Reply to Walker et al

To the Editor—We thank Walker et al for their interest in our work [1]. Our study found no evidence of difference in clinical severity of *Clostridium difficile* infection (CDI) between patients infected with ribotype 027/078 strains compared with others, when adjusted for other covariates [2]. Adjustment for factors on the hypothesized causal pathway between exposure (ribotype) and outcome (severity), such as leukocyte count, has been addressed elsewhere [3]. Removing the leukocyte count as a covariate or including it in the definition of severe disease did not alter our findings [3].

We appreciate the concern regarding the fact that the resultant *P* values were close to the standard *α* level of .05. We used the customary cut-point for *α* found in the scientific literature but appreciate its limitations. It is possible, with more patients, that an association may be found. However, a secondary analysis of our entire dataset ([Supplementary Table 1][2]) was conducted with a total of 413 CDI cases. The association between ribotype 027/078 and severe disease in this analysis yielded an odds ratio of 1.34 (95% confidence interval, 0.67–2.58) when only adjusted for age, sex, and CDI surveillance definition—factors that existed prior to CDI diagnosis.

Contrary to Walker et al’s assertion, we did not intend to claim “evidence of no difference” in disease severity for patients infected with ribotype 027/078 strains. We sought to test the hypothesis that infection with ribotype 027/078...
strains predicts severe CDI. Our analysis implies that there is no evidence to reject the null hypothesis (“no evidence of difference”). We do not claim that, by not rejecting the null hypothesis, we provided “evidence of no difference.”

Our study was limited by population size and restriction to a single hospital system and our methods appear to differ from those in a new study referred to by Walker et al, unavailable to us at the time of this response. Our cases were defined by clinical suspicion of disease coupled with a positive culture and a positive test by either toxin enzyme immunoassay (EIA) or tcdB gene polymerase chain reaction (PCR) [2]. Because toxin EIA-negative/PCR-positive patients with gastrointestinal symptoms might be colonized rather than truly infected [4], the possible inclusion of colonized individuals in our study may have impacted the results.

The extent to which Walker and associates controlled for host factors that could confound their results is unclear as their study is not available at present. Because 027 strains are antibiotic-resistant and largely healthcare associated, they tend to infect patients who are older and more frail than patients infected with other strains, particularly during epidemics [5]. It is unlikely that either of our studies captured nuanced differences between hosts infected with strains of different ribotypes, which is a limitation of study design. However, if there are unique virulence characteristics of 027 strains that impact outcome (as opposed to transmission [6]), the absolute risk to severity posed by these strains is unclear, and less clear is whether treatment decisions based on ribotype are warranted.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online (http://cid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyrighted. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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.

Seth T. Walk,1,2,a Dejan Micic,1
Andrej T. Galecki,1,3,b Mary A. M. Rogers,1
Laraine Washer,1,5 Duane W. Newton,1,6
Preeti N. Malani,1,2,a Vincent B. Young,1,2,a and
David M. Aronoff1,2,b

1Department of Internal Medicine, 2Division of Infectious Diseases, 3Division of Geriatric Medicine, 4Department of Biostatistics, 5Department of Infection Control and Epidemiology, 6Clinical Microbiology Laboratories, 7Department of Pathology, and 8Department of Microbiology, University of Michigan Health System; and 9Veterans Affairs Affairs Ann Arbor Healthcare System, Geriatric Research Education and Clinical Center, Ann Arbor, Michigan

References


a Present affiliation: Department of Microbiology, Montana State University, Bozeman. Correspondence: David M. Aronoff, MD, University of Michigan Health System, 5510-E MSRB I, 1150 W Medical Center Dr, Ann Arbor, MI 48109-5680 (aronoff@umich.edu).

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