Author’s response to reviews

Title: Prescriber and patient-oriented behavioural interventions to improve use of malaria rapid diagnostic tests in Tanzania: facility-based cluster randomised trial

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Author’s response to reviews: see over
Dear Dr Lin Lee,

Response to Comments by Reviewers
Re: Prescriber and patient-oriented behavioural interventions to improve use of malaria rapid diagnostic tests in Tanzania: facility-based cluster randomised trial

We would like to thank the reviewers for their very useful and supportive comments which have helped to improve the manuscript. We have provided a point by point response to the comments below, with reference to any relevant changes that have been made in the manuscript.

The study was approved by the Ethical Review Boards of the National Institute for Medical Research in Tanzania (NIMR/HQ/R.8cNoL. 11/24) and the London School of Hygiene and Tropical Medicine (#5877). The trial was prospectively registered with ClinicalTrials.gov (#NCT01292707) but unfortunately our initial submission to the PRS system contained the error that the 'oversight authority' was not presented in the approved format and the note that this had to be corrected slipped our attention. For this reason the PRS has only recently been fully approved and we apologise for this omission. The date of initial trial registration was 29th January 2011, and this has now been added at the end of the abstracts per guidelines. We have also submitted a screenshot of the registration page to confirm this.

Reviewer 1

Minor essential

• Abstract

1. Clarify that the main problem is over-prescribing of anti-malarial in the face of a negative RDT result

We have added this to the abstract.

• Background
2. ‘formative mixed-methods research’. This approach needs explaining – it is clarified by reading the reference 19 outlining how the intervention was developed, but not all readers will access that information. 

We have now provided a brief outline of the key stages of the formative research, whilst remaining mindful of the manuscript length.

3. One reason for clinicians ignoring the RDT results is that they may not trust that they are accurate. Some information about the ‘real-life’ accuracy of RDTs in this sort of setting is therefore required.

We have added in a couple of references with regards to the RDT performance to the manuscript in the last para of the outcomes. As part of this study we collected sample of RDTs from the facilities and re-tested them in a lab against serum of a confirmed slide positive case with a parasite density of 5000 parasites per mcl. All RDTs in the sample registered positive. In addition all RDTs had been batch tested according to WHO standards before receipt of the tests.

4. The practical implications of adding in the patient component of the intervention are not clear – were the patients supposed to query to prescriber if they felt they were not getting the appropriate advice/treatment?

The purpose of the ‘patient component’ was to assess whether prescribing practices would improve if the prescriber was aware that the patient had seen posters at the health centre and been provided with a leaflet that promoted an expectation of RDT testing if malaria was suspected, and adherence with test results. Patients were not asked or expected to make any particular response to the prescriber, although the prescribers could use the leaflets to explain their decision making if they wished to do so. We have clarified this in the methods section when describing this aspect of the intervention.

• Methods

5. Typo - ‘very poor in this in previous’

Thank you. This has now been corrected.

6. ‘Consenting patients’ are mentioned but many data were from children so information needs to be provided about the consent process for them.

Verbal consent was obtained from all patients for participation. If the patient was a child under the age of 15 the carer provided consent on their behalf. This has been clarified in the manuscript.

7. It would be helpful to know how many facilities there were in total in the catchment areas, and how many were considered for inclusion before the final decision about
eligibility was made. Were they all government facilities since the RDT training was provided by the government? Apart from this the inclusion criteria are well described.

The total number of primary care health facilities in the study areas was 90. All 90 facilities were assessed for eligibility as indicated in Figure 1. The eligibility criteria specified that facilities were registered as health facilities with the local District Medical Officer and had been approved to receive supplies of drugs from the Government stock. Such facilities in Tanzania are subject to MOH guidelines and supervised by visits from the District Medical Officer or his team. We have outlined the eligibility criteria within the methods section of the manuscript.

