Author's response to reviews

Title: Extreme Precipitation and Emergency Room Visits for Influenza in Massachusetts: A Case-Crossover Analysis

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Response to Reviewers, Environmental Health ENHE-D-17-00137

We thank the reviewers for their time and their thoughtful and helpful comments and suggestions.

Reviewer #1

Reviewer #1: The article entitled « Extreme Precipitation and Emergency Room Visits for Influenza in Massachusetts: a case-crossover Analysis » focuses on an interesting issue: the impact of weather conditions on influenza dynamics in temperate areas. Considering that extreme climatic events are likely to become more frequent in the next decades due to climate change, improving our knowledge of their impact on public health might prove essential to enable the adaptation of disease control measures.

Yet, the authors could enhance the interest of the paper by clarifying some points and completing the discussion part. It would notably be important to discuss the choice of the Emergency Room Visits as a proxy of Influenza dynamics and to develop the perspective to explain how the presented results could help in adapting disease control measures.

Thus I recommend accepting this article for publication with major revision.
Detailed comments:

Abstract:

The conclusion part in its current version just make a summary of the results while it could present hypotheses explaining these results and suggest some ways to use them to adapt public health measures.

Response: We have now revised the abstract conclusion to reflect the reviewer’s suggestion.

Background:

"Extreme rainfall such as that […] influenza occurrence". This part could be completed. Indeed some studies showed that rainfall is negatively associated with Influenza Incidence while, as said in the paper, extreme rainfall events have been shown to increase this incidence. Thus there is an interesting distinction to underline here based on references between the impact of environmental conditions (more humidity, less influenza persistence, see for example the table in Vittecoq et al. 2015 Epidemiol. Infect. 143, 3384-3393) and behavioural impacts of extreme events (heavy rain, more crowding).

Response: We agree with the reviewer that there is an important distinction between impacts of extreme precipitation on behavioral response and environmental conditions (low/high humidity) that should be noted. We have now noted the literature in the background and expounded upon this previous research in the discussion section of the manuscript.

Methods:

Environmental data: It would be useful to add a reference to justify the use of Kriging in the determination of precipitation distribution. It seems also important to explain how the definition of extreme events (values exceeding the 99th percentile of daily local precipitation) was chosen since this choice as a considerable impact on the results.

Response: Multiple references are now included to justify the use of kriging to determine precipitation distribution. Analyses conducted using lower cut points for rainfall showed positive, but nonsignificant associations. Although the definition of extreme rainfall varies among locations, previous research in this study area identified the 99th percentile as distinguishing between heavy and extreme precipitation; see Jyotsna S. Jagai, Quanlin Li, Shiliang Wang, Kyle P. Messier, Timothy J. Wade, Elizabeth D. Hilborn. Extreme precipitation and emergency room visits for gastrointestinal illness in areas with and without combined sewer systems: an analysis of Massachusetts data, 2003 – 2007. Environmental Health Perspectives. 2015. 123(9):873-879.
Originate

P7, Line 14: The socioeconomic status is mentioned while it was not used in the analysis. Why?

Response: Because we analyzed the association between extreme precipitation and ER visits for influenza using a case-crossover approach, each case was self-matched which inherently controls for individual confounding factors like socioeconomic status. Also, since the analysis made use of hospital administrative data, individual-level data on socioeconomic status was not available.

Results:

P9, Lines 13-32: It was weird in this part to mix American units (e.g. inches/day) with metric system (e.g. μg/m3) could it be homogenized?

Response: While we acknowledge the metric and Imperial units are mixed, this paper is originating in the US, and these are the units commonly used for each variable we reference; these are the units commonly reported in the literature.

P9, Line 53: I did not understand the meaning of "Individual" in "significant association at lags 2 and 3. Individual."

Response: This was a typo and has been removed from the text.

Discussion:

It seems important to discuss somewhere the choice of the ER visits as a proxy of influenza cases in the studied area. Some references should be cited to confirm that it's a good choice and possible bias should be mentioned. As an example it's not clear if the patients have been tested for influenza virus infection or if they just presented influenza like illness. According to the definition of the "code 487" I guess they presented ILI but it should be clearly stated in the paper.

