Author’s response to reviews

Title: The challenge of maintaining microscopist capacity at basic levels for malaria elimination in Jiangsu Province, China

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Author’s response to reviews:

17 Dec, 2017

Prof. Natalie Pafitis,

Re: PUBH-D-17-01857
Dear Natalie Pafitis,

Please find a revised version of our manuscript titled “The challenge of maintaining microscopist capacity at basic levels for malaria elimination in Jiangsu Province, China” (No: PUBH-D-17-01857). We are very grateful for the opportunity to revise our manuscript based on those valuable comments from reviewers. The specific changes made in response to the reviewer’s comments are provided below.

Sincerely yours

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In response to Editor comments

Editor Comments:

(1) Please provide a 'Declarations' section heading after your 'Conclusions' section.

The “Declarations” section was added after “Conclusions” section. (Line 345)

(2) Considering the nature of your study, we would have expected you to have received ethics approval and also obtained consent from the participants. In light of this, please let us know whether you discussed your study with an ethics committee and whether you obtained informed
consent. Your explanation should be reflected within your 'Ethics approval and consent to participate' section of your manuscript.

Thanks for the comment, we have added “This study was reviewed and approved by the Institutional Ethics Committee of Jiangsu Institute of Parasitic Diseases (JIPD). The written informed consent was obtained from all participants before the interview or evaluation.”(Line 377-379)

In response to reviewer #1

(Reviewer 1):

PI Thank you for this interesting article on a very important operational issue - maintaining quality surveillance. It would be useful in the background to describe how these health workers at various levels initially received their skills in microscopy, if any regular refresher training or quality assurance method (eg sample test slides sent out and then reviewed) is regularly undertaken, and how the Master microscopists have their capacity maintained.

Thanks for the comment, we added “In this province, the regular refresher training courses are organized by both provincial and prefecture level every year to maintain the microscopical test skills, and there are two mutual-checking microscopists meetings per-year, in which the microscopists from all the 13 prefectures bring their positive and negative slides and checked by each other, in addition, the quality control system for the whole provincial microscopical test has been established, provincial reference lab for malaria diagnosis collect the slides quarterly and reviewed the reading accuracy and feedback the result to the administrative department.”(Line 90-99)

It would also be useful to understand more on why China has not adopted RDTs more extensively, as this may end up being a barrier to the scale up you suggest.

Thanks for the query, as we mentioned in the manuscript, limited RDT products for malaria have been registered with the State Food and Drug Administration (SFDA) in China(Line 103-104),
we don’t have many choice at that time, the import products from other countries such as SD, Binaxnow, are relatively more expensive, that’s why China has not adopted RDTs more extensively, however, due to the decreasing of the cost and enhancement of the quality, we may scale up this in the near future.

Would also be useful to understand whether the lower level microscopists are used for their programmes and if they also have either problems with the quality assurance of the diagnosis and/or if they have refresher programmes that could have malaria integrated into them.

Thanks for the query, as mentioned above, the network of quality control for malaria diagnosis in the whole province has been well established, all the hospitals prepare at least 2 slides when checking the fever patients seeking treatment, and the county CDC checked the slides within 3 days after reporting the malaria cases, also, the county CDC monthly collect all the negative slides from the hospitals for double check, and the provincial reference lab collect quarterly all the reported positive slides and 10% of the negative slides for quality control, by using both of the microscopy and PCR-based method.

Also in the conclusion you discuss perhaps the role of RDTs at local level but earlier you discussed the lack of sensitivity of these at low parasitaemia levels. How would you reconcile this issue?