8. There is some lack of clarity and inconsistency about the term ‘prescriber’, ‘health worker’, ‘workers’, ‘providers’, ‘colleagues’ and representatives from facilities (results, para 2) – how do these differ, and how do they relate to each other, and what are their roles in the study? Because of the diversity of these terms it is not always clear who and how many of the different cadres were trained or contributed to the data obtained in the study (for example in the ‘implementation of the intervention’ section). It is therefore not possible to get a clear idea of the proportion of total health workers in the facilities that were actually involved in the study and the training they received.

We apologise for the confusion around the various uses of these terms. We have now amended the manuscript such that consistent terminology is used throughout and any differences explained. To summarise, all health workers who were responsible for prescribing were invited to participate in the trial (study design and participants paragraph). The characteristics, including the cadre, of the prescribers participating in the trial are summarised in Table 1. Baseline data at the health facility level indicate that on average 75-90% of health workers are regular prescribers. We have included this information in the manuscript and in Table 1 which also shows the average (range) of health workers in the study facilities.

As outlined in the first paragraph of results, patients included in the evaluation of the primary outcome could have seen any of the health workers present at the facility on the day of the exit surveys. Therefore, the patient may not necessarily have been in consultation with a health worker who was a regular prescriber that attended the training. Similarly, some of the trained prescribers were not present on the days of the patient exit surveys and therefore did not treat any patients included in the evaluation of the outcome. Also, any new prescriber who joined the health facilities during the study were also eligible and were included if they consented. We did carry out an analysis based on exit survey data from those patients who were treated by a prescriber who participated in the study and received the training (see additional file 3) and the results were very similar to those from all patients attending the study facilities.
9. The purpose of recording the stock-outs is not clear. Since the research team were providing supplies through the trial why did stock outs occur at all? If stockouts are a significant problem in routine facilities, the effect of this on implementing the study findings on a large scale could be covered in the discussion.

ACT supply was through the usual channels; the study did not supply ACTs to the study facilities. Therefore, we recorded details of stock-outs to observe prescribing practices when the recommended antimalarial drug was not available, and to carry out sensitivity analysis to examine the intervention effect when there were no stock-outs. Since some facilities did experience periods of stock-out then the results of this study provides an indication of the intervention effect that could be expected in a similar setting experiencing a similar degree of stock-outs if implementing the study on a large scale.

10. The purpose of the SMS and feedback summary to providers provided by staff is not clear in the methods, although the purpose can be partly deduced later in the paper. Was this data included in the final analysis?

Data from all consenting patients attending the facilities on the days of the exit surveys have been included in the final analysis. These exit surveys took place throughout the duration of the trial and during the various stages of intervention implementation, including the period when prescribers received feedback and motivational SMS. We have added in further detail about the purpose of these SMS into the methods.

11. More information is needed about the process for checking blood slides and the number of slides checked, since they were used for quality assurance of the RDTs.

We sampled RDTs from the clinic supply and checked them against blood from a confirmed slide-positive case at Teule Hospital, a site where staff are subject to external QA to meet the demands of clinical trials. All tests were concordant. The number of research blood slides available for quality assurance check of the RDT results recorded in MTUHA register was 105. We have now included this in the results.

12. Some information should be included about the contexts of the survey administrated by interviewers to those exiting the facilities

All patients exiting a consultation were briefly interviewed to determine if they had suspected malaria and if so whether they had been prescribed an antimalarial or antibiotic and if they had been tested by RDT. We have added further detail in the manuscript.

13. More information is needed about the observations of provider performance including the length of time they were observed for, how patient interactions were observed and what was actually being observed (e.g. was there an observation checklist?)

Prescribers use of RDTs was checked at supervisory visits for following the test procedure as presented in the standard MoH RDT training. No other aspect of the consultation was...
documented or commented upon. Observations of performance were conducted if eligible patients were being treated on the day of the supervision visit. A total of 143 observations were performed, and the numbers were similar across study arms. We have provided further clarification about these observations in the manuscript under the methods and results.

