Author's response to reviews

Title: A real-time automatic hospital-wide surveillance of nosocomial infections and outbreaks in Chinese large tertiary hospital

Authors:

Mingmei Du (dumingm@163.com)
Yubin Xing (xyb70@yahoo.com.cn)
Jijiang Suo (si191919@yahoo.com.cn)
Bowie Liu (liubowieiabcd@126.com)
Na Jia (jiana79_41@hotmail.com)
Rui Huo (huoray@xinglin-tech.com)
Chunping Chen (chenchunping@xinglin-tech.com)
Yunxi Liu (yunxiliu6511@sohu.com)

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Author's response to reviews: see over
Cover Letter

Dear editor,

Thank you for your kind consideration and the reviewers’ valuable suggestions. We have revised our manuscript carefully following the suggestions, and would be very grateful if it could be accepted for publication in your journal. The cover letter gives a point-by-point response to the reviewers’ comments.

Reviewer’s report
Title: A New Real-time Automatic Hospital-wide Surveillance of Inpatients with Nosocomial Infections and Outbreaks in Chinese large tertiary hospital
Version: 4 Date: 18 November 2013
Reviewer: Walter Koller
Reviewer’s report:
General:
1. Is the question posed by the authors well defined?
   Yes, but in poor English
2. Are the methods appropriate and well described?
   Yes, methods are appropriate; descriptions are concise but sufficient
3. Are the data sound?
   Yes
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes
5. Are the discussion and conclusions well balanced and adequately supported by the data?
   Yes/No
6. Are limitations of the work clearly stated?
   Yes, but insufficient
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   Not quite. Compared with the large bundle of different fields addressed, the reference list is rather selective and short.
8. Do the title and abstract accurately convey what has been found?
   Yes, but in poor English
9. Is the writing acceptable?
   No, not at all

MAJOR COMPULSORY REVISIONS
Writing of most parts needs urgent revision, especially title, abstract, table and figure-legends. In some parts of the text and the graphs it remains obscure what the authors
want to say. I cannot exclude that translation into correct English reveals major flaws which presently are hidden behind imprecise or not understandable wording.

**Reply**——Thank you so much for your positive comments and valuable suggestions. We have revised our manuscript carefully as you suggested. And we have sought the assistance of native-English speaker in revising this manuscript.

**Table 1: text of footnote not clear**
**Reply**——We have revised the footnote of table 1 making it clearly.

**all Figures: legends need unmistakable writing**
**Reply**——The legends of all five figures had been revised as suggested.

**Figure 1: What means “access middleware fetch” in the graph?**
**Reply**——We have explained “access middleware fetch” in figure 1.

**MINOR ESSENTIAL REVISIONS**
**Figure 4: legend header says figure 3**
**Reply**——We are sorry about the careless error. We have changed the number “3” to “4” in the revised manuscript.

In condensing NI prewarning alerts into correct NI diagnoses, how is precision of ICPs decision controlled?

**Reply**——In our study, the precision of ICPs confirmation is very important. It determined the accuracy of relative NIs rate. The controlling methods: The profession of ICPs charging for the NIs confirmation must have clinical specialty and have more than two years clinical work experience. After he or she accepted NI professional training, we have two aspects checking. The one is the NIs confirmation by RT-NISS exam in our department. And the other is checking the ICP’s NIs confirmation with the clinical doctor. In the study on 14th Mar 2013, the kappa of ICP’s diagnosis was 0.93. In fact, there are two ICPs in the subjected hospital charging for NIs confirmation. The kappa of their diagnosis is good. We have explained this question in figure 1.

ICP diagnosis decreased sensitivity:
The Comparison Between RT-NISS and Manual Survey
“RT-NISS prewarned 146 suspicious NIs, with a sensitivity of 98.8% (84 of 85) and specificity of 93.0% (827 of 889) (Table 1).
The ICP diagnosed 80 NIs from RT-NISS detected 146 prewarning alerts with a sensitivity of 94.1% (80 of 85) and specificity of 99.3% (883 of 889)” Impairment of sensitivity by ICP diagnosis should be adressed in the discussion
**Reply**——We have added the reason for impairment of sensitivity (from 98.8% to 94.1%) by ICP diagnosis in the discussion. *(Page15, first paragraph, line 8-12)*
RT-NISS NIs Computer Algorithm (Professional Suspicious NIs Screening Criteria)

How can AB usage be used as a valid criterion for presence of NI when inappropriate (over)use of AB is known to be highly prevalent?

