Reviewer’s report

Title: The impact of healthcare visit timing on reported pertussis cough duration: Selection bias and disease pattern from reported cases in Michigan, USA, 2000-2010.

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Reviewer: Flor Munoz

Reviewer’s report:

The authors present a model, simulated population analysis of the impact of healthcare visit timing on reported cough duration in cases of pertussis.

It is difficult in many parts of the manuscript to follow the logic presented to describe the rationale for this project, which deserves further clarification.

Specific comments:

Background

Page 3, Second paragraph, last sentence, arguments regarding lack of effect of antibiotic therapy on cough duration, "even when antibiotics (like erythromycin) are prescribed prophylactically". Note that when antibiotics are given prophylactically, it is evident that this is a time when the patient is asymptomatic, and therefore there should be no measurable effect in the duration of cough, as patients should not be coughing - this definition of prophylactic treatment is not clear throughout the document. Also note that the of certain macrolides and compliance with either treatment or prophylaxis regimens might vary given the presence of side effects, particularly with erythromycin. The "effectiveness" of the antimicrobial would be altered if the treatment is no completed. This was probably the case when erythromycin was in use, as in the period covered by most of the references cited in this section, which are old, except for the Cochrane review of 2007. Finally, it is important to clearly state that the reason for starting antibiotic treatment in symptomatic patients is NOT to decrease the duration of cough, but rather, to reduce shedding and transmission of the B. pertussis pathogen. The authors might want to include some background on the pathophysiology of pertussis, or what is understood of it, including that cough is not directly associated with the presence of the organism in the upper airway, but rather toxin mediated effects which may be long lasting given the injury to respiratory epithelium and other local inflammatory effects as a result of the host response to the pathogen.

Page 3, third paragraph, the example given to explain care seeking bias is confusing as it relates to pertussis and vaccine. Would suggest to use a different example.

Page 4, top paragraph, last sentence - is not clear - in part because there seems to be cut and paste issues, and in part because it continues to talk about vaccination and pertussis while the main
focus of the paper is cough symptoms in pertussis. Consider a different example to make this confusion disappear.

Although one would agree that there is care seeking bias in the results of surveillance for pertussis, and that the number of cases identified do not represent all pertussis infection in a particular population, the explanation provided is confusing when trying to understand the effects of these biases in the duration of cough.

Page 4, second paragraph - Explanation of case exclusion bias - please indicate WHY would cases who delay the initial visit be "under-represented" in the data?

Similarly, why is it assumed that cases with a mild or short duration of symptoms (two different things), may be less likely to seek care?

Again, one can agree that mild cases will likely be fewer than severe cases (case selection bias) among those who seek medical care, but the rationale presented here is not clear.

Methods

Page 5, the assumptions are clearly stated.

Results:

Page 6, first paragraph - there seems to be an issue with data interpretation when the actual duration of cough is not known in the reported surveillance, given that the majority (82.2%) of patients were still coughing at the time the report was finalized.

The findings reported for cases presenting later in the clinical course of their disease are as expected.

However, the comment regarding the use of prophylactic antibiotics is confusing - if prophylaxis was used, it would have been in asymptomatic patients, otherwise, it is not prophylaxis, rather treatment. What is unclear is when the cough started in relation to the use of prophylaxis (failure of prevention), and how severe the cough was in this group, versus those who presented in the first two weeks of cough onset, as severity of symptoms would be a more likely indicator for the healthcare visit, rather than the duration of cough.

Discussion

Page 7 - the premise that "those who used antibiotics prophylactically should have had the shortest duration of cough" does not make sense. Prophylaxis is given after exposure, not after onset of symptoms, including cough. Persons on prophylaxis are not ill yet, although they might
be infected. Again, the symptoms of pertussis, including cough, are not likely to be affected by antibiotic treatment.

The finding that there is a 13 day difference in reported cough length between those seeking care in the first week vs. the third week after cough onset is not surprising, as this is the difference of time in cough duration. It is not clear what the author's message is about this finding.

It would be interesting to know what other factors the authors consider would influence their findings, for example, patient age, vaccination history, type of exposure, comorbidities, etc. There is no mention about this.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
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