- Discussion

14. A description of the suggested intervention for scale up should be included outlining the potential challenges to be considered if this is taken up outside a trial setting, as well as the benefits

We do not feel that we should be prescriptive about the intervention for scale up but have provided a discussion around the interpretation of what may have contributed to the intervention’s effect and challenges associated with implementation that can inform both other researchers and policy makers. This is a pragmatic trial to help inform intervention choice in routine settings rather than prescribing an intervention for scale up.

Table 3

15. Add in information about the actual timing and duration of the ‘periods’. These also appear in figure 1 – maybe consider having a text box with the timings

We did initially have this information included in Table 3 and Figure 2 but removed it prior to submission since we felt it made the Table and Figure too cluttered. We have therefore provided a text box with timings as suggested.

Figure 1

16. The components of the 3 modules need to be explained

Does the reviewer mean Figure 2? We have added a brief description of these modules into the text under the description of the intervention.

Discretionary

17. It may be helpful to readers to explain that part of the problem of over-prescribing of ACTs may be related to a lack of diagnostic and treatment options for non-malaria fevers.

18. The finding that 21% of those who were afebrile and tested, had a positive RDT is interesting and the authors may consider expanding on this in the discussion

We thank the reviewer for raising important points which relate to the scale-ability of the intervention. In response to point 17 we found that in our setting they were (relatively) well
equipped to provide alternative diagnoses and treatments. We have expanded the discussion to reflect these points.

**Reviewer 2**

**Major revisions**

1. **Timeline:** It would be helpful to have a clearer timeline (revise Figure 2?) since different interventions were introduced at different times during the study period. This would help clarify the dates for study implementation and particularly in relation to the different rounds of data collection. For example, please make clear in this figure that the workshops were introduced 4-6 weeks after RDT training, and the different lengths of time each intervention was running prior to its evaluation.

   In response to this comment and that from reviewer 1 we have added a text box to the manuscript to define the timings for implementation of the intervention, outcome data collection periods and evaluation.

2. **Outcome:** More clarity needed in terms of outcomes.
   
   a. Please provide more precise definitions, including labels in figures/tables (e.g. eligible and ineligible RDT? rAM or AM?)

   Definitions to the components of the primary outcome, including non-malarial illness and recommended antimalarial are provided in the outcomes section of the manuscript and in the footnote to Table 3. Figure 3 illustrates the definitions for eligible and ineligible RDT but to clarify this we have added the definition into the labelling within this Figure too.

   b. Lack of clarity also stems from reporting many various indicators, and not just the most critical ones (e.g. Table 4). For example, does this paper need to present “quality of RDT reporting” indicators when it is not central to the discussion or their implications? Does Table 4 need to report all indicators listed or could you refine to only the most important?

   We feel that the reporting of the various indicators and the detailed tables are required to provide a comprehensive overview of what is a complex trial. In particular, RDT uptake and adherence to results are important components of effective case management of malaria and are therefore of interest to those within the research community and policy makers, and overuse of antibiotics is a serious issue currently generating a lot of debate.

   c. I am also not clear if you are consistently reporting the same outcome, e.g. ACT or any anti-malarial treatment (e.g. Table 4 is not clearly labeled and differs from Table 3 in this regard?).

   As outlined in the titles, Table 3 is reporting on recommended antimalarial treatment and Table 4 more generally on antimalarial and antibiotic prescribing. Table 3 reports on
recommended antimalarial treatment since this was the primary outcome. Table 4 reports on prescribing of recommended antimalarial treatment to RDT positives since this is in accordance with the treatment guidelines. For adherence to negative tests we have presented any antimalarial because we felt that if we narrowed it to recommended antimalarial we would be saying it is ‘appropriate’ to give another antimalarial to an RDT negative case.

d. I find Figure 3 hard to follow and it makes me wonder if the primary outcome should simply be inappropriate RDT use and adherence rather than inappropriate malaria treatment for non-malaria non-severe illness, which is a tricky outcome to define and leads to some of this confusion as captured in Figure 3. Does capturing the (small?) issue of AM treatment to non-fevers, UTIs that are not tested (or eligible/ineligible for testing?) muddy the outcome and take away from the central problem of use/adherence to RDTs to improve treatment of non-malaria illness, as defined by a RDT-negative result.

We agree with this comment although obviously it’s not possible to change outcomes at this stage.

3. Tables and Figures need to be streamlined and consolidated, and present only the most important information with clear labels and definitions. For example, could Table 1 and 2 be consolidated? In Additional Table 1, what is HWC – is that same as HWP? In Tables 3 and 4, how is prevalence defined? what is RDT eligible and ineligible? Are you reporting on recommended anti-malarial or any anti-malarial treatment, and if the latter, why? Need to reduce the number of indicators reported to only the few most important in this table as well as in other figures/tables. I also think Table 4 should show results for each evaluation period, and also stratified by age (under five or older patient), which would be quite informative. Finally there needs to be better harmonization between figures and numbers cited in text. This is now always consistently done (see paragraph starting “Table 3….”. In other instances, it is not clear how numbers cited in text are derived from the figure (e.g. Figure 3 and relevant text). Please clarify.

As mentioned above we feel that the detailed tables are required to provide a comprehensive overview of what is a complex trial, and also present the required data according to the CONSORT. Tables 1 and 2 provide the baseline characteristics of those contributing to the various levels of the clustering and can therefore need to be included. They could be combined into one large table and we are happy to do this if the editors wish us to do so. Table 3 reports on the primary outcome and Table 4 the secondary outcomes. Therefore we do not agree that these should be consolidated. In response to the specific comments:

• HWC in the additional Table 1 is a typo and we have corrected this to HWP.
• Prevalence in Tables 3 and 4 is your standard prevalence of the number of patients with the outcome of interested divided by the number of patients.
• Definition of RDT eligible and ineligible have been defined further – see earlier response.
• The titles of the tables and the outcomes within the tables clearly state whether we are reporting recommended antimalarial treatment or treatment with any antimalarial.
• Stratifying the outcomes in Table 4 by evaluation period and age would present us with issues around multiple testing and the increased risk of a Type I error and therefore do not feel comfortable doing this. In addition, some of the numbers with the outcome would be too small to present stratified results.
• We have checked the harmonization between figures and numbers cited in the text and feel this is now clear.

4. Facility selection and randomization: Why did 25 of 90 facilities refuse exclusive use of RDTs? It is also not clear why/how only 36 of 55 eligible facilities were selected and then randomized. Please clarify.

We did not collect information on why facilities refused exclusive use of RDTs. Only 36 facilities were required according to the sample size calculations. As outlined in the paragraph on selection of facilities, randomisation and blinding these 36 facilities were selected from the 55 eligible at random using a computer generated programme.

5. Malaria transmission: Need to be clear on differences in malaria transmission across study districts and over time during the study period, and to state clearly how this is handled in analysis and then its implications for study results. For example, in the methods section, how is low and moderate transmission specifically defined for the two districts and among facilities? How specifically did transmission differ over time as briefly mentioned in the methods section but not fully discussed elsewhere? It seems you stratified by malaria consultations but you do not state a threshold level for this stratification, nor if malaria consultations were defined by a clinical or confirmed at in the design/analysis. Finally, did data collection occur during peak or off-peak malaria transmission seasons – or was it a mix for different evaluation periods? How does all of this potentially affect results, particularly the result that the control arm with standard training also showed significant declines?