Response: the following text has been added to address the reviewers concerns: “The use of hospital administrative data, specifically ICD-9 diagnostic codes, means we cannot rule out the possibility that some patients presented influenza like illness and were not actually tested for infection with influenza virus, however this misclassification is likely nondifferential with respect to exposure status. Additionally, emergency department data is often used for influenza syndromic surveillance, acting as a general indicator of influenza morbidity in the target population”.

P11 line 35: "This observation consistent with existing literature…", "is" is missing here.

Response: Thank you for finding this omission – the statement has been corrected.
"This observation is consistent with existing literature which shows Blacks having higher rates of influenza hospitalization than whites." I'm not certain to understand this explanation. Black people may be more vulnerable to influenza infection in general but here the result is not "there are more blacks that went to the hospital due to influenza" but rather "the association between ER visits and extreme rainfall events was stronger in Black than in other ethnic groups" and here it seems to me that an hypothesis is missing. Do the crowdings have more impacts in this group and why? Besides, the relative proportions of ER visits in the different ethnic groups could have been compared to the proportion of these groups in the general population of the State to see if there is indeed an excess of visits among black people or not. Finally socioeconomic vulnerability is also presented as a potential risk factor for influenza infection in Blacks and in the method section data on socioeconomic status were mentioned. Could they be used to disentangle the role of poverty versus other factors in the ethnic differences highlighted here?

Response: We agree that the statement made were not clear. We have taken the reviewer's suggestion and clarified the text, as well as, compared the proportion ER visits for influenza to the MA general population. While disentangling the socioeconomic vulnerabilities within the study population would add valuable information to draw conclusions upon, these data were not available for this study. There were no data available on crowding. This paragraph has been revised to address the issues stated above.

P12, 114 "this may be reflective of congregation in indoor school settings, which often temporally coincides with increased reports of influenza" Could the effect of the "holidays" factor be discussed here?

Response: We discuss holidays in the last line of page 13 in the discussion section: "Factors that did vary with time were assessed as confounders in the analysis. For example, holidays which are time-varying, can potentially affect rates of hospitalization, and may reduce influenza transmission, were included in the final model."

P13, L31 The word "present" is repeated two times here.

Response: We have corrected the text.

Conclusion

It could be interesting to be more specific on the adaptations that could be made in public health measures and to cite other pathogens that might have the same dynamics and thus be impacted if extreme rainfall events were to become more frequent.

Response: We have now expanded the conclusion section to include the above suggestions.

Reviewer #2:
Reviewer #2: Extreme Precipitation Emergency Room Visits Influenza Mass, Case-crossover Analysis

In tropical regions, precipitation, temperature, and humidity are systematically related to the timing and number of influenza cases. The study authors wonder if a similar relationship could be found in a more temperate climate. The study uses a high quality data set of classified influenza emergency room visits over 2002-2008 in Boston, MA. The statistical analysis was conducted through a standard case-crossover approach. Extreme precipitation events in the preceding week increased the odds of recording a severe influenza case. The authors subsequently discuss potential mechanisms for this association such as overcrowding and virus survival outside of a host. The manuscript is relatively well written.

Response: Thank you for your response to our submitted manuscript.

Major Comment

* The study neglects the larger literature on specific humidity and influenza transmission. The study should also reference transmission mechanisms related to specific humidity. Previous studies have shown that seasonal influenza activity in the tropics is associated with high levels of specific humidity (Tamerius et al. 2013a; Soebiyanto et al. 2014; Soebiyanto et al. 2015; Thai et al. 2015). Although there is mixed evidence, some studies found a positive relationship between specific humidity and influenza virus survival outside of a host and transmission risk.

Response: Although the primary focus of our investigation is extreme precipitation, we agree with the reviewer that current studies show mixed evidence in relation to humidity and influenza and this important point should be noted. The background section has been revised to acknowledge literature on humidity and influenza transmission.