Author's response to reviews

Title: Progress towards implementation of ACT malaria case-management in public health facilities in northern Sudan: a cluster-sample survey

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Version: 2 Date: 3 November 2011

Author's response to reviews:

Dear Editor,

Many thanks for the chance to submit a revised version of our manuscript. We also thank the reviewers for their detailed comments. Please find below our responses to their reviews together with the revised version of the manuscript.

Responses to reviewers’ comments

Reviewer: Patrizio Pezzotti

Reviewer’s report:

Statistical advice only

Although the statistical methods used are appropriate, the authors should clarify in the survey design section how they calculated 244 health facilities out of 5,716 in the country as sample size. I feel that they defined the expected precision but this is not clarified. Furthermore the authors, in the same section, should clarify what they consider as size of the stratum. The number of visited patients, the population residing in that area, something else?

Authors’ responses:

Thank you for this advice. We have revised manuscript to provide sample size calculation (Methods, survey design, pg 6). With respect to stratum size, this refers to the number of facilities in the stratum and this is now explained in the section describing sampling strategy in the revised manuscript (pg 6).

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

Reviewer: Beth Kangwana
Reviewer’s report:

Major Compulsory Revisions
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The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

1) Under methods, survey design, line 6-7 ‘From each stratum a simple random sample of facilities was drawn in proportion to the size of the stratum’: Could the authors provide the ratio of facilities to size of stratum that was used to select the sample? I feel this important information especially for purposes of replication.

Authors responses
Thank you for this comment. The survey design section was revised and expanded to provide details on the sample size calculation and the sampling strategy applied (pg 6).

2) Under results, sample description: The authors mention that 4,140 patients were screened, of which 2,433 patients were (197) referred, (61) admitted or hospitalised, (362) pregnant’ (420) follow up visits, (50) aged 2 months, (41) less than 5kg, (1,365) presented without fever. The numbers add up to 2,496 instead of 2,433. Could the authors please clarify the discrepancy.

Authors responses:
The numbers add up to more than 2,433 patients because some patients may have had more than one of the six assessed exclusion criteria. This is now specified on pg 9.

3) Under results, health facility and health worker readiness to implement ACT policy, paragraph 2, line 3: it states that ‘At least one of the four AL weight-specific packs was in stock at only 9.0% of facilities’. Table 1 shows AL (at least one pack) =24.6%. Could the authors please clarify the discrepancy.

Authors responses:
The results in the main text referred to all facilities while in the Table 2 they were
restricted to the subsample of health facilities for reasons explained in the footnote. We have now revised the main text throughout the paper to provide results as presented in the Table 2 (24.6%). Thank you for this observation.

4) Table 3: could the authors review their numbers. Under ‘treatment for test positive patients’, ‘other antimalarials’, there is total of 14 patients, yet under footnote b, it describes antimalarials for only 13 patients. The same problem exists in table 4.

Authors responses:
We have done corrections in both Tables.

Minor Essential Revisions
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The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.

1) Table 4: Could the authors please check the ordering of their footnotes. I think the second ‘a’ should be ‘b’?

Authors responses:
We have corrected footnotes.

2) Under methods, indicators and definitions, paragraph 2, line 3, suggested change of ‘non-pregnant patients aged 2 month’ to ‘non-pregnant patients aged 2 months’

Authors responses:
Thank you, we have corrected this.

3) Under discussion, malaria case-management practices, paragraph 3, first line, suggest changing from …refer to patients’… to refers to patients

Authors responses:
We have corrected grammar in this sentence.

4) Under discussion, study limitations, in the last sentence of this paragraph it states that the authors do not know if patients were prescribed the appropriate drug dosage component of antimalarial treatment. I wanted to confirm if this is also true for health workers explaining what to if vomiting took place. Do the authors know if all patients that were explained on what to do if vomiting took place were given the correct advice? Also from this manuscript, it is not clear what the correct advice should be?

Authors responses:
Thank you for this observation. The vomiting advice information in table 5 is based on patients’ report if any advice in case of vomiting was provided during
the facility visit. It was strikingly low - only 6% (22 patients) reported any advice. The content of the information to judge the quality of advice on vomiting was unfortunately not collected. Nevertheless, the correct advice should be that in case of vomiting within 30 minutes another dose should be given and patient/caretaker should return to the facility for the replacement dose.

5) Table 1: Could the authors annotate on the table that the RDTs listed under ‘availability of malaria diagnostics on survey day’ are non-expired RDTs, as written in the text.

Authors’ responses:
Thank you for this suggestion, we have inserted “non-expired” wording in Table 1.

Discretionary Revisions
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These are recommendations for improvement which the author can choose to ignore. For example clarifications, data that would be useful but not essential.

1) Under results, sample description: I feel that displaying the data provided on a table will make it easier for readers to scan through the numbers.

Authors’ responses
Thank you for the suggestion, however we felt that this section is clearly laid out and given that we already have 5 tables and 2 figures this would be unnecessary extension of the manuscript.

2) Under methods, study design, second line: the authors mention ‘non-government public health facilities’. Could the authors please provide some clarification on this phrase as it is not clear to me how the facility is a public facility yet is owned by a non-governmental organisation.

Authors responses:
In Sudanese context public health facilities managed by Federal Ministry of Health include governmental and non-governmental facilities.

3) In the text, the authors mention ‘significant difference’ for example under results, malaria diagnostic and treatment practices, paragraph 4 and 5. I assume the authors are referring to real differences observed between percentages as oppose to statistical significance, based on confidence intervals that do not overlap. In which case this seems fine. However if the authors mean statistical significance, could they rephrase this to ‘apparent significant difference’ since no hypothesis testing was carried out.

Authors responses:
Thank you for this observation. As also suggested by another reviewer we have revised the Tables and results section to undertake formal significance tests for comparison of proportions between age groups.
4) Table 2, under pre-service training, could the authors list in the footnote who these ‘other cadres’ are

Authors responses:
Unfortunately for 12 (4%) health workers in the category “other cadres” we have no information what specific cadres they are. We only know that they are not doctors, medical assistants, nurses or CHWs.

Minor issues not for publication
N/A

Level of interest: An article whose findings are important to those with closely related research interests

Reviewer's report

Title: Malaria case-management in the era of artemisinin-based combination therapy across 15 northern states in the Sudan

Version: 1 Date: 22 September 2011

Reviewer: Kenneth L Leonard

Reviewer's report:

Malaria Case-Management in the era of artemisinin-based combination therapy across 15 northern states in the Sudan.

Summary:
This paper presents the results of survey designed to measure the degree of compliance with new national protocols on the management of malaria cases.

They find that the old therapy has been effectively eliminated from malaria management but that recommended first line therapy is not universal, in particular, a significant proportion of facilities do not have the recommended medicines on site. The most disappointing results are seen in the compliance with protocol; too many patients receive injectable therapy when it is not indicated, too few patients are tested for malaria, and too many patients receive medication despite testing negative for malaria. However, the authors state that these results are similar to results found in other countries. The primary recommendation of the research is that the supply of medicines and tests be improved, allowing more facilities to properly implement the protocols. These gains are expected to come from current government plans to increase the use of RDTs.

Review:
The research project is well designed. In particular, the authors have taken care
to study the question recognizing the important difference between capacity and effort. In collecting data on supplies as well as the practices, they are explicitly allowing for the know-do gap, in which health workers are capable of properly administering protocol but choose not so to do. This is very different from health workers who do not follow protocol because they cannot (when they are missing supplies). In addition, they are aware of the possibility of the Hawthorne effect and take that into account in their design.

Overall, it is clear that the authors have answered the question they set out to answer: how are the new protocols being implemented?

My concerns with this paper rest with the implications of their findings. As far as I can tell, the results are not particularly surprising given the experience in other countries. (If they are different from the experience in other countries, the author(s) have not adequately communicated this and I would like to see the differences more clearly outlined.) For example the comparison of Northern Sudan with other African countries on the rates of testing and the explanation that there are more doctors and that there is a greater tradition of testing, is illuminating (page 13). Furthermore, the simple conclusion appears to be: “The program has not adequately taken hold, so we need more of what we have already done.” I realize I am oversimplifying the case, but it does appear that most of the problems with the implementation are the kinds of things that could have been anticipated ahead of time. The fact that RDTs are not available excuses the health workers in a particular clinic (maybe the lack of supplies is the health workers responsibility—the paper does not clarify) but it does not excuse the implementation.

