

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

## ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Adding proactive and reactive case detection into the integrated community case management system (iCCM+) to optimise diagnosis and treatment of malaria in a high transmission setting of Cameroon: an observational quality improvement study
<b>AUTHORS</b>	Bekolo, Cavin; Williams, Thomas

## VERSION 1 – REVIEW

<b>REVIEWER</b>	Kelly M. Searle University of Minnesota School of Public Health, Epidemiology and Community Health
<b>REVIEW RETURNED</b>	16-Oct-2018

<b>GENERAL COMMENTS</b>	<p>Manuscript ID: bmjopen-2018-026678</p> <p>Proactive and reactive case detection to optimise integrated community case management of malaria in a high transmission setting in Cameroon</p> <p>The authors present the findings of a case report on a pilot study implementing active case detection for malaria infections into the existing integrated community case management system in Bare-Bakem, Cameroon. The analysis showed positive findings that adding in active case detection can lead to increased diagnosis and treatment of infected individuals in this area. From these results, the authors then recommend that this be implemented through national malaria control programme. One of the major limitations of this study is the premise of the intervention itself. Proactive and reactive case detection is not recommended in high, or even moderate transmission settings. Currently, it is primarily recommended in low transmission settings and areas approaching elimination, as it is designed as an elimination strategy to interrupt transmission. The authors do address this as the objective of implementing it in this setting is not as an eliminate malaria, or impact transmission, but to identify additional cases as part of case management. However, they mention the already existing challenges to the existing integrated case management system and the lack of education, health-care seeking, and access to health facilities in the area. In light of these, it is obvious that active case detection would increase the number of cases identified. But in this area this is likely to be an incredibly intensive intervention with mounting logistic and operational challenges that limit its sustainability. It would be much more suitable to make improvements to the existing iCCM program to improve education, prevention, and access to community health workers. This is made clear as all of the 'index' cases identified were simply febrile</p>
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	<p>children that should be regularly tested and treated in these areas by a community health worker. A more reasonable approach is to improve this program to increase care seeking behaviours for cases of fever in the community and even the schools as well. Expanding on that program before it is well established and functioning can lead to failures. The authors themselves even note in the discussion that the infrastructure is currently not in place for this to sustain on its own. It seems as though a better course of action in this area is to focus on the action of getting febrile children (and adults) to seek care through community health workers and build infrastructure around that as the main aspect of iCCM.</p> <p>Additional comments:</p> <p><b>Abstract</b>          The abstract presents the primary and secondary outcome measures read as if this is an RCT comparing standard of care to an intervention.</p> <p>The conclusion indicates that all or nearly all undiagnosed infections could be mopped-up or identified with this approach, which is not true.</p> <p>Throughout the abstract and manuscript the authors' language is a little unclear, particularly with the use of 'case' and 'index case'. In this manuscript the authors seem to be referring to a case of suspected fever (or confirmed fever), this is unclear. Then index cases are those with suspected fever who are then diagnosed with malaria via RDT. This can be confusing in the text. Typically cases only refer to cases of malaria, not suspected fever. Index cases then only refer to those confirmed cases that trigger a reactive event. This should be cleared up in the text.</p> <p><b>Introduction</b>          Page 3, Line 13 – The authors refer to malaria mortality and present percentages. Please clarify the specific measurement. It looks like a case fatality ratio, but isn't specified.          Page 3, Line 20 – All case morbidity should be all-cause morbidity.          Page 3, Lines 40-45 – The authors lay out significant challenges facing the current iCCM, which are numerous. These include stockouts of diagnostics and treatment and inadequate supervision. The response to these being proposed is to expand the current program to include expanded activities that require more oversight and increase the need for diagnostics which is a large operational challenge. The current situation laid out doesn't provide much justification for a program scale-up, but a focus on creating an infrastructure for the current iCCM to provide community level education, outreach, and increase health-care seeking behavior to screen febrile individuals for malaria.          Page 4, Line 3-4 – Integrating active case detection with iCCM has not been documented in a high transmission setting, because it is not recommended as it is and elimination strategy and iCCM should be screening suspected malaria cases as part of their established program.          Here and throughout the manuscript <i>Plasmodium</i> should be italicized.</p> <p><b>Methods</b></p>
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	<p>Page 4, Lines 24-28 – The wording here is a little confusing for laying out the environmental features that foster high levels of malaria transmission.</p> <p>Page 4, Lines 50-53 – The last sentence reads as if prompt and expanded access to malaria treatment is in contrast to a focus on malaria prevention and education. Typically, all of these aspects are contained within an iCCM program.</p> <p>Intervention description and evaluation</p> <p>Page 5 – The authors introduce CHWs to refer to community health workers in the introduction, then shift to the French terminology of ASC then use them interchangeably moving forward. It would be easier to follow if one was chosen and used consistently throughout the manuscript.</p> <p>Page 5, Line 28 – The use of ‘effectiveness’ here isn’t entirely accurate and this doesn’t appear to have been measured in this study. Something more like ‘accuracy’ or ‘completeness’.</p> <p>Page 5 – The overview of steps taken here could be improved. Perhaps a diagram or flow-chart describing how febrile cases were identified and where and how reactive events were triggered. The terminology of an index case should also be addressed. It reads as if all febrile children were index cases before any malaria screening. Typically, in reactive case detection, index cases are confirmed malaria cases, not febrile, suspected cases.</p> <p>Page 6, Line 15 – Gender is listed as a variable collected, where it is more likely sex is what was collected.</p> <p>Page 6, last sentence – Was only statistical significance considered for the final model, or were other important factors considered to be included apriori from a conceptual framework based on previous publications and hypotheses?</p> <p><b>Results</b></p> <p>Detection and management of febrile cases</p> <p>Throughout this section, it is difficult to discern the difference between an index case and a febrile case. This should be clarified.</p> <p>Page 9, Line 10-12 – The authors indicate a lag phase during the first half of the project to lower numbers of cases identified and an increase after establishing the project. Is there a likelihood that there was an increase in cases over this time due to seasonality of transmission in this area?</p> <p><b>Discussion</b></p> <p>Page 10, Line 41 – The authors don’t lay explain how the 67.5% was calculated and what specifically it is in reference to. As there wasn’t a comparison it’s not accurate to conclude that adding in proactive and reactive case detection improved iCCM by 67.5% without a comparison group.</p> <p>Page 11, Lines 3-12 – The authors describe the CHWs not needing additional resources to perform this intervention, but note in the introduction that they typically have frequent and prolonged stock-outs of diagnostics and treatment. It has been published that reactive case detection is operationally challenging due to having to maintain a high level of RDTs in a continuous supply chain for passive case detection of febrile individuals and reactive screening in addition.</p> <p>Page 12, Lines 29-35 – The authors indicate that older school age children were not included in the school-based screening, but would have been identified at the community level. This statement may not be completely accurate because older school age</p>
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	children are typically asymptomatic and afebrile in endemic areas when they are infected and represent an asymptomatic reservoir for transmission. This age group is typically targeted in proactive case detection in low-transmission and pre-elimination settings.
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<b>REVIEWER</b>	Roly Gosling University of California San Francisco, Namibia
<b>REVIEW RETURNED</b>	02-Nov-2018

