Reviewer's report

Title: Clostridium difficile exposure as an insidious source of infection in healthcare settings: An epidemiological model

Version: 1  Date: 12 June 2013

Reviewer: Jan Lindstrom

Reviewer's report:

This is an interesting analysis and I do not have any serious criticism, but rather some suggestions and questions about the parts which I did not understand quite as well I would like to.

Major compulsory revisions

1) I did not understand the model formulation in some respects:
   - Fig. 1 shows the possible transitions between the seven states, however, I do not understand why the transition matrix in the supplementary material only shows transitions between five states.
   - Table 2 in the supplementary material shows the transition probabilities and state changes. Why does the state change take two time steps, from -1 to +1, rather than just one, from -1 to 1? Please clarify.

2) The Results and discussion section says that the outcome is relatively insensitive to antimicrobial prescription; I am a bit puzzled by this result. Is this because in this context you mean antimicrobials used to treat the C. difficile infection, not the antimicrobials which make patients more vulnerable C. difficile infection. Please clarify.

3) As the approach taken here requires a rather parameter-rich model, the issue of adequate sensitivity analysis becomes inevitable. There are a number of parameters taken with a varying degree of justification: it was assumed that 25% of new admissions were taking (or had recently been taken) antimicrobials, 50% of hospital inpatients were currently on antimicrobials, and a few others. How robust are the results to these assumptions made?

4) As the authors state, the C. difficile epidemiology has shifted in recent years so that it does not only affect elderly patients after antimicrobials but also individuals of all age groups, even without a recent history of antimicrobials. Has this shift been associated with any changes in the parameters relevant to the model presented here? As the authors use parameter values based on published research, I wonder if any of these are ‘outdated’.

Another closely related question: as the parameter values are from different studies, they are presumably also based on different strains. As different strains may have different correlations between the parameter values, is it possible that the ‘model strain’ created here is based on a bundle of parameter values which
would not actually occur together?
Perhaps these issues could be addressed in the Discussion.

Minor essential revisions

5) Fig. 3 shows the means of 1,000 simulation rounds but it would be good to see
some other indicators of those underlying distributions. If they are symmetrical,
means are obviously fine but presenting medians and some other percentiles (25
and 75, or perhaps 2.5 and 97.5) might be more informative.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a
statistician.

**Declaration of competing interests:**

I declare that I have no competing interests