What would be interesting to the potential reader of this article is some understanding of the reasons for the failures, not a suggestion that some future program may fix it. I think the authors have in hand the data to start to understand the components of the shortfalls in the program, even though overall, it achieved many of its gains. There are, within the data, multiple levels, multiple systems and multiple distances from major urban centers. Is the lack of supplies determined by distance to urban centers and it is the same in public and non-public? Question such as these will help the reader to understand what could be done to improve a program like this in Sudan as well as what could be done for such a program in another country. Indeed, the multiple necessary inputs for this program (knowledge, effort, diagnostic tests and medicines) is something likely to be repeated in other programs on different therapies. As it is, the paper is too narrowly focused to be of much use to future program implementers. The statement that further research is needed is inadequate—the researchers have the data to do a better job and if not, they should have realized that such data would have been necessary before they did the first research project. Are the authors really willing to say that they did an in depth study of whether the program was working, were surprised to discover that it was not working perfectly and now need more money to go and find out why?

Authors responses:

We thank the reviewer for acknowledging the appropriateness of research design
and the success in answering the study question. The reviewer however raised two important questions. First, are the Sudanese findings anyhow different than what was previously reported in other African settings? Second, what further analysis/research would be required to answer questions “why” and better inform policy implementers? With respect to the former, there are at least three important areas where substantial differences were observed compared to other countries where similar surveys were undertaken. On positive side, we observed higher rates of patients tested and fewer patients with negative test results disregarded by health workers, yet on negative side, the inappropriate use of injectable artemether was higher than observed in other countries. For each of these findings we have approached discussion in balanced way suggesting possible contextual explanations and highlighting differences between Sudan and other countries. Most importantly, we believe, but as also suggested by another reviewer, that qualitative research is indeed critical to provide explanations why some of the challenges exist. Such investigations should look at the whole supply chain to answer questions around the availability of commodities, and include desk reviews and in-depth interviews with programme implementers as well as with health workers and patients to better understand practices. While we could be criticized that we have not included in-depth qualitative investigations around health systems and behavior issues, it should be however acknowledged that the primary aim of this work was entirely for M&E purposes providing national quantitative indicators for measuring progress in the implementation of the new case-management policy, and this was however successfully accomplished. We indeed believe that qualitative research is indispensable to disentangle subtle differences in relation to the systems and behavior and we have reemphasized this in the conclusion section of the manuscript and in the abstract.

Level of interest: An article of limited interest

Quality of written English: Acceptable

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.

Reviewer's report

Title: Malaria case-management in the era of artemisinin-based combination therapy across 15 northern states in the Sudan

Version: 1 Date: 16 September 2011

Reviewer: Carole Fogg

Reviewer's report:

General comments
This is a clearly described and detailed piece of work, highlighting some important issues in malaria case management 'in practice'.

Major compulsory revisions

1. Please provide sample size calculation, or a rationale for the number of facilities surveyed. The data management and analysis section glosses over the power and precision considered to be required for the survey, and what the primary outcome that the survey was based on was, or if the number of facilities were in fact the number you could feasibly visit.

Authors responses:

Thank you for this comment. The survey design section was expanded to provide details of the sample size calculation and the sampling strategy (Pg 6).

2. You state that ‘there were no significant differences in practices for patients below and above 5 years of age’ (last sentence, Results section of abstract). What is this based on? Although the sample in table 3 for test positive patients is small, there is a trend towards greater use of AS/SP for test positive patients under 5 vs greater use of artemether injection for patients >=5 (the latter is statistically significant). Test negative patients do not show anything, but the difference between the age groups in treatment with NO test is statistically significant both for AS+SP and artemether (watch your spelling...!) injection. I would suggest that you abandon the confidence intervals in this table, and insert a column with simple test of 2 proportions results. Then repeat the process for Table 4 (for which it looks like the pattern is similar, although smaller differences, as you say). Then, suggest you adjust this statement in the abstract, and consider discussing these significant findings in the results/discussion. Similar differences between age groups in terms of prescribing first line/alternative line according to knowledge of parasitological results were found in Ghana (Dodoo et al Mal Journal 2009) (?add as reference?) and this is something which warrants further, perhaps qualitative, research (you could mention this in the conclusions?)