<b>GENERAL COMMENTS</b>	<p>Review of BMJ Open Bekolo and Williams</p> <p>Thank you for giving me the opportunity to review this paper. I think that the reporting of this kind of program activity is good. I think that if the authors really worked hard to describe what they did, what they wanted to measure, what they did measure, and wrote up with clarity what they found – it would be worthwhile publishing.</p> <p>However, at the moment, I could not replicate what the authors have done, because I cant easily understand what they did and what they found. I am unclear if the outcome they are saying is very important is important. Just finding more cases may not help the community but be resource intensive. Also, how do we know that doing this method is any better than doing another method of screening more people – presumably the more people you screen the more people you find, especially in an area of high prevalence of infection.</p> <p>I recommend rejection of this manuscript but would allow the authors a go at redrafting as the malaria field does need to think about how to make ICCM more effective. I would recommend the authors looking at other reports of quality improvement to understand how to draft it.</p> <p>Specific comments:</p> <ol style="list-style-type: none"> <li>1. Title should tell us what you did this is an Observational study...</li> <li>2. Abstract – Design: We want the epidemiological trial design here not a loose description</li> <li>3. Abstract – Primary and secondary endpoint measures: What is the numerator and what is the denominator .... I can t tell.</li> <li>4. Abstract – results: I don't understand what is being presented. It can t see the primary end point in each arm nor a comparison between arms</li> <li>5. Abstract conclusions: Conclusions don't seem to be based on the results</li> <li>6. Strengths and weaknesses of the study: What does “clinical relevance mean”?</li> <li>7. Strengths and weaknesses of the study Line 54: should be “targeted”</li> <li>8. Strengths and weaknesses of the study: Page 3 line 3 – there are many more weaknesses that need to be noted!</li> <li>9. Page 3 lines 11 and 12 – what do the percentages mean? What is the numerator and what is the denominator? Are these of all illnesses? Are these all deaths? Maybe give numbers of reported cases and deaths in the two date periods and tell us the reduction as a %.</li> <li>10. Page 3 lines 34-37 – English needs correcting</li> <li>11. Page 3 line42: what does passiveness in operation mean</li> <li>12. Page 4 line 6 – “a” CHW? Or a number of CHW”s”?</li> </ol>
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	<p>13. Page 4 lines 33 and 34: what age of patients are you talking about – 40% in under 5s or total age group</p> <p>14. Page 4 Lines 51 -53: Need editing</p> <p>15. Page 5 Lines 34- 37: What proportion of children attending school are under 5 year old. In many settings this would be very few in number. Seems more worthwhile to spread the testing to older kids.... This is probably for the discussion.</p> <p>16. Page 5 line 39 : do you mean :”freely” as at “no cost” or “willingly”... please correct to what you mean by “freely”</p> <p>17. Page 5 Line 48 – 51: What proportion of cases did you miss? I can only imagine that relatively few under 5 year old attend school.</p> <p>18. Page 6 lines 3-9: We need to know more details! Remember with the methods sections you are writing it so I can repeat your experiment. What exactly did you do? Did you go to the household, make a list of everyone who lives there, and then attempt to screen everyone (adult, child, person calling in for coffee.... Who did you include and who did you exclude), Did you only test fevers or people feeling unwell or did you test everyone.</p> <p>19. Page 7 Lines 7 -10: this is another type of intervention and should be fully described. How did you select these areas -was there any bias? Did you select them because of the CHWs who worked there? How did you do your door-to- door, what happened if someone wasn't in, did you take a list of all people resident nad note the people who were not in to understand your bias?</p> <p>20. Page 7 lines 12-15. Again a full description of how community participation was driven. Remember again that if we like your results we will want to do what you did. By not including what you did means that we might try and fail. So you really want us to understand what you did.</p> <p>21. Page 7 Line 19: Consent was sought? I don't see a consenting process written into the methods. There was a letter that went out to the parents.. was that it?</p> <p>22. Methods section – there is no clear section describing what you were or are looking for- ie what do you intend to measure, and how you define those measures.</p> <p>23. Page 7 lines 30-34 Results section: Very difficult to understand your percentages, perhaps write the numerator over the denominator so we can see what are proportions of what.</p> <p>24. Page 7 Line 37 “likely to be boys”? What does that mean?</p> <p>25. Page 7 Lines 41 and 42. Shouldn't all index cases have a positive RDT? I think that this is where a strong methods section would help. If you defined what an index case was you may not run into these challenges in the results.</p> <p>26. Page 7 results section could do with a flow diagram that would clearly show index cases recruited from school, index cases recruited from houses, numbers in each screened with an RDT, those positive, those uncomplicated, those complicated.</p> <p>27. Table 1: Why are the index numbers similar to the RACD arm... You should include the total number screened at the top not just the positive cases.</p> <p>28. Page 9 lines 1-12: In your methods you should have a comment about seasonality. Does Figure 1 just reflect seasonal variation. You could plot rainfall on Figure 1, or health facility malaria cases..</p> <p>29. Page 9 Paragraph starting line 15 – starts with LLIN ownership and then goes into describing index cases. These should be separate paragraphs – its confusing for the reader. These latter descriptions should be in the first paragraph of the results with the suggested flow diagram.</p>
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	<p>30. Page 9 Lines 25 – 28: Your statement assumes that finding cases is good, perhaps those cases would ve appeared later at the health facility, or self-resolved and so ACD was not needed. Just be careful of making a subjective statement when you are not actually measuring the outcome.</p> <p>31. Lines 28 -43 an increase of 125% compared to what? Could this just be a seasonal increase? Nothing to do with the ACD? You were doing your activity when cases where high?</p> <p>32. Page 9 lines 48- 54: females are more often found at home – this is an accepted bias of doing home visits. Did you collect information on who you were not screening, who was not at home when you went? What are the cultural habits of the population? Do people tend to send male children to school rather than girls..?</p> <p>33. Limitations do not include that there is no control arm, apriori assumptions are not stated – ie what we are going to measure, what we are looking for etc</p> <p>34. Conclusion is actually ok, although this study doesn't prove anything as it has not design to assess causality. My question to the authors is if they just did occasional screen and treat cross sectional surveys – would that have achieved the same output? If random households had been chosen instead of following index cases- would that have worked? There is no attempt to see if this actually any better from anything else, the authors are assuming it.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Kelly M. Searle

