Reviewer's report

Title: Antibiotic susceptibility of Clostridium difficile is unchanged despite widespread use of broad spectrum antibiotics

Version: 3 Date: 22 September 2014

Reviewer: Andrew M Morris

Reviewer's report:

I have been asked to review from a statistical perspective only. I found this paper interesting and thought-provoking however, my comments are limited to statistical methodology and conclusions:

Minor Essential Revisions

1. The rationale behind sampling is unclear, as the data set does not contain one continuous period, and therefore may result in bias.

Major Compulsory Revisions

1. The data set only contains 90 samples. The authors have drawn conclusions on 10 different classes of antimicrobials. Sample size precludes inferences from the number of variables they have considered. Additonally, reasonable conclusions cannot be made using the analysis they have used, as they use univariate methods. Because a majority of patients were on more than one antimicrobial prior to CDI diagnosis, multivariate methods are required. A regression model seems considerably more appropriate here, and would largely account for sample size issues.

2. It is unclear how many patients were on antecedent antimicrobials. From Supplementary Table 2, it appears that only 59 patients were on prior antimicrobials. Using n=94, this would make the percentage of patients receiving antecedent antimicrobials at 63%, even though they mention 83% in the manuscript. This requires clarification in the manuscript.

3. Time on antimicrobials--especially in this kind of study--is relevant. A proper analysis exploring the role of each antimicrobial in contributing to risk should also explore the time each patient was on an antimicrobial (e.g. antimicrobials utilized for 1 day should not be considered in the same manner as antimicrobials utilized for 14 days).

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.