Reviewer’s report

Title: Factors associated with Human West Nile Virus Infection in Ontario: A Generalized Linear Mixed Modeling Approach

Version: 1  Date: 24 Feb 2018

Reviewer: Tommy Hing-cheung Tang

Reviewer's report:

***General comments***

Unlike Japanese encephalitis virus, no vaccine is currently available to protect humans from the West Nile virus (WNV). Early warning systems to predict severe human WNV season is necessary to reduce WNV related morbidity and mortality.

The authors have conducted a modeling study relating annual WNV incidence in southern Ontario to specific parameters in climate (temperature and rainfall), environment (land cover), human population (age and gender composition), and vectors (proportion of WNV infection in captured mosquitoes). This is a timely study to supplement additional information to existing knowledge about WNV presence in the region. The manuscript is a good try, however, as previous review has pointed out, the flow is a bit disconnected in methods. May the authors further explain why a new, separate model was constructed to investigate association between "early season" climate variables and annual WNV incidence?

The authors may aware a very similar study by Giordano et al. (PLoS One. 2017 Aug 22;12(8):e0183568. doi: 10.1371/journal.pone.0183568. eCollection 2017.) which also described seasonal and geographical trends in WNV activity in southern Ontario. Non-Canadian readers may gain useful insights by reading the work by Giordano et al. to understand the background. The authors may consider adding some essential information. For example, there are 36 public health units in the province of Ontario, the reason of grouping Culex pipens and Culex restuans under the group Culex pipens/restuans etc. Also, the authors should consider to include this article in their references since it addressed and investigated the issues alike.

During the peer review process of the first submission (INFD-D-17-1640), Reviewer 1 has asked the data about frequency of precipitation (days per month). The authors' reply was "Unfortunately, data on the frequency of precipitation were not available." I would like to point out that, the data is openly available from the Government of Canada webpage (address: http://climate.weather.gc.ca/prods_servs/cdn_climate_summary_e.html), recorded in spreadsheets summarizing monthly climatic data. One of the columns is "Number of days with Precipitation 1.0 mm or more (Pd)". Short term but large increase in precipitation may have a
negative impact in both larval and adult mosquito survival (Jones et al. J Med Entomol. 2012 May;49(3):467-73.).

One of the special features of the manuscript is the usage of land cover data. As the authors pointed out that environment have influence on WNV transmission via its effect on ecology. May the authors walk the extra mile to utilize these data? A US group has published a remarkable ecological niche model of the estimated probability of Culex tritaeniorhynchus presence, and thus Japanese encephalitis in Asia (Miller et al. PLoS Negl Trop Dis. 2012;6(6):e1678. doi: 10.1371/journal.pntd.0001678.).

The basis to understand WNV transmission is that WNV infection a zoonosis. Transmission of the WNV involves the enzootic cycle with birds as amplifying hosts. The statistical model would be enhanced if avian data is incorporated. The Canadian Wildlife Health Cooperative (CWHC) has the WNV surveillance in dead birds available (2009-present, address: http://www.cwhc-rsff.ca/data_products_wnv.php). The Canadian Cooperative Wildlife Health Centre (CCWHC) (probably the same organization as the CWHC) has published dead bird surveillance reports specific to individual Canadian provinces (for example, the 2005 data can be found in the following address: https://digitalcommons.unl.edu/cgi/viewcontent.cgi?referer=&httpsredir=1&article=1046&context=icwdmcwwhcnw). In addition, the authors may mention the role of migratory birds as they may contribute to the long range transport of WNV (Drebot et al. Can J Infect Dis. 2003 Mar;14(2):105-14.). Migratory birds travel across Ontario and bird sanctuaries are located some PHUs. For example, the Jack Miner Migratory Bird Sanctuary in the Windsor-Essex County PHU with the highest incidence.

***Specific comments***

Line 105: What is the case definition of both confirmed and probable human WNV infections? Please state or provide reference.

Line 229 to 237: Is there any other biologically plausible explanation for a higher spring temperatures and WNV incidence? Like, quicker thawing may increase flow of water bodies which is unfavourable for larval survival?

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.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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