Data collection was across an entire year and therefore spanned the different malaria seasons within each of the different transmission areas. The evaluations of the intervention effects are thus capture the full range in seasonal variation in consultation and RDT positivity rates (as would be the conditions under routine implementation). No adjustment was therefore made for this in the analysis. The study was stratified by malaria transmission (i.e. by district) and the proportion of all consultations that were diagnosed with malaria in the previous year. We have clarified in the manuscript that the malaria consultations were
as reported by the health workers as part of the routine Health Management Information System (MTUHA book). As described in the last sentence of study design and participants no threshold level was used for the stratification but rather facilities were ranked, within district, according to the proportion of malaria consultations and split into two equal categories. We have reworded the text to make this clearer. We have also included a reference in the methods related to the local transmission intensity where readers may peruse the question of declining malaria transmission in the area. The actual parasite prevalence in febrile subjects (as measured through RDT positivity) is shown in the trial results and is our best estimate of transmission at the time of the trial.

6. Discussion - Need to more fully discuss the following important issues:
   a. The limited nature of the patient intervention (e.g. targeting only patients already presenting at facilities and not community sensitization; implementation challenges – did all patients actually receive the leaflet? Were all patients able to read the leaflet?). Could alternative methods to improve community sensitization to diagnosis and treatment have improved results in the HWP arm?
   b. Malaria transmission intensity – This is mentioned in the methods section but not in the discussion about its implications for results. Could declining malaria transmission affect these results, and if so, how? Are there contextual factors or other programs operating in these districts that could raise awareness about malaria case management and then also affect results? Reductions in inappropriate treatment in the control arm with standard training require further thought and explanation, possibly due in part to other factors?
   c. The standard training (control arm) had quite significant reductions without any additional provider or patient oriented interventions, and I think this needs more thought and discussion. Why do you think this occurred? What are program implications of these results? Specifically, when should a program consider doing only the standard training (which also led to significant declines) and when should a program consider implementing additional interventions for the provider alone or for both provider and patient? What other types of interventions should be further researched, e.g. community sensitization?

We agree with the thrust of these comments and have added some additional points to the discussion. We are a bit cautious about speculating at length on interventions we did not undertake- clearly there are multiple ones which in theory we could have undertaken, but this did follow formative work backed up by many years working in this area of Tanzania. On reductions in incidence- we think these are likely to lead over time to better targeting and indeed some of the improvement in all arms may have been due to this. We agree community sensitization is an additional intervention- but would point out that compared to only a few years ago the targeting seen in this trial is massively better than that seen
previously. To get further significant improvement will be difficult (and would need a massive trial to test its effect).

7. Footnotes: All factual statements need footnotes, which is not consistently done (e.g. first sentence and last sentence in second para of background section; “…despite large number of training interventions…” in background section; footnote evidence for important correlates to primary outcome in methods section; etc.etc

We respectfully disagree with the referee. We do not want to over-reference this on obvious points as this unnecessarily lengthens the paper (and patronises the expert reader). We think key factual statements, or ones which are not known widely are the ones to concentrate on for footnoting.

Minor essential revisions

8. Title: - Is the outcome to improve RDT use or to reduce inappropriate malaria treatment? Your primary seems to be outcome the latter – so does not necessarily support the title phrasing as it appears now.

The primary outcome is about treatment of non-malarial fevers when prescribers are supported with RDTs. We disagree that it is solely about inappropriate malaria treatment as this could also relate to malaria positive patients receiving a non-recommended antimalarial. The points about antibiotics are also important and topical. We would therefore prefer to keep the title as it stands.

• Abstract:

9. Need for high quality evidence to improve prescribers’ practices is certainly more to do with mixed program success in terms of RDT adherence rather than simply increased RDT investments (if increased investments was met with strong programs there would be no need for this study, correct?)

We agree with the reviewer and recognise that there is also a need to improve adherence to RDTs for such programs to be successful. We have now clarified this in the abstract.

10. Clarify outcomes – is it any anti-malarial or first line treatment? See other comments on outcomes.

As defined in the outcomes section the primary outcome is the incorrect prescribing of a (recommended) antimalarial. We have included the term ‘recommended’ in the abstract. See also earlier responses.

• Background:
11. Second paragraph “…due to persistent preference” – this is too simplistic since RDT non-adherence is result of complex patient-provider interactions and other factors e.g. RDT mistrust. Rephrase.

