**To the Editor Bulletin of the World Health Organization**

Dear Dr Maria Gustafsson Trajkovska

We would like to thank you for the opportunity given us to re-submit a revised version. We are happy with the positive and constructive comments raised by the editorial team and external reviewers. We have addressed the concerns of the editorial committee and specific points made by each reviewer (in bold). Our reaction is in normal typeface. We have attached the revised version of the manuscript with track changes on denoting where the text has been changed (uploaded as a supporting information file) and the final version without track changes.

We took the comments by the editorial committee seriously particularly, the one which asked us to take into consideration the Cochrane review from March 11 2015 "Circulating antigen tests and urine reagent strips for diagnosis of active schistosomiasis in endemic areas" and what ours seeks to add. We have put our review into context of that review to address the concerns raised. TO ANSWER THE EDITORIAL COMMENT ON COCHRANE REVIEW HERE

Please find below the responses to our reviewers’ and editorial team’s comments.

Yours sincerely,

Dr Anthony Danso-Appiah

(on behalf of co-authors)

**Reviewer 1**

**General comments**

**We are happy with the useful comments that no doubt will help improve the quality of the paper, thank you. We have addressed all comments in our reactions below.**

**Specific comments:**

**Comment 1: The author’s name and corresponding affiliation in alphabetical order should be written in full according to the style of Bulletin of the World Health Organization.**

Reaction: Thank you, we have edited the author list and affiliation to match Bulletin of the World Health Organization’s in-house style.

**ABSTRACT**

**Comment 2a: *Objectives*: An information on POC-CAA should be indicated.**

Reaction: We have replaced the background information with an “Objective” on POC-CCA as follows: “We assessed diagnostic accuracy of POC-CCA test for schistosome infections using Kato-Katz thick smear (for *S. mansoni* and *S. japonicum*) or 10 mL urine filtration (for *S. haematobium*) as reference standard”.

**Comment 2b: *Methods:* Methods are not described enough and should be rewritten with special reference to the time interval of selected manuscripts.**

Reaction: Thank you for this comment. We were hampered by the restriction on word count. Based on your comments, we have introduced additional making reference to the period in which studies included in the review were selected (1994 and September 2015) as follows “We searched MEDLINE, EMBASE and LILACS from inception to 30th September 2014 (and updated the search to 30th September 2015) with no language restrictions. We also searched the Cochrane Library 2015, reference lists of articles and grey literature and contacted experts for additional or unpublished studies.” We have added the sentence “Twenty-eight studies published between 1994 and September 2015 met the inclusion criteria” to the section “Selection of studies” (pg. 5, para. 2).

Comment 2c: **95% credible intervals (CrIs)”as a measure of association is no longer used in the review and should be changed to “95% confidence intervals (CIs)”.**

Reaction: Thank you for this comment, we can undsertand the confusion as we have used “confidence interval (CI)” in the main Methods but “credible intervals (CrIs)” in the Abstract. We have replaced “credible intervals (CrIs)” with “confidence interval (CI)”.

**Comment 2d: Also, the abbreviation “SROC curves” should be changed to “HSROC curves” and the abbreviation LCBM (as written in page 15) might be used.**

Reaction: Thank you for this important comment. We have used a slightly modified version that works the same as ‘HSROC’ but not necessarily ‘HSROC’. We explained this in the section “Data synthesis” (pages 5 & 6, lines 2-7) that “The meta-analyses were performed using the bivariate model specified inReitsma 2005, using the Mada package in the R programming environment. The function fits the bivariate model described by Reitsma 2005 that Habord 2007 showed to be equivalent to the Hierarchical Summary Receiver Operating Characteristics (HSROC) by Rutter 2001”.

Dear Tony, I think that your reaction is not correct. The point is that we can use a Bivariate Model (BM) or a Hierarchical Summary ROC (HSROC) model but the pplotted curves are always called SROC curves (e.g. Figure 2, page 247 on Harbord et al. 2007). LCBM stands for Latent Class Bivariate Model.

**Comment 3 *Findings:* Major findings were only indicated. However, no data regarding secondary objectives of the review were indicated.**

Reaction: Thank you, we limited the findings to the main or primary objective because of lack of space. Adding findings of the secondary objectives would have moved the abstract well beyond the required word count of 300. [DEAR CO-AUTHORS, ANY SUGGESTION? I THINK THAT IF THERE IS SPACE AT THE END WE CAN ADD ONE OR TWO SECONDARY FINDINGS, OTHERWISE WE HAVE TO MAINTAIN AS IS]

**MAIN DOCUMENT**

**Comment 4a: *Background:* The background lakes information on the history and development of CCA assay which should be indicated (See related references). The following related references should be cited and discussed.**

***Related References:***

1. De Jonge N, et al. Presence of the schistosome circulating anodic antigen (CAA) in urine of patients with *Schistosoma mansoni* or *S. haematobium* infections. Am. J. Trop. Med. Hyg. 1989;41:563–569.