The authors present the findings of a case report on a pilot study implementing active case detection for malaria infections into the existing integrated community case management system in Bare-Bakem, Cameroon. The analysis showed positive findings that adding in active case detection can lead to increased diagnosis and treatment of infected individuals in this area. From these results, the authors then recommend that this be implemented through national malaria control programme. One of the major limitations of this study is the premise of the intervention itself. Proactive and reactive case detection is not recommended in high, or even moderate transmission settings. Currently, it is primarily recommended in low transmission settings and areas approaching elimination, as it is designed as an elimination strategy to interrupt transmission. The authors do address this as the objective of implementing it in this setting is not as an eliminate malaria, or impact transmission, but to identify additional cases as part of case management. However, they mention the already existing challenges to the existing integrated case management system and the lack of education, health-care seeking, and access to health facilities in the area. In light of these, it is obvious that active case detection would increase the number of cases identified. But in this area this is likely to be an incredibly intensive intervention with mounting logistic and operational challenges that limit its sustainability. It would be much more suitable to make improvements to the existing iCCM program to improve education, prevention, and access to community health workers. This is made clear as all of the 'index' cases identified were simply febrile children that should be regularly tested and treated in these areas by a community health worker. A more reasonable approach is to improve this program to increase care seeking behaviours for cases of fever in the community and even the schools as well. Expanding on that program before it is well established and functioning can lead to failures. The authors themselves even note in the discussion that the infrastructure is currently not in place for this to sustain on its own. It seems as though a better course of action in this area is to focus on the action

of getting febrile children (and adults) to seek care through community health workers and build infrastructure around that as the main aspect of iCCM.

We totally agree with the reviewer's concerns because we also raised those challenges too in the introduction and discussion. While the process is labour intensive, CHWs were happy with the once-a-week activity to canvas their respective intervention neighbourhoods. Health education and prevention are integral parts of iCCM and of the NMCP control measures which are beyond the scope of this work. We focused our attention on how iCCM could be improved to diagnose and treat more cases given the specific challenges of this rural community which has very limited access to healthcare facility.

