Author’s response to reviews

Title: Lessons from an active surveillance pilot to assess the Pneumonia of Unknown Etiology Surveillance System in China, 2016: the need to increase clinician participation in the detection and reporting of emerging respiratory infectious diseases

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Dear Dr Li,

Your manuscript "Enhancing surveillance for emerging respiratory infectious diseases through clinician participation: an assessment of pneumonia of unknown etiology surveillance in China, 2016" (INFD-D-18-01610) has been assessed by our reviewers. They have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in BMC Infectious Diseases.

Their reports, together with any other comments, are below. Please also take a moment to check our website at https://www.editorialmanager.com/infd/ for any additional comments that were saved as attachments.

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I look forward to receiving your revised manuscript and please do not hesitate to contact us if you have any questions.

Best wishes,

Robin L. Cassady-Cain, PhD
Editor Comments:

Please thoroughly copyedit your manuscript text for grammar and understanding.

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Reviewer reports:

Fiona Russell (Reviewer 1):

This observational study describes a surveillance system for acute respiratory emerging infections in two hospitals in China and compares clinician reporting with surveillance officer reporting.

Response: Please note: the pneumonia of unknown etiology system in China, the surveillance system for acute respiratory emerging infections, includes all healthcare facilities in China. This paper describes the 2nd phase of a surveillance system assessment that built upon a clinician and health administrator knowledge, attitudes and practices study conducted in 43 healthcare facilities. In the introduction we explain: “A 2015 assessment of clinician and health administrator knowledge, attitude and practices related to PUE surveillance conducted within 43 healthcare facilities revealed a willingness to report PUE cases, but identified limited awareness of the PUE system, lack of understanding of the reporting process, and failure to follow the case definition [7].”

Title: the title needs to be more specific and reflect the methods and results

Response: Thank you for this suggestion. We have revised the title to one that is more specific and reflects both methods and results: “Lessons from an active surveillance pilot to assess the
Abstract; the methods do not describe the analytical methods used to answer the research question— it just describes the reporting. The results do not reflect the main results. The conclusion does not reflect the main findings.

Response: We have modified the methods section of the abstract to reflect the research questions, and we have expanded the conclusion section to ensure that it reflects the main findings. The results section reflects the study’s main results: none of the 335 cases meeting the PUE case definition were reported to the PUE system; <10% of the PUE case medical records documented exposures relevant to respiratory infections; and the most common reasons for not reporting were no awareness of the PUE system and not understanding the case definition.

Introduction: needs to have a specific research aim at the end of the Introduction

Response: Our specific research aim appears at the end of the Introduction on page 5: “…we piloted a 3-month active surveillance program in two hospitals to quantify the number of cases meeting the PUE case definition, the number reported, and to identify ways to improve the PUE surveillance system’s detection of respiratory infections of public health significance.”

Methods

Does not describe the statistical tests used to make comparisons

Response: We have added “using the chi-square test for comparisons” to the Data analysis section of the methods.

Results

The first paragraph should be moved to the methods as a description of the study sites

Response: Thank you for this suggestion. We have moved the first paragraph of the Results section to the description of the study sites in the Methods.
A statistical test (p value) should be applied to compare the results obtained by the clinicians and surveillance officers (Table 2)

Response: Thank you for this suggestion. We have added the p value to results presented in the table 2.

Discussion

There are 3 main findings:

1. If all the cases that met the case definition were reported, the numbers would be so great it would not be feasible. There are no recommendations made such as reporting just on selected days, selecting a random sample, or until a certain threshold is met. These and other potential options need to be discussed.
2. Underreporting by clinicians due to lack of awareness
3. Differences in reporting between the 2 hospitals

These should be mentioned in the both abstract and the discussion

Response: We agree that underreporting by clinicians due to lack of awareness is a main finding, and we have added this to the conclusion of the abstract as you have suggested. We believe that the differences in reporting between the two hospitals is not a main finding, but rather, the main finding is that none of the cases meeting the PUE case definition in either hospital was reported. We have included this finding in both the abstract and the discussion. Finally, we agree that the first point you list is one of the main reasons that the PUE system is not feasible. However, this is not a finding from our study, but rather, an interpretation of our findings. We have therefore chosen to make this point in our discussion.