2. Deelder AM, et al. Schistosoma: analysis of monoclonal antibodies reactive with the

circulating antigens CAA and CCA. Parasitol. 1996;112:21–35.

3. van Lieshout L, et al. Immunodiagnosis of schistosomiasis by determination of the

circulating antigens CAA and CCA, in particular in individuals with recent or light

infections. Acta Trop. 2000;77:69–80.

4. Ochodo EA, et al. Circulating antigen tests and urine reagent strips for diagnosis of active schistosomiasis in endemic areas. Cochrane Database Syst Rev. 2015; 11(3):CD009579.

5. Van Dam GJ, et al. Evaluation of banked urine samples for the detection of circulating

anodic and cathodic antigens in *Schistosoma mekongi* and *S. japonicum* infections: a proofof- concept study. Acta Trop. 2015;141(Pt B):198-203

Reaction: We agree that such information is useful and should have been included as part of the manuscript. Actually, in our main review document submitted to the WHO (this is a paper resulting from WHO-commissioned systematic review in support of its policy shift on schistosomiasis diagnosis) there was detailed information about history and development of CCA assay of which the listed references were cited. We also had a section detailing existing tests, their strengths and limitations as well as those in development. Unfortunately, we had to leave these out because of restrictions on word count. However, based on the comment we have revised paragraph 3 of the Background and added the following which has been borrowed from Reviewer 1 “The prevalence and intensity of infection have fallen significantly in most endemic areas through mass drug administration within the preventive chemotherapy strategy (ref). Undoubtedly, routinely used diagnostic tests such as Kato–Katz thick smear and urine filtration techniques are no longer sensitive. Therefore, sensitive and easy-to-use at low cost diagnostic is a necessity. Detection of *Schistosoma* circulating antigens using specific monoclonal antibodies has shown promise (ref). High sensitivities in detecting active infections have been achieved with assays for circulating cathodic antigen (CCA) and circulating anodic antigen (CAA) in serum or urine. Research based on CCA (refs) has produced the point-of-care (POC) lateral flow urine cassette assay for diagnosis of schistosome infection (van Dam et al.), which has been validated in several studies (refs).

**Comment 4b: The information in the third paragraph should be referenced.**

Reaction: We have provided appropriate references in support of the statements

**Comment 4c: The use of single author name (e.g. Katz 1972) to indicate a manuscript should be changed (i.e. Katz et al., 1972) or written in numbers according to the style of Bulletin of the World Health Organization.**

Reaction: Thank you, we have revised the citations according to the style of Bulletin of the World Health Organization.

**Comment 5a: *Criteria for considering studies for this review*, A statement regarding the use of an eligibility standard forms based on predefined inclusion criteria should be indicated.**

Reaction: We clearly stated this as part of “Selection of studies”. We have now added a statement on this also to Criteria for considering studies for this review and Data extraction and management.

**Comment 5b: *Types of participants*, The last sentence (For Kato-Katz…….).is not complete**

Reaction: We have deleted “For Kato-Katz. It was left there by mistake.

**Comment 5c: *Diagnostic thresholds,* Does the authors mean that all eligible studies applied the specified diagnostic thresholds of POC-CCA and Kato-Katz or urine filtration. The heavy infection of Kato Katz reference standard “(> 400 EPG)” should be corrected to “(≥ 400 EPG)”.**

Reaction: Thank you for this critique. No, what we meant was that in this review we used the WHO classification of intensity thresholds to define the intensity categories, not necessarily that all eligible studies applied the specified diagnostic thresholds. We have made the necessary changes to address the confusion. The section now reads as “We used the commonly applied intensity of infection thresholds based on WHO classification for interpreting our data. POC-CCA has usually been classified as “trace as negative (-)”, “trace as positive (tr)”, “single positive (+)”, “double positive (++)” and “triple positive (+++)”; Kato-Katz as “light infection (< 100 EPG)”, “moderate infection (100-399 EPG)” and “heavy infection (≥ 400 EPG); and the standard 10 mL urine filtration test as light infection (≤ 50 eggs/10mL of urine) and heavy infection (> 50 eggs/10mL of urine)”.