Additional comments:

#### Abstract

The abstract presents the primary and secondary outcome measures read as if this is an RCT comparing standard of care to an intervention.

The design is a cross sectional survey that compares the modified iCCM (which we now call iCCM+) to the existing one but taking into account the inherent bias of observational studies. We intend to design it as an RCT in future to improve the strength of our recommendations

The conclusion indicates that all or nearly all undiagnosed infections could be mopped-up or identified with this approach, which is not true.

The sentence now uses 'most of these cases' rather than 'these...' in relative terms (line 49)

Throughout the abstract and manuscript the authors' language is a little unclear, particularly with the use of 'case' and 'index case'. In this manuscript the authors seem to be referring to a case of suspected fever (or confirmed fever), this is unclear. Then index cases are those with suspected fever who are then diagnosed with malaria via RDT. This can be confusing in the text. Typically cases only refer to cases of malaria, not suspected fever. Index cases then only refer to those confirmed cases that trigger a reactive event. This should be cleared up in the text.

We have revised the definition of cases (index and secondary) to mean a case of confirmed malaria throughout the manuscript

#### Introduction

Page 3, Line 13 – The authors refer to malaria mortality and present percentages. Please clarify the specific measurement. It looks like a case fatality ratio, but isn't specified.

It's a proportional mortality and has now been specified as such in line 66

Page 3, Line 20 – All case morbidity should be all-cause morbidity.

The sentence now reads ... all-cause morbidity in line 71

Page 3, Lines 40-45 – The authors lay out significant challenges facing the current iCCM, which are numerous. These include stockouts of diagnostics and treatment and inadequate supervision. The response to these being proposed is to expand the current program to include expanded activities that require more oversight and increase the need for diagnostics which is a large operational challenge. The current situation laid out doesn't provide much justification for a program scale-up, but a focus on creating an infrastructure for the current iCCM to provide community level education, outreach, and increase health-care seeking behavior to screen febrile individuals for malaria.

We are equally making efforts with support from the malaria control programme and partners to address these challenges at all levels. Yet, we have identified a crucial issue of access to malaria care and have just made an attempt to resolve it to some extent through action research

Page 4, Line 3-4 – Integrating active case detection with iCCM has not been documented in a high transmission setting, because it is not recommended as it is and elimination strategy and iCCM should be screening suspected malaria cases as part of their established program.

We thought it was intuitive to buy the principle of ACD in order to bring services to otherwise "forgotten" cases and we were not disappointed with are results obtained so far

Here and throughout the manuscript *Plasmodium* should be italicized.

*Plasmodium* has been written in italics as advised

## Methods

Page 4, Lines 24-28 – The wording here is a little confusing for laying out the environmental features that foster high levels of malaria transmission.

The sentence now reads: “The locality’s low elevation and its warm and wet equatorial climate are conducive for high levels of malaria transmission”

Page 4, Lines 50-53 – The last sentence reads as if prompt and expanded access to malaria treatment is in contrast to a focus on malaria prevention and education. Typically, all of these aspects are contained within an iCCM program.

We do agree, we were laying emphasis on the priority aspect of particular interest to us

Intervention description and evaluation

Page 5 – The authors introduce CHWs to refer to community health workers in the introduction, then shift to the French terminology of ASC then use them interchangeably moving forward. It would be easier to follow if one was chosen and used consistently throughout the manuscript.

CHW has been chosen and is used consistently

Page 5, Line 28 – The use of ‘effectiveness’ here isn’t entirely accurate and this doesn’t appear to have been measured in this study. Something more like ‘accuracy’ or ‘completeness’.

... ‘effectiveness’ has been replaced by ‘completeness’ in line 145

Page 5 – The overview of steps taken here could be improved. Perhaps a diagram or flow-chart describing how febrile cases were identified and where and how reactive events were triggered. The terminology of an index case should also be addressed. It reads as if all febrile children were index cases before any malaria screening. Typically, in reactive case detection, index cases are confirmed malaria cases, not febrile, suspected cases.

A flow-chart has been added and the definition of index and secondary cases clearly mentioned in Figures 1 and 3

Page 6, Line 15 – Gender is listed as a variable collected, where it is more likely sex is what was collected.

‘Gender’ has been replaced by ‘sex’

Page 6, last sentence – Was only statistical significance considered for the final model, or were other important factors considered to be included a priori from a conceptual framework based on previous publications and hypotheses?

Sex, age, use of LLIN and household size were factors considered for the multivariate model with clustering around CHW

## Results

Detection and management of febrile cases

Throughout this section, it is difficult to discern the difference between an index case and a febrile case. This should be clarified.

Clarification has been done where a case refers to only a confirmed case of malaria

Page 9, Line 10-12 – The authors indicate a lag phase during the first half of the project to lower numbers of cases identified and an increase after establishing the project. Is there a likelihood that there was an increase in cases over this time due to seasonality of transmission in this area?

The effect of seasonality is likely but the study was carried out during the high transmission season only

## Discussion

Page 10, Line 41 – The authors don’t lay explain how the 67.5% was calculated and what specifically it is in reference to. As there wasn’t a comparison it’s not accurate to conclude that adding in proactive and reactive case detection improved iCCM by 67.5% without a comparison group.

67.5% is the proportion of all cases identified by adding PACD and RACD in iCCM compared to the 24% identified by iCCM alone and the 8.5% seeking care in health facilities



Page 11, Lines 3-12 – The authors describe the CHWs not needing additional resources to perform this intervention, but note in the introduction that they typically have frequent and prolonged stock-outs of diagnostics and treatment. It has been published that reactive case detection is operationally challenging due to having to maintain a high level of RDTs in a continuous supply chain for passive case detection of febrile individuals and reactive screening in addition.

We want to bring out the point that, as per iCCM guidelines, CHW do not need additional extra resources to implement iCCM+ but we have acknowledged the challenges the malaria programme needs to overcome to ensure a smooth delivery of RDTs. In fact, RDT stockouts are always artificial stockouts because the CHW are unable to procure them directly from the provincial level and depend on health facilities. In this study, the supply of RDTs was independent of health facilities.

Page 12, Lines 29-35 – The authors indicate that older school age children were not included in the school-based screening, but would have been identified at the community level. This statement may not be completely accurate because older school age children are typically asymptomatic and afebrile in endemic areas when they are infected and represent an asymptomatic reservoir for transmission. This age group is typically targeted in proactive case detection in low-transmission and pre-elimination settings.

In Cameroon, the current practice is that asymptomatic cases are not targets for treatment or we might have to treat entire communities or schools. We had to respect these instructions from the NMCP who provided the RDTs for this work

Reviewer: 2

Reviewer Name: Roly Gosling

Thank you for giving me the opportunity to review this paper. I think that the reporting of this kind of program activity is good. I think that if the authors really worked hard to describe what they did, what they wanted to measure, what they did measure, and wrote up with clarity what they found – it would be worthwhile publishing.

However, at the moment, I could not replicate what the authors have done, because I can't easily understand what they did and what they found. I am unclear if the outcome they are saying is very important is important. Just finding more cases may not help the community but be resource intensive. Also, how do we know that doing this method is any better than doing another method of screening more people – presumably the more people you screen the more people you find, especially in an area of high prevalence of infection.

I recommend rejection of this manuscript but would allow the authors a go at redrafting as the malaria field does need to think about how to make ICCM more effective. I would recommend the authors looking at other reports of quality improvement to understand how to draft it.

We have now included a flow chart to illustrate the idea of the project for better understanding of what we did.

Finding and treating more cases who otherwise must have had no treatment at all because of existing barriers to malaria care is very important to us, to this community following an initial community needs assessment

We agree and have recognised in the introduction that iCCM is an important intervention to fight child mortality but we have found that the programme as implemented was underperforming in this community and thus needed measures to make it more efficient.

Specific comments:

1. Title should tell us what you did this is an Observational study...

The title now reads "Adding proactive and reactive case detection into the integrated community case management system (iCCM+) to optimise diagnosis and treatment of malaria in a high transmission setting of Cameroon"

2. Abstract – Design: We want the epidemiological trial design here not a loose description

The design now reads “A community-led cross-sectional survey to measure the proportion of Plasmodium infection diagnosed and treated under iCCM+ compared with iCCM alone”

3. Abstract – Primary and secondary endpoint measures: What is the numerator and what is the denominator .... I can't tell.

The proportion of cases was defined as number of confirmed malaria infected individuals as numerator and the number screened by RDT

4. Abstract – results: I don't understand what is being presented. It can't see the primary endpoint in each arm nor a comparison between arms

We have presented the cases in numbers and proportions found by implementing iCCM alone compared (using the difference) to cases found by implementing iCCM+

5. Abstract conclusions: Conclusions don't seem to be based on the results  
Conclusions have been derived from the relative contributions of each strategy to the detection of malaria cases

6. Strengths and weaknesses of the study: What does “clinical relevance mean”?  
... 'relevance' has been replaced by 'importance'

7. Strengths and weaknesses of the study Line 54: should be “targeted”  
... 'targeted' has replaced 'target'

8. Strengths and weaknesses of the study: Page 3 line 3 – there are many more weaknesses that need to be noted!

These has been included in the limitation section of the manuscript as the journal requires just a few pertinent ones in this section

9. Page 3 lines 11 and 12 – what do the percentages mean? What is the numerator and what is the denominator? Are these of all illnesses? Are these all deaths? Maybe give numbers of reported cases and deaths in the two date periods and tell us the reduction as a %.

We were presenting proportional mortality and morbidity attributed to malaria

10. Page 3 lines 34-37 – English needs correcting  
'All-case mortality' replaced by 'all-cause mortality'...

11. Page 3 line 42: what does passiveness in operation mean

We meant operating passively rather than actively in case detection as it reads now in line 84

12. Page 4 line 6 – “a” CHW? Or a number of CHW“s”?  
CHWs

13. Page 4 lines 33 and 34: what age of patients are you talking about – 40% in under 5s or total age group

Overall U-5 mortality

14. Page 4 Lines 51 -53: Need editing

15. Page 5 Lines 34- 37: What proportion of children attending school are under 5 year old. In many settings this would be very few in number. Seems more worthwhile to spread the testing to older kids.... This is probably for the discussion.

