

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.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Adverse Events Following Immunization (AEFI) of COVISHIELD Vaccination Among Healthcare Workers in Ghana
AUTHORS	Marfoh, Kissinger; Samba, Ali; Okyere, Eunice; Acheampong, Frankline; Owusu, Elsie; Darko, Dorothy Naa Ashokor; Zakariah, Joseph; Mensa, Hillary; Aidoo, Ernestina; Mohammed, Yasmin

VERSION 1 – REVIEW

REVIEWER	Gopaul, Chavin D North Central Regional Health Authority
REVIEW RETURNED	12-Apr-2022

GENERAL COMMENTS	<p>Dear authors,</p> <p>Thank you for your esteemed efforts in adding to our knowledge of AEFIs with the COVISHIELD vaccine. Please see my comments below which are intended to help improve your manuscript.</p> <p>1. Abstract</p> <p>-Participants: lines 14-16 should be included in the Design section of the abstract and removed from the Participants section. Use the Participants section to indicate eligibility, exclusion criteria and the number of participants completing the study. Also, the order of the statements in lines 14-16 implies that the online questionnaire was filled out after 1st and 2nd dose receipt. The methodology section however implies that the questionnaire was filled out before receipt of any dose. This could be clarified in the Abstract by first stating that the eligible healthcare workers filled out the online questionnaire with baseline data and then mentioning that they were followed-up after 1st and 2nd dose receipt.</p> <p>-Results: error in line 22, 70.3% would be an incidence rate of 703 per 1000 doses.</p> <p>2. Introduction</p> <p>-The links provided to references 1 & 5 in the Reference section do not work. Please update these references.</p> <p>-In addition, the authors should clarify where the classifications and definitions of serious and non-serious AEFIs came from. Are these WHO terms?</p>
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3. Materials and Methods

Overall, the methods section should be structured according to the STROBE guidelines for cohort studies (study design, setting, participants, variables, etc.)

Participants and Recruitment:

-The authors have not indicated if sampling was done or if all eligible healthcare workers of the teaching hospital were recruited.

-Was receiving vaccines other than COVISHIELD an exclusion criterion? If so, this should be stated.

-Also, please indicate how the 4000 initially recruited healthcare workers became 3022 participants e.g. did the 978 healthcare workers (who were not followed up) not meet the eligibility criteria/ did they not receive a 1st dose of COVISHIELD/ did they not receive a 2nd dose of COVISHIELD/did they not agree to participate?

Data collection and Follow-up:

-Again, the timeline for the healthcare workers' completion of the online questionnaire relative to their receipt of the vaccine should be clarified.

-Lines 10-11 state that all participants had both 1st and 2nd doses of the COVISHIELD vaccine. Was receipt of both doses of the COVISHIELD vaccine an inclusion criterion for this study? If so, this should be stated in the Participants section and also noted as a study limitation since healthcare workers who experienced serious AEFIs after the 1st dose might have opted out of getting the 2nd dose, and therefore their 1st dose data would have been excluded.

-Line 13 which states the average follow-up time is inconsistent with what was stated in the abstract (56 days vs. 56 hours). Please clarify. Additionally, this sentence should be moved to the results section and not included in the Methods section.

-Lines 15-16: please clarify if the daily and weekly follow-up calls were made after the 1st dose was received and if the same procedure was then repeated after the 2nd dose was received.

-How did the research team verify that the healthcare workers included in this study received the COVISHIELD vaccine e.g. was this verified at the outset of the follow-up call or did healthcare workers have to present an immunization card to be included in the follow-ups? This would be valuable to include in the Methods section.

4. Results

Factors Affect Onset and Duration of Adverse Events Following Immunisation (lines 29-30): did the group of "participants who use paracetamol" include those who used it prophylactically (before symptom onset) or those who used it therapeutically (after symptom onset), or both? This could be valuable information to disclose.

5. Discussion

Line 38: A study should be referenced after "India (57.0%)".

	<p>6. Figure 2: The figure description could be improved. “Onset of AEFI by the various time of the day” should be changed to a more appropriate description e.g. “Onset of AEFIs by time interval after inoculation”.</p> <p>7. Though I have indicated that the standard of English is acceptable for publication, a thorough revision of the manuscript for improvements to the English language should still be done since some errors in grammar (lack of pluralization, tenses), spelling (some instances of COVISHIELD, treatment) and syntax have been made throughout the manuscript. An important error which should be corrected is line 25 of the Introduction: “However, this vaccine is without adverse events.” It should be “...not without adverse events”.</p>
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REVIEWER	Hidayat, Rakhmad University of Indonesia
REVIEW RETURNED	13-Sep-2022

GENERAL COMMENTS	<p>We can accept this paper with a minor revisions that must be corrected by the author.</p> <p>'The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.'</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer # 1 Comments

Thank you for your esteemed efforts in adding to our knowledge of AEFIs with the COVISHIELD vaccine.

Response: We thank the reviewer for carefully reading the paper and appreciating its strength. We appreciate his comments.

Abstract

-Participants: lines 14-16 should be included in the Design section of the abstract and removed from the Participants section. Use the Participants section to indicate eligibility, exclusion criteria and the number of participants completing the study. Also, the order of the statements in lines 14-16 implies that the online questionnaire was filled out after 1st and 2nd dose receipt.

The methodology section however implies that the questionnaire was filled out before receipt of any dose. This could be clarified in the Abstract by first stating that the eligible healthcare workers filled out the online questionnaire with baseline data and then mentioning that they were followed-up after 1st and 2nd dose receipt

Response: All these sentences have been revised as recommended.

Results: error in line 22, 70.3% would be an incidence rate of 703 per 1000 doses.

