Author’s response to reviews

Title: The interplay between individual social behavior and clinical symptoms in small clustered groups

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RESPONSE TO REVIEWERS
INFD-D-16-01715

The interplay between individual social behavior and clinical symptoms in small clustered groups

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BMC Infectious Diseases

Editor:

Your manuscript "The interplay between individual social behavior and clinical symptoms in small clustered groups" (INFD-D-16-01715) has been assessed by our reviewers. Based on these reports, and my own assessment as Editor, I am pleased to inform you that it is potentially acceptable for publication in BMC Infectious Diseases, once you have carried out some essential revisions suggested by our reviewers.

We are grateful to the editor and the reviewers for their positive comments on the manuscript. We think that suggestions provided helped to make the manuscript clearer and more accurate.

We have done our best to thoroughly address all reviewers’ comments and we dare to hope that the new version of the manuscript can be now considered suitable for publication in BMC Infectious Disease.
Reviewer reports:

Ngai Sze Wong, PhD (Reviewer 1):

1. Methods, individual social activity and dynamic proximity network: the symbol cannot be shown normally in the pdf version. Please double check and revise.

We are sorry for this. In the new version of the manuscript, we have fixed this problem, so that all formulas in the text should be visible in the pdf version of the manuscript as well.

2. Line 105-110: I would consider these sentences as limitation instead of METHODS. You may relocate to limitation part.

We agree with the reviewer and moved this text in the discussion accordingly (please see lines 216-218 and 230-234 of the new version of the manuscript)

3. It would be easier for readers if the exact figure of incubation period and serial interval is shown in text, e.g. duration of the incubation period (xx days)

Addressed. The incubation period and serial interval are now shown in Fig.1 of the main text.

4. 1st sentence (line 129-131), Result: this sentence should be stated in METHODS instead of Results. Also, for the "absence of isolated (disconnected) clusters of individuals", I don't understand fully. Do you mean individuals who ever had any connection with other individuals? And how did you define connection? Is there any cut-off value (e.g. an individual met with another individual for >1 minutes)?

We agree with the reviewer that this point was not sufficiently clear in the previous version of the manuscript. In our analysis, connections between two individuals were defined as potential interactions between two study participants (e.g. verbal or physical contacts) that may have occurred as a consequence of their physical proximity. No cut-off values on the time spent in physical proximity were considered to define potential individuals’ interactions. However, as already stated in the methods, the software on individuals’ smartphones scanned for Bluetooth wireless devices in proximity every 6 minutes, a compromise between sensing short-term social interactions and battery life.

We now also clearly describe how connections are defined on the basis of physical proximity (lines 92-95 of the new version of the manuscript).
On the other hand, we preferred to leave the brief description of the topological properties we found for the considered network in the results in order to better highlight differences that can emerge by considering dynamic networks of contacts vs considering aggregated static networks of contacts. Nonetheless, we agree that the description of these results was not sufficiently clear in the previous version of the manuscript. As a consequence, we have rewritten the initial paragraph of the results. Please see lines 127-131 in the new version of the manuscript.

5. Line 135: when presenting the average time spent, could you include the standard deviation as well?

Addressed. We also added standard deviations associated with the other measures of individuals’ social activity level presented in the same paragraph (at lines 133-136).

6. Paragraph of "epidemiological links associated with influenza-like illness", Results: this paragraph seems to be a mix of results and discussion. Please note that "results" are presentation of study findings only. Please restructure and relocate relevant parts to discussion.

In order to address the reviewer’s comment, we have rewritten this sub-section of the results and a part of the discussion. We think that findings and comments are now properly placed in the manuscript. Please see lines 176-187 and lines 220-229.

7. Line 179, "less than 50% of cases observed during follow-up period": when calculating the proportion, I'm wondering if there was a wash out period at the very beginning. It's common for the first case to have infection outside the network if he/she was infected before the study started, and you may want to exclude that.

By considering potential transmission events caused by individuals’ physical proximity with observed clinical influenza cases, we identified 7 separate chains of transmission. However, no wash out of study participants was observed during the period under study. As a consequence, the spread of influenza among the study participants may have occurred either through infections generated outside the considered network of contacts or through transmission events caused by asymptomatic infectious cases. We now clearly state these two points at lines 178-180 and 184-187. Please note that a proper discussion on the potential role played by asymptomatic carriers (i.e. infected individuals showing no symptoms) and influenza subclinical cases (i.e. symptomatic cases that do not meet the criteria for Influenza-like illness) in the spread of the infection is also provided at lines 204-212.
8. Discussion: it's a bit strange for having no reference cited and no previous studies compared and discussed here. You may want to expand this further, besides relocating the sentences as stated in Comment 6.

Following the review suggestion we have expanded both the discussion and the conclusions of our manuscript to discuss our findings with respect to evidences coming from other published works. Relevant studies are now cited in the discussion as well.

9. Please don't cite the previous work by "suggested by [23]", "observed [24]". Please either show the name of author followed by [ref], or delete "suggested by [23]" and directly cite [23] at the end of the sentence.

Addressed.

Varduhi Ghazaryan (Reviewer 2): This is very interesting topic. However, I would recommend to highlight more the clinical/public health significance of the study; what are the implications; what are the next steps.

We thank the reviewer for positive comments on our manuscript. We have done our best to highlight possible significant implications of the obtained results. Please notice that to such an aim both the Discussion and the Conclusions have been extended.

In particular, we now suggest that

1. changes in contact patterns caused by influenza are mainly driven by the onset of fever and that these two symptomatic conditions mainly affect the duration of individuals’ contacts, rather than the number of individuals with whom they have social interactions; please see lines 241-244 of the new version of the manuscript.

2. remarkable differences in social behavior can also emerge among individuals characterized by similar daily routines and may influence the onset of super-spreading events within small clustered communities; see lines 200-203 and 246-248;

3. silent transmission caused by asymptomatic cases can be crucial to sustain infection transmission in small communities and may remarkably contribute to spread the infection in the population.
In particular, as for the latter point, we discuss the potential role in the infection transmission of patients with influenza who have very few or no symptoms (see at lines 204-212 and 248-253), also highlighting the need for further studies aimed at estimating the differential infectiousness between asymptomatic and symptomatic cases.