Agreed but his older group has more of asymptomatic infections which we were targeting but were picked up the community in case of sickness

16. Page 5 line 39 : do you mean :“freely” as at “no cost” or “willingly”... please correct to what you mean by “freely”

At no cost as mentioned now in line 151

17. Page 5 Line 48 – 51: What proportion of cases did you miss? I can only imagine that relatively few under 5 year old attend school.

This was not determined as missed cases were followed to their homes

18. Page 6 lines 3-9: We need to know more details! Remember with the methods sections you are writing it so I can repeat your experiment. What exactly did you do? Did you go to the household, make a list of everyone who lives there, and then attempt to screen everyone (adult, child, person calling in for coffee.... Who did you include and who did you exclude), Did you only test fevers or people feeling unwell or did you test everyone.

A flow diagram has been added to clarify the procedure. A list of every household member was made and we tested only fevers in the previous week

19. Page 7 Lines 7 -10: this is another type of intervention and should be fully described. How did you select these areas -was there any bias? Did you select them because of the CHWs who worked there? How did you do your door-to- door, what happened if someone wasn't in, did you take a list of all people resident nad note the people who were not in to understand your bias?

Every CHW has a catchment area where he/she lives. The door-to-door intervention was an M&E activity to verify if CHW were actually visiting households and how many cases were missed by them. We have now deleted this activity in the manuscript to avoid confusion

20. Page 7 lines 12-15. Again a full description of how community participation was driven. Remember again that if we like your results we will want to do what you did. By not including what you did means that we might try and fail. So you really want us to understand what you did.

This section as per the journal requires the authors to mention if any, there was community participation and not much detail. However, the whole of this project was run by the community with support from health authorities and partners

21. Page 7 Line 19: Consent was sought? I don't see a consenting process written into the methods. There was a letter that went out to the parents.. was that it?

An information letter was sent to parents and local administrations, and was announced in community meeting or worshipping places as mentioned in lines 138 and 203-5

22. Methods section – there is no clear section describing what you were or are looking for- ie what do you intend to measure, and how you define those measures.

The intervention description section has been modified to include a flow-chart to describe what was done and what we measured

23. Page 7 lines 30-34 Results section: Very difficult to understand your percentages, perhaps write the numerator over the denominator so we can see what are proportions of what.

We have added figure 3 to indicate this numbers

24. Page 7 Line 37 “likely to be boys”? What does that mean?

'Likely' has been replaced to read 'mostly'

25. Page 7 Lines 41 and 42. Shouldn't all index cases have a positive RDT? I think that this is where a strong methods section would help. If you defined what an index case was you may not run into these challenges in the results.

Any case whether index or secondary now refers to one with a positive RDT as shown in table 1

26. Page 7 results section could do with a flow diagram that would clearly show index cases recruited from school, index cases recruited from houses, numbers in each screened with an RDT, those positive, those uncomplicated, those complicated.

Figure 3 has been added to corroborate this view

27. Table 1: Why are the index numbers similar to the RACD arm... You should include the total number screened at the top not just the positive cases.

RACD identifies secondary cases triggered by the index cases. After deleting RDT negative cases, the difference is clear

28. Page 9 lines 1-12: In your methods you should have a comment about seasonality. Does Figure 1 just reflect seasonal variation. You could plot rainfall on Figure 1, or health facility malaria cases..

The effect of seasonality is likely but the study was carried out during the high transmission or rainy season only

29. Page 9 Paragraph starting line 15 – starts with LLIN ownership and then goes into describing index cases. These should be separate paragraphs – its confusing for the reader. These latter descriptions should be in the first paragraph of the results with the suggested flow diagram.

The sentences have been separated and the flow chart added as suggested

30. Page 9 Lines 25 – 28: Your statement assumes that finding cases is good, perhaps those cases would ve appeared later at the health facility, or self-resolved and so ACD was not needed. Just be careful of making a subjective statement when you are not actually measuring the outcome. Statement has been removed
31. Lines 28 -43 an increase of 125% compared to what? Could this just be a seasonal increase? Nothing to do with the ACD? You were doing your activity when cases where high? The comparison between 2017 and 2018 high transmission seasons
32. Page 9 lines 48- 54: females are more often found at home – this is an accepted bias of doing home visits. Did you collect information on who you were not screening, who was not at home when you went? What are the cultural habits of the population? Do people tend to send male children to school rather than girls..?  
In the rural communities, though the trend is changing, we find more boys in schools than girls  
Information was collected on every member of the household whether present or absent or ill or not
33. Limitations do not include that there is no control arm, apriori assumptions are not stated – ie what we are going to measure, what we are looking for etc  
This has been included in the limitations in lines 314-16
34. Conclusion is actually ok, although this study doesn't prove anything as it has not design to assess causality. My question to the authors is if they just did occasional screen and treat cross sectional surveys – would that have achieved the same output? If random households had been chosen instead of following index cases- would that have worked? There is no attempt to see if this actually any better from anything else, the authors are assuming it.  
These are the right questions we might want to explore in further attempts. We did weekly surveys in reality and we are convinced that it was better than what was going on before then.