Reply—— Only depending AB usage was shown to be sensitive but not very specific, as there are many unreasonable excessive antibiotic usage leading to false positive findings, such as surgical operation prophylactic antibiotics. The AB usage alerts in Computer Algorithm considering the new AB usage after surgical operation, and excluding the kind of AB using for operation. This could decrease false positive findings. (Page 6, first paragraph, line 9-10; Page14, second paragraph, line3-6)

How can „specimen taken for microbiology“ be a valid criterion for NI when it for a long period is neglected by physicians and later a significant increase of microbiological testing is enforced by hospital regulations? How do such changes in underlying criteria change the RT-NNIS output?

Reply—— Yes, the change of rate of microbiological testing would influence the output of RT-NNIS (the rate of NIs prewarning alerts). It was the main reason of the different rates in the two studies (15% vs 8.8%). Because the positive result of microbiological testing was an important criterion for NIs computer screening algorithm. Only depending microbiological testing was shown to be specific but not very sensitive, because the physicians didn’t always prescribe microbiology cultures for NIs. The good sensitivity and specificity was the performance of all the screening algorithms. We have explained this question in the discussion as reviewer’s suggested. (Page15, second paragraph, line 1-10)

„continual fever (temperature ≥38.0°C) for two days after surgery excluding surgical reacting fever (in 72 hr after surgery)“:

Who discriminates the two entities and on which criteria? Attending physicians or ICPs? Degree of fever? Why is surgical reacting fever watched for 72 hr after surgery and fever alerting for SSI only for two days after surgery? Why not longer?

Reply—— Sorry for the confusion caused by improper expression. We want to express one valid criterion for NI computer Algorithm: continual fever (temperature ≥38.0°C) for two days after surgery ignoring the temperature in 72 hr after surgery. Because most surgical reacting fever happened in 72 hr after surgery, it would bring about much false positive alerts. We have revised this sentence in the Methods (Page 6, first paragraph, line 6-8)

The RT-NISS discriminates the two entities.

We selected the degree of the temperature (≥38.0°C) according to the Chinese NIs diagnosis criterion. (reference 10 in the revised manuscript)

Why we selected fever for 2 days? Why not longer?

Because when we selected each criterion for NI computer algorithm, we have
ascertained this algorithm performance. For example, selecting “fever for 1 days ” would bring about much false positive alerts. “fever for 3 or 4 days ” would lose some NIs.

RT_NISS as presented in the manuscript provides no post discharge surveillance
– discuss under limitations
Reply——Yes, most NIs happened when inpatients discharged would be out of RT-NISS surveillance. We have discussed this question in the limitation as suggested. (Page 16, second paragraph, line 8-11)

RT-NISS NIs Outbreak Prewarning
“In order to realize sensitive outbreak prewarning, the prewarning threshold combines NIs with community infections. And the microbiological reports included confirmed infection, colonization, or contamination.”
Explain in short why NI and CI are combined, also why not only confirmed infection is reported.
Reply—— Most outbreak concerned NI and CI cases. Under some circumstances, the CI is the source of outbreak. Combination of NIs and CI could increase the sensitivity of outbreak alerts. For example, if one CI case (MRSA detected) spread two NI cases (MRSA detected), the outbreak alert will be triggered. This alert is a cluster not outbreak.
Likewise, microbiological reports included all detected results in spite of confirmed infection, colonization, or contamination. Because the cross-spread pathogen may cause infection, colonization or contamination. In order to increase the sensitivity of outbreak alerts, the RT-NISS selected the prewarning threshold according to different kind of cluster.
We have explained this question clearly in the new manuscript as suggested. (Page 8, first paragraph, line 5-6; line 14-19)

Results
“After ICPs made a final confirmation of all prewarning NIs alerts, the RT-NISS would record all confirmed NIs with their information and would do time-serial alignment in order to identify the daily new suspicious NIs. Then the system could realize the real-time hospital-wide surveillance everyday.”
Why suspicious and not confirmed?
Reply—— There were most suspicious NIs alerts confirmed by ICPs, and the others were excluded because they were community infections, colonizations or not NIs yet. We have explained it in Figure 2.

Rates of prewarnings:
The Comparison Between RT-NISS and Manual Survey
“However it took only 3.5 hours for one ICP using RT-NISS to diagnosis 146 prewarned suspicious NIs from 974 inpatients” = 15%.
In the abstract it says under „Results“, as well as under ICPs Daily Work with the
Help of RT-NISS: “... new suspicious NIs alerts usually accounted for about 2% out of all inpatients......It took about two hours for one infection control practitioner (ICP) to deal with around 70 new suspicious NIs cases among 3500 inpatients each day in the study hospital.”