We have also replaced (> 400 EPG) with (≥ 400 EPG) .

**COMMENT 6: REVIEW METHODS**

***Comment 6a: Data synthesis,* The source of the program used to perform the statistical analysis of data was not indicated. Positive and negative Likelihood ratios were not shown in the data presentation and should be removed.**

Reaction: JON AND PAOLO TO REACT TO THE COMMENT ON SOURCE OF THE PROGRAM USED TO PERFORM THE STATISTICAL ANALYSIS OF DATA.

We agree Positive and Negative Likelihood ratios were not eventually used so we have deleted them.

Source for mada: Philipp Doebler (2015). mada: Meta-Analysis of Diagnostic Accuracy. R package version 0.5.7. <http://CRAN.R-project.org/package=mada>

Source for LatentGOLD: Vermunt, Jeroen K., and Jay Magidson. "Technical Guide for Latent GOLD 5.0: Basic, Advanced, and Syntax." Statistical Innovations Inc., Belmont (2013). <http://www.statisticalinnovations.com/latent-gold-5-1/>

**Comment 6b: *Assessment of heterogeneity and sub-group analysis,* Chi2 should be corrected to “Chi square” or “c2”. The source of latent GOLD v4.5 should be indicated.**

Reaction: Thank you, we have replaced “Chi2” with “X2”. I would prefer “Chi square”.

JON AND PAOLO WHAT DO YOU THINK ABOUT THE SOURCE OF LATENT GOLD?

I have indicated above new source for Latent Gold 5. It is the upgrade of the previous version.

**COMMENT 7: RESULTS**

**Comment 7a: Generally, the results are ill described and should be re-written clearly.**

Reaction: Thank you, we took this comment seriously revising and rearranging the results section.

**Comment 7b: All figures and tables should be omitted from the text and presented in separate pages at the end of manuscript text. The quality of all figures and tables should be improved.**

Reaction: We have improved the Figures and Tables and placed them on separate pages at the end of the manuscript.

**Comment 7b: The information in the footnotes of figures 4, 5, and 7 is not clear enough and should be improved.**

Reaction: We have revised footnotes of figures.

**Comment 7c: In table 1, the alphabetical order of the eligible studies is not informative. These studies should be classified or grouped if possible e.g. according to diagnostic criteria or characteristics of participants to facilitate comparison and draw conclusions. In page 1 of Table 1, column 3 (Country) “thiopia” should be corrected to “Ethiopia”.**

Reaction: THIS IS WHAT IM GOING TO DO NEXT

**Comment 7d: As it approximately has drawn the same conclusion, the following five subtitles compared POC-CCA test with Kato-Katz reference standard should be merged and presented under one subtitle.**

1. ***SINGLE POC-CCA TEST VERSUS SINGLE KATO-KATZ REFERENCE STANDARD***
2. ***SINGLE POC-CCA VERSUS THREE KATO-KATZ TESTS***
3. ***THREE POC-CCA VERUS THREE KATO-KATZ TESTS***
4. ***POC-CCA VERSUS COMBINED POC-CCA/KATO-KATZ GOLD STANDARD***
5. ***GLOBAL PERFORMANCE OF POC-CCA VERSUS KATO-KATZ***

Reaction: Thank you, the suggested presentation of the results will improve the result section considerably. We have created one subheading “POC-CCA VERSUS KATO-KATZ” withthe five forming subtitles as follows:

1. *Single POC-CCA versus single Kato-Katz*
2. *Single POC-CCA versus three KATO-KATZ tests*
3. *Three POC-CCA versus three KATO-KATZ tests*
4. *Global performance of POC-CCA* versus KATO-KATZ
5. *POC-CCA versus combined POC-CCA/Kato-Katz*

**Comment 7e: As it has drawn from a few number of studies, the following three subtitles investigate the effect of endemicity, threshold and age on performances of POC-CCA test should be merged and presented under one subtitle.**

***1. ASSESSMENT OF POC-CCA BYBACKGROUND ENDEMICITY***

***2. THRESHOLD EFFECT OF POC-CCA TEST***

***3. EFFECT OF AGE ON POC-CCA ACCURACY***

Reaction: Thank you, we have created one subheading “THE EFFECT OF ENDEMICITY, THRESHOLD AND AGE ON PERFORMANCES OF POC-CCA” withthe three forming subtitles as follows:

1. *Background endemicity*
2. *Threshold effect on POC-CCA*
3. *Effect of age on POC-CCA*

**Comment 7f: In addition, statistical analyses are not satisfactory. The stability of the results should be evaluated and whether any one study had an excessive influence on the meta-analysis need to be tested (e.g. Normand SL. Meta-analysis: formulating, evaluating, combining, and reporting. Stat Med. 1999; 18(3):321-59). It is not clear how the authors analyzed the qualitative against quantitative findings. The use of conventional level (P < 0.05) or recommended level (P < 0.1) to test statistical significance was not indicated in the results. Is the p value one-side or two-sided**.