### VERSION 2 – REVIEW

<b>REVIEWER</b>	Kelly M. Searle University of Minnesota, School of Public Health, Minneapolis, MN, USA
<b>REVIEW RETURNED</b>	13-Feb-2019

<b>GENERAL COMMENTS</b>	<p>Bmjopen-2018-026678.R1</p> <p>Thank you for the opportunity to review the revisions of this manuscript. This is much clearer in the methods and the flow charts created were incredibly helpful. The authors addressed most of the specific comments, however it is still unclear how adding in active case detection in this manner is preferred to improving the current iCCM program where CHWs should be identifying, testing, and treating suspected (febrile) members of the community and act as a community link to health care. Along this line, if the iCCM program in place has major challenges and is underperforming, efforts to improve this directly will also result in more infections identified and treated. The primary finding was that testing more febrile community members identifies more malaria infections and iCCM+ identifies more febrile community members.</p> <p>One major comment that was not addressed in the manuscript was about the issue of RDT stockouts among the CHWs. The authors responded that these are artificial stockouts because the CHWs cannot procure them from the provincial level, but only through the health facilities. If the health facilities do not have</p>
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	<p>RDTs but the provincial level does, this is a breakdown in the distribution pipeline, and is a stockout. These issues definitely need to be addressed on a programmatic level to ensure that CHWs have adequate testing material to do their jobs.</p> <p>Additionally, in this study, since the RDTs were provided outside of the established system, then in practice iCCM+ would be impacted by the breakdown in the distribution pipeline. Therefore, the same logistic and operational challenges present with iCCM would also be experienced with iCCM+, perhaps more so. This should be addressed as a limitation, and if the study is providing the RDTs outside of the established public health system, then it is not accurate to say that this intervention does not require additional resources.</p> <p><b>Abstract</b></p> <p><b>Design:</b> This doesn't seem to qualify as a cross-sectional survey by design. In the discussion it is described as a quality improvement study, which is more accurate. Perhaps change this to 'observational quality improvement study'.</p> <p><b>Conclusion:</b> Since you don't know the denominator for undiagnosed cases, it's not accurate to state that 'most of these undiagnosed cases can be mopped-up by iCCM+'.</p> <p><b>Introduction</b></p> <p>Page 3, line 84: Since the design on iCCM is a passive case detection system in the community to alleviate the barrier to travel to health facilities for care, being passive rather than active case detection isn't necessarily a challenge.</p> <p><b>Methods</b></p> <p>Page 5, line 126-127: The authors describe that the shortcomings of iCCM led to the introduction of iCCM+, which implicates that iCCM is now the standard intervention implemented by the NMCP, but in reality, is being tested here as a potential alternative.</p> <p>The authors are still using ASC and CHW inconsistently.</p> <p>Page 5 line 147-148: It is mentioned that health centres were conducting PACD and that CHWs were doing malaria testing of admitted febrile children at the health centres that were identified by health care workers. It is unclear here why these children aren't getting tested and treated by care workers as the standard of care with CHWs doing the reactive case detection in their households.</p> <p>Page 6 line 182: Were patterns of missingness in the data explored in any way? It sounds like missingness was assumed to be completely random, but missingness not at random and conditional of other variables was not considered.</p> <p>Page 7 lines 193-198: I asked this in my initial review, but it wasn't properly addressed. Was the only deciding factor for inclusion in the multivariable model statistical significance with at an alpha of 0.05 or were other factors (such as apriori knowledge) used for inclusion? Additionally, with the final model, was only statistical significance used to decide variables for the final model or was other information considered?</p> <p><b>Results</b></p> <p>First paragraph: The percentages presented (e.g. 84.4% overall), are presented as prevalence, which is not accurate as the</p>
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	<p>denominator is only febrile participants that were tested. For a prevalence the denominator would be a random sample of the entire population. In this case what is being presented is a test-positivity.</p> <p>Table 1: What are 'Referrals'? This wasn't mentioned in the text.</p> <p>Conclusion In the last sentence the authors indicate that this intervention in this setting and reduce the burden of malaria in communities. Impacts of this intervention on the community prevalence of malaria nor malaria transmission were evaluated. The results showed that more infections were identified, which is what would be expected when more people are tested. The impact on malaria burden was not evaluated.</p>
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<b>REVIEWER</b>	Roly Gosling University of California San Francisco, Namibia
<b>REVIEW RETURNED</b>	18-Jan-2019

<b>GENERAL COMMENTS</b>	<p>Thank you for allowing me to review this much improved manuscript. Please see attached comments in your marked up word document.</p> <p>1. The abstract needs work to match the main manuscript. 2. The methods need to be shortened, with excessive descriptive words taken out, and we need to know what is the standard iCCM.</p> <p>- The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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### VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Kelly M. Searle

Thank you for the opportunity to review the revisions of this manuscript. This is much clearer in the methods and the flow charts created were incredibly helpful. The authors addressed most of the specific comments, however it is still unclear how adding in active case detection in this manner is preferred to improving the current iCCM program where CHWs should be identifying, testing, and treating suspected (febrile) members of the community and act as a community link to health care. Along this line, if the iCCM program in place has major challenges and is underperforming, efforts to improve this directly will also result in more infections identified and treated. The primary finding was that testing more febrile community members identifies more malaria infections and iCCM+ identifies more febrile community members.

We do agree with the reviewer that the current challenges faced by the programme need to be addressed directly and that is what the programme managers are (supposed to be) doing. Yet, there is no single way of approaching this. We are somehow proposing one of such approaches to make the ongoing programme perform better at least in the setting we are describing by addressing in particular the low uptake and low performance due to the passive nature of iCCM.

