Author’s response to reviews


Authors:
Ayesha De Costa (deay@who.int)

Version: 1 Date: 12 Oct 2019

Author’s response to reviews:

Dear Editor,

Please find attached our responses to the review comments for our protocol TRLS-D-19-00643

Kind regards,

Ayesha De Costa on behalf of the ABCD study group
11th Oct 2019

Ayesha Mariette De Costa MD, PhD
Scientist, Dept of Maternal, newborn, child and adolescent health,
World Health Organization, Geneva
deay@who.int
Tel: +41 227-911-965

Item 11d: relevant concomitant care field needs completing and ensure information in the protocol. Perhaps you could state that using the antibiotic azithromycin will not require alteration to current usual care (including use of any medication) for both trial arms.

Response: Assignment to either study drug (azithromycin or placebo) will not require alteration to current standard of care has been inserted into the text on Page 9 (lines 162-163)

Item 15: this is currently blank, please insert into the protocol information on recruitment strategy to ensure adequate participant enrolment to reach sample size. You need to state in the protocol how you will recruit and for instance the recruitment period. Where and extra measures taken to recruit sufficient number.
Response: Site specific recruitment plans were made. Each site will discuss the protocol and its implementation with medical staff, community health workers in the area and community leaders in order to increase awareness of the trial, as well as to encourage referral of eligible children to enrolling sites. This has now been included on page 10 (lines 150-153)

Item 18b: please complete and state why not applicable if that is the case and insert the information into the protocol.

Response: Participant retention will be encouraged with the frequent follow-up during days 1-3, the provision to caretakers of a study phone number for questions, and the follow-up schedule noted in Figure 2. Caretakers of enrolled children provided study staff with their home address and the closest available telephone number they could be contacted on. Attempts to trace the vital status of a participant at day 180 and enquire about hospitalizations will be made for children who deviate from protocol (miss visits). This is mentioned on page 13 (lines 242-247)

Item 20b: please complete methods for any subgroup analysis, if not please state this.

Response: Effect modification by site, age, sex, anthropometry and socioeconomic status will be explored. This is planned to be exploratory. No testing within any stratum is envisaged as there is unlikely to be adequate power to test within a stratum. This is mentioned on page 18 (lines 367-369)

Item 20c: please complete: Analysis needs completion - how will missing data be handled? How will you analyse those that are randomised to the intervention but do not adhere to the intervention? Edit the protocol and put in page number in SPIRIT checklist.

Response: The way missing outcomes will be treated in the primary ITT for each co primary has now been added (pages 17 and 18 respectively – lines 344, 356-357). A secondary per protocol approach has also been inserted on page 18 (lines 365-366)

Item 26b: Additional consent provisions for collection and use of participant data and biological specimens. E.g. state if there is additional information on the consent form requesting use of participant data they choose to withdraw from the trial. Also if the research team can share relevant data with people if relevant. Plus perhaps state that "No biological specimens will be collected".

Response: This information is stated in the consent form that was submitted with the paper. The last two paragraphs on page 2 of the consent form provide information on the samples, their storage and use. The caregiver’s right to request discontinuation of storage and destruction of samples collected from the child is in this part of the consent form. The two top paragraphs on page 3 of the consent form speak to withdrawal from the trial. This is on Page 9 (lines 178-181)

Item 30: you could state "There is no anticipated harm and compensation for trial participation" and it would be helpful to know if there will be any provision for post-trial care.

Response: The presenting diarrhoeal episode and any serious illnesses will be treated at the time of presentation. Page 15 (lines 303-304). No post trial care will be provided as this is an acute illness episode.
Item 31a: You state on line 434, page 22 "The datasets generated during the current study are available from the corresponding author on reasonable request." So please correct the checklist details.

Response: This has been edited in the SPIRIT checklist.

Item 31b: page 25 you state the author contributions please insert into checklist. You could also state "All named authors adhere to the authorship guidelines of Trials. All authors have agreed to publication."

Response: The following text has been added to page 25. ‘All named authors adhere to the authorship guidelines of Trials. All authors have agreed to publication’.

Item 33: See above 26b there will be no biological specimens collected.

Response: This has been edited in the SPIRIT guideline. As stated on page 6 (lines 86-90), stool samples and nasopharyngeal swabs are being collected.

References:
There was 1 article that could not be validated so please check references. There are also 7 articles that could not be checked, please check format for websites, include date checked and check for typos. But key is removing all references that are not essential

Response: The single reference that could bit be validated had a typographical error (no space) in one of the author names. This has been corrected.

The 7 articles that could not be checked:
2 of these are websites. The date checked are included in the reference list. We have checked again on Oct 11 2019 to confirm that these are still accessible.
A typo in a third unchecked reference has been rectified. The remaining four have been checked and they are correct.
All the references in the paper are deemed necessary.