Author’s response to reviews

Title: A randomized controlled trial of an intervention delivered by mobile phone app instant messaging to increase the acceptability of effective contraception among young people in Tajikistan

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Reviewer reports:

Additional comments from Associate Editor:

Please address the comments principally from reviewer 2.

Reviewer #1: It is a pity that the control arm was contaminated with intervention material delivered passively through the mobile app to both arms. Given that this contamination made it impossible to answer the primary research question that the trial aimed to answer, perhaps a commentary or a methods review would be a more appropriate format in which to present this study.
It would be good if there were some valid way to present the findings from the data, which do suggest an effect on attitudes toward contraception associated with mobile delivery of targeted health behavioral content. It is, however, unclear what is the value of presenting the original study in such detail, since the failure of the trial resulted from a design flaw in the trial and not from null effect, with the major takeaway as such being related to the study design (make sure there is no contamination of the control arm) and not the intervention itself.

Would it be possible to combine the data on all content that was received by both arms in the trial through the app, and use it to conduct a retrospective matched cohort study?

Alternatively, could the paper be rewritten to condense the failed trial process and outcomes into the background and introduction section of an alternative paper presenting the results of the post hoc non-random McNemar's chi squared test, reporting on the difference between baseline and endline for the whole study cohort in reported acceptability of at least one contraceptive method? In this case the takeaway could be that a mobile application appeared to be effective in changing baseline attitudes toward contraception, with no difference observed when push IM messages were added...

RESPONSE: Thank you for your suggestions. We see the contamination not as a problem that occurred in the design phase, rather a problem that occurred in implementation of the design. This was the result of the challenges related to working in a collaboration across countries and languages, in a service environment new to conducting trials and with a management set up whereby the research team did not have primary responsibility for the content of the new usual care control arm. Therefore, this was a problem with communication and trial management, from which we agree there are lessons to be learned. We anticipate publishing the lessons we have learned about making such collaborations separately, so others too can learn from what happened.

In line with best practice regarding the conduct of randomised controlled trials, we have pre-specified the methods by publishing the protocol and registering the trial on an international, publicly available registry (Clinical trials.gov). We feel that it is necessary to report the results as they are currently in the interest of transparency and in accordance with the intention-to-treat principal. We agree that a more detailed analysis on the pre-post difference would be of interest, but that this should be in addition to the trial results rather than instead of it.

Reviewer #2: General comments

This article is interesting and relevant to the burgeoning field of mobile medical and health apps. I appreciate the opportunity to review this article.

The text on page 4 lines 50-59 and page 5 lines 1-6 is key to understanding the differences between the study arms and understanding how the research question changed because of the misunderstanding between collaborators, but is not presented clearly. I did not fully comprehend these changes until the discussion section. The first paragraph of the discussion provides a clear
and concise description of the revised study objectives. The authors should consider incorporating this paragraph into the methods section.

RESPONSE: Thank you. On page 4 & 5, we have incorporated some of the wording of the first paragraph of the Discussion section into this paragraph, have separated it into two paragraphs and have signposted it by giving it the heading, ‘Contamination’ (below). Hopefully this will make it easier for the reader to understand. We have kept the details about the content included on the app, but if the editor thinks that this level of detail is not necessary, we can omit the text from the sentence beginning with, “For example, 57% of the female-married intervention messages…”.

“Contamination

Participants allocated to the intervention arm had access to the app plus the intervention instant messages. Participants allocated to the control arm had access to the app plus control instant messages about trial participation. Contrary to what was planned in the trial protocol (44), the app contained intervention content. The app was intended to contain only basic information about contraception and no behaviour change methods. This contamination occurred due to a misunderstanding between the partners collaborating in the research.

The app contraception pages included just under a third of the intervention content. Specifically, 57% of the female-married intervention messages that provide accurate information about the effective contraceptive methods and 36% of the messages that use the BCM ‘belief selection’ were included on the app. Forty-four percent of the female-married intervention content included on the app used the same words as the intervention messages (56% did not use the same words but was very similar and conveyed the same meaning). The intervention content included on the app aimed to help individuals: name the effective methods, describe how the effective methods work, list services that provide effective contraception, list the risks and benefits of the effective methods, describe how methods are used, express positive attitudes towards the effective methods and differentiate between real potential side-effects and misconceptions about the methods.”

Although the authors reference the publication of the trial protocol (citation #44), the manuscript would benefit from more details of the protocol in the methods section of the present manuscript. It is unclear whether and how the intervention messages differed according to gender and/or marital status. I initially thought the intervention was consistent across all participants in the intervention arm of the study, but line 57 on page 4 suggests otherwise (‘57% of the female-married intervention messages’). The authors present results stratified by marital status and gender, so differences, if any, in the interventions for these groups should be touched upon. If there were no differences, however, I would remove 'female-married' from page 4.

RESPONSE: In the Intervention and control section on p4, we have added more detail about the intervention messages as follows: “The messages are tailored according to marital status and gender, resulting in four sets of messages (female-married, female-not married, male-married and male-not married). Most of the messages in the four sets are the same, with minor tailoring
so that the messages are relevant to these groups. (Marital status was used as a proxy for sexual activity because the target group and TFPA considered it inappropriate to ask directly about sexual activity.)

The background section presents statistics specific to Tajik women, and the study includes a mix of men and women. Are there any statistics specific to men that can be included?

RESPONSE: The 2012 Tajikistan Demographic and Health Survey (the best resource providing data on unmet need and unintended pregnancy in Tajikistan) only interviewed women.

As the authors note, participation in the trial, not the intervention itself, could explain the observed increase in acceptability from baseline to 4 months as participants were aware that the trial involved changing attitudes towards contraception. Similarly, there is a possibility that those who enrolled in the study were systematically different than those who did not enroll. According to the consort diagram, approximately 40% of people assessed did not enroll in the study - 20% for reasons unknown/not recorded. Can the authors comment on selection bias of this nature affecting the results?

RESPONSE: We have added the following to p13 Strengths and limitations: “Thirty six percent of people assessed for eligibility (328/908) were excluded from the study. The reason for ineligibility was not recorded for 85 people, which could limit the generalizability of the trial findings. While the recording of this information was not complete, of those that are known, the majority appear to have been excluded because they either did not have an Android phone (n = 99). If those who do not own a smartphone are less likely to find at least one method of effective contraception acceptable, this could affect the generalisability of the results. Smartphone ownership is rapidly increasing however, and ownership could be an option for a greater proportion of young people across different socioeconomic communities in the near future.”

The authors discuss inclusion/exclusion criteria in the study design and participants