One major comment that was not addressed in the manuscript was about the issue of RDT stockouts among the CHWs. The authors responded that these are artificial stockouts because the CHWs cannot procure them from the provincial level, but only through the health facilities. If the health facilities do not have RDTs but the provincial level does, this is a breakdown in the distribution pipeline, and is a stockout. These issues definitely need to be addressed on a programmatic level to ensure that CHWs have adequate testing material to do their jobs. Additionally, in this study, since the RDTs were provided outside of the established system, then in practice iCCM+ would be impacted by the breakdown in the distribution pipeline. Therefore, the same logistic and operational challenges present with iCCM would also be experienced with iCCM+, perhaps more so. This should be addressed as a limitation, and if the study is providing the RDTs outside of the established public health system, then it is not accurate to say that this intervention does not require additional resources.

We had earlier recognised this issue in lines 314-316. we have also acknowledged the ongoing effort by the programme managers at the regional/provincial level to resolve the problem by distributing malaria commodities to health facilities instead of waiting upon the latter to purchase and pick them up from their regional offices (lines 218-323).

#### Abstract

**Design:** This doesn't seem to qualify as a cross-sectional survey by design. In the discussion it is described as a quality improvement study, which is more accurate. Perhaps change this to 'observational quality improvement study'.

The suggestion has been applied as an "observational quality improvement study" both in the title and the design sections

**Conclusion:** Since you don't know the denominator for undiagnosed cases, it's not accurate to state that 'most of these undiagnosed cases can be mopped-up by iCCM+'.

That's right and that's why we did not give a figure to represent how many of such cases can be detected in specific terms. We have now used the term '...more cases can be diagnosed and treated by iCCM+'

#### Introduction

Page 3, line 84: Since the design on iCCM is a passive case detection system in the community to alleviate the barrier to travel to health facilities for care, being passive rather than active case detection isn't necessarily a challenge.

Accepted and modified as -... low uptake inherent to its passive nature...lines 91-92

#### Methods

Page 5, line 126-127: The authors describe that the shortcomings of iCCM led to the introduction of iCCM+, which implicates that iCCM is now the standard intervention implemented by the NMCP, but in reality, is being tested here as a potential alternative.

That's true

The authors are still using ASC and CHW inconsistently.

We have succeeded in locating the remaining 'ASCs' and have changed them to CHWs

Page 5 line 147-148: It is mentioned that health centres were conducting PACD and that CHWs were doing malaria testing of admitted febrile children at the health centres that were identified by health care workers. It is unclear here why these children aren't getting tested and treated by care workers as the standard of care with CHWs doing the reactive case detection in their households.

CHWs are NOT doing malaria testing in health centres but do collaborate with HCW to locate children with malaria/fever they have admitted or treated in their health facilities so that CHW can then visit their homes in search for more cases.

Page 6 line 182: Were patterns of missingness in the data explored in any way? It sounds like missingness was assumed to be completely random, but missingness not at random and conditional of other variables was not considered.

We collected few variables to ease the work of CHWs and just by (cross) tabulation, we noticed that missing values were very few (Table 1 shows that n was usually 100% for the selected variables)

Page 7 lines 193-198: I asked this in my initial review, but it wasn't properly addressed. Was the only deciding factor for inclusion in the multivariable model statistical significance with at an alpha of 0.05 or were other factors (such as apriori knowledge) used for inclusion? Additionally, with the final model, was only statistical significance used to decide variables for the final model or was other information considered?

All the variables (few indeed) were included in the initial model. The final model did retain variables only on the basis of a p-value <0,05.

## Results

First paragraph: The percentages presented (e.g. 84.4% overall), are presented as prevalence, which is not accurate as the denominator is only febrile participants that were tested. For a prevalence the denominator would be a random sample of the entire population. In this case what is being presented is a test-positivity.

That's very correct. We have changed prevalence to test positivity rate

Table 1: What are 'Referrals'? This wasn't mentioned in the text.

We mean cases of severe malaria or RDT-negatives that were referred to the health facilities. We have now made it more precise to read as such.

## Conclusion

In the last sentence the authors indicate that this intervention in this setting and reduce the burden of malaria in communities. Impacts of this intervention on the community prevalence of malaria nor malaria transmission were evaluated. The results showed that more infections were identified, which is what would be expected when more people are tested. The impact on malaria burden was not evaluated.

We have removed the statement making allusion to impact of the intervention as rightly suggested because this was not measured though that may be the ultimate goal. We have now indicated that the intervention could detect and treat more infections

THANK YOU VERY MUCH INDEED!!



Reviewer: 2

Reviewer Name: Roly Gosling

Thank you for allowing me to review this much improved manuscript. Please see attached comments in your marked-up word document.

We have addressed the points raised directly onto the new marked-up document

1.The abstract needs work to match the main manuscript.

We have reworked the abstract in the light of the suggestions made by reviewers. The background, design and conclusion have been revised.

2. The methods need to be shortened, with excessive descriptive words taken out, and we need to know what is the standard iCCM.

We have removed that portion of the text highlighted in the setting

A paragraph to describe the standard iCCM has been added just before the description of iCCM+