Author’s response to reviews

Title: Assessing Chikungunya risk in a metropolitan area of Argentina through satellite images and mathematical models

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Version: 1 Date: 20 Sep 2015

Author’s response to reviews:

September-20-2015

BMC Infectious Diseases

Dear Editors,

Please find enclosed with this letter the revised version of my manuscript “Assessing Chikungunya risk in a metropolitan area of Argentina through satellite images and mathematical models” by D. Ruiz-Moreno (diego.ruizmoreno.phd@gmail.com) which I would like to submit for publication as an article in BMC Infectious Diseases.

I would like to thank both reviewers for their insightful comments, as these comments led to a significant improvement on the manuscript that I am submitting. This revision reflects all the suggestions proposed by the reviewers as you can see in the detailed list bellow. As suggested the Results, Discussion and Conclusion sections were modified to improve the implications and constrains of the model. The equations of the model are still showed in the supplemental material, but a description of the dynamic of the model is now included in the methods section. I hope with these revisions the main focus of the manuscript is enhanced and the modeling details are sufficiently clear without overwhelming the readers with the equations of the model —that are still available in the supplementary material. In addition to that, I would like to thank the reviewers for the suggestions on future directions for this modeling approach some of which are already in progress.
Yours sincerely,

D. Ruiz-Moreno

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Reviewer #1—Major Compulsory Revisions

Methods

1. Line 131, up to 50% of the population was allowed to move between neighborhoods. Could you clarify how long the period was referred to?

The text was expanded to clarify that the human movements are intended to simulate the daily routine of humans, and therefore these movements are in the scale of hours.

2. Line 133, please clarify "mosquito movement was restricted to a small fraction of the available population". Do you mean the movement was restricted geographically?

The text was expanded to incorporate the data that only ~5% of the adult mosquito population was allowed to move. In the original text (and in the revision) the sentence that followed clarifies that the movement was restricted to at most 200 meters per event.

3. Line 134, is there a seasonality pattern in the flight distance of mosquito?

No seasonal pattern is included in the flight distance of mosquitoes. We had the intention of perform experiments to measure flight distance during the study year. Unfortunately, unforeseen financial and extreme climatic difficulties made experimentation impossible at the study area.

4. Line 134, could you provide the details how the flight distance is incorporated in the model?

This is how the movement works. For each location a set of up to ~5% of the adult population was selected to move to another location. The set of possible destination was set to be only those
locations that are located at no more than 200 meters of the departure location. Mosquitoes (selected to move) were uniformly distributed among the possible destinations.

5. Line 152-154. Is the local data for rainfall available? The wetness obtained by satellite image provides the geographical detail but lacked the time resolution (6 measurements in 1.5 years) and is a limitation. If rainfall data is available, would it be possible to combine the two measures?

There is no really any (official) local measurement of rainfall, because of that we want to use remote sensing as a proxy for environmental conditions. The (new) local university is setting up a meteorological station for the area, however only one (incomplete) year of data was collected. In addition to that, in that year there were several extreme rainfall events (up to 400 millimeters per hrs) that made the time series extremely unusual. As you can imagine, that time series was not really useful for this particular modeling exercise.

6. Line 156, could you provide some detail of the wetness index, so the readers can understand what -50 means.

The text was expanded to incorporate information of the method used to determine the value of the index. Once again, the impossibility of perform experiments was the main reason to relay in these approach.

7. Line 164, what was the time step used for the simulation?

The time step in the model is one tenth of a day, (2 hour and 24 minutes). The text was expanded to incorporate this information.

8. Line 165-167. The main focus of the study is to assess the effect of introduction of Chikungunya virus. It is important to provide details about how the virus was seeded into the population in the simulation. For example, what is the location, timing during the month, etc.

The text was expanded to incorporate detailed information on disease introduction.

9. The model results depend on the parameters. It is essential to describe how the model parameters were selected.
The text was expanded to incorporate detailed information on the parameters and their value is reported in Table 1.

Results

10. Line 159, it would be informative to provide a figure with the smoothed values for the total area in the results.

The text was expanded to incorporate a Figure with this data.

11. Were the results sensitive to how the virus was seeded?

The results hold if the virus was introduced in different locations.

12. The model incorporated symptomatic and asymptomatic infections. It will also be interesting to see how the two numbers increased over time in the simulated epidemic.

Because the model assumes that inside each neighborhood there is perfect (or homogeneous) mixing the ratio of symptomatic to asymptomatic is on average 3:1. The variability displayed in the simulations is due to demographic stochasticity. Models that include heterogeneity in the human population (i.e., a model where age structure determined commuting rates) may be more interesting to follow asymptomatic and symptomatic individuals.

13. Line 186, a very high probability of Chikungunya outbreak (95%) was estimated for March, and high probability for December to July. To understand the performance of the model prediction, does that match with the reported case in Florencio Varela in March for the previous years?

Up to this point there are no cases of Chikungunya in Argentina. One of the goal of this work is to inform about the potential risk of the introduction of the disease.

14. Figure 5, y-axis, do you mean 'infected' instead of 'affected' population?

The caption and the label of axis were modified to avoid the confusing wording.
15. Figure 5, there was a sudden drop in % of affected population in each neighborhood. There was no such subtle change in temperature (Fig 3) or probability of invasion (Fig 4). What was the reason of this result? Also, is this consistent with the number of reported Chikungunya case in May?

The sudden drop seems to be related with habitat quality and therefore the number of vector.

16. It is informative to provide the simulated mosquito population size over time.

The text was expanded to incorporate a Figure with this data.

17. Figure 6. Could you clarify what do you mean by saying the population 'at risk'? do you mean expected number of infections or other meaning?

It is the mean number of infected (based on the simulations).

Discussion

18. Line 215, please clarify which outcomes in this study were consistent with the listed works?

The text was expanded to incorporate information on the finding of the listed works.

19. Line 227-230, while the preventive measures (1) and (2) are probably effective. However, the corresponding results were not reported in the study.

This work is a part of a research project that includes a detailed evaluation of the effect of different control measures. To better quantify the effects of control measures a calibration of the model seems to be required. This process will include (a) sampling mosquito populations to better understand the vector:host ratio, (b) set up (or use) local meteorological stations, (c) include rainfall (or superficial water-flow) as a part of the model, and (d) fit disease data. For that the model should be set up in a location with either endemic or epidemic Chikungunya.

20. The limitations of the study was not described.

The text was expanded to incorporate information on limitations of the model (lines 295-316)

Supporting Material
21. Please define the states, (G, D, C, etc.)

These are now included in the introductory description of the model (lines 116-120)

Minor Essential Revisions

22. Line 212, typo "hight"

Fixed

Reviewer #2—Specific comments

1) It is not clear from the manuscript how human travel/movement is implemented. It is stated that this is proportional to population size but does this determine the rate to or from a population centre or both? It is stated in the supplementary material that this is determined by a matrix but this matrix is not given.

The human movement is implemented via a matrix that specifies the rate of movement between neighborhoods. Each neighborhood can act as source or destination. The matrix is the result of the attractiveness of each destination from the source (of the movement) perspective, thus, a big neighborhood (in population size) is more attractive for a small (in population size) neighborhood than for a big (in population size) neighborhood. The supplementary material was expanded to include this information.

2) Lines 176-178: "...it was possible to test whether a difference arise from considering epidemic thresholds from symptomatic or asymptomatic individuals...". It is not clear to me what this means or how it was analysed.

Several different threshold levels were used to define the event that disease invasion was considered successful. With these different definitions, the probability of a successful invasion was calculated. For example, we estimated the probability of invasion counting a success whenever there were more than 5 symptomatic infected cases in the simulations (i.e., outbreaks with only 2, 3, and 4 symptomatic cases and any number of asymptomatic cases, were ignored). The figure suggest that outbreaks do not have an intermediate size (therefore the differences between 5 and 50 cases is negligible). This is facilitated by the fact that under the assumption of homogenous mixing inside each neighborhood, disease spread quite easily once a couple of cases are generated. The main text was modified to clarify these criteria.
3) Methods lines 173-180: the description of "measures used to quantify the probability of an outbreak" is inadequate and it is thus difficult to know how to interpret Figures 4 and S1. Furthermore, there should be some discussion of Figure S1 where these probabilities appear to be identical across all months except for a small difference for the red bars in June and a bigger difference in July. How do the authors explain this?

The text was expanded to incorporate information on the calculations and also results from Fig 4 and S1 were addressed in that section and in the conclusions.

4) Conclusions lines 228-230: the authors state that "(1) reducing the movement of exposed individuals could reduce the spread of the disease and (2) reducing the population size of the vector could reduce the probability of disease transmission". This begs the obvious question, why not use the model to explore this? The paper would have far more impact if the impact of these potential interventions (and perhaps others) were investigated.

This work is part of a research project that includes a detailed evaluation of the effect of different control measures. To better quantify the effects of control measures a calibration of the model seems to be required. This process will include (a) sampling mosquito populations to better understand the vector:host ratio, (b) set up (or use) local meteorological stations, (c) include rainfall (or superficial water-flow) as a part of the model, and (d) fit disease data. For that the model should be set up in a location with either endemic or epidemic Chikungunya.

Minor comments:

1) Abstract lines 18-19: it should be stated that "In America, it is transmitted mainly by the MOSQUITO Aedes aegypti...". Similarly add "...and at that time THE MOSQUITO Ae. aegypti appeared to be the main vector..." at line 52 in Background.

The text was expanded to incorporate this information.

2) Abstract lines 21-22: the name of city should be given, i.e., "...in the metropolitan area of Buenos Aires, the capital city of Argentina."

The text was expanded to incorporate this information.

3) Line 77: it is not clear to me what an "intrinsic" incubation period is?

The intrinsic incubation period is the time from the contagium event up to the point of developing symptoms in the human host, as opposite to the extrinsic incubation period which is
the equivalent time period by in the vector. Although both terms are common in the vector borne disease readership, we incorporate modified the main text to clarify this point.

4) There are numerous abbreviations throughout the manuscript that are not defined. Each abbreviation should be defined the first time it appears in the manuscript.

The text was modified to define each term and abbreviation.

5) The format used for references is not the correct format for BMC Infectious Diseases. These should be numbered and the authors should refer to the instructions to authors for the correct format.

The format was modified.