Reviewer's report

Title: Measles Outbreak in an Office Building in the Crowded Metropolis of Beijing, China

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Reviewer: Vicky Sheppeard

Reviewer's report:

I think this is an interesting incident, with lessons to be drawn from the response. As presented the paper is not properly focused and I make suggestions to improve the structure and content of the paper to better focus on the key issues (transmissibility of measles in a high rise setting and effective control measures). I also draw attention to some aspects of the approach which I am unable to substantiate, either because there are no references, or the only references are in Chinese. Where these diverge significantly from established international practice I think that evidence should be provided, or the paper reviewed by someone who can understand the Chinese references.

Focus:

Firstly the paper seems to indicate that the outbreak in the office building is the main focus, yet there are several distracting references to spread elsewhere that are not resolved. The authors make a valid point that the outbreak in a building where workers come from many precincts risks a widespread outbreak, and this should be retained, there is no data provided to suggest that secondary cases did arise outside of the building. Hence I question the following: Abstract line 9 "and residences" and line 21 qualify "wider distribution of cases" (should be potentially wide geographic distribution of cases"); p12 line 4 "and spread to 9 of Beijing's 16 districts" - this indicates secondary cases did occur, or do you mean "infected workers from 9 of 16 districts"? and line 9 - same wording as abstract regarding "wider distribution of cases"; same statement is also repeated in Conclusion line 9.

The second aspect of focus is that there is insufficient time describing the response, yet quite a lot of time spent describing IgM and PCR results. As the main focus of the paper is on the outbreak setting and effective control I don't think it necessary to dwell on IgM evolution over time, nor even the change in vaccination status during the outbreak - these matters can be described with simple statements rather than excessive text and tables. Yet there is minimal description of the vaccination and active surveillance approach, which must be inferred from the figure and the discussion - these should be properly described in the methods and results. Lines 9-11 on p.7 are the only reference to the vaccination response in the results, yet are poorly written and do not give the reader any appreciation of the vaccination process or key decision points in the evolution of the response. In addition, most of the "Outbreak Setting" section on p.7 should be moved to the beginning of the Results so that readers can understand the significance of the "Chronology of the Outbreak". Also in the "Outbreak Setting" include the population numbers for the building and each of the subsections (Company A, Company B, commercial,
other). Another example - the risk of the elevator is mentioned twice in the discussion, yet only in results once to describe what floors the elevator services - nothing about how the investigators came to determine it was an important exposure site (Discussion p. 12 line 17). Also "the working area of the source case" is first mentioned on p.10 as having the highest attack rate. This is interesting. His working area should be described in the outbreak chronology or outbreak setting sections - how many co-workers? was the area physically separated from the rest of Company A? did the index case also work in this area?

By contrast we are given too much detail about Laboratory results - as we are already told the criteria by which cases are confirmed, and this is not a paper investigating specificity and sensitivity of measles diagnostic methods, much of the detail can be omitted. Particularly, p. 8 lines 20-21 can be simplified "Forty four percent (19/43) of cases were IgM positive and 81% (34/43) were PCR positive for measles" - please add how many were confirmed by clinical evidence alone? I suggest deleting Table 2. In the Discussion, p.14, lines 20 -22, there is reference back to the relative performance of IgM and PCR, yet it is not apparent about the point of including this. Do the Beijing measles control guidelines not recommend confirming measles with PCR and caution about the sensitivity of IgM in the first few days following rash? If this is the case then it does deserve a paragraph in the Discussion, if not, then omit the sentence.

My final major concern is where the local guidance appears to vary from international guidance, yet I am unable to substantiate the reasons for this. This is mainly along two lines - requiring MCV for adults not vaccinated in the past 5 years and a longer infectious period for cases with pneumonia. It may well be this is what the Beijing measles control guidelines state, but I am unable to verify that and the references provided do not substantiate the claims made. This applies to p.11 lines 3-4 and lines 10-11, p13 lines 3-8. I note that reference 4 does not mention poor immunogenicity of Chinese measles vaccines, nor does it mention cold chain as a problem, except as a constraint in expanding the vaccination program prior to the 1980's. A major issue described by Ma seems to be inaccurate measurement of coverage. Reference 24 is in Chinese so I am unable to ascertain if it verifies these claims. I am unable to find any other English references to poor performance of Chinese measles vaccines, including regarding the Beijing 55 strain. on p.14 lines 4-5 the authors suggest that Beijing could refer to the "current" US recommendations or Japan's strategies for adult immunization". Reference 26 refers to the 1998 US guidelines (2013 is current) - nevertheless, neither recommend anything more innovative than ensuring all adults have two lifetime doses of measles containing vaccine. The reference for cases with pneumonia having a longer infectious period is a South African autopsy study. I cannot find any evidence there about transmissibility - certainly much of the pneumonia associated with measles is due to secondary viral or bacterial infection, and I cannot find any reference that pneumonia indicates prolonged transmissibility of measles. If the authors have such references I would be grateful to be directed to them. Further, just because measles virus can still be detected by PCR a couple of weeks after rash onset does not mean that it is viable or infectious.

