

## 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>	Uptake of Four or More Doses of Sulfadoxine Pyrimethamine for Intermittent Preventive Treatment of Malaria during Pregnancy in Zambia: Findings from the 2018 Malaria in Pregnancy Survey
<b>AUTHORS</b>	Sinyange, Danny; Mukumbuta, Nawa; Mutale, Lwito; Mumbole, Hudson; Hamainza, Busiku; Sialubanje, Cephas

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Stephen Rogerson University of Melbourne, Medicine and Radiology
<b>REVIEW RETURNED</b>	22-Mar-2023

<b>GENERAL COMMENTS</b>	<p>Dr Sialubunje and colleagues have analysed data from the 2018 Zambian Malaria Indicator Survey, to try to identify factors that might explain the relatively low uptake of the 4th dose of SP IPTp identified in that survey, and in the country more generally. Zambia apparently recommends at least 4 doses of SP IPTp in pregnancy, which is one dose more than the WHO which recommends three or more. Given how hard it has been for many countries to reach the 3+ dose threshold, it is not surprising that Zambia's efforts to increase this to 4 doses, which started relatively recently, in 2016, have met with limited success. More positively, it should be noted that just over 70% of participants in this study reported taking three doses of SP.</p> <p>Major comments</p> <ol style="list-style-type: none"><li>1. I struggled to find the reference for the 4 dose SP policy, reference 10 cited on page 6 line ~27 does not contain the information. This is relevant because few other countries specify a 4 dose policy, and WHO recommends at least three doses.</li><li>2. The authors write about "wealth quintiles" in the analysis, but it seems they are discussing three groups commonly referred to as tertiles.</li><li>3. First paragraph Page 5: The authors should reference the meta analysis of Kayentao et al in JAMA (2013) which provides the most comprehensive case for 3 or more cases of SP IPTp.</li><li>4. In table 1 it is clear that for some Provinces sample sizes were quite small, and the authors should be more cautious in their interpretation of some of the differences by Province, given low sample size e.g. in Copper Belt.</li><li>5. The table 1 format with two sets of parallel pairs of columns is unusual and could be confusing.</li><li>6. Table 2, there appears to be an error in the row Urban residence. The Ns and percentage appear right, but the OR, CI and P value do not seem to be derived from this urban vs rural comparison.</li><li>7. Discussion first paragraph. I suggest not highlighting findings that were only significant in unadjusted and not in adjusted analyses,</li></ol>
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	<p>such as knowledge and media exposure.</p> <p>8. Discussion page 16 line 44-5: I do not believe WHO specifically recommends 4 doses of SP, and could not find a dosage recommendation on the RBM web site. Please carefully check these sources and add a relevant reference.</p> <p>9. The authors' conclusion that "Strategies and interventions aimed at improving uptake and coverage of IPTp-SP must focus on women in high wealth quintile from urban areas with low malaria transmission in the country" is debatable. Would not resources be best deployed targeting increased coverage from current very low levels in Provinces with much higher malaria burden, where the risk is greatest and the ability to afford health care lowest? Wouldn't more MIP related morbidity be prevented this way, which should be the Malaria Control Programme's main aim?</p> <p>Minor comments</p> <ol style="list-style-type: none"> <li>1. Strengths and weaknesses, the first point re the data set is rather hard to follow and needs rewriting</li> <li>2. Introduction page 4, please define WHO at first use.</li> <li>3. Bottom page 4: these are not "recent findings" regarding the impact of malaria in pregnancy. Perhaps "As recently reviewed..."</li> <li>4. Page 5 line 35, stray use of word "information, please remove.</li> <li>5. Please generally check for abbreviations that are only used once or twice and don't use these.</li> <li>6. Page 7 line 12, please provide a citation for the 2018 Zambia MIS</li> <li>7. Page 9 Demographic characteristics, there is a duplication of (48.9%)</li> <li>8. Page 9 last lines, the summary of SP doses seems inaccurate. The statement "most (77.9%) took less than 4 doses of SP" does not agree with the table or other text which implies that 95% of women took fewer than 4 doses.</li> <li>9. Page 12, there is mention of (appendix 3) which was not included with my review copy.</li> <li>10. Page 15 Discussion paragraph 3 mentions SP uptake in women with post secondary education. Given these data are not separately presented in results it is not appropriate to separately discuss them.</li> <li>11. Line 34 "contrast" not contract</li> <li>12. Line 46: there is a hanging phrase, what point about women with less education is being intended here?</li> <li>13. Page 16, re teenage mothers, while this is an important group, the authors have not shown us the data on teenage mothers, who form part of 15-24 year olds. They should either split the age data in tables 1 and 2 or drop this point.</li> <li>14. Next paragraph line 33: please cite the literature being referred to. Is it just reference 36 cited later in the paragraph? There are other studies.</li> <li>15. What does this mean: "The GTFCC supported the country with OCV stocks". Please spell out in full .</li> <li>16. Reference 11 and ref 21, please write author name and/or document name in normal text.</li> <li>17. Ref 17, errors in capitalization</li> <li>18. Ref 38, initials precede authors when they should follow them</li> <li>19. References 39 and 42 are duplicates.</li> </ol>
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<b>REVIEWER</b>	David Dosoo Kintampo Health Research Centre
<b>REVIEW RETURNED</b>	31-Mar-2023

<b>GENERAL COMMENTS</b>	The authors found the prevalence of uptake of IPTp-SP in Zambia and the factors associated with uptake. The manuscript is well-
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	<p>written. Below are some comments for consideration:</p> <p>Abstract:</p> <ol style="list-style-type: none"> <li>1. Page 2 Line 21: the authors indicate p-values &lt;0.05 were computed. However, all p-values are computed and those &lt;0.05 considered as statistically significant. Please revise that sentence.</li> <li>2. Please include the statistical package that was used for the statistical analysis.</li> </ol> <p>Methods:</p> <ol style="list-style-type: none"> <li>3. Page 3 Line 8: “.... Zambia reduces makes the finding ....” Should be “.... Zambia makes the finding ....”</li> </ol> <p>Results:</p> <ol style="list-style-type: none"> <li>4. Please re-check the summation of percentages for the uptake of IPTp-SP in Table 1. The current total is 100.1%</li> <li>5. In Fig 1, the number of women who were excluded because they delivered before 2016 was not indicated in the figure.</li> </ol> <ol style="list-style-type: none"> <li>6. Page 14 Line 34: Reference is made to “appendix 3” but this could not be found</li> </ol>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Major comments

Query 1: I struggled to find the reference for the 4 dose SP policy, reference 10 cited on page 6 line ~27 does not contain the information. This is relevant because few other countries specify a 4-dose policy, and WHO recommends at least three doses.

Response: We thank the reviewer for the observation. We have now included the reference on the 4 doses of IPTp-SP policy (see reference # 14).

Query 2: The authors write about “wealth quintiles” in the analysis, but it seems they are discussing three groups commonly referred to as tertiles.

Response: We appreciate the reviewer’s comment. We have now corrected this to read tertile

Query 3 : First paragraph Page 5: The authors should reference the meta-analysis of Kayentao et al in JAMA (2013) which provides the most comprehensive case for 3 or more cases of SP IPTp

Response: We have included this reference (see page 5, reference # 21)

Query 4: In table 1 it is clear that for some Provinces sample sizes were quite small, and the authors should be more cautious in their interpretation of some of the differences by Province, given low sample size e.g. in Copper Belt.

Response: We have taken note of this observation and have included a statement to on the interpretation of the result (See page 12)

Query 5: The table 1 format with two sets of parallel pairs of columns is unusual and could be confusing

Response 5: We have edited table 1 and removed the parallel columns (see page 10)

Query 6: Table 2, there appears to be an error in the row Urban residence. The Ns and percentage appear right, but the OR, CI and P value do not seem to be derived from this urban vs rural comparison

Response 6: We appreciated the comment. We have gone through the analysis and confirm that the figures are correct

Query 7: Discussion first paragraph. I suggest not highlighting findings that were only significant in unadjusted and not in adjusted analyses, such as knowledge and media exposure.

Response 7: We appreciate the comment by the reviewer. We have now edited this section and removed the findings which were not significant on adjusted analysis (see page 15)

Query 8: Discussion page 16 line 44-5: I do not believe WHO specifically recommends 4 doses of SP and could not find a dosage recommendation on the RBM web site. Please carefully check these sources and add a relevant reference.

Response 8: We thank the reviewer for this observation. We have edited this section accordingly (page 16)

Query 9: The authors' conclusion that "Strategies and interventions aimed at improving uptake and coverage of IPTp-SP must focus on women in high wealth quintile from urban areas with low malaria transmission in the country" is debatable. Would not resources be best deployed targeting increased coverage from current very low levels in Provinces with much higher malaria burden, where the risk is greatest and the ability to afford health care lowest? Wouldn't more MIP related morbidity be prevented this way, which should be the Malaria Control Programme's main aim?

Response 9: We thank the reviewer for this comment. The conclusion has been edited accordingly (see page 17).

Minor comments

Query 1: Strengths and weaknesses, the first point on the data set is rather hard to follow and needs rewriting

Response 1: We have edited this section (see page 3)

Query 2: Introduction page 4, please define WHO at first use

Response 2: WHO has been written in full before use of the abbreviation (see page 3)

Query 3: Bottom page 4: these are not "recent findings" regarding the impact of malaria in pregnancy. Perhaps "As recently reviewed..."

Response 3: We appreciate the observation. We have edited the sentence to read: "Previous studies in Zambia and elsewhere....."(see page 5)

Query 4: Page 5 line 35, stray use of word "information, please remove.

Response 4: The stray word has been removed accordingly (see page 5)

Query 5: Please generally check for abbreviations that are only used once or twice and don't use these.