Reaction: I AGREE IT WOULD HAVE BEEN A GOOD IDEA IF WE RAN SENSITIVITY ANALYSIS TO TEST THE ROBUST OF OUR FINDINGS. JON IS IT POSSIBLE FOR YOU TO RUN SENSITIVITY ANALYSIS? CAN YOU ALSO REACT TO THE REMAINING COMMENTS ON P-VALUE AND WHETHER P-VALUE USED IS ONE-SIDED OR TWO-SIDED?

One option is to test for outliers using the modchk option in the midas routine in STATA. modchk(inf) produces a spikeplot for checking for particularly influential observations using Cook’s distance. If Jon prepares an excel file with one sheet per analysis I can do it easily. Another option would be to produce a Baujat plot diagnostic accuracy review but this could be an idea for a small methodological paper.

JON:

If the p value question relates to the chi-squared test, then this is always a one tailed test.

Paulo: could you indicate the preferred format for the data with one sheet per analysis? i.e. what columns and rows should be in each sheet?

I think we covered the sensitivity analyses quite well in the sense of looking at many subgroup analyses. In terms which of the analyses were most susceptible to leverage from a single study, that would be those with fewest studies and observations. The Mada package produces warnings about few primary studies for the following subgroup analyses: study 4, study 6, study 7, study 8, study 9.

As one rough-and-ready approach to addressing the question of sensitivity analyses, I’ve calculated the effect of leaving out each individual study, within each of the analyses, on the AUC. The results are below, with the column ‘dif\_AUC’ showing the effect of leaving that row’s study out on the AUC. The two studies with the greatest leverage according to this measure are Coulibaly 2011 in A01, and Tchuem Tchuente 2012 in A06. I hope this helps.

> lever\_A01

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Shane 2011 0.863 0.859 0.005

2 Tchuem Tchuente 2012 0.858 0.859 -0.001

3 Coulibaly 2011 0.730 0.859 -0.129

4 Adriko 2014 0.855 0.859 -0.004

5 Erko 2013 0.858 0.859 -0.001

6 Standley 2010 0.861 0.859 0.002

7 Sousa-Figueiredo 2013 0.889 0.859 0.031

> lever\_A02

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Coulibaly 2011-study 1 0.847 0.845 0.002

2 Coulibaly 2011-study 2 0.841 0.845 -0.004

3 Coulibaly 2011-study 3 0.840 0.845 -0.006

4 Dawson 2013 0.847 0.845 0.002

5 Erko 2013 0.838 0.845 -0.008

6 Legesse 2008 0.855 0.845 0.009

7 Tchuem Tchuente 2012-study 1 0.848 0.845 0.002

8 Tchuem Tchuente 2012-study 2 0.848 0.845 0.003

9 Tchuem Tchuente 2012-study 3 0.845 0.845 0.000

10 Koukounari 2013-study 1 0.844 0.845 -0.001

11 Koukounari 2013-study 2 0.839 0.845 -0.006

12 Legesse 2007 0.849 0.845 0.004

13 Coulibaly 2013 0.846 0.845 0.000

14 Adriko 2014 0.846 0.845 0.001

> lever\_A03

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Coulibaly 2011-study 1 0.882 0.857 0.025

2 Coulibaly 2011-study 2 0.849 0.857 -0.008

3 Coulibaly 2011-study 3 0.847 0.857 -0.010

4 Erko 2013 0.844 0.857 -0.013

5 Tchuem Tchuente 2012-study 1 0.857 0.857 0.000

6 Tchuem Tchuente 2012-study 2 0.863 0.857 0.006

7 Tchuem Tchuente 2012-study 3 0.858 0.857 0.001

8 Coulibaly 2013 0.857 0.857 0.000

> lever\_A04

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Midzi 2009 0.603 0.617 -0.013

2 Ayele 2008 0.668 0.617 0.051

> lever\_A05

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Coulibaly 2011-study 1 0.816 0.823 -0.007