We have rephrased this.

12. Third paragraph first sentence “increasing investments in RDT…” as reason for this study, but isn’t the primary reason actually mixed program results to date – see abstract comment on same point.

See points above.

13. Third paragraph – how was design of intervention based on mixed-methods research – what did this research show and how did it influence the design of this study. Please elaborate. This is also brought up in the discussion section as a unique strength of the trial but it is not well discussed there.

See response to reviewer 1. We have now included further details on this in the background.

• Methods:

14. Patient intervention is only among patients already coming to health facilities and not a community intervention to target ‘potential patients’. Is this correct? Need to be clearer in the methods and discussion about the limited nature of the patient intervention, and how this could affect results.

See earlier comment on this re: the discussion.

15. Figure 2 - Please clarify why there is only data collection in 9 HW-arm facilities during Period 1? Why were there fewer patients in Period 1 and 4 data collection rounds? How does this affect analysis?

The difference in the patient numbers (and health facilities) in the different periods of data collection reflects the natural variation in the duration of the period of data collection and the number of patients visiting the facilities during these periods. We did not power the study to formally assess the intervention effects within each period. Rather we have presented these results to provide a greater insight into the primary outcome.

16. Characteristics of study population – give figures in this first paragraph. Higher proportion of poorest patients found in HWP-arm. How would this affect results?

In the interests of conciseness we have chosen not to present figures associated with characteristics of the study population in the text since these can all be viewed in the Tables.
17. HWP-arm – was there any check that these posters and leaflets were consistently displayed or given out to patients at facilities throughout intervention period, if so, how? What about illiterate caregivers that may not read posters or leaflets, and higher proportion of poorest caregivers in HWP arm is problematic for this reason, correct? Where were posters displayed? When and by who gave out leaflets to patients? How was this intervention actually done? Please clarify, and also more fully describe the limited nature of this patient-oriented intervention in the discussion as compared to the provider intervention.

We did not collect any evaluation data on this aspect of the intervention.

- Discussion and Conclusion

18. “Formalizing such a process requires....” I think it is more complicated than discussed. Consider revising.

We are referring here to the process of change we were attempting to initiate and consolidate through communities of practice in the peer group meetings. We have amended the sentence in the discussion to clarify this.

19. Conclusion says the study demonstrates “that a combination of provider and patient behavioral interventions...” is not necessarily correct since this study did not demonstrate real added benefit of the patient oriented intervention. Moreover, the control arm also showed quite significant declines that has program implications as well and should be raised more fully in the discussion and conclusion.

We think the statement we made is accurate based on the data presented.

Discretionary revisions

- Abstract:

20. Second sentence – ‘both outcomes’ please clarify, not clear what this means

We think the reviewer is referring to ‘both interventions’. We have chosen not to change this since we feel as though it is clarified by presenting the results from each intervention arm with the control further on in this sentence.

- Background:

21. You state RDT is affordable and accurate, but isn’t a main reason is that RDT in fact allows for diagnosis in remote, rural facilities where it was not previously possible.

RDTs have many other advantages, as laid out in the introduction and discussion.

22. Footnote 19 duplicates previous reference, is this correct?
We have checked and cannot identify any duplicate references (but appreciate the referee checking).

**Methods:**

23. “Training materials were delivered as planned and well-received” This is not specific and I would think assumed to be the case unless otherwise stated. Consider deleting this sentence.

We have considered this but on balance decided to keep this in as an insight into the fidelity of the intervention.

**Reviewer 3**

**Major Compulsory Revisions**

1. **Figure 2 vs. Table 1** - The actual numbers of $N_{hw} = 35$ in Table 1 did not match those in Figure 2 (HWs: 34 to 35) – why? Am I missing something?