Response 5: We have checked all the abbreviations and corrected accordingly

Query 6: Page 7 line 12, please provide a citation for the 2018 Zambia MIS

Response 6: The citation has been provided earlier under the introduction section (see page 5)

Query 7: Page 9 Demographic characteristics, there is a duplication of (48.9%)

Response 7: The duplication has been noted and corrected (see page 9)

Query 8: Page 9 last lines, the summary of SP doses seems inaccurate. The statement "most (77.9%) took less than 4 doses of SP" does not agree with the table or other text which implies that 95% of women took fewer than 4 doses

Response 8: This has been noted and corrected to read: "most (92.5%) took less than 4 doses of SP" (see page 10)

Query 9: Page 12, there is mention of (appendix 3) which was not included with my review copy.

Response 9: The error has been noted and (appendix 3) has been removed

Query 10: Page 15 Discussion paragraph 3 mentions SP uptake in women with post-secondary education. Given these data are not separately presented in results it is not appropriate to separately discuss them.

Response 10: We have taken note of this error and edited the sentence accordingly (see page 15)

Query 10: Line 34 "contrast" not contract

Response 10: This has been corrected (see page 15)

Query 11: Line 46: there is a hanging phrase, what point about women with less education is being intended here?

Response 11: The hanging phrase has been corrected to read, "The differences in the findings could be as a result of using different methods. It could also be due to selection bias; a large proportion of study participants were those with primary level education who mainly resided in rural areas".

Query 12: Page 16, re teenage mothers, while this is an important group, the authors have not shown us the data on teenage mothers, who form part of 15–24-year-olds. They should either split the age data in tables 1 and 2 or drop this point.

Response 12: The sentence has been corrected. The term youth, which denotes the age group 15 to 24 has been used instead of teenage mothers (see page 16)

Query 13: Next paragraph line 33: please cite the literature being referred to. Is it just reference 36 cited later in the paragraph? There are other studies.

Response 13: The sentence has been rephrased and the citation has been placed correctly (see page 16)

Question 14: What does this mean: "The GTFCC supported the country with OCV stocks". Please spell out in full

Response 14: This was error and has been removed, it is not part of this study (see page 18)

Question 15: Reference 11 and ref 21, please write author name and/or document name in normal text.

Responses 15: The references have been corrected and written in full

Query 16: Ref 17, errors in capitalization

Response 16: This has been corrected

Query 17: References 39 and 42 are duplicates

Response 17: The duplication has been removed

Reviewer 2

Query 1: Page 2 Line 21: the authors indicate p-values <0.05 were computed. However, all p-values are computed and those <0.05 considered as statistically significant. Please revise that sentence.

Response 1: The sentence has been corrected to read: explanatory variables with a p-value less than 0.20 on univariate analysis were included in the multivariable logistic regression model and crude and adjusted odds ratios (AORs) along with their 95% confidence intervals (CIs) were computed (p<0.05) (see page 2).

Query 2: Please include the statistical package that was used for the statistical analysis.

Response 2: This has been done (see page 2)

Query 3: Page 3 Line 8: "... Zambia reduces makes the finding ...." Should be "... Zambia makes the finding ...."

Response 3: This has been noted and corrected (see page 3)

Query 4: Please re-check the summation of percentages for the uptake of IPTp-SP in Table 1. The current total is 100.1%

Response 4: The summation has been corrected

Query 5: In Fig 1, the number of women who were excluded because they delivered before 2016 was not indicated in the figure.

Response 5: We appreciate the observation; this information has been included in the figure 1

Query 6: Page 14 Line 34: Reference is made to "appendix 3" but this could not be found

Response 6: This was an error and has been removed.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Stephen Rogerson University of Melbourne, Medicine and Radiology
<b>REVIEW RETURNED</b>	19-Apr-2023

<b>GENERAL COMMENTS</b>	The authors have satisfactorily addressed my initial comments. I have a few further minor corrections: Page 4, (7-9) in curved brackets rather than square? Page 4 last paragraph line 2 "involve" not involves Page 5 2nd paragraph IPTp not ITPp Page 9 Patient and public involvement: sentence starting "However, since the study..." needs revision Table 1 Non-Christian (not Non-christian) Page 16 last paragraph, turtle not quintile Page 17 paragraph 2 There WERE no significant associations Page 18 representative not presentative
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<b>REVIEWER</b>	David Dosoo Kintampo Health Research Centre
<b>REVIEW RETURNED</b>	07-May-2023

<b>GENERAL COMMENTS</b>	Thank you for submitting the revised manuscript. The revision addresses my earlier comments.
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### **VERSION 2 – AUTHOR RESPONSE**

Reviewer: 1

Prof. Stephen Rogerson, University of Melbourne

Comments to the Author:

The authors have satisfactorily addressed my initial comments. I have a few further minor corrections:

Page 4, (7-9) in curved brackets rather than square?

Page 4 last paragraph line 2 "involve" not involves

Page 5 2nd paragraph IPTp not ITPp

Page 9 Patient and public involvement: sentence starting "However, since the study..." needs revision

Table 1 Non-Christian (not Non-christian)

Page 16 last paragraph, turtle not quintile

Page 17 paragraph 2 There WERE no significant associations

Page 18 representative not presentative

Response: We appreciate the corrections by the reviewer. We have now corrected all the typographic and grammatic errors in the document.