2 Coulibaly 2011-study 2 0.812 0.823 -0.010

3 Coulibaly 2011-study 3 0.817 0.823 -0.006

4 Dawson 2013 0.823 0.823 0.001

5 Erko 2013 0.818 0.823 -0.005

6 Legesse 2008 0.829 0.823 0.006

7 Shane 2011 0.823 0.823 0.000

8 Tchuem Tchuente 2012-study 1 0.823 0.823 0.001

9 Tchuem Tchuente 2012-study 2 0.824 0.823 0.001

10 Tchuem Tchuente 2012-study 3 0.822 0.823 -0.001

11 Coulibaly 2013 0.823 0.823 0.001

12 Koukounari 2013-study 1 0.821 0.823 -0.001

13 Koukounari 2013-study 2 0.813 0.823 -0.009

14 Legesse 2007 0.825 0.823 0.002

15 Adriko 2014 0.823 0.823 0.000

16 Sousa-Figueiredo 2013-study 1 0.831 0.823 0.008

17 Sousa-Figueiredo 2013-study 2 0.825 0.823 0.002

18 Sousa-Figueiredo 2013-study 3 0.833 0.823 0.010

19 Standley 2010 0.823 0.823 0.000

> lever\_A06

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Adriko 2014 0.760 0.757 0.004

2 Sousa-Figueiredo 2013 0.815 0.757 0.059

3 Tchuem Tchuente 2012 0.666 0.757 -0.091

4 Coulibaly 2011 0.767 0.757 0.011

> lever\_A07

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Adriko 2014 0.836 0.832 0.003

2 Sousa-Figueiredo 2013 0.834 0.832 0.002

3 Tchuem Tchuente 2012 0.824 0.832 -0.008

4 Coulibaly 2011 0.808 0.832 -0.024

> lever\_A08

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Adriko 2014 0.660 0.657 0.003

2 Sousa-Figueiredo 2013 0.726 0.657 0.069

3 Standley 2010 0.643 0.657 -0.014

4 Coulibaly 2013 0.659 0.657 0.002

> lever\_A09

Study\_ID local\_AUC global\_AUC dif\_AUC

1 Adriko 2014 0.831 0.836 -0.006

2 Sousa-Figueiredo 2013 0.848 0.836 0.011

3 Standley 2010 0.839 0.836 0.002

4 Coulibaly 2013 0.836 0.836 0.000

**Comment 7g: *Latent class analysis of POC-CCA Test,* The information under this subsection should be re-written clearly. Data presented in Table 2 are repetitions of that in the text and consequently Table 2 of no value and should be deleted. Figure 8 is not indicated in the text of the manuscript.**

Reaction: PAOLO CAN YOU HELP?

I have rewritten this section.

**Comment 8a: *Discussion,* The authors to somewhat discus most of the obtained data and indicate the limitations of their analyses especially the few number of eligible studies in the last paragraph of the discussion. An additional potential limitation is that none of the studies compared POC-CCA before and after specific treatment included in the meta analyses. However, these limitations represent a major drawback of this review to approve the final conclusions and further studies regarding parameters affect performance characteristics of POC-CCA test are still required. Moreover, their findings may be affected by other unknown confounding factors that were not adjusted for.**

Reaction: I’M GOING TO DRAFT THIS NEXT

**Comment8b: Finally, some recent and relevant studies should be addressed and discus e.g.**

**1. Degarege A, Legesse M, Medhin G, Teklehaymanot T, Erko B. Day-to-day fluctuation of point-of-care circulating cathodic antigen test scores and faecal egg counts in children infected with *Schistosoma mansoni* in Ethiopia. BMC Infect Dis. 2014;14:210.**

**2. Lamberton PH, , et al. Sensitivity and specificity of multiple Kato-Katz thick smears and a circulating cathodic antigen test for *Schistosoma mansoni* diagnosis pre- and post-repeated praziquantel treatment. PLoS Negl Trop Dis. 2014;8(9):e3139.**

**3. Mwinzi PN, , et al. Additional Evaluation of the Point-of-Contact Circulating Cathodic Antigen Assay for *Schistosoma mansoni* Infection. Front Public Health. 2015; 3: 48.**

**4. Van Dam GJ, et al. Evaluation of banked urine samples for the detection of circulating anodic and cathodic antigens in *Schistosoma mekongi* and *S. japonicum* infections: a proofof-concept study. Acta Trop. 2015;141(Pt B):198-203.**

Reaction: I’M GOING TO DRAFT THIS BUT WE HAVE TO BE CAREFUL AS WE CAN INCLUDE ONLY 50 REFERENCES. MY LAST SEARCH FOR NEW STUDIES RETRIEVED ABOUT 5 STUDIES. ALTHOUGH THEY DID NOT MEET THE INCLUSION CRITERIA, WE HAVE TO TALK ABOUT THEM. TOGETHER WITH REFERENCES FOR THE SECTION ON HISTORY OF CCA, THE REFERENCES LIST MIGHT WELL EXCEED 50. THEREFORE, WE HAVE TO ACCEPT SOME OF THESE COMMENTS IN THE LIGHT OF THIS. PLEASE LET HEAR FROM YOU CO-AUTHORS.

Maybe we can just ask to the editors if we can go beyond this limit (you may find my suggestion trivial or optimistic)

**Comment 9: *References*, References of the review do not conform off the instructions to authors of Bulletin of World Health Organization and should be rewritten.**

Reaction: We have rearranged all the citations in the text and the reference list in line with Bulletin of the World Health Organization standards.

**Minor Essential Revisions**

**Comment 1: The manuscript needs major revision of the English.**

Reaction: Thank you, we have taken this seriously and run spell and grammar check.

**Comment 2: Several typos also need correction.**

Reaction: We have run spell check to take care of typos.

**Reviewer 2**

**Comment: You and your co-authors have done a good work as far as I am concerned. However, you should effect all my observations and corrections to eliminate typographical**

Reaction: We are pleased to receive such a compliment, thank you. We have addressed all the comments below.

**Comment 1: Author’s name and corresponding affiliation in alphabetical order**

Reaction: Thank you, we have rearranged the authors’ names and affiliations in alphabetical order.

**Comment 2a: The referencing style of the Bulletin of the World Health Organization should be used by the author please. For e.g.: use the numeric style of referencing in the text.**

Reaction: Thank you, we have followed Stefanie Vandevijvere et al. 2015 and revised our referencing to Bulletin of the World Health Organization style.

**Comment 2b: It is biologically wrong to write names of microorganisms as ordinary text e.g. Schistosoma mansoni as you did in your reference section instead of Schistosoma mansoni or S. mansoni. Hence, implement same to references 6, 7, 8, 11, 12, 15, 18, 21, 25, 30, 31, 33 and 42. See your example in reference number 3 line 2. The genus and species are written in italics (Schistosoma mansoni or S. mansoni). Keeping in mind that you abbreviated the names of the parasites! As from page 2 in your write up.**

Reaction: We have made all the necessary changes.

**Comment 2c: Why don`t you maintain that style in your references as you did at the**

**beginning of your write-up?**

Reaction: Thank you, we have checked to make sure our referencing is consistent throughout the document.

**Comment 3: On page 13 figure 7 legend: Line 1…at the same time. You should either end the sentence with a full stop or add the missing word/statement**.

Reaction: Thank you, we have introduced a full stop to end the sentence there.

**Comment 4: It is alright that you abbreviated the names of your referenced journals. Also, most of your journals were abbreviated in plain text, so write the journal in reference 13 as plain or ordinary text because but you have written the name of reference number 13 in italics while others were not. Write it in ordinary or plain text please!**

Reaction: We have checked and introduced consistency throughout the manuscript.

**Comment 5: Also, Parasitology should be abbreviated as Parasitol. See your example in**

**reference 12. Reference 3 is written in italics. Correct it to a plain text please!**

Reaction: Thank you, we have checked and corrected them.

**Comment 6: Also you cannot write in full as well as well as abbreviation at the same time. See references 39, 40 and 43.**

**Kindly look for the correct abbreviation for Parasite and Vectors and Lancet please! If you cannot find the above, you can forget it and leave them as they are in your references.**

Reaction: There is no abbreviation for “Parasite and Vectors” so we have maintained it and checked for consistency.

**Comment 7: Kindly abbreviate all your journals written in full in references 3, 11, 15, 38, 39, and 40.**

Reaction: Thank you, we have abbreviated all our references.

**Comment 8: On your Table 1 pages 24-29. Schoolchildren should be separated as School**

**children for consistency on pages 25 [S/no 1], 28 [S/no 26], 29 [S/no 27and 28].**

Reaction: We have checked and made the necessary corrections and introduced consistency.

**Comment 9: Finally, I commend you and your co-authors the ability to relate the reviews of past authors in coincided manner as it relates to your research article.**

Reaction: Thank you very much, we appreciate your compliment.