Author's response to reviews

Title: A bibliometric analysis of childhood immunisation research productivity in Africa since the onset of the Expanded Programme on Immunisation in 1974

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Version: 2 Date: 24 September 2012

Author's response to reviews: see over
The BMC Medicine Editorial Team

Re: MS: 1071507553719442
A bibliometric analysis of childhood immunisation research productivity in Africa since the onset of the Expanded Programme on Immunisation in 1974.
Charles S Wiysonge, Olalekan A Uthman, Peter M Ndumbe, and Gregory D Hussey

Dear Editor,

We are pleased to submit the revised manuscript referenced above according to the reviewers' comments. We have made every effort to revise our manuscript based on the reviewers' suggestions and recommendations, which we believe made our paper stronger and better.

In the following pages we provide a point-by-point response to the reviewers. We have put the comments in bold, with the response below each comment.

We would like to thank you in advance for your consideration.

Sincerely,
Charles Wiysonge, for all authors
Reviewer 01: Christopher John Clements

This is a well-written article that lays out its premise, method and conclusions clearly. It is of importance to the African community and has a high interest level. I am not competent to comment on the statistical methods used.

Reply: Thank you for the encouraging comments. The revisions have been done as indicated below.

The only error I detected was line 3 of the discussion – I think the number of countries is incorrect.

Reply: Thanks, for pointing this out. We have now corrected the number of countries from “two” to “three”.

I accept the final conclusions that the most significant determinant of immunization research productivity in sub-Saharan Africa is private health expenditure, which may be a surrogate measure of the economic ranking of a country. However, I would like to have seen a discussion regarding the contribution of world-class research teams or institutes funded by overseas governments. In particular, I am thinking of the British MRC unit in the Gambia and the Danish group in Guinea-Bissau (Peter Aaby’s group). Are such institutes offering a better model than funding by national health authorities?

Reply: Thanks for pointing this out. This was mentioned in the manuscript, and we have now made mention of Peter Aaby’s group:

“Multiple medical schools and research institutions in South Africa, Nigeria, and Egypt may account for the large number of publications from these three countries. Similarly, the presence of the British Medical Research Council, the Kenyan Medical Research Institute, and a Danish research group (Bandim Health Project) may be the drivers of publications from The Gambia, Kenya, and Guinea-Bissau respectively.”

It would have been useful if the authors had also commented on the type of research that might usefully be undertaken – not simply encouraging research in general. Clearly some research is going to have a greater impact than others. There is an enormous range of research that could be undertaken to support routine immunization. Ultimately, implementation of strategic plans, rather than additional research is likely to have the greatest impact on raising immunization coverage and preventing disease, disability, and death (Clements et al. Vaccine 2011 Nov 3:29(47):8477-82.)

Reply: We agree. In a related study, our group has done a detailed analysis of the type of immunisation research that has been conducted. We have now added the following:

“Locally-relevant health research is needed to ensure the effectiveness, efficiency, and equity of immunisation policies in Africa. In general, health
research helps to answer questions, to generate the evidence required to guide policy, and to identify new tools. A descriptive analysis of study types, quality, and outcomes was beyond the scope of our bibliometric analysis. However in a related study, Shingai Machingaidze and colleagues have conducted a detailed descriptive analysis of a random sample of 881 childhood immunisation research publications from Africa between 1970 and 2010 [ref 35]. The studies were classified as clinical (442/881 or 50.2%) or operational (n=439) research. Among clinical research studies, 41% were phase 1-4 controlled trials, 23% were burden of disease or epidemiology, and 36% were other clinical studies. Among studies classified as operational research, 76% were on programme management, 19% on immunisation policy issues, and 5% related to vaccine financing. There is clearly a need for increased immunisation research productivity from Africa, especially locally-relevant operational research."
Reviewer 02: Jean-Marie Okwo Bele

This research topic is timely and relevant.
The following comments are meant to increase the potential impact of the paper-
Reply: Thank you for the encouraging comments. The revisions have been done
as indicated below. Generally your remarks were very useful and thought-
provoking.

