Author's response to reviews

Title: The influence of geographic and climate factors on the timing of dengue epidemics in Peru, 1994-2008

Authors:

  Gerardo Chowell (gchowell@asu.edu)
  Bernard Cazelles (cazelles@biologie.ens.fr)
  Helene Broutin (broutinh@mail.nih.gov)
  Cesar V Munayco (cvmunayco@dge.gob.pe)

Version: 2 Date: 18 January 2011

Author's response to reviews: see over
Submission of a research article

Tempe, December 31, 2010

Dear Editor,

Please find enclosed a manuscript, “The influence of geographic and climate factors on the timing of dengue epidemics in Perú, 1994-2008”, by Gerardo Chowell, Bernard Cazelles, Helene Broutin, Cesar V. Munayco, which we wish to resubmit for publication in *BMC Infectious Diseases*.

We have significantly revised our manuscript following the Reviewer comments. In particular, we have simplified the presentation of the article and focused on the main findings of the paper to improve its readability. The paper has been shortened considerably as a result of this simplification.

Dengue represents an increasing public health problem in Latin American nations including Perú, a geographically diverse country. Increasing our understanding of the transmission patterns of dengue at different spatio-temporal scales could suggest improved intervention strategies particularly in the context of limited resources. We studied the spatial-temporal patterns of dengue in Perú across three distinct geographic regions. We found that dengue is highly persistent in the jungle region where epidemics peak most frequently near March when rainfall is abundant. Moreover, findings indicated that the timing of dengue epidemics between the jungle
and coastal regions could be explained by the timing of the seasonal cycle of ambient
temperature. Jungle regions and cities of other dengue-endemic neighboring countries may be
the source of outbreaks in the coastal regions where dengue incidence typically reaches low
levels during the dry season. Our results demonstrate the advantages of using high-resolution
spatio-temporal data to detect heterogeneity in the timing of epidemics, and thus, have
implications for dengue control strategies.

We believe that this paper presents results that could lead to improved control interventions
against dengue to many nations experiencing similar patterns of dengue transmission.

This paper has not been submitted elsewhere, and all authors have approved the final version of
the manuscript.

Thank you very much for your consideration.

Sincerely,

Gerardo Chowell

Corresponding author:
Gerardo Chowell, PhD
Assistant Professor
School of Human Evolution and Social Change
Arizona State University
And
Fogarty International Center, NIH

Box 872402
Tempe, AZ 85287
Phone: 480-965-4730
Fax: 480-965-7671
Email: gchowell@asu.edu
Reviewer #1

Reviewer's report
Title: The influence of geographic and climate factors on the timing of dengue epidemics in Peru, 1994-2008
Version: 1 Date: 26 August 2010
Reviewer: scott ritchie

Reviewer's report:
This ms details epidemiological patterns for purported dengue outbreaks in Peru from 1994-2008. Patterns from jungle, mountainous and coastal areas are described. The authors state that the patterns suggest that persistent endemic dengue in jungle areas serves as a reservoir that sparks dengue in other areas. Unfortunately, there is no real data to indicate this. Ultimately, analysis of imported coastal/mountain cases with a travel history from jungle areas would be useful.

Response:
We have investigated the statistical associations between dengue incidence during the period 1994-2008 and demographic and climate factors across geographic regions of the country by using statistical methods and wavelet time series analysis. The statements made in this manuscript are by no means conclusive (as we explain in the paper), but we provide evidence for "differences in the timing of dengue epidemics in jungle and coastal regions are significantly associated with the seasonal temperature cycle."

Response:
We have shortened the manuscript which we have now focused on the main findings. We have made an effort to provide detailed descriptions of the spatio-temporal patterns of dengue dynamics in Peru to be able to support our findings namely "support the presence of significant differences in the timing of dengue epidemics between jungle and coastal regions, with differences associated with the timing of the seasonal cycle of mean temperature."

Response:
We note that similar analyses to the ones conducted in our study have been used widely for a number of infectious diseases including the study of dengue dynamics in several countries including Thailand, Mexico and Puerto Rico (Cazelles et al. Plos Med 2005; Johansson et al. PLoS Med 2009), and more recently on the spatio-temporal patterns of dengue in southern Vietnam (Thai et al. PLoS Negl Trop Dis 2010). In our paper we have carried out both statistical and wavelet time series analysis to detect heterogeneous levels in the spatio-temporal dynamics of dengue epidemics across geographic regions.

Response:
On Page 7: case defintion based on fever + headache and bodyache??? Sounds like flu to me! And you only state 18% of the cases were confirmed by IgM. I am worried that the definition is too broad and will include other illness in addition to dengue. I really think, based upon the ambiguous case definition, that probable cases should be excluded from the analysis. This will mean redoing the analysis. But I do think you must use confirmed dengue cases, not suspected ones.

Response:
The use of data consisting of probable (epidemiologically-linked) dengue cases for the study of the spatio-temporal
The dynamics of dengue is not uncommon (e.g., Chowell et al. Epi & Inf 2008; Thai et al. PLoS Negl Trop Dis 2010). As we state in our manuscript we use case definitions for probable and confirmed dengue cases as specified by the World Health Organization (WHO) guidelines. The amount resources necessary to achieve high sampling rates limits the number of probable cases that can be tested in the laboratory particularly in developing countries. We have included this limitation in a new caveats paragraph in the discussion.

References:


Johansson MA, Cummings DAT, Glass GE


Reviewer # 2

Reviewer's report
Title: The influence of geographic and climate factors on the timing of dengue epidemics in Peru, 1994-2008
Version: 1 Date: 27 September 2010
Reviewer: Wenbiao Hu
Reviewer's report:
Discretionary revisions
This is a well-written, clear, concise, and interesting paper about the influence of geographic and climate factor on the timing of dengue epidemics in Peru. Both methods and conclusions obtained from the results are adequate and the paper is worth to be published with minor changes.

Response:
We are glad that the Reviewer found our paper interesting and the results and conclusions to be sound. We have further simplified the manuscript as suggested by the first reviewer by focusing on the main findings.

I have few comments that follow.
1. Authors used a simple correlation (Spearman rho) to examine the “moves” from jungle provinces to mountain and coastal provinces. It would be better to use a regression model (e.g., logistic regression) to assess the “move” after adjusting for confounders.

Response:
We thank the Reviewer for this comment on the methodology used in our paper. Our analyses have taken into account the role of geographic, climate, epidemiological and demographic factors. Moreover, our data has been analyzed at several spatial scales (national, regional and province levels). Furthermore, to partially account for the
introduction of new serotypes in Perú, two time periods were assessed in our analysis: 1994-1999 (1st time period) and 2000-2008 (2nd time period). These time periods correspond to the time intervals before and after all four dengue virus serotypes started to co-circulate in Perú. We note that we have use both statistical and wavelet time series methods to detect heterogeneous levels in the spatio-temporal dynamics of dengue epidemics across geographic regions as in several previous studies (e.g., Cazelles et al. Plos Med 2005; Johansson et al. PLoS Med 2009). Our wavelet time series analyses are used to quantify the non-stationary relationship between dengue time series and climate variables through wavelet coherence analysis by geographic region.

2. To improve the presentation, I would advise using a regression line in figure 6.

Response: Addressed as indicated.

3. The study suffers from the usual problems of an ecological design such as ecological fallacy. The authors should acknowledge the limitation as well as the roles of social, economic and tourism factors in dengue transmission in discussion section.

We have included a caveats paragraph in the discussion of the paper to collect the limitations of our study as suggested by the Reviewer.

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests