Reviewer's report

Title: Risk Factors for Recurrent Clostridium difficile Infection (CDI) Hospitalization Among Hospitalized Patients with an Initial CDI Episode: A Retrospective Cohort Study

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Reviewer: Bryan F Curtin

Reviewer's report:

1. Is the question posed by the authors well defined?

This manuscript highlights the increasing problem of Clostridium Difficile Infections (CDI) and recurrence of disease and then proceeds to identify potential risk factors for recurrent CDI. The goals and question posed by the author are clear and well defined.

2. Are the methods appropriate and well described?

The methods for the most part are comprehensive and well described. One area I think needs more detail is the definition of the high-risk and low-risk antibiotic choices. The authors define which antibiotics they consider high and low risk and cite two papers that appear to have been published by the same group. I think the authors could address this by acknowledging that their antibiotic classifications are based on studies done at the same institution, or by including other studies that have looked at classifying antibiotics by their risk of CDI.

The following paper was recently published and has similar findings of which antibiotics are high risk:


This is a Minor Essential Revision and should be addressed prior to publication.

3. Are the data sound?

The data collected from retrospective review the authors performed appears sound and well stratified.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?
The discussion and conclusion sections are well balanced and supported by their data. However, I think the discussion section is conspicuously lacking a paragraph suggesting possible interventions as a result of their findings, aside from a few sentences at the very end in the conclusions section. While it is important to recognize the importance of modifiable risk factors in the development of rCDI, which of these risk factors can we realistically modify on a large scale. It would be interesting to hear the authors' viewpoints on specific intervention strategies regarding their findings. At minimum the importance of educational initiatives or antibiotic stewardship should be at least mentioned.

In addition, while the authors mention that they found no difference between PPI and H2 blocker and the development of CDI in their preliminary data and past work, there have been multiple studies released in the past few years that suggest H2 blockers may be safer, and this should be acknowledged. Examples include:


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6. Are limitations of the work clearly stated?

The authors clearly and effectively state the limitations of their work in the context of a retrospective observational study.

However, while the authors cite the updated 2010 SHEA/IDSA guidelines on multiple occasions, including discussion about the hyper-virulent strain of Clostridium Difficile and our current knowledge on the risk of acid suppressant therapy, they do not acknowledge one of the most essential elements of those guidelines, which was the stratification of CDI into mild-moderate, severe, severe-complicated cases and the new recommendation of oral vancomycin as a sole first line agent in more severe cases. The patient population they observed was between 2003 and 2009, which would not have been treated according to updated guidelines and thus represents a significant limitation.

This is a Minor Essential Revision and should be addressed prior to publication.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

The authors clearly acknowledge work their are building upon, which is in multiple cases their own published work from prior retrospective studies. As mentioned in my earlier comments, in such occurrences other studies should be mentioned in these cases to give the reader more broadened perspective.
8. Do the title and abstract accurately convey what has been found?
Yes, although I would re-word the Background portion of the abstract so that (rCDI) is preceded by the words "Recurrent Clostridium Difficile infection" and not "Clostridium Difficile Infection recurs" with according changes to the rest of the sentence to make it grammatically appropriate.

This is a Discretionary Revision and the authors can choose to ignore it.

9. Is the writing acceptable?
The writing is acceptable and is of high quality.

Overall this study provide a through and very interesting retrospective observation look at a wide variety of risk factors. While I think that some sections can be further expounded upon (see my previous comments), I would say that the entire body of work is quality and worthy of publication.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

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