Major Compulsory Revisions: the conclusions could be further
strengthened if the authors address the following points:

1. The authors conclude that private health expenditure (the only variable
significantly associated with research productivity in multivariate analysis)
“may be a proxy for the economic development status of a country”. A
discussion on existing data supporting private health expenditure as an
indicator of economic development status, including why this would be a
better indicator of economic development than total health expenditure or
GDP, would be a useful justification for this conclusion.
Reply: We have not found data to support the statement that private health
expenditure “may be a proxy for the economic development status of a country”.
We have now withdrawn this statement.

1.2. Given the strong association with private health expenditure, a brief
explanation of how this indicator was measured in the source reports
might yield more understanding
Reply: The method used to measure private health expenditure is now explained
in the manuscript:

“[Private health expenditure was measured as out-of-pocket health expenditure].
The latter refers to the sum of money spent on health by private entities, such as
households, commercial or mutual health insurance, non-profit institutions
serving households, and resident corporations and quasi-corporations with a
health services delivery or financing function. The out-of-pocket health
expenditure includes gratuities and in-kind payments, to health practitioners and
suppliers of pharmaceuticals, therapeutic appliances, and other goods and
services whose primary intent is to contribute to the restoration or enhancement
of the health status of individuals or population groups.”

1.3. The conclusion that the study results (lack of association between
coverage and research productivity) may indicate lack of communication
between health decision-makers, programme managers and researchers is
not justified by the study findings
Reply: Thanks, we agree with your comment. However, this conclusion is a hypothesis, which we have now modified as follows:

“The implementation of strategic immunisation plans whose development is informed by available locally-relevant research evidence should raise immunisation coverage and prevent disease, disability, and death in Africa. In general, health research helps to answer questions, generate the evidence required to guide policy, and identify new tools.”

….The lack of association between research productivity and immunisation coverage may be an indication of lack of interactive communication between health decision-makers, programme managers, and researchers; to ensure that immunisation plans are always informed by the best available evidence.”

Minor essential revisions:

1. An important variable that is not addressed is that of research capacity, which could be a significant factor in the number, quality and type of immunization research conducted. Some measures of capacity could be number of medical schools and public health schools and health research institutions in the country.

Reply: Thanks for pointing this out. Unfortunately, there is no reliable database to retrieve information on number of medical schools in each country in Africa.

2. While in the introduction the authors cite the ‘inter-related components of the immunization programme, there is no indication of what the research papers published in Africa is addressing. We believe such information is useful in such a paper.

Reply: Thank you for pointing this out. We have now added the following text:

“A descriptive analysis of study types, quality, and outcomes was beyond the scope of our bibliometric analysis. However in a related study, Shingai Machingaidze and colleagues have conducted a detailed descriptive analysis of a random sample of 881 childhood immunisation research publications from Africa between 1970 and 2010 [Ref. 35]. The studies were classified as clinical (442/881 or 50.2%) or operational (n=439) research. Among clinical research studies, 41% were phase 1-4 controlled trials, 23% were burden of disease or epidemiology, and 36% were other clinical studies. Among studies classified as operational research, 76% were on programme management, 19% on immunisation policy issues, and 5% related to vaccine financing.”

3. The reference to research priority capacity development in the discussion section is not substantiated. While doing this, the authors could refer to the Lancet series on the Decade of Vaccines, published in June 2011.

Reply: We have now made reference to two papers in the Lancet series on the Decade of Vaccines.
Reviewer 03: Sheng T Luo

This manuscript investigated the factors that influenced the productivity of research on children immunization in Africa. The overall presentation and the quality of written English are acceptable. But I believe the manuscript is NOT of sufficient importance to be published in BMC Medicine for the following reasons:

Reply: Thank you for the pertinent comments, which helped to improve the quality of the manuscript. We have addressed them as indicated below.