Authors responses:

The primary study objective was to report stand alone values with precision estimates and this is the reason why confidence intervals were reported. Yet we have accepted the reviewer’s suggestion and removed CIs for age specific estimates and performed significance test comparing proportions between age groups. This is now provided in Tables 3-5 and also reported in the results section on the indicators we deemed the most important in the context of the new diagnostic and treatment policy. Furthermore, the reference to age groups comparisons was deleted in the abstract and the focus here remained on all age results. The discussion section was also amended to highlight somewhat higher trend in the use of AS+SP for children vs artemether injection in adults. With respect to patients without test performed we performed exploratory analysis restricting it to the patients who had any antimalarial prescribed and no difference in AS+SP use was observed between children (80.0%) and patients 5 years and
older (81.8%) and the age-specific effect was due to somewhat lower proportions of children treated for malaria. Since the new policy is promoting testing for febrile patients, this category of patients without test done was not focus of our discussion. Finally, the need for qualitative research investigating supply chain and clinical practices, as rightly stated by the reviewer, is highlighted in the discussion as well as in the conclusion sections of the revised manuscript and the abstract.

3. I was not over fond of the confidence interval columns in any of the tables, especially in the absence of a sample size calculation – are they necessary?

Authors responses:
Thank you for this observation, this has been addressed; kindly see responses under points 1 and 2.

Minor essential revisions

4. Title: - should reflect the fact that this survey was in public health facilities only. Also, title focuses on case-management, when in fact the focus of the paper is all aspects of adherence to the change in strategy – perhaps you can update this?

Suggestion: ‘Adherence to / progress towards implementation of ACT malaria case-management in public health facilities in northern Sudan: a cluster-sample survey (or audit..or ‘mid-term’ audit...)

Authors responses:
Thank you for this suggestion. We have amended the title of the manuscript to state “Progress towards implementation of ACT malaria case-management in public health facilities in northern Sudan: a cluster-sample survey”

5. In table 3 and 4, rather than the ‘Any AM prescribed’ row, for consistency it would be good to have the ‘no treatment’ row (then the reader can add up the numbers rather than having to subtract figures from the denominators). Or perhaps just add in a ‘no treatment’ row above the ‘Any AM’ row.

Authors responses:
We have added the row “no antimalarial treatment” as suggested by the reviewer. The row “any antimalarial treatment” was kept only for reference to treatment of test negative results.

6. You refer to RDT roll-out in the discussion – can you please specify if the intention is that the health workers rather than lab personnel are intended to use these? Or are the health workers already performing microscopy? For example – you say that ‘only 23.5% of outpatient health workers were trained on RDT use’ – would you expect them all to be trained, or do lab personnel also have a role? Lab personnel were not mentioned in this manuscript, so I was not entirely sure where the diagnostic responsibilities lay.
Authors responses:

Unfortunately we do not have information on the laboratory personnel since the focus of our evaluation was case-management from clinicians’ perspective. We have reported coverage on RDT training for all health workers because despite a general orientation that RDT deployment should be prioritized to facilities without microscopy, the future training activities on RDT use are directed towards clinicians and laboratory personnel at all levels of health system.

7. Paragraph 2 of results ‘health facility and health worker readiness etc’ – it is not clear whether expired blisters were found at different facilities to non-expired (i.e. did the units actually have some expired and some non-expired, or were they totally different units?) Are all types of units expected to have all medications? E.g. is a basic health unit expected to have quinine injections, or would you expect these to be mainly at referral units? It is sometimes difficult to ascertain the ‘expected’ denominator for these factors when just % are given.

Authors responses:

Regarding the distribution of expired drugs, of 7 facilities where these drugs are found 6 had both expired and non-expired drugs while only 1 had only expired drugs. Since there were only 7 (2.9%) facilities with expired AS+SP, the problem was considered minor and we have not explored further on this topic. Thank you for observation on denominators – we have restricted now analysis on injectable antimalarials to health centres and hospitals, the levels of care which are supposed to stock these items.

8. Still on the subject of denominators – another example under ‘Quality of ACT dispensing and counseling’ – you state ‘6.1% were weighed’ – but how many patients would you expect to be weighed? Just the kids? Unlikely to routinely weigh adults at outpatient consultations? If just the kids, for example, you could state ‘x% of children under x years were weighed’, which may represent a more meaningful statistic.