Niranjan Bhat, M.D. (Reviewer 2): Overall Comments

Public health significance: This manuscript reports on an important issue regarding the quality of surveillance for emerging infectious diseases in China. This is particularly important, as the area has been at the epicenter of several emerging infectious diseases, such as various avian influenza subtypes and SARS. Having said that, this report examines a relatively small part of the system. The authors raise some provocative points and the study has the potential to raise some larger questions about the approach of the national authorities in developing the particular case definition, the feasibility or practicality of the system if complete reporting was done, and the methods in which the surveillance was established and maintained. However, the authors do not follow through with recommendations that address all of the issues that they raise.
Specifically, one of the objectives states for the study was to identify ways to improve the system's detection. However, while the authors propose modifications to improve participation and awareness of the system, which would increase its sensitivity, they do not address the problem identified of potentially overwhelming the system with false positive cases, in other words to improve specificity.

Response: Thank you for this excellent point. We had intended to suggest that modifying the case definition to include epidemiologic criteria related to emerging respiratory diseases would improve specificity. We have now stated this more explicitly. At the end of the second Discussion paragraph, we have introduced this idea broadly: “Modifying the system to decrease the number of cases that meet the PUE case definition but are not emerging respiratory infections of public health significance will increase the system’s feasibility, acceptability and usefulness.” After the discussion of the documentation of respiratory infection-related exposures, we have added the following text (in bold) to address this idea more specifically: “Adding items related to exposure to live poultry or swine and other exposures relevant to emerging respiratory infections to the standard infectious disease history checklist for priority inpatient wards in China may prompt clinicians to ask about these exposures, and in turn, improve the detection and reporting of emerging respiratory infections. First, increasing documentation of relevant exposures for persons with respiratory infections may facilitate the addition of more specific epidemiologic criteria to the PUE case definition to reduce the number of cases meeting the case definition that are not infections of public health concern. Second, clinicians who identify concerning exposures in patients with respiratory diseases may be reminded of emerging infectious diseases and therefore may be more likely to report these cases to the PUE system.” Finally, we added text to the Conclusions and Recommendations section to emphasize the need to increase the specificity of the case definition.

Originality: Surveillance system evaluations are necessary, but not unique, and the investigators do not use any innovative techniques to assess the performance of the system, although this may not be necessary.

Response: We agree that surveillance system evaluations are necessary and that we have used standard techniques in our evaluation. Additional techniques were not needed in this particular instance to identify a major weakness in this surveillance system. We do, however, believe that the findings from this evaluation demonstrate significant shortcomings of the current surveillance system, and the compelling need for system modification.
Reader interest: This topic is of relevance to mainly PH practitioners in terms of sharing the realities and practicalities of implementing national surveillance at a grassroots level. The interest of this report is potentially undercut by the absolute lack of functionality of the system; it might be more interesting if it were at least somewhat operational, thus providing the opportunity for a more nuanced look at the strengths and weaknesses of such a system; the lack of detection of any emerging disease cases also reduces the interest level. Perhaps a repeat evaluation after an intervention, or during the course of an outbreak would provide some valuable comparative data.

Response: Thank you for this thoughtful comment. We agree that public health practitioners will have interest in learning more about the realities and practicalities of implementing a national surveillance system (within the most populous country in the world) that attempts to detect rare events. Public health practitioners will also be interested to learn more about the reasons associated with clinician reporting behavior. We appreciate your suggestions for future study. We agree that given our findings, this evaluation should lead to system modification followed by a repeat evaluation. We also plan to reassess the modified system’s utility during the course of an outbreak.

Specific comments

Background

The background section is generally concise and informative.

Response: Thank you.

Methods

Would be better to change the order of the paragraphs, grouping together the description of the surveillance system ("PUE reporting description", PUE case definition) and description of the evaluation study ("Evaluation sites", description of evaluation study enrollment, etc.)

