Reviewer's report

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

Version: 3 Date: 5 August 2014

Reviewer: Nitish Khanna

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Overall
The authors have answered most of the queries relating to the paper, however, in doing so, numerous grammatical and spelling mistakes have been created. In addition, grammatical issues relating to colloquialisms not detected on the first draft have been found. Therefore, I would recommend a detailed grammatical and spelling check be performed ensuring that each sentence reads well and contains only the essential information. Pay close attention to antibiotic names as still numerous spelling mistakes, Also in supplementary material as well. Advised to review all documents and amend as necessary. Examples found include nitromidazoles, lincosamid, cephalosporines, glykopeptides

Major Compulsory Revisions
None

Minor Essential Revisions
Line 61 – “exemplary” does not make sense: Should be “For example”
Line 63/64 – Review English as does not make sense. Should be: “All strains were susceptible to metronidazole. One strain was resistant to vancomycin”
Line 89 – „Irrespective of ribotype 027, the mortality rate appears to have increased in other parts of the world“ – Can you reference this?
Line 96 – Review English – Drop “an” from sentence: “Various antibiotics have an antimicrobial activity against C. difficile.”
Line 115 – Should be “repeat” and not “repeated” - “There were no repeated stool specimens from patients with recurrent CDI”
Line 204 – „Inpatients were hospitalized during 17.2 days in”
Does not make sense. Do you mean inpatients were hospitalized for 17.2 days on average?
Line 206-9 - Thirty patients (32.6%) underwent one or several complications: 20 patients (21.7%) suffered from infectious complications, and further complications spanned the entire spectrum of medicine (Suppl. Table 12). Seven patients (7.4%) died shortly thereafter, of causes unrelated to CDI.
Review English as does not make sense: You do not undergo a complication. You undergo surgery. Also should be „one or more“ instead of „several“.
Line 210 – “Before the first positive culture, 83.3% of the patients were prescribed antimicrobials, 37.832.2% antifungal medication…”

Clarify this: Do you mean that in the proceeding 8 weeks prior to 1st positive culture, as you have mentioned in your methods?

Line 224 - We believe that the observed resistance is a laboratory artifact.
What evidence do you have to say this?

Line 281 – review grammar

Line 306 – „intermediate“ instead of „intermediates“

Line 317-321 - Review this entire sentence as does not read well/make sense: eg: „high activity“, spelling of „suffered“, „under CDI“ does not make sense

Line 327 – „but for“ does not make sense: should be „apart from“

Line 329 – review „rather“

Line 331 – “and the absence of an outbreak in ZH”
Do you mean absence of an 027 outbreak or outbreak in general? Suggest removing this as does not make sense in current form

Line 339 – Review and/or remove: „reported in a seminal work“

Line 348-51 – „acknowledge that interpretations must be done cautiously and put in a bigger context in concert with published data. While we made a major effort to get hands on a homogenous cohort, the changes in microbiological assays over the time may be regarded as a confounder for diagnosing CDI. Irrespective of this confounder, we are pretty convinced that the retrospective identification of the“

Remove colloquialisms such as “bigger”, “hands on” and “pretty convinced”. These are not scientific terms and should be removed

Supplementary table 1 - Confusion is not a systemic disease? Was there an underlying diagnosis found?

Discretionary Revisions

5. Line 187 - some evidence that antifungals may predispose to CDI. Worth commenting on.

Evidence for this comes from following papers:

Prevalence and clinical features of Clostridium difficile-associated diarrhea in a tertiary hospital in northern Taiwan.
Hsu MS1, Wang JT, Huang WK, Liu YC, Chang SC.

Does Candida species overgrowth protect against Clostridium difficile infection?
Manian FA, Bryant A.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I have received funding for research and fees for public speaking from AstraZeneca