Nevertheless apparently this in the Beijing measles surveillance guidelines which I do not wish to question, however international readers should be able to review the evidence base for this guidance, which is not possible as the guidelines are in Chinese. Depending on how this is
resolved, there may need to be subsequent corrections to p.6 lines 14-15 as according to most international guidelines the source patient would not be considered infectious on March 7 & 8. Finally, some specific corrections:

p. 2 line 15 - do you mean after "rash" onset?
p. 2 line 15 - reported to whom? the NNDRS? the local CDC?
p.2 line 22 - do you mean "emphasizes the difficulty"?
p.4 line 12 - "in Beijing in recent years"
p.6 line 14 - "before he went to hospital"
p.6 line 15 & 16 - specify company A and describe his work area.
p. 6 line 18 - specify company A
p. 7 line 22 - is it correct to say "each have separate dedicated entrances"?
p.8 line 6: you state here that 30 were migrants, however in Table 1 it gives 30 not migrants - which is correct?
p.8 lines 8-10 - this meaning of this sentence "The proportion of cases...."is not clear - can it be omitted?
p.8 lines 11-12 this sentence is not clear. Are you referring to just cases, or to all workers in the building? Do you mean that workers without documented measles vaccinated were recalled for vaccination? or that the vaccination status of cases was obtained either through reviewing documentation or recall?
p.8 line 12 - "Nine cases (20.9%) had received measles vaccine;"
P.8 line 13-14 - is this information about hospital attendance and travel provided to demonstrate there could be other sources of infection for some cases? If so, introduce the sentence to orient the reader: "Some cases may have contracted measles infection elsewhere...."
p. 8 line 16: reported to whom? the NNDRS? the local CDC?
p.8 lines 17-18 - Do you mean that 17.4% of cases who visited a hospital were not reported, compared to 55.8% of those who received primary health care only? If so, please restructure the sentence to improve clarity.
p. 11 lines 6-7: were any cases identified in the residential communities? If so please provide details, if not, please state that none were found there.
p.12 line 2: building should be plural (buildings)
p.12 line 6: "on" should be "one"
p. 12 line 9: "will be emphasized" doesn't make sense. Maybe just "will be challenging for measles elimination..."
p.13 line 1: do you mean "vaccinated in the early stage of the expanded.."?
P.13 lines 13-15: do you mean: 'Delayed recognition of measles cases could have meant that the optimal time for controlling spread was missed, leading to an even larger outbreak'?
p.14 lines 1-2: without more background about how the measles vaccine is offered to adults, and who should be vaccinated, it is hard to know whether its a matter of acceptability, or other factors leading to low uptake of apparent recommendations for adults. I think to include this point more information is needed to support the contention, or other factors discussed.
p.14 line 13: missing "of" between Isolation and fever
p.15 lines 10-11: The phrase "especially pubic traffics" is not clear, similarly "by exposure made in public contact".
p.15 line 17: do you mean "avidity"?
p.15 line 21 - as for p.13 lines 13-15, "Early recognition of cases is the key to controlling an outbreak" (by the time you have an epidemic it is by definition already an outbreak)

p.16 lines 9-10: do you mean "emphasizes the difficulty of measles eradication in crowded cities"?

Table 1: no need to include vaccination by end of outbreak in the table. Simply state in the text that four individuals who received measles vaccine as part of the response went on to develop measles infection - two of whom had no prior doses and two had an unknown vaccination history.

p.24 line 1: I think you mean "cases who didn't go to hospital are unknown"?
Figure 1: please correct typo in legend "other companies"

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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