Author's response to reviews

Title: Investigation of an Influenza A (H3N2) Outbreak in Evacuation Centres following the Great East Japan Earthquake, 2011

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Author's response to reviews: see over
Dear Dr Pafitis

Re: MS1272534689101964 Investigation of an Influenza A (H3N2) Outbreak in Evacuation Centres following the Great East Japan Earthquake, 2011

Please find enclosed our revised manuscript titled “Investigation of an Influenza A (H3N2) Outbreak in Evacuation Centres following the Great East Japan Earthquake, 2011” for consideration as Research Articles for publication in *BMC Public Health*.

Reviewers’ comments were highly insightful and enabled us to greatly improve the quality of our manuscript. Revisions in the text are preserved as tracked changes. In following pages are our point-by-point responses to each of the comments of the reviewers;

We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in *BMC Public Health*.

We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

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Reviewer 1

The case definition is not well detailed, it seems to be only febrile patients. If it is the case the definition was very large. How many symptomatic patients (febrile) or had influenza like illness have been tested with POC, how many were negative. In the situation of a typical clinical influenza infection with a negative POC test, was a PCR performed as we know that sensitivity of rapid diagnostic tests is not so good and the diagnosis can be improved with PCR. What kind of tests are considered point of care in Japan. To address this issue is important because the outbreak can be underestimated.

We appreciate this comment. Together with the second comment from reviewer 2, we amended the description of case definition. In fact, to maximize the possibility to detect influenza cases there, we used either self-reporting feverish and reported fever as the first screening. Unfortunately, we could not have a number of those negatives. However, the period when the Great East Japan Earthquake occurred was certainly in the meantime of influenza epidemic in Japan. In this sense, commercial rapid test kits could detect influenza to a certain extent of the level.

Two PCR were described in the method paragraph to confirm influenza infection but in results only RT PCR is mentioned, it seems no real time PCR have been performed

We appreciate this comment. We removed RT-PCR test in the text body accordingly.

Why only 27/105 residues were tested, 22/27 (81%) were tested positive, how to explain this discrepancy, usually PCR is more specific than rapid diagnostic tests. If it is the case, we can have an overestimation of the number of false positive cases with regard to the POC test.

Principally clinician used commercial rapid test kits for influenza confirmation in the field and we aimed to monitor the types of influenza virus in not only this outbreak investigation but surrounding affected areas by performing gene detection of influenza virus from residues of POC tests (Tohma K et al. Jpn. J. Infect. Dis.2012). We found influenza virus was detected in 89% of all residues and believed influenza virus

If we count the cases joined with a link on the fig 2, they are 16 cases in EC B, which is less than the 43% of familial cases in the text (16/60 is 26%)/10/31 are mentioned in the EC C (31%) less than the 38% in the text. May be I don’t read the figure properly. The legend could help to better understand the
reading of the figure. The living in the same room seems to be the major reason to get influenza.

We appreciate this comment for our further revision. We redraw the figure to emphasize the familial link and recalculate the proportion. We totally agree that sharing rooms and spaces were the major reason to get influenza among our cases.

*How many of the cases were vaccinated, the information is given only for B and C EC, with the highest AR, what was the vaccine uptake in the lowest AR in the other ECs, are differences within the age ranges to explain that the AR is also more frequent in adults < 65 y.*

We also would like to address this possibility by presenting vaccination rates but there was no data available except evacuation centre B and C. In general, influenza vaccination rate among the elderly aged over 65 years has reached more than 50% (Charu V et al. PLoS One 2011) and that rate seems homogenous partly due to the government recommendation as well as to subsidy service from local government. It was possible that difference of age distribution among evacuees affected the extent of difference in AR. However we believed that extent would not be large since there was no order/recommendation for evacuees to stay a specific evacuation center and evacuees naturally stayed at a nearest evacuation center because of lack of transportation at the early phase of after-disaster.

*Only physical barriers were implemented, why a prophylactic use of neuraminidase inhibitors has not been implemented?*

We appreciate this comment. Prophylactic administration of neuraminidase inhibitors was not implemented in this setting but early detection of cases and isolation of cases in specific rooms (i.e. social distancing) was intensively implemented.

*It could be interesting to have data on the pre earthquake situation of the influenza epidemic in Japan, AR, death rate with regard to the age range.*

We do appreciate this comment and included the brief description of influenza situation in Japan in Background.
The authors stated that the index cases were from outside the EC and was associated with the through search and rescue activities. If we consider this explanation how to explain the difference of AR between the different EC. Were the preventions methods followed in the same way in each EC.

There was no clear reason why we had lower AR in some EC, however lower AR was observed in two ECs where cases were reported in the latter part of this outbreak and both outbreak investigation as well as standardized response to influenza was implemented at that time. We added “in the early phase of this outbreak” for the sake of making this speculation more clear.

The authors also propose as with Cholera in Haiti that influenza virus was introduced by foreign rescuers. To affirm this causal relation, the strains of influenza must be determined. I assume Cholera outbreaks is not the same thing.

We do appreciate this comment. We drew the phylogenetic tree with samples of before and after the earthquake in previous study and observed a different clade of influenza A(H3N2) was identified in affected areas after the earthquake (Tohma K et al. Jpn. J. Infect. Dis. 2012). We could not identify the origin of this clade, however we believe there was a possibility of influenza virus from outside in these areas.

Reviewer 2

The AR value of EC (B), how can 60 of the 702 be 11.1 %? Shouldn't it be 8.6%? Please confirm or explain it.

We appreciate this helping comment. We modified the figure accordingly.

Their definition of influenza infection case is a little unclear. During epidemic of influenza, High febrile patients in the same evacuation center must have been infected influenza. However, who did undertake "point of case test" after febrile patients was identified? Was it Physician's diagnosis? Using Rapid Diagnostic Testing for Influenza? or combined them?

We appreciate this clarification and amended the definition accordingly. Please also see the first answer to Reviewer 1.