1. The authors failed to make a convincing argument of the importance and necessity of this research. The relevance of this research to public health and medicine is unclear and unsubstantiated.

Reply: This was stated in the background section. In addition, we have added more rationale to the background section:

“Research publications have an important role in the scientific process providing a key linkage between knowledge generation, uptake, and use. For long, bibliometrics has been the method of choice for quantitative assessments of academic research at international, national, institutional, and individual levels. Bibliometric analysis is also a feasible tool to comprehensively recognise the research advances in the past and future research trends in a specific field. In the context of the African continent, to date, factors related to variation in immunisation research productivity have not been examined; although bibliometric studies with data on Africa exist in other disciplines. Therefore, this study aims to fill some of the gaps in existing research by providing insights into the history and growth of childhood immunisation research in Africa.”

2. The validity of using the number of articles as a surrogate of research productivity was not supported. As a minimum, a short literature review and some references should be provided.

Reply: The choice and limitations of number of publications indexed in PUBMED as surrogate for research productivity was mentioned in the discussion section:

“PubMed has been widely used for bibliometric analysis, but it is important to note that the database is dominated by English-language journals; therefore possibly contributing to selection bias due to language barriers. By using the author addresses listed in the by-lines of research articles, one can only identify countries and organisations where the authors were employed when the research was done or where the article was written, or both. These limitations notwithstanding, we believe that this study is a good reflection of research productivity in the field of childhood immunisation in Africa.”

3. The authors made a strong argument that negative binomial regression should be used due to overdispersion, but they neither checked the
overdispersion parameter nor conducted the likelihood ratio test to compare the negative binomial and Poisson models. Some descriptive statistics and plots should be presented to support the existence of overdispersion.

Reply: To make research findings more accessible (easy read) and not distract the general audience of the paper, we decided to keep the statistical details in the manuscript minimal.

As suggested, the details of the model fit statistics and model comparisons as implemented is now reported as an online appendix for the audience with advanced statistical interests. The following tests were conducted:

- Test 1: The probability distributions which underpin the two models were examined to see how they fit the observed data
- Test 2: The likelihood ratio test was used to test for overdispersion in Poisson regression model
- Test 3: The Bayesian Information Criterion (BIC), based on log likelihood was used as a measure of how well our different models fitted the data. A lower value on BIC indicates a better fit of the model

4. The multivariate analysis only included the covariates that were significant (with p value 0.05) in the univariate analyses, which may be too stringent. Usually, the covariates with p values smaller than 0.2 in the univariate analysis should be included in the multivariate analysis. Alternatively, some variable selection should be conducted.

Reply: There is no golden rule on choice of p-value cut-offs for inclusion in multivariable models. As suggested, the cut-off of p<0.2 is now implemented in the multivariable model. Only one additional variable (number of physicians) met the inclusion criterion. The inclusion of this variable did not change the results of our final full model.

5. On page 5, in the 3rd paragraph, it said that “We observed continuous increase in the production of research articles from all African sub-regions during the period 1974 to 2010”, but Figure 2 displays a large drop for Southern Africa.

Reply: This has been corrected:
“Apart from Central Africa and Southern Africa which experienced a drop between 2001 and 2010, there was a continuous increase in the production of research articles from all African sub-regions during the period 1974 to 2010.”

6. On page 5, in the 4th paragraph, it said that “A unit increase in private expenditure on health”. It is much more informative to be explicit what that unit was.

Reply: This has been corrected.
7. The authors failed to provide insight and discussion why some covariates were insignificant and why private expenditure on health was significant.

Reply: Thanks for pointing this out, we have now added a few sentences about this in the manuscript:

“One possible explanation for the lack of a statistically significant association for most factors included in the multivariable model is the small sample size (that is, number of countries included in the analysis). In 2010 there were only 53 countries on the African continent. The model may not be adequately powered to reach statistical significance with these variables.”