Response: We have made this change.

In the screening list of ARI diagnoses, can we assume that the term (in English) "bronchiolitis", which is the most common reason for hospitalization in infants, is covered by the diagnoses numbered 41-43?
Response: Yes, “bronchiolitis” is included within the diagnoses numbered 41-43.

In terms of the data analysis, how were the reported 95% confidence intervals calculated?

Response: We calculated the lower and upper limits of the 95% confidence interval for a proportion, according to the Wilson procedure described in: Newcombe, Robert G. "Two-Sided Confidence Intervals for the Single Proportion: Comparison of Seven Methods," Statistics in Medicine, 17, 857-872 (1998). We also added the following to the Data analysis section of the methods: statement in the statistic method section as following: "Wilson score was used to calculate 95% confidence intervals (CI) for proportions."

Results

It would be helpful to provide more characteristics of the hospitals that were ultimately chosen. For instance, later in the manuscript we learn that the Fuyang hospital is an infectious disease hospital, and has experience with avian flu cases, while Lu’an hospital is more general and has no experience.

Response: Per another reviewer’s suggestion, we moved the information about the two hospitals to the Methods section, and we expanded the description to provide more characteristics, per your suggestion. The relevant text in the Methods is now: “We selected two tertiary hospitals in Anhui Province: the Second People’s Hospital of Fuyang City, a 1400-bed facility, which from February through May 2013-2015, admitted an average of 231 pneumonia patients per month, and Lu’an City People’s Hospital, a 2300-bed facility, which over the same time period admitted an average of 252 pneumonia patients per month. While Fuyang Hospital, an infectious disease hospital, had experience treating human infections with avian influenza, Lu’an Hospital, a general hospital, did not.”

For Table 1, places the column regarding total ARI admissions first (in other words to the left), then the column showing the percentage of those that met the PUE case definition would potentially flow more logically. The column describing those that did not meet the case definition is not necessary, as one can easily calculate from the yes column. It may be helpful to somehow show what percentage of overall PUE cases come from each department.

Response: We have revised accordingly.
In terms of laboratory results, nasopharyngeal swabs may be more sensitive in detecting the relevant pathogens compared to throat swabs, but this varies by pathogen. In the future, it may be more useful to obtain from both sites; they can be placed in the same container.

Response: Thank you for this suggestion.

Regarding the recording of relevant exposures, it may be useful to describe any forms used by clinicians, particularly the use of a checklist, as mentioned later in the manuscript. What are all the items that are required in the medical history? Occupation is mentioned, and apparently contact with hepatitis B, tuberculosis, and schistosomiasis are as well.

Response: The exposures you mentioned are asked as part of routine practice by Chinese clinicians when completing the “personal history” section of the medical record. It is not a formalized checklist on the actual form itself. We have clarified the language related to this practice and have also made it more clear that our intention would be to leverage the electronic medical record to create a more standardized approach to asking about relevant respiratory infectious disease exposures. “About half of the medical records from identified PUE cases documented any contact with parasites-infected water, because asking about “any exposure to parasites-infected water” is a routine practice among Chinese clinicians when completing the “personal history” section of the medical record [17]. This finding suggests that clinicians are more likely to ask about specific exposures when they are part of routine practice as opposed to exposure that may only be asked intermittently as part of non-routine practice. The widespread use of electronic medical records in China provides an opportunity for prompting clinicians to ask about certain exposures relevant to infectious diseases that can be documented in a standardized way in patient’s medical record. By developing a checklist within the electronic medical record with questions related to exposure to live poultry or swine and other exposures relevant to emerging respiratory infections for priority use in inpatient wards in China, clinicians would be prompted to ask about these exposures. This may in turn improve their ability to detect and report emerging respiratory infections. First, increasing documentation of relevant exposures for persons with respiratory infections may facilitate the addition of more specific epidemiologic criteria to the PUE case definition to reduce the number of cases meeting the case definition that are not infections of public health concern. Second, clinicians who identify concerning exposures in patients with respiratory diseases may be more likely to report these cases to the PUE system.

