Author's response to reviews

Title: Assessing the role of contact tracing in a suspected H7N2 influenza A outbreak in humans in Wales

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Author's response to reviews: see over
Dear Sir/Madam,

Please find enclosed a revised version of our manuscript “Assessing the role of contact tracing in a suspected H7N2 influenza A outbreak in humans in Wales” for consideration for publication in BMC Infectious Diseases.

Following the comments provided by two referees, we have made a number of changes to the manuscript, and have in particular worked hard to improve its clarity. We believe that the second referee has misunderstood the aims and methods of the manuscript, but recognise that this misunderstanding may be a result of a lack of clarity on our part. We have substantially rethought and rearranged the text, and have added additional information and clarification where it was suggested by the referees.

We believe that we have satisfactorily answered the referees’ queries (details are given below), and we therefore submit this manuscript for your further consideration.

Yours faithfully,

Ken Eames.

**Detailed response to referees’ reports (referees’ comments in normal text, our response in italics).**

Referee 1:

**Reviewer’s report**

This is an interesting paper that describes the role of contact tracing in preventing an outbreak of possible avian influenza. The authors use a compilation of hospital data to pinpoint cases and suspected cases with influenza-like illness. The authors conclude that CT is a useful tool in controlling an outbreak and that in many cases the experience of the personnel in prioritizing is very important. This is particularly the case where quick and precise laboratory tests are not available.

While this is a worthwhile analysis, I felt that the paper is not easy to read and it does not flow well. I think this paper can be improved to provide a more complete and clearer story.
The paper should have page numbers (line numbers would be nice too) so that comments can be more easily targeted to specific parts/sections.

While there are no major revisions from analysis point of view, I encourage the authors to thoroughly revise the paper to improve the presentation and clarity.

We have substantially restructured the manuscript to aid the flow and clarity. Much of the narrative of the contact tracing and control effort has been moved from the “Background” to the “Results” section, to allow relevant definitions (in “Methods”) to be introduced before the main bulk of the manuscript. We agree with the criticism, and hope that the restructured manuscript is more appropriate.

Specific comments:

In abstract->results:

- provide examples for ?other encounters?

We have provided additional examples and explanations of each of the types of contacts in the “Methods” section but, in the interests of brevity, have not changed this part of the abstract.

In Background:

- provide more background or a reference about the ?UK guidance?

We have reworked this section, and provided a reference to UK guidance.

- ?individuals were show to be? ->?individuals were shown to have? or ?to be infected with?

Amended.

- ?contact tracing overnight identified 6 suspected ?? ? was this CT from the 4 confirmed H7 cases?

Yes it was. We realise that this section was confusing, without being particularly instructive even had it been clearer. We have therefore substantially rewritten it.

- what is the difference here between ?suspected? cases and ?contacts?? does suspected mean contact with one of the 4 cases and also ILI?

We have reworded the “Methods” section to clarify the case definitions used by the outbreak response team.
- how many days back is the contact history compiled for?

We have added a section to the “Methods” section to explain the contact tracing methodology. Generally speaking, the contact history was compiled from one day before symptoms began until 8 days after symptom onset, where appropriate (we have also added that for those cases traced some time after their symptoms not all contacts could be recalled).

- was CT carried out only from suspected cases?

CT was carried out from cases and also from individuals who were thought to be cases or likely to become cases. This precautionary contact tracing meant that the response had the opportunity to get ahead of the infection.

- a suspected case initiates CT and then those contacts that have ILI initiate further tracing?

In general yes, but see above.

- more details about the data-base would be useful. who recorded the data in the first place, is the data available etc?

We have added more details about the compilation of the database to the “Background” section.

In Contact Tracing

- [2.3]–>[2,3]

Amended.

In Results:

- according to the analysis presented, the network only displays heterogeneity in degree distribution (or number of contacts). Can the authors clarify the meaning of wide range of heterogeneities?

We have rewritten this to clarify our meaning.

- caption of Fig 1: squares are ?poultry flocks??

We have rewritten the caption to clarify this.

- there seems to be at least one blue node that is not linked to a red circle or square, this should not happen according to the description

As explained above, contact tracing was carried out from individuals who did not, in the final analysis, end up being classed as cases, which is why this node appears.

- in the caption the total number of nodes of different type and the number of links of different type should also appear.
We have added to the caption to give the total numbers of nodes of each type.
- does Figure 2 tell us anything interesting?

Figure 2 tells us about the variability within the population in terms of the numbers of contacts they identify in the different settings. It illustrates that the burden of contact tracing can vary widely from person to person. We have added further discussion of this figure to the text.

- Figure 4 is very informative

In Discussion:

1st paragraph:

- where did case 1 acquired large number of contacts, in hospital? was he/she not isolated?

That is corrected, and is now stated explicitly.

- were there resources for CT stretched at any point? how many more days before CT resources would have been considerably stretched?

A paragraph addressing this point has been added to the discussion.

Referee 2:

Reviewer's report This manuscript describes contact tracing activities which occurred in the context of an avian Influenza A H7N2 outbreak in poultry, with transmission to humans.

The research question described by the authors is not well defined, although it is stated (in the abstract only) that the aim of the study was to examine the role of contact tracing in preventing an outbreak of possible avian human influenza in humans. Most importantly, the methods as described by the authors are not well described and as presented are not appropriate considering the objectives of the study.

The manuscript offers a description of the outbreak and the control effort, in particular the use of contact tracing. We have amended the abstract to clarify this, and have rewritten the Methods section. We believe that the methods used are entirely appropriate for this purpose.