Authors responses:

Good clinical practice suggests that all patients should be weighed, certainly all children. In addition to age-specific data provided in Table 5, we have now revised results section to report age specific results (despite somewhat better results only 14% of children are weighed).

9. Discussion – 2nd paragraph – monotherapy has large been successful phased out – would think the relevant % here is 95% - i.e. you found no CQ in 95% of facilities.

Authors’ response:

We have corrected this figure as suggested.

10. Your point about the Hawthorne effect can be expanded a bit – for example the much higher rate of patient microscopy/RDT testing than expected is highly
likely to have been a result of this! Did you look in the lab log books to see if this was an unexpected ‘peak’ on the survey day? This could have had a knock-on effect therefore in how the patients actually got treated – you could imagine that on a ‘normal’ day, more patients would have been treated as per your last rows in Tables 3 and 4 (‘treatment when no test done’) – and therefore lower rates of case-management adherence seen – this warrants discussion.

Authors’ responses:
Thank you for this question. The Hawthorn effect cannot be entirely ruled out and we have indeed acknowledged this under the study limitations but we have also considered this carefully when deciding upon data collection methods to minimize it, as well noted by another reviewer, an expert on Hawthorn effect. Despite somewhat better adherence results observed than in other countries which applied the same methodologies, the adherence is still far from perfect and we feel that we discussed an overall performance with all limitations in a balanced way highlighting both positive and negative findings. We unfortunately cannot comment on the record reviews since the study did not include this component.

11. Instead of the map, could you put in a flow chart of the decision tree for health workers? i.e. what are the recommendations they are supposed to follow – febrile Y/N, test positive/negative etc with the treatment regiments? (I imagine there is something like this in the health worker guidelines?) You can replace the map with a sentence saying something like the sample of health facilities was evenly spread among the population of north Sudan...

Authors responses:
We have included the flowchart in the manuscript as the Figure 2..

Discretionary revisions
12. Although this work is described as a ‘survey’, it actually appears to be an audit – i.e. you are evaluating the proportions of certain factors/processes which you expect to be in place (e.g. you expect 0% of chloroquine in health facilities according to policy recommendations, but you find 5%). Perhaps you could consider using this terminology at some point in the manuscript.

Authors’ responses
The study falls within the category of “health facility surveys” measuring inputs and processes and this is why we prefer to use “survey” terminology.

13. Would like to know whether the policies extend to private facilities, and if so, why they were not included in the survey? If not, would be good to state that this is the reason they were not included.

Authors’ responses:
Private health facilities were not included because they are not supplied with
ACTs and diagnostics by the Federal Ministry of Health. This is specified now under the survey design section (pg 5).

14. Table 3 Title – perhaps make clear this is a patient denominator, rather than facility.

Authors' responses:
In Tables 3 and 4 we have revised titles as suggested

15. As regards point (2) above, >5’s are known to vomit more – perhaps this could be a reason for utilising injections? Was this symptomatic information collected at baseline?

Authors responses:
We have observed the opposite pattern than suggested by the reviewer - children had higher rates of vomiting (17%) than patients 5 years and older (8%). To our view this is an expected age pattern.

16. It would be nice to see the point about future qualitative research required in the conclusions. There are several studies now published very similar to this one, but I was left wondering WHY health workers had not attended ACT based case-management training (didn’t know? No access? No funds? Not interested? Etc etc), WHY do health workers not follow the recommendations even when they have the tests/medications etc....these are the questions which need to be answered from this kind of ‘audit’ work, and you could highlight this here. Some qualitative work would be necessary to understand the reasons for the shortfalls / non-compliance with recommendations before large scale implementation of RDTs, for example, particularly the non-adherence to first-line recommendations for positive patients, and the continued treatment of negative patients – why is this happening, and how can it be addressed to avoid potential future waste of resources?

Authors' responses:
We agree with the reviewers’ comment - the future qualitative work investigating quantitative deficiencies revealed in the study is indispensible. We have revised the manuscript to make this point clear in the conclusion section.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being Published

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
Yours Sincerely
Abdisalan M Noor, on behalf of all authors