Thanks for the query. Currently, the available RDT could not completely solve the problem of the diagnosis accuracy of low parasitemia, however, most of high quality RDT exhibited high accuracy when parasitemia is more than 100 per micro-liter and identifying the deadly species plasmodium falciparum. Based on the result of this study, we recommend scaling up the using of RDTs especially at lower levels, such as the township hospitals,(we have added “especially at a lower level ”at the end of the conclusions section)(Line 343), as we mentioned in the manuscript, since the staff in township hospitals in particular are responsible for many disease diagnoses and treatments, it is difficult to perform well under time constraints and a heavy workload (Line 323-325). Therefore, application of RDTs in low level should able to help improving the malaria diagnosis, especially in the setting of elimination. However, at the upper level, such as the county hospitals and CDCs, the maintaining of the microscopical ability are critically required,
for the purpose of case confirmation and species identification, which providing important information for following foci investigation and reaction.

Edits

Abstract:

Not There were inaccurate rate should be Inaccuracy rate (also line 51)

Thanks for the suggestion, we have corrected it as suggested: “Inaccurate rate with 13.49% and 7.32%, respectively, in 2013 and 2014,”(Line 51)

Suggest adding full stop and a new sentence to start "or villages; the staff at" That is "villages. The staff

Thanks for the suggestion, we have corrected it as suggested “however, none of these cases received confirmed diagnosis of malaria in townships or villages. The staff at county CDCs and hospitals with a higher education background performed better at making and interpreting blood smears than staff from townships” (Line 55-58)

Page 2 Better re-wording of "However, whether the current capacity of microscopists to manage malaria cases in hospitals and public health facilities can meet the surveillance needs to eliminate and prevent the reintroduction of malaria is unknown." Would be "However, the current capacity of microscopists to manage malaria cases in hospitals and public health facilities to meet the surveillance needs to eliminate and prevent the reintroduction of malaria is unknown”.

Thanks for the comment, we have corrected it as suggested. (Line 40-43)

Line 81-82 scale of their use for malaria detection HAS (not have) increased rapidly
Thanks for the correction, we have corrected it as suggested: “The number of rapid diagnostic tests (RDTs) that are available and the scale of their use for malaria detection has increased rapidly over the past few years”. (Line 100)

Line 113-115 one microscopist or clinician from each county CDC and county hospital and half of the township hospitals WAS (not were) randomly

Thanks for the correction, we have corrected it as suggested: “To assess operational ability of microscopy examination for malaria diagnosis, half of the township hospitals were randomly selected in Nantong, and one microscopist from each county CDC (8), county hospital (8), and selected township hospitals (36) was randomly selected to assess their skill at interpreting blood smears and tests to identify malaria parasites.” (Line 131-136)

Line 201 There WAS A (not were) total of 19 and 168 microscopists

Thanks for the correction, we have corrected it as suggested: “There was a total of 19 and 168 microscopists involved with malaria diagnosis in 8 county CDCs and 88 township public health centers (PHCs), respectively”. (Line 210)

Additional information

Page 2 More information - When was the National Malaria Elimination Action Plan launched in China?

Thanks for the comment, we have added: “Local malaria transmission has decreased rapidly since the National Malaria Elimination Action Plan was launched in China in 2010”. (Line 37)

Line 113 What is this " certification from the World Health Organization” and how recent was it?
In 2012, 2014 and 2015, Jiangsu Institute of Parasitic Diseases (JIPD) sent three microscopists from provincial reference lab to participate the malaria diagnosis ability assessment in Shanghai, organized by WHO and National Institute of Parasitic Diseases (NIPD), China. All of them passed the assessment and received the certification issued by WHO (two obtained first class certification, one obtained second class certification).

In response to reviewer #2

(Reviewer 2):

The article "The challenge of maintaining microscopist capacity at basic levels for malaria elimination in Jiangsu Province, China" presents an interesting analysis of microscopy diagnosis for malaria in China which is pursuing malaria elimination. The ability to maintain high quality diagnostics is important, given the levels of imported malaria that are being reported.

Major comments

1. I suggest the authors follow the STROBE guidelines for reporting an observational epidemiological study. These guidelines would help the authors organize the manuscript better - right now it's a bit difficult to understand what exactly the authors are doing.

Thanks for the suggestion, providing us the STROBE guidelines for reporting an observational epidemiological study. In this study, we investigated the relationship between the distribution of education background, working experiences and age with the performance of blood smear making in county CDCs, county and township hospitals, which belongs to the observational study, however, we also delivered the test slides on-site and assessed their parasites reading ability, which seemed not belong to any of the prospective, retrospective, or investigative study, that’s why the manuscript was not completely written in accordance with the “STROBE” method. We have revised the manuscript according to the reviewers’ comments, wish it now became more understandable than before.
2. The authors need to include better description of their sampling plan. It appears that they randomly selected one microscopist or clinician from each county CDC and hospital. They also take one microscopist or clinician from half of the township hospitals. Were half the hospitals selected randomly, or by convenience?

Thanks for the query, there are 8 counties in Nantong Prefecture, and there are totally 72 township hospitals. To make it clear, we rewrote” To assess operational ability of microscopy examination for malaria diagnosis, half of the township hospitals were randomly selected in Nantong, and one microscopist from each county CDC (8), county hospital (8), and selected township hospitals (36) was randomly selected to assess their skill at interpreting blood smears and tests to identify malaria parasites”.(Line 131-136)

3. Can the authors explain better whether they took slides from the microscopist or clinician's case load, or whether they had a pack of "training" slides that they used to assess the microscopist or clinician's expertise? It appears they may have done both, but this section was confusing to read. Following the STROBE guidelines will help to clarify what was done and why.

Yes, we have done both of them, 1) for the blood smear preparation and staining, the slides made by the microscopist from CDC or hospital were used, we wrote in the manuscript ”Ten blood smears from febrile patients diagnosed as non-malaria cases at a CDC or hospital were investigated and scored”; 2) for the parasites identification ability assessment, those slides were prepared by the test organizer, we wrote:”In addition, five blood smears comprising the four main malaria parasite species and a negative were randomly distributed on-site and tested by a microscopist or clinician”. (Line 135-137, Line143-146)

4. There is no mention of sensitivity or specificity of the individuals surveyed. My opinion is that these would be the primary outcomes when assessing accuracy of the microscopists or clinicians.

Thanks for the comment. We do agree that sensitivity and specificity is the primary outcomes. However, it may not be very objective with limited number cases in the setting of elimination,
and the capacity of microscopists can not be simply measured if we just using sensitivity and specificity only. For example, the ability of identifying the parasite species, which is also very important for following foci treatment in terms of the transmission assessment. Additionally, the quality of blood smear preparation is very critical for reading.

5. The ANOVA does not appear to be the appropriate statistical test for the problem presented in the manuscript. I would suggest using a logistic regression.

Thanks for the comment, in this study, chi-square test was used to compare the distribution of educational background, work experience and age between the county and lower levels in Nantong, and ANOVA test was used to 1) compare the ability to accurately interpret parasites among the staff from county and lower levels; 2) analyze the relationship between the educational background, work experience and age played with the preparation of blood smears and the interpretation of parasites among the staff of county and lower levels. We compared the ANOVA and suggested logistic regression method, and exhibited similar result as showed in the study, please find the below paper recently published, in which the ANOVA method were also used for similar analysis.


6. The authors report an increasing trend in imported cases. How is this determined? Could the authors explain more in the introduction or methods how imported cases are determined (my guess is by travel history)?

Thanks for the query, the number of annual malaria cases were collected from web-based notifiable disease reporting system, the increasing trend in imported cases can be found clearly from the annually reported data (reference 3, 4, 15-18). For the determination of the imported cases, we do rely mostly on the travel history, according to the national malaria elimination
guideline. However, the other factors are also considered, for example, which season the cases reported? If the cases reported in transmission season, the active case screening will be performed, to exclude the possibility of local malaria transmission. In addition, we are developing the molecular-based method to make supplement for the determine, such as using the population genetic method through whole genome sequencing to identify the origination of the parasites strain.

Minor comments

7. Lines 147-157 belong more in the introduction.

Thanks for the comment, we agree with the reviewer, we deleted the subtitle of “malaria surveillance network” in “Result ”section, and moved the contents to the “background” section, and adjusted the related reference and figure order in the manuscript accordingly. (Line 80-90)

In response to reviewer #3

(Reviewer 3): Comments

General comments.

A well written and timely manuscript, a problem faced by many countries that have eliminated malaria and those countries in the process of doing so. There is no mention if ethical clearance was obtained as human subjects were interviewed.

Back ground

The background is insufficient, more details on the malaria situation in the provinces studies should be included. The prevalence of malaria before elimination, how many imported malaria cases yearly since elimination up until the study period and why this particular region was chosen should be included. Why was this particular period selected for this study.
Thanks for the comment, for the prevalence of malaria before elimination in recent years, we wrote in the “Discussion” section as: “After concerted efforts from the national to regional levels, malaria transmission has been well controlled recently, and only hundreds of malaria cases have been reported in Jiangsu annually, despite fluctuations after a re-emergence of vivax malaria in central China from 2004 to 2006. No additional local malaria cases have been observed and reported since 2011; however, the total number of malaria cases increased markedly in the last several years because of oversea laborers who export and trade in China but have contact with areas of endemic malaria (reference 4, 15, 16, 17, 18).” The reason why Nantong prefecture was chosen is that it shows a pattern of malaria spread that this similar malaria prevalence situation to that of the entire province and therefore is a good current representative. (Line 241-249)

Line 75 delete cases

Thanks for the comment, we deleted the “cases” as suggested.(Line 75)

Methods

Malaria in Jiangsu and Nantong from 2000 to 2014, Suggest re-writing the paragraph, it lacks clarity.

Thanks for the comment, we have corrected it as suggested.(Line 168-178)

All figures do not have legends nor titles.

Sorry for the confusing, please find the legends and titles at the end of the manuscript, after the section of “references”. (Line 459-471)

Figure 3 and figure 4 What is A and B?
Sorry for the confusing, please find it at the end of the manuscript, after the section of “references”. (Line 463-467)

Line 165 delete second.

Thanks for the suggestion, may I request to reserve this, since the “second” is followed by the above “first”. (Line 168-178)

Capacity of microscopists at a basic level

- describe more on the experience of the microscopists. It is mentioned in the table but not in the text.

Thanks for the comment, in this paragraph, we provided the detail about the 1) distribution of the basic information from microscopists and clinicians in county CDC, county and township hospitals, including the age, education degree and working experience, 2) the reading and preparing the slides through on-site assessment from and microscopists and clinicians.

It is important to address the relationship between experience and skills in diagnosis in the results and discussion

Yes, we totally agree with the reviewer. In this study, we described in the “Capacity of microscopists at a basic level” under “Result” section, 1) the staff with higher education background exhibited better than lower education degree for both of the blood smear reading and preparation, 2) the aged from 40 to 50 exhibited better than those younger than 30 for blood reading, accordingly, we described the relationship between the experience and skills based on the different education background, as a result, we wrote in the discussion section: “Consequently, it is imperative to encourage more young and promising graduates with a higher education level to join the malaria control and elimination network.” (Line 222-234)
Line 263 eradicated or eliminated

Thanks for the suggestion, we have revised as: “An impressive lesson demonstrating a re-emerging infection was observed in Greece, where a vivax malaria outbreak occurred in 2009 after malaria was declared eliminated in 1973.”(Line 272)

I feel it is better to give a few more examples of re-emergence of the disease

Thanks for the comment, we added “in addition, more countries including Italy, Cyprus and Costa Rica have reported the re-emerging infection recently”.(Line 272-274)

Replace line 311 and 312 "other morphological confused materials, i.e. the impurities or blood components". with artifacts

Thanks for the suggestion, we replaced the "other morphological confused materials, i.e. the impurities or blood components" with “artifacts” as suggested.(Line 322)