Major Compulsory Revisions
1. Background as it is written is not adequate and present information about the outbreak and contact tracing which should be described in results. Relevant background to the study is not presented and the aims of the study are not clearly stated in this section. Reports of other avian influenza outbreaks and human transmission which occurred in recent years and its investigation should be included in this section.

Thank you; we agree that the manuscript was not sufficiently clear, and have reworked and rewritten much of the material to aid clarity.

2. The research question posed by the authors is not well defined. This study described contact tracing activities conducted during an outbreak of influenza A H7N2 initiated in a poultry flock which resulted in human cases. Despite being an important tool during outbreak investigation and control, contact tracing usually by itself cannot prevent an outbreak.

We have rewritten the abstract and the text of the manuscript to clarify our aims. We agree that contact tracing cannot necessarily be relied upon to prevent an outbreak, though it nevertheless has important uses in determining important parameters of transmission.

3. The end of the background section states that an analysis of the database of cases, and contacts in presented. This is different than what is indicated in the abstract, in which it is indicated that the objective of this study is to examine the role of contact tracing in preventing an outbreak of possible avian influenza in humans.

We have rewritten the abstract and the text of the manuscript to clarify our aims.

4. According to BMC instruction to authors, methods section should include the design of the study, the setting, the type of participants or materials involved, a clear description of all interventions and comparisons, and the type of analysis used, including a power calculation if appropriate. None of this was clearly described in the methods section.

We have rewritten the methods section to clarify our methodology. Since the manuscript presents a retrospective descriptive analysis of an outbreak and the response to the outbreak, a power calculation is not appropriate.

5. The authors mention that this study was conducted to examine the role of contact tracing in preventing an outbreak, however it not clear what were the methods used to assess this, and the authors do not define clearly what are the measures of outcome of this observational study. Was it number or cases, time between symptom onset and treatment/prophylaxis? This should be clearly stated.

The outcome was the progress of the outbreak and the response, in particular looking at the numbers of contacts identified by cases, the timing of new cases, the time taken for cases to be notified to the outbreak control team, and the time for contacts to be traced. This is now made clear in the abstract.

6. Methods for the analysis of likelihood of transmission depending on type of contact (home, work and other) should be presented.
These methods are extremely straightforward, and are therefore presented alongside their results in the “results” section. We believe that this is the clearest way of presenting this information.

7. Social network analysis results are presented, but the authors did not describe its methods in any detail in the manuscript.

We have added a paragraph to the methods section to explain the use of social networks.

8. As the authors indicate in the results section, laboratory confirmation was only possible in 2 of the 14 suspected cases. This is a major flaw in the study. In addition, the authors do not inform whether this was not possible because testing was done, or whether testing was done but did not result positive.

This flaw is recognised and discussed in some detail in several places throughout the manuscript. It is also noted that the response proceeded as though the infection were a novel strain of influenza, and therefore the lessons to be learnt from it are instructive.

9. Information presented on cases and contacts in the first paragraph of results section is difficult to relate to previous information described in the background section. This should be made clearer and all results of contact tracing should be presented in results section.

We have reworked the manuscript to clear up this confusing section, and are grateful for the suggestion.

10. Second paragraph of results should be better described in methods section. The authors indicate that suspected cases and contacts were linked together through a network of social contacts and this plot allows for identification of individuals likely to be at increased risk of infection. As presented here, this is not an adequate risk measure and should not be used as a single method to identify high risk individuals. Furthermore, no measure of risk can be estimated and therefore it is not adequate to indicate that “home and workplace encounters were more likely to result in transmission”.

We have reworked the manuscript to clarify the use to which social network analysis is customarily put. We strongly disagree with the suggestion that no measure of risk can be estimated – we have explained our estimate of risk and are confident in our conclusions.

11. Discussion and conclusions as are presented are not adequately supported by the data provided by this study. The authors indicate in the conclusion section that the setting of this study provides a natural experiment for interventions that have been envisaged in pandemic planning for early stages of pandemic flu. This cannot be concluded considering the results of this study and is therefore not appropriate to be stated.

We strongly disagree with this statement. We cannot think of a better natural experiment for the response to a novel flu strain than the emergence of what appears to have been a novel flu strain. The response that took place was exactly that which would have been mounted in the early stages of a bird-to-human flu outbreak.
Minor Essential Revisions

Background:

12. It is not clear whether contact tracing was conducted in Wales or also in North West England. Considered contacts from bird only or also contacts from human cases?

We have clarified these issues.

13. It is indicated that "Contact tracing overnight identified 6 suspected human cases and 13 contacts". Later in this paragraph, the authors mention that "contact histories were obtained from 12 suspected cases" - How to these 12 refer to the 6 suspected and 13 contacts described earlier? Likewise, how do the 142 contacts identified relate to the previous identified suspected cases, and contacts? Are these contacts either close birds or human contacts?

We have substantially rewritten this section, and hope to have clarified what was previously a somewhat confusing section.

Methods-

14. First paragraph of “contact tracing” section in methods should go to background or discussion section, as it refers to the literature and uses of contact tracing, but not methods.

We agree, and have made the suggested changes.

15. Definitions:

- Suspected case potential case is used in the study but not defined in methods. It is not clear whether “suspected case” is the same as ”potential case”.

- Contact (general term) is used throughout the manuscript. In methods, only "close bird" and "close human contact” are defined. Does contact refer to any one of these?

- Definition of Home, work, and other contact should be described in this section.

In the interests of clarity, we have made the suggested changes.