Response: This sentence is corrected, percentages removed, and replaced with incidence and 95% confidence interval.

Introduction

The links provided to references 1 & 5 in the Reference section do not work. Please update these references

Response: We have updated the two references accordingly.

In addition, the authors should clarify where the classifications and definitions of serious and nonserious AEFIs came from. Are these WHO terms?

Response: Thank you for this comment. The definitions of serious and nonserious AEFI are WHO terms. We included the WHO definitions to make it more clear. "WHO operational definition. The AEFI is defined as any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine .

The AEFI were classified into non-serious and serious AEFI based on WHO definition. Non-serious adverse events were defined as any event that is not serious and does not pose a potential risk to the health of the recipient. Serious adverse events were defined as events involving hospitalization, prolongation of existing hospitalization, life-threatening illness, or permanent disability or death"

Materials and Methods

Overall, the methods section should be structured according to the STROBE guidelines for cohort studies (study design, setting, participants, variables, etc.)

Response: We have structured the materials and methods section according to the strobe guidelines.

Participants and Recruitment:

-The authors have not indicated if sampling was done or if all eligible healthcare workers of the teaching hospital were recruited.

Response: This was an oversight. We have revised the participants and recruitment section to include this statement "All eligible healthcare were invited to participate in the study."

Was receiving vaccines other than COVISHIELD an exclusion criterion? If so, this should be stated.

Response: Vaccines other than COVISHIELD were not included in the exclusion criteria because, during the study, the only vaccine available in Ghana was COVISHIELD.

-Also, please indicate how the 4000 initially recruited healthcare workers became 3022 participants e.g. did the 978 healthcare workers (who were not followed up) not meet the eligibility criteria/ did they not receive a 1st dose of COVISHIELD/ did they not receive a 2nd dose of COVISHIELD/did they not agree to participate?

Response: We thank the reviewer for this comments. We have revised the data collection and follow-up section to include how the initial 4000 healthcare workers became 3022. We have also included a flow chart (Figure 1) describing how we got 3022 healthcare workers.

Data collection and Follow-up:

-Again, the timeline for the healthcare workers' completion of the online questionnaire relative to their receipt of the vaccine should be clarified.

Response: This is an important point. We have rephrased the sentence for clarity. " At the baseline, pre-vaccination online questionnaire "

Lines 10-11 state that all participants had both 1st and 2nd doses of the COVISHIELD vaccine. Was receipt of both doses of the COVISHIELD vaccine an inclusion criterion for this study? If so, this should be stated in the Participants section and also noted as a study limitation since healthcare workers who experienced serious AEFIs after the 1st dose might have opted out of getting the 2nd dose, and therefore their 1st dose data would have been excluded.

Response: We did not include receiving both the 1st and 2nd doses of the COVISHIELD vaccine in the inclusion criteria because none of the participants were vaccinated at the begin of enrollment. But in the analysis, we included only participants who received both 1st and 2nd doses. This is because those who took the first dose only provided little or no information about their adverse events were excluded from the study (Figure 1).

-Line 13 which states the average follow-up time is inconsistent with what was stated in the abstract (56 days vs. 56 hours). Please clarify. Additionally, this sentence should be moved to the results section and not included in the Methods section.

Response: We have moved this sentence, as recommended to the result section. 56 days is the average follow-up time, and 56 hours is the median time to onset of AEFI.

Lines 15-16: please clarify if the daily and weekly follow-up calls were made after the 1st dose was received and if the same procedure was then repeated after the 2nd dose was received.

Response: We have revised the sentence to make clearer.

-How did the research team verify that the healthcare workers included in this study received the COVISHIELD vaccine e.g. was this verified at the outset of the follow-up call or did healthcare workers have to present an immunization card to be included in the follow-ups? This would be valuable to include in the Methods section.

Response: We thank you for this excellent point. This lets us know the reviewer's understanding of our research is excellent. We have included sentences to explain how the vaccination status of the healthcare workers were verified.

. Results

Factors Affect Onset and Duration of Adverse Events Following Immunisation (lines 29-30): did the group of "participants who use paracetamol" include those who used it prophylactically (before symptom onset) or those who used it therapeutically (after symptom onset), or both? This could be valuable information to disclose.

Response: The participants used paracetamol after the onset of AEFI (treatment). We have included a statement in the result section that indicates that participants used paracetamol after the onset of AEFI.

5. Discussion

Line 38: A study should be referenced after "India (57.0%)".

Response: We have revised the sentence to include the reference.

. Figure 2: The figure description could be improved. "Onset of AEFI by the various time of the day" should be changed to a more appropriate description e.g. "Onset of AEFIs by time interval after inoculation".

Response: We have changed the title of the graph as suggested.

Though I have indicated that the standard of English is acceptable for publication, a thorough revision of the manuscript for improvements to the English language should still be done since some errors in grammar (lack of pluralization, tenses), spelling (some instances of COVISHIELD, treatment) and syntax have been made throughout the manuscript. An important error which should be corrected is line 25 of the Introduction: "However, this vaccine is without adverse events." It should be "...not without adverse events".

Response: We thank you for these comments. We have revised the manuscript by carefully proofreading it to improve the English language.

Reviewer #2

Abstract

Percentages do not need to be in line 22 to 23

Response: Thank you for this comment. We have deleted the percentage as suggested.

Introduction

The second and third paragraphs should be swapped. The second paragraph becomes the third paragraph, and vice versa.

Response: We agreed with this comment and have edited it as recommended.

Method

Data collection and follow-up should be made into a flow chart and given clear explanations to make it easier for readers to understand.

Response Thank you for this comment, we have included data collection and follow-up to the flow chart as suggested.