm was attributed to CDI in only one of the cases as an immediate cause of death, and in their discussion the authors state, “none of the deaths could be attributed to the combination of metronidazole and rifampin.”

The other deaths appear to have been related to additional infections, congestive heart failure, respiratory failure, or pancreatic cancer, as shown in Table 3.2 Thus, it is not at all certain that increased mortality is related to the treatment regimen for CDI. In preparing the guidelines, we discouraged use of antibiotic combinations for CDI, hence the statement: “There is no evidence to support administration of combination therapy to patients with uncomplicated CDI.”

The letter by Dr Drekonja1 only serves to reinforce this recommendation; however, it is not at all certain that there was attributable harm to patients from combination treatment with metronidazole plus rifampin.2

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S.J. reports that he has been an advisor to Astellas, Bio-K+, Optimer, and ViroPharma.

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