Author's response to reviews

Title: Measles vaccine coverage estimates in an outbreak three years after the nation-wide campaign in China: implications for measles elimination, 2013

Authors:

Chao Ma (maachao@163.com)
Fangjun Li (fangjunliself678@sina.com)
Xiang Zheng (xiaoyucool88@163.com)
Hong Zhang (6184778524@qq.com)
Mengjuan Duan (duan123mengjuan@163.com)
Yanhua Yang (hncdcyyh@163.com)
Lixin Hao (lixinh2010@163.com)
Qiru Su (shine_firefly@126.com)
Lance Rodewald (rodewaldl@wpro.who.int)
Bosong Guo (361778524@qq.com)
Shanliang Xiao (1178273088@qq.com)
Huating Wang (hwang@vip.sina.com)
Li Li (llsdjn@163.com)
Junhua Li (867663530@qq.com)
Huiming Luo (Luohm@Chinacdc.cn)
Lidong Gao (gldlj@hotmail.com)

Version: 2
Date: 16 December 2014

Author's response to reviews: see over
Dear Editor Philippa Harris,

Thank you very much for your re-sending our manuscript for peer review, positive comments, and encouragement to us. We especially thank Dr. Felicity T Cutts’s for the careful review and comments, and we have extensively revised the manuscript accordingly. And below are our responses to the reviewer comments point-by-point. Our responses are written in blue font.

We have also formatted the manuscript according to the format, as required. Please don’t hesitate to tell us if any revision is needed.

Thanks again, and best wishes,

Yours sincerely,

Huiming Luo, On behalf the co-authors

December 16, 2014

**Reviewer 2: 1023500303152404_comment**

**Major Compulsory Revisions**

Line 67 and lines 248-9. The recent national survey showed over 99% coverage for MCV1 and 93% for MCV2 – although the authors have provided a little more information about that survey, these findings do not support the conclusion that reported coverage is exaggerated. The journal that published the 2011 survey is not easily accessible. Some discussion of why the survey found such high coverage is needed – e.g. the authors could comment on the sampling method used (simply saying that children were randomly sampled is not enough – in reality it is rare that true random selection is feasible), and on data quality control in that survey compared to international guidelines, could be helpful.

In lines 248-9: the authors reference surveys that support their own findings but ignore the 2011 survey which did not. It is here that some discussion of why the 2011 survey results may also have been inflated is needed.

Response: Thanks for pointing out this. It’s true that the 2011 national survey showed pretty high coverage, which is not consistent with our findings of “low coverage” compared with administratively high reported coverage. We added more detail in method of the survey in line 67-69, and cited that the survey also found low coverage areas (see line 251-253), which means, under high “average” coverage, pocket/pocket areas exists with low coverage, which might allow measles virus transmission to be sustained.

It is good to see a section on limitations. The following additional limitations should be discussed:
- laboratory methods need to be discussed. How do the titers measured by the Virion EIA compare to other assays? Was the international reference serum used in the runs? How sensitive and specific is this assay compared to the gold standard plaque reduction neutralisation assay? There is presumably a chance of misclassification of serological status and this should be included in the limitations.
Response: Thanks, and we have added this point in limitation section (see line 320-323): “and previous studies comparing commercially available EIA assay versus the gold standard plaque reduction–neutralization assay have demonstrated that EIA was less sensitive, but is a reliable identifier of measles-seronegative individuals”, and added a reference NO. 28 for this.

- Lines 169 and 175 show that there were more MCV2 doses administered than MCV1, and coverage was higher for MCV2 than MCV1 in some clinics. This is not possible as a child cannot have a 2nd dose of vaccine without having received a first dose. It implies that there is some migration between clinics, so that children who received a 1st dose elsewhere came for their 2nd dose, or alternatively that some doses were mis-recorded as second dose when in fact they were first dose.

Response: Yes. This is a good point, since it could confuse the reader. Either of the reviewer’s explanations may be true, but it is not possible to distinguish which is the case from our data. However, given the large urban migration in China, changing clinics is a frequent occurrence, and is the most likely explanation. To address this point, we added a sentence in the Methods Section (see line 106-108) says, “Because this method is ecologic, the number of MCV2 doses can exceed the number of MCV1 doses when children change clinics.” We also added a sentence to the note under Table 1 that says, “The number of MCV2 doses can exceed the number of MCV1 doses when children change clinics.”

Minor essential revisions
Lines 117 and 123 and 133 – in their response to previous comments, the authors clarified that coverage was measured among children aged 9 months or older. Therefore should the methods also state children aged 9 months to 15 years old etc.?

Response: Yes, the reviewer is right. It should be consistent in abstract, method, and in results. We have carefully checked and revised.

Lines 149-150. “Sera samples for which the results were equivocal were retested using the same method and then categorized as negative or positive.” This is still not quite clear. What if the 2nd result was also equivocal?

Response: Thanks the reviewer point out this. We made this clear in the text, in line 152-153, saying: “Sera samples for which the results were equivocal were retested using the same method; if again equivocal, we considered the result negative.”

Line 159 – thank you for including the incidence rates, but can you add the denominator (rates per 1000 or 100,000 or million population)?

Response: Thanks and we have added the denominator.

Lines 279 – 290. These are important points but the authors should point out that if the administrative coverage estimates used birth cohorts as the denominator rather than children registered at clinics, the resulting coverage would be very similar to that found by all the other methods. Given that the data on birth cohorts are readily available, it would seem that the first step to take is to
re-calculate coverage rates using the numerator data reported by clinics and the denominators from the statistics offices. If this does not help to explain why outbreaks are occurring then community-based surveys may be needed, and when they are done, they should use rigorous methods with probability sampling (and please provide some references for readers on coverage survey methods, e.g. recent papers available in open-access journals).

**Response:** Thanks. This is a helpful comment and addition to make to the manuscript. We have added a sentence (see line 297-301) says, “When a measles outbreak occurs in a community, an initial step for public health officials can be to use population estimates to determine whether the number of children registered in community clinics is consistent with population estimates. If inconsistent, community based surveys using rigorous methodology may be indicated.” We have also included a recent review of community immunization survey methods, (see REF NO.26: Measuring Coverage in MNCH: Design, Implementation, and Interpretation Challenges Associated with Tracking Vaccination Coverage Using Household Surveys, PLOS Medicine, 2013;10(5): e1001404).