In Table 3, are items with zero positive responses included in the table because they were asked? It would be helpful to indicate this.

Response: Thank you for this question. During the clinician interviews, surveillance officers asked the open-ended question: “Why didn’t you report the PUE case?” When clinicians
answered, the surveillance officer selected the option that corresponded to the clinician’s response, or if the appropriate response option was not available, the surveillance officer wrote in the response. To avoid confusion, we have removed the rows with zero positive responses in Table 3. These items were options that were included in the survey check-list but were never the clinicians’ responses.

In describing the one PUE case that was reported up to the local CDC, the authors do not investigate why the case was not reported to the national system. More could be said here, or in the discussion section, regarding why cases are or are not reported to the various entities.

Response: The PUE case that was reported to the local CDC was not reported to the national system because the specimen tested negative for avian influenza virus. We have added this explanation to the discussion. The third paragraph of the Discussion explores the most common reasons clinicians did not report PUE cases to the system.

Discussion

In the first paragraph, the authors summarize key points and express valid criticism of the feasibility of the existing PUE system, as it would likely be overwhelmed if all eligible cases were reported. However, the rest of the section discusses the issue of under-reporting and how rates can be improved. More could be said about ways to refine the PUE case definition to be more specific, or other modifications to the surveillance system that would make it more targeted and manageable. The conclusions and recommendations paragraph reflect this same imbalance, stating the problem of potentially overwhelming the system, but only providing recommendations on how to increase reporting.

Response: Thank you for this excellent point. We had intended to suggest that modifying the case definition to include epidemiologic criteria related to emerging respiratory diseases would improve specificity. We have now stated this more explicitly. At the end of the second Discussion paragraph, we have introduced this idea broadly: “Modifying the system to decrease the number of cases that meet the PUE case definition but are not emerging respiratory infections of public health significance will increase the system’s feasibility, acceptability and usefulness.” After the discussion of the documentation of respiratory infection-related exposures, we have added the following text to address this idea more specifically: “By developing a checklist within the electronic medical record with questions related to exposure to live poultry or swine and other exposures relevant to emerging respiratory infections for priority use in inpatient wards in China, clinicians would be prompted to ask about these exposures. This may in turn improve
their ability to detect and report emerging respiratory infections. First, increasing documentation of relevant exposures for persons with respiratory infections may facilitate the addition of more specific epidemiologic criteria to the PUE case definition to reduce the number of cases meeting the case definition that are not infections of public health concern. Second, clinicians who identify concerning exposures in patients with respiratory diseases may be more likely to report these cases to the PUE system.” Finally, we added text to the Conclusions and Recommendations section to emphasize the need to increase the specificity of the case definition.

The authors place significant importance on the national training on PUE surveillance conducted in 2008. They reasonably suggest that better initial training as clinicians enter the workforce and refresher courses may be helpful. They also suggest adding more items to the "standard infectious disease history checklist", as they would become required elements. Other means to improve reporting that could occur on a continuous basis should be considered, such as structural modifications, including posting notices in clinical areas, incorporating public health issues into hospital policies, or assigning personnel to screen admission diagnoses, could be proposed.

Response: We agree that a multi-pronged approach is needed to incorporate public health practice into clinical settings. We have expanded the third recommendation in our Conclusion section to address this comment: “3) Providing clinicians with frequent public-health related training and communications will ensure that clinicians are aware of public health reporting requirements. A multi-pronged approach to incorporating public health practice into clinical settings may include: offering training to clinicians as they enter the workforce followed by annual refresher courses, posting public-health related updates and notices in clinical areas, incorporating public health guidance into hospital policies, engaging clinicians in the development of clinically-appropriate and easy-to-apply case definitions, and regularly sharing local and national public health data of interest with clinicians, to enhance their appreciation of the public health importance of their work.”

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Response: We have included these mandatory sub-sections between the “Conclusions and Recommendations” section and the “References”.

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