Author’s response to reviews

Title: Risk of transmission via medical employees and importance of routine infection prevention policy in a nosocomial outbreak of Middle East respiratory syndrome (MERS): a descriptive analysis from a tertiary care hospital in South Korea

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Author’s response to reviews:

Dear editor and reviewers

We appreciate kind comments by reviewer, which greatly improved our manuscript. Our replies to the comments of reviewers and amended manuscript are as follow:

Editor Comments:

1) Please state whether the maps in Figure 1 and the schematic diagram in Figure 2 have been taken from other sources. Please acknowledge the source in the figure legend, and if it is under copyright, also state the written permission given to use and adapt it.

Reply: All figures were redrawn by the authors. In Figure 1, the transmission map was redrawn using background Korean maps which do not require copyright permission.

Reviewer reports:

Maria D. Van Kerkhove (Reviewer 1): The authors provide a very detailed review of human-to-human transmission within their hospital adding valuable information about exposures resulting in infection. Having travelled to the Republic of Korea during the outbreak and several times
afterwards, I witnessed the thorough investigations that took place to evaluate human-to-human transmission.

Major Comments

Consider a new figure outlining the timing and location of all of the MERS-infected patients and their contact with one another (perhaps a transmission tree). The current Figure 2 does not adequately capture the detail contained in the text, and it would be extremely valuable to see an illustration of the human-to-human transmission before and at this hospital.

Reply: As the reviewer mentioned, we added a new figure (fig 2) illustrated timeline transmission tree of all of the MERS-infected patients in the revised manuscript.

Suggest a full English review of the manuscript (some examples, not comprehensive of the entire manuscript, are below).

Reply: As the reviewer suggested, we edited the revised version by the English editing service.

Throughout the MS, the authors refer to several MERS patients as superspreaders, I, and many others, question whether these were actual superspreaders vs superspreading events. There is compelling evidence that these were superspreading events - caused by several factors that resulted in a few individuals infecting many others in this outbreak. Consider calling these superspreading events.

Reply: As the reviewer suggested, super-spreading event was correct. We corrected them in the revised manuscript (page 5, line 1 and 6; page 15, line 9, 10,12 and 17; page 16, line 6)

PDF Page 7, lines 5-39, please provide references for these procedures implemented during the outbreak, if possible.

Reply: In July of 2015, the MERS-CoV Infection Prevention and Control Guideline Development Committee were constituted with experts recommended by the joint panel of the Korean Society of Infectious Diseases, Korean Society for Healthcare-associated Infection, and Korean Association of Infection Control Nurses. Based on this guideline, the national infection control guidelines of the Korean Ministry of Health was established. We added this reference in the revised version. (page 7, line 9 and 17)
Results, PDF page 9, lines 3-27, these are not results of the authors analyses and should be removed from the results section. Suggest moving this paragraph to the introduction. Again, I would argue that the first case seeding several superspreading events, and was not necessarily a super-spreader himself.

Reply: As you suggested, we moved this paragraph to the introduction, and rewrite some sentences. (page 4, lines 11-23; page 5 lines 1-8)

Results: With regards to the isolation, were there any lessons learned about the isolation procedures implemented for the 1019 contacts isolated during this event? If so, can these be provided in the discussion section?

Reply: We think that this is very important recommendation. We initially missed the tenth and eleventh patients during the first isolation phase. This had a disastrous outcome. They went around everywhere in the hospital before they were isolated. As a result, numerous people were exposed to the tenth and eleventh MERS infected patients or shared space and time with MERS patients. Although we thought that other people may seldom become infected because of the early isolation of infected patients, we should have performed extensive quarantine procedures for all people in the hospital because of the national fear of MERS transmission and the urgency of abating MERS transmission. Fortunately, among the 1,019 people, there were no transmission cases. This showed that our following concrete infection control measures may greatly contribute to preventing further transmission of MERS. But, implementing unnecessarily broad isolations of hospital employees could cause a lack of adequate manpower and increased fatigue among non-isolated medical employees. During the national MERS outbreak, most hospitals suffering from nosocomial MERS transmission experienced the same, which may have resulted in the crisis of a lack of medical services in some regions. Unrecognized MERS patient often caused super-spreading events, especially in large volume hospitals, which can threaten not only a hospital system but also the regional medical service system. We added further discussion regarding this issue in the revised manuscript. (page 19, lines 11-23; page 20, lines 1-7)

Results: Can the authors provide any results on the use of PPE, specifically used during aerosolizing procedures? If so, please include this in the manuscript.

Reply: During ED and GW stays, the index patient had no complaints of respiratory symptoms and there were no aerosol-generating procedures before the initiation of isolation. After isolation began, two doctors and nine nurses cared for index patient routinely wearing level D equipment (N95 mask, head cover, goggles, surgical glove, disposable coverall and waterproof boots) during all aerosolizing procedures. We inserted it to the revised manuscript (page 14, lines 1-7)
Table 1: for the cases where the incubation period is listed at >14 days, are there no other possible exposures prior to day 14 that could have resulted in infection? Possibly environmental contamination? Please provide input on this in the manuscript.