The Comparison of Monthly NIs Prevalence Between RT-NISS and Other Traditional Report:
“...... 10765). The RT-NISS prewarned 948 NIs suspicious alerts” = 8.8%

Somewhere in the manuscript the difference between new suspicious NIs alerts in daily routine and the NIs alerts in the two studies should be addressed and explained. Also the different rates in the two studies (15% vs 8.8%) should be discussed.

Reply—— We have explained the different rates of RT-NISS prewarning alerts in the two studies (15% vs 8.8%) and daily routine work (2%) in the Discussion. (Page 15, second paragraph, line 1-10)

ICPs Daily Work with the Help of RT-NISS
“Firstly, the system would provide an audio-visual infections time-serial chart......”

What kind of audio components?
Reply—— We are sorry about the incorrect word “audio”. We have deleted the misusage of the terms. Now we have replaced it with the correct word “visualized time-serial chart” in the Results and Figure 3. (Page 9, third paragraph, line 4; Figure 3)

The Comparison of Monthly NIs Prevalence Between RT-NISS and Other Traditional Report
“We compared the NIs prevalence calculated by three methods in July 2011 out of 10765 outpatients”
Why outpatients?
Reply—— We are sorry about this incorrect word “outpatients”. We have replaced the “outpatients” with “inpatients who discharged in July 2011” and corrected the same error in other part (Figure 2) in the revised manuscript (changing “outpatients” into “discharged inpatients”). We have revised the misusage of medical terms according to the standard English medical usage. (Page 11, second paragraph, line 2; Figure 2)

Different predictive values:
“negative-predictive value was 91.19 % (9817/10765), that is to say, the system successfully reduced the number of patients (around 10 times) whom ICPs would manual review for surveillance.”
In the study The Comparison Between RT-NISS and Manual Survey the corresponding figures were: 828/974 which is 85% In this sample the ICPs had to review 15% of all patients.

Comment on the difference

**Reply**—— We have explained the different rates of RT-NISS prewarning alerts in the two studies(15% vs 8.8%) in the Discussion. (Page15, second paragraph, line 1-10)

RT-NISS NI Clusters or Outbreaks Alerts
Difference between cluster und outbreak not defined. Define and reference.

**Reply**—— The definitions for cluster and outbreak were the definitions established by the Chinese Ministry of Public Health in 2009. We added the definitions of cluster and outbreak in the Methods as suggested. (Page 7, last paragraph, line 1-8)

We have added this reference as reference 12 in the revised manuscript.

Discussion

“Stephen E. et al reported a successful hospital-wide prospective system ………..specificity were 0.86 and 0.98 respectively14.”

Reference 14 is Brossette et al.

There is no “Stephen E. et al.” in the Reference list, only a Stephen M Shortell as second author in reference 11 (Halpin H et al.)

**Reply**——The reference 14 (the reference 16 in the revised manuscript) was the correct cited reference. The first author is Brossette SE(Stephen E. Brossette). Now we have revised the obscure “Stephen E” to “Brossette SE” in the revised manuscript. (Page 14, second paragraph, line 10)

DISCRETIONARY REVISIONS

References

In relation to the large bundle of different fields addressed, the reference list is rather selective and short. E.g. none of the work our group has published is referenced though it is closely related, e.g.


This could be cited in chapter Background close to references 5-8.

**Reply**—— We have read the above study carefully. Now we have cited the above reference (studying NIs automated surveillance in ICU ) in the background as reference 9.

Additional remark:

Congratulations to the authors and to all of their co-workers!

Having been active in this field since long and knowing all sorts of obstacles in
establishing a centralised hospital wide electronic NI alerting and reporting service I read this success story with much joy and respect. The work presented here reflects a real breakthrough in IT-supported infection surveillance. And it shows us that with substantial resources and backup (as stated in the acknowledgements), a system of sophisticated IT which is intelligently interlaced with ICP supervision can provide highly efficient, timely, and comprehensive infection surveillance and control. And this in turn helps in focussing ICP work capacity on the relevant issues of NI and outbreak prevention. I encourage the authors to improve this manuscript because it deserves to be put forward to the community of all who are active in infection prevention and control.

Reply——Thank you very much. We have revised our manuscript carefully as you suggested.

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Not suitable for publication unless extensively edited
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests