Author's response to reviews

Title: A Mass Vaccination Campaign Targeting Adults and Children to Prevent Typhoid Fever in Hechi; Expanding the Use of Vi Polysaccharide Vaccine in Southeast China: A Cluster-Randomized Trial

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Author's response to reviews: see over
Dear Editors,

I would first like to thank on behalf of all the authors. I hereby reply to both reviewers, point-by-point, which all are incorporated into the manuscript. The revised manuscript is also uploaded with this cover letter.

Sincerely,

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Reply to the reviewers:

Dr. Szu:

“This group has performed similar study at different sites and should include a section to review results found from other sites.”

The DOMI (Diseases of the Most Impoverished) program has similar studies in Pakistan, Vietnam, and Indonesia, but we decided not to include the results from these sites, because: a) there is a rationale and design paper submitted to another journal; b) that each mass vaccination targeted different age group, and addressed a different vaccination strategy; c) authors (PIs) decided to submit separate papers to other journals.

“Accept after minor essential revisions”

Revisions have been made to incorporate Dr. Robbins’ comments. Many ambiguous sentences have been re-written, which we believe it would be considered within the “minor essential revisions.”

Dr. Robbins:

“Methods: The targeted population was inhabitants that were>5 and <60 years-old. "...were documented and systematically recorded." is ornate. The authors also had to breathe during this time but they do not have to describe this activity.”

The sentence has been re-written.

“Results: I do not understand the last sentence. The subject was the identification of adverse events as occurring in 0.07% of the participants and among these fever (how high?) was recorded in 21%, etc.”

The sentence has been re-written. Details on fever cases are written in the main body.

“Conclusions: Line 1, delete "logistically" Line 3. Delete "targeting typhoid fever". A "mop-up" strategy was not shown to be specific for typhoid fever vaccines.”

The sentence has been re-written.
“Background change "leaded" to "led". Change "Vi polysaccharide (PS) vaccine to "Vi vaccine" – Vi means polysaccharide.”

Changed accordingly. “Vi vaccine” is now used in all sections.

“The original studies demonstrating the efficacy of Vi vaccine should be cited.”

The sentence has been re-written and included the citations.

“Remarkably, there is no mention of the specifications published by the WHO for Vi”

The sentence has been re-written and included the citations.

“What is a "local vaccine institute"? Delete "local".”

Deleted.

“What has been the effect of the use of Vi vaccine in the PRC?”

The sentence now includes: “Although the reduction in typhoid fever cases from government surveillance has been reported, to date, there has been no formal assessment of the effectiveness of the Vi vaccine use as a public health tool.”

“I do not understand this sentence, "Guangxi Province plans to expand the Vi PS vaccine strategy by reaching other age groups affected by the typhoid fever burden". What is "policy-relevant data"? The paragraph should be rewritten to explain the purpose of this program. Is it related to reference 7?”

The sentence has been re-worded and a citation has been included. The article explains the policy-relevant data. “Deroeck D, Clemens JD, Nyamete A, Mahoney RT. Policymakers' views regarding the introduction of new-generation vaccines against typhoid fever, shigellosis and cholera in Asia. Vaccine. 2005 Apr 15;23(21):2762-74”

“Methods: Please explain why "Ethical and research clearance" was necessary for 2 licensed vaccines?”

Although the study uses licensed and commercially available vaccines, there are components of research such as 2-year follow-up and blood drawing. Ethical and research clearance were made to take into account of such research-specific requirements. Sentence in the body has also been clarified.

“I do not understand the sentence "Vaccination coverage by cluster was calculated from the vaccination record books database.””

The sentence has been re-written.

“The paragraph starting with "Safety profiles..." must be rewritten to explain what was measured, by who, and how long.”

The sentence has been re-written.

“Results: Rewrite the first paragraph to remove the redundancies that are confusing.”
The sentence has been re-written.

“What is "vaccine-specific coverage"? Delete "specific".”

Deleted.

“Describe the "Three needle-stick injuries".”

The sentence has been re-written and includes now the descriptions of the injuries.

Delete "capture". There was no crime. Use "identify".

Word replaced.

“What was the range of fever? Do the authors have an idea of the background level of fever especially in the children? Was the temperature of the vaccinees taken before the immunization? Were febrile individuals excluded from the vaccination?”

The sentence has been re-written and includes the range of fever (37.5 – 39.5 degrees). Fever cases recorded as adverse events are based on what attending doctors consider causal to vaccination. Background (considered non-causal) cases are not included. Everybody was asked for presence of fever and those reported of fever and having fever higher than 37.5 degree was excluded from vaccination. (See the method section.) They were re-invited for another day.

“Conclusion: The last sentence of the first paragraph is not based upon data from this study.”

The sentence has been removed.

“The fourth paragraph is confusing. Did not cost estimates precede the study? How is the term "affordable" reached? Affordable for who? How much disease was prevented? The last sentence is silly.”

The sentence has been re-written. Cost estimates here meant the cost effectiveness, when delivery cost is compared with the total cost averted. It will be available at the end of the study. Affordable was for public health program, which was the case in Vietnam study.

“The fifth paragraph is "hype". Delete the first sentence and start the second sentence with "A "mop-up" strategy increased the vaccine coverage by 9.6%.”

The sentence has been re-written.

“Personally, I would not publish this manuscript without a description of the surveillance for the two diseases covered by the vaccines and the efficacy data.”

We believe that description of the disease surveillance and efficacy data are not pertinent to this manuscript that describes the feasibility, logistics, etc. (Vi effectiveness results paper is planed later on after finishing 2 years of surveillance). Both cost-effectiveness and logistics/feasibility are equally important in order to expand the use of Vi vaccine. Since this is the first time that Vi vaccine is offered to all ages (5 – 60) in China and therefore this results/paper are/is essential to tailor the vaccine delivery strategy to expend Vi use as a public health tool.
“Lastly, the authors have not mentioned the advances in the field of Vi polysaccharide-based vaccines.”

The sentence has been re-written and included the citation.

We, authors, hereby thank the reviewers for their times and giving us precious comments in improving the manuscript.