Author's response to reviews

Title: Potential for international spread of wild poliovirus via travellers

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Responses to Reviewers

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Dear Editor,

We updated the manuscript with the year 2014 data and some newer references.

Our specific changes are listed point-by-point below:

Reviewer 1:
Stephen Cochi

General Comments:
The authors have made a valiant effort to quantify, through a mathematical model, the risk and extent of international spread of polioviruses from polio-infected countries with active transmission to polio-free countries.

Specific Comments:
Introduction, line 4 -- The WHA did indeed declare polio eradication a "programmatic emergency" in 2012. However, this was a low level of alert, and only a prelude to WHO declaring in May 2014 the situation "A public health emergency of international concern" (PHEIC) under the International Health Regulations that govern all member countries of WHO (this is noted in the Abstract)--- regulations which have only been invoked on two other occasions for pandemic influenza and Ebola, in addition to polio. This distinction should be made here and reinforced on the next page where the PHEIC is discussed.
Response: We have revised the manuscript accordingly.

Introduction, paragraph 3 -- there is updated information related to the first sentence regarding the costs of importation events -- see Cochi et al. A world without polio. J Infect Dis 2014 (Suppl 1):S1-S4 -- "....from 2003 to 2014, there were 191 new importation events into previously polio-free countries, resulting in 3,763 reported cases of paralytic polio in 43 countries and costing $1.15 billion in additional funds from international organization and agencies alone for outbreak control, ..."

Response: Updated accordingly and added the reference.

Introduction, bottom of p.1 -- the outbreak of 199 polio cases in Somalia in 2013-14 due to an introduction of poliovirus of Nigerian origin should be mentioned.

Response: Updated accordingly.

Introduction, p.2, middle -- reference 12 does not apply here, as it refers to the Hajj, not to the situation in India.

Response: not sure what is meant here. But we checked all the references and believe that they are correct.

Introduction, last page - Figure 1 does NOT, as stated, show the number of travelers to India in 2013. These data are in Table 4.

Response: thank you, we have rectified the mistake.

Table 2 - The data for 2014 are now essentially complete and would be highly relevant and timely for this paper to present these data as well. Can the authors add this analysis for 2014? This would provide a current perspective along with the 2013 observations, and increase the value of this paper tremendously.

Response: we obtained the data for 2014, calculated the 2014 estimates, and added the new estimates to all the tables and figures, and revised the manuscript accordingly.

Discussion - please add discussion of the 2014 data, and how they compare with 2013.

Response: done accordingly.

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

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Reviewer 2: Zindoga Mukandavire

Reviewer's report:
The authors developed a mathematical model to estimate the international spread of polio infections which has been described as a public health concern by the WHO. This paper covers a very interesting topic. I have the following comments:

Major
1. The model description is not clear. There is need to include more detail on the model formulation and clarity on how different data sets were used in the model analysis and validation.

Answer: We included a substantial amount of detail in the model's description in the revised version and moved the equations to a new Box 1.

2. It is not clear as to how asymptomatic and symptomatic cases were factored in the model.

Answer: as mentioned in the original version "Published estimates of the ratio of inapparent to paralytic illness vary from 50:1 to 1,000: 1 (usually 200:1).14We assumed a ratio of 200:1". We included a new phrase that reads: "As we assumed a 200:1 asymptomatic to symptomatic ratio we multiplied the number of reported cases at year in country i ( in equation (3) of Box 1)." We hope this is clearer now.

3. Explicitly show how vaccination and importation of cases were incorporated in the model.

Answer: Vaccination is included in the estimation of the number of susceptible, as mentioned in the revised Table 1: "Calculated from the total population in country i at year t times the probability of not being vaccinated". Cases imported to each particular country is computed in the total number of reported cases.

4. Is there evidence to support that disease incidence is constant as assumed in equation (3)?
Answer: In fact the disease incidence varies from year to year but we assumed no seasonal variation in each year and so the term "constant along the year" in the new version.

Minor

1. Equations in the Methods section should be moved to a Supplementary Methods (i.e. equations (1-4)).

Answer: The model's equations were removed to a new Box 1. Boxes 2 and 2 can be used as supplements, although we prefer these boxes to be in the text as the model and the sensitivity analyses are integral to this manuscript and not just a supplement. But we leave this decision to the editor.

2. Page 3, Paragraph 2, Rephrase to avoid repetition “In response to ongoing importations of poliovirus into polio-free countries, on 5 May 2014, the WHO's Director-General declared the international spread of wild poliovirus a public health emergency of international concern (PHEIC).”

Answer: text was revised accordingly.

3. Table 1 should also include table parameter values and references.

Answer: We did this in the revised manuscript

4. Lines 4-7 of paragraph 1 in the Discussion section should be moved to the Methods section.

Answer: The methods section includes a detailed description of the model using many mathematical terms. We feel it is important to repeat some of the model description in the discussion using less mathematical terms so that the readers fully understand the advantages of our model. Hence, we did not move this text to the methods section, as the methods section already contains the description (now also partially moved to the Boxes in response to the other comments). However, we did condense the description of the model in the discussion to avoid any (or too much) repetition with the text in the methods.

Quality of written English: Acceptable

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

Declaration of competing interests:

We declare that we have no competing interests