Reply: Generally, incubation periods of MERS was known as 1-2 weeks. Therefore some infected patients (third, fourth, tenth and eleventh patients) had incubation period > 14days might be infected from contaminated environment after several days later. However, third and fourth infected case in Kyung Hee hospital were isolated at 6 May (within 10hrs after contacting with patients) then they could not have a chance of contacting the contaminated environment. Tenth and eleventh in our hospital may have been infected from a contaminated environment on this floor after MERS patient was isolated. However, this is seldom a possible route of action because of the following facts. When we identified index patient, we cleaned all environments of hospital. The following day, we began checking daily for presence of the MERS virus for several days and confirmed no existence of the MERS virus. We think that there were no possibilities of contaminating from infected environments. We added some discussion regarding this issue (page 17, line 23; page 18, lines 1-7)

Table 2: Can the authors stratify results by use of PPE?

Reply: We stratify PPE results by referencing of the WHO recommendation (WHO rapid advice guideline) in revised table 2.

Discussion, page 17, lines 10-12 - consider revision of the sentence suggesting that the last 2 cases were "an embarrassment for our hospital's infection control team". Breaches in IPC have been common in MERS outbreaks, unfortunately, but IPC can always be improved.

Reply: We rephrased this sentence in the revised manuscript (page 17, lines 20-22)

Discussion, can the authors provide concrete examples of measures taken/implemented following the MERS outbreak in their hospital?

Reply: We added following infection control measures (strengthen the early identification and encouraging of hand washing and wearing surgical mask) to the method section in the revised manuscript (Page 11 lines 3-9)
Line 49-51, consider rephrasing this sentence "We performed a post-outbreak analysis and obtained some unique data" to We performed a post-outbreak analysis with detailed observational data from our hospital" or similar.

Reply: We corrected this sentence in the revised manuscript (page 5, lines 9-10).

PDF page 6, line 49-51, can the authors describe further the strengthening of systems before the MERS patient arrived?

Reply: We added further description of our triage system for early identification suspected MERS patient in the revised manuscript (page 6, lines 12-19).

Revision of many sentences/phrases throughout the manuscript are required: For example:

Results, PDF page 9, line 37, the patient "had" been receiving treatment, not "has"

o Results, PDF page 9, line 47, missing a "the" in front of index patient.

Reply: We corrected them as reviewer recommended. In addition, we corrected all English grammar errors via English editing service.

o Results, PDF page 10, lines 18-22, "She was first admitted to a 2-bed room but was then transferred to a single-bed room after 5 min by claiming from caregiver of other patient who staying in this room already" - please clarify the meaning of this sentence. It is not clear what "claiming from caregiver of other patient..." means.

Reply: When index patient admitted to a 2-bed room, caregiver of other patient who staying in this room already didn’t want to share the room with index patient. We rewrite this sentence (page 9, lines 20-23).

Alexandre Bleibtreu, MD; PhD (Reviewer 2): PULM-D-18-00628 is about nosocomial cross transmission of MERS-CoV during the 2015 South korean Outbreak. Many published articles had related and explored tranmission chain with in particular superspredre identification.

This manuscript give a new way to understand reasons of this spreading. They intensively redraw the contacts and routes used by one of these spreader. The most remarkable contribution
of this article is to highlight that standard protection and hygiene measures can contain the spread of the MERS-CoV virus.

I think this manuscript is suitable for publication in BMC Pulmonary Medicine after minor revisions listed below.

- In Background:
  - remove new lethal in the first sentence
  
  Reply: We removed it in revised manuscript (Page 4, line 2).

- remove new in the last sentence of the first paragraph
  
  Reply: We removed it in revised manuscript. (Page 4, line 11).

In Results:
- in The Index patient section:
  - I think you made a mistake in dates because first you wrote 7 June then 7 May.

  Reply: Index patients visited our hospital 5 June. We corrected April to May, and May to June. We corrected all errors of days in manuscript (page 9, line 2, 4, 9 and 10).

Globally:

What are the differences between X-Ray and Roentograms?

Reply: I checked the meanings of two words in the English dictionary. X-ray means “A photon of electromagnetic radiation of very short wavelength” primarily. It also means “A photograph taken with x-rays (same with Roenterogram)” or “the act or process of taking such a photograph”. I think that there was no different meaning between two words, but x-ray may be more suitable to our manuscript because it had more broad meaning. I corrected it (page 12, lines 1, 3).
For numbers between one to ten I prefer when they are fully written.

Reply: As you suggested, we corrected them (page 11, line 13, 15 and 23; page 12, lines 5,7,8,9, 15 and 19; page 17, line 22; page 19, line 11 and 15)