We acknowledge the differences in the number of prescribers between Table 1 and Figure 2. Table 1 provides the profile of all prescribers who consented to participate in the study. This includes prescribers new to the facilities during the study period (as outlined in the footnote). Figure 2 shows the number of prescribers who received the initial training as it was held. A total of 35 prescribers in the control arm were included in the study but 1 prescriber joined the study after the initial RDT training period and therefore is not included in the number receiving this training in Figure 2. They did still receive the training, just at a later date. The number of prescribers in the HWP arm in Figure 2 is an error and we have amended this in the revised version.

We did have a version of the flow chart indicating the movement of prescribers in and out of the study but we removed this information as we felt it made the figure too busy. We can include this information if the editors feel that it would aid readers with the understanding.

2. **Figure 2** - The number “all eligible patients” at the bottom (end of trial) in Figure 2 were reported as “15,931”; but should it be the sum of patient numbers cumulatively from evaluation period 1 to 4 ($702 + 6,630 + 3,973 + 2,269 = 13,574$)? – Please explain or double check the numbers. Similar puzzle for control arm: 14, 217(reported) vs. 9050 (the actual sum).

The numbers of patients listed in the total data collection box at the bottom of Figure 2 are the total number of patients who presented at the study facilities during period i.e. from the end of the standard RDT training until the final exit survey was conducted. The numbers are not simply the sum of the numbers in the different outcome evaluation periods because we did not include in the evaluation periods the patients presenting during the intervention implementation activities. We did this to be able to estimate the (incremental) effect of
each additional intervention activity, after it had been fully implemented. We have added extra information in the footnote to clarify this.

Minor Essential Revisions:

3. Abstract - To be more informative, please add study period (e.g. 2007 – 2009 in Table 1 or 2011-2012 in Results, 1st paragraph?) and intervention follow-up time frame (“6-weekly supervisory visits”?)

We have added in the information study period as requested. We do not feel that it is necessary to add information about the 6-weekly supervisory visits as these took place across all study arms and therefore not a distinguishing component of the intervention. Further detail on this would take us over the word limit for the abstract and we do not feel that any current detail can be removed to keep within the word limit without making the abstract less informative in other respects.

The period 2007-2009 referred to in the footnote of Table 1 is pre-study information that was available on proportion of consultations diagnosed with malaria to provide the reader with information on patients presenting and prescribing practices prior to the intervention. The period 2011-12 referred to in the 1st paragraph of the results is the period of patient recruitment. As outlined in Table 2, randomisation, baseline data collection and mRDT training.

4. Statistical Methods - Any multiple comparison issues for this 3 arms stratified cluster randomized trials?

We recognise that we have used the control arm data twice in the analysis (to compare each intervention with the control), and therefore this raises the multiplicity question. However, we do not feel that a multiplicity adjustment is required for this study since i) we powered the study to be able to detect an intervention effect for comparing each intervention arm separately with the control; and ii) we did not perform an interim analysis.

5. Statistical Methods - Please specify what alpha level is regards as statistical significant and which statistical software to conduct the analysis.

The first paragraph of the statistical methods specifies that STATA version 12.0 was used to conduct the analysis. We have now included that formal hypothesis testing was assessed at the 5% significance level.

6. In terms of the trade-off between sensitivity and specificity of the RDT diagnostic test, are both properties improved after the intervention?

RDTs were only evaluated during the study period, with the sensitivity/specificity as reported in the manuscript. There were no RDTs in the study facilities prior to the intervention and since the intervention RDTs have been introduced into the facilities but we have no data to be able to evaluate sensitivity and specificity.
Discretionary Revisions

7. Figure Numbers only mentioned in the overall Figure Legends page; but Figure Number was absence in each actual figure page. It is not convenient for reading and the issues may also be easy to have errors or mis-matches.

We apologise for this inconvenience but we were following the instruction for authors for the submission of figures for publication which stated that figure titles and legends should be provided in the main manuscript and not in the graphic file. We will ensure that we correctly adhere to the guidelines when we resubmit.

Yours sincerely

Bonnie Cundill
For the authors