Reviewer's report

Title: Emergence of chikungunya seropositivity in healthy Malaysian adults residing in outbreak-free locations

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Reviewer: Luke Mease

Reviewer's report:

This paper provides new information on the epidemiology of Chikungunya, particularly regarding infection and spread in non-epidemic areas of a country to which CHIK has (presumably) arrived within the past 15 years. Given CHIK’s importance as an emerging infection with the potential for global spread (e.g. to Latin America) causing severe morbidity, this work merits publication, provided that the authors address several important issues with the manuscript as currently written. These are discussed below.

Major Compulsory Revisions

1) Maps/spatial analysis. This is the biggest issue with this manuscript. This manuscript should not be published unless these issues are resolved or the discussion about spatial analysis and the maps are removed. The manuscript would still merit publication if these were removed, but the manuscript will be much stronger if they are corrected. Specific issues follow:

- “Spatial analysis.” I consider this term to refer to methods-based quantitative analysis of spatial data. Did you do a quantitative analysis? If so, which methodology (or methodologies) did you use and what were your results? Or were you methods purely quantitative (i.e. creating a map and then looking at it)? Either one is OK, but please be more clear in the paper.

- What made a “cluster?” in your analysis? Was this quantitative or qualitative (e.g. defined by consensus)? Please give more details.

- The maps, as currently prepared are unclear. A small locator map, included as part of the larger maps would be very helpful. The color scheme of the maps is also unclear. What do the boundary lines represent? Are all of the small geographic units shown on the maps necessary? It is unclear to me, with the current maps, where the boundaries between the different regions are. Indicating the location of previous outbreaks would be useful.

Minor Essential Revisions

1) The writing is a bit wordy throughout and could use careful revision for grammar.

2) Malaysian Cohort. This seems like an interesting, useful project. However, as currently written, the objectives and methods behind the cohort are not clearly
explained. For example, the paper says that it “is a national project initiated in 2006 to recruit 100,000 individuals...” Surely the project has more purpose than this. If there is an existing peer reviewed publication that explains the purpose and processes behind the cohort, it would be useful to cite this in the paper. If not, you might consider preparing such a manuscript in the future and including the Cohort’s website in this manuscript (or its references).

3) Logistic regression. As written, it is not entirely clear to me how you did your logistic regression. For example, it says that univariate and multivariate logistic regression were performed only in the Results section, not in the Methods section. Also, how did you build your multivariate models. Were all factors included in these models?

4) Please include some discussion of the regional and global implications of the findings from this study. As it stands the discussion is fairly Malaysia-centric. Chikungunya is important because it has spread a great deal in the last decade and has the potential to continue to do so in the coming years. This study would be strengthened by further discussion of how its findings help us better understand this disease and its spread.

5) Please include a section in this paper discussing its limitations.

Discretionary Revisions

1) Comparison of Chikungunya seroprevalence rates. The first paragraph of Discussion section compares the seroprevalence rates from your study with other studies. I think that this comparison is misleading, as your study was looking at seroprevalence in non-epidemic areas, but the other studies cited looked at seroprevalence rates post-epidemic. Similarly, I think that comparing the urban/rural rates in Malaysia with those of Lamu island may not be appropriate, since the difference between urban and rural Malaysia is very different from the difference between urban and rural in Lamu.

2) I am interested in the mobility of the Malaysian population. How mobile is the population? Does the fact that a study participant doesn’t currently live in an epidemic area tell us that they likely were not in the epidemic area in previous years?

In summary, this paper presents important information and merits publication, provided that several important issues are first resolved.

Level of interest: An article of importance in its field

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

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