Reviewer’s report

Title: Human Infection and Environment Contamination with Avian Influenza A(H7N9) Virus in Zhejiang Province, China: Risk Trend Across the Three Waves

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Reviewer: Alexander J. Millman

Reviewer’s report:

This manuscript describes H7N9 detections in human cases and the environment in Zhejiang Province during the three waves. The article shows that there have been changes in areas of detection over the course of the three waves.

Major Compulsory Revisions

The methods of this article need to be described in more detail to lend support to authors' conclusion that there are changes to where the detection are occurring. Over the course of the three waves, surveillance for H7N9 has changed and areas where surveillance is conducted have expanded. It is unclear if the trends described in H7N9 detection are truly due to changes in the range of the virus or changes due to increased surveillance. Additionally, sampling methodology needs to be described in greater detail.

1. Discuss changes in H7N9 human and environmental surveillance over the course of the three wave. It seems unlikely that the surveillance practices were equally the same during the first and third waves for example, but maybe they were. This needs to be clarified as it is essential for interpreting the findings reported. Was surveillance conducted equally in urban and rural areas across the three waves? Were there changes to the frequency of surveillance activities conducted? How were sites that underwent environmental sampling chosen? Were they chosen because of identified cases of human infection or was it random? In addition the following specific areas need to be addressed:

Abstract:

Methods Section. This does not provide an adequate description as to what was done. Please provide more information specifically mentioning surveillance for human case identification, surveillance for environmental samples, and serological surveillance among poultry-related workers.

Page 4 lines 88-97: Please describe how environmental sampling sites were identified. Was this by random sampling? Was another methodology used? Were they based on association with known human cases? How were these sites identified? Were the same sites included across the three waves or were some included at some points in time but not others?

Page 4 Lines 98-99. How were the poultry-related workers identified? How did you determine if they had direct contact with poultry? Were they randomly
sampled or was it a convenience sample or another methodology? The results state that 912 poultry-related workers were recruited from 95 premises of 75 towns, but more specific details of how they were identified are needed in the methods.

2. Clarification of the three waves
Page 3 line 76-79: Please clarify the start and end days of the waves. For example, does the second wave start on 1 October 2013 or 30 October 2013?

3. Clarification of human case definition
Page 3 line 82-86. If a patient has acute pneumonia and an RT-PCR positive for H7N9 but has an elevated WBC count at early stage of illness onset, is the person considered a case? If not, why not? Can you also clarify the severe versus non-severe case definitions?

4. Clarification on serological survey
Page 7, lines 185-188. How were these poultry-related workers identified and sampled? Were they randomly sampled from these 95 premises? Was it a convenience sample? Similarly, how were the 95 premises from which the poultry workers recruited identified?

5. Page 8 lines 207-209. Please explain how you came to the conclusion that the closure of LPMs in central towns forced the contaminated poultry to be forwarded to rural markets. Was surveillance being conducted equally in rural and urban markets during all the waves? Is it possible that the virus was circulating in rural markets in earlier waves and those cases were not identified?

6. Please include a limitations section in your discussion

Minor Essential Revisions

1. Please define how you classify an area as urban versus rural.

2. Page 2 lines 54-55. Please provide exact dates when discussing timing of the waves (i.e. what does second half of 2014 correspond to and is February 2015 the first day of the month or last day of the month?)

3. Page 6 line 150 “Most cases concentrated in January 2014.” Do you mean most cases were detected in January 2014?

4. Page 8 line 213-214. How many of the urban cases were found to have had a rural market exposure? Include this in your results.

5. Your discussion about illegal poultry trading in the Discussion and the conclusion of your abstract is an important one. Aside from reference 17 which is only an editorial commentary, what evidence do you have that this was occurring in Zhejiang? Did you identify an operations that were conducting illegal trading? Do you have any thoughts on what can be done to curtail it if it is source of H7N9 transmission?
Discretionary Revisions

1. Page 8 Lines 230-232. The additional analysis finding a high positive rate of H7N9 virus in premises testing positive for both H7 and H9 is interesting but would probably be better suited for the results than the discussion section. Can you present more of these results and the actual data in the results section?

**Level of interest:** An article whose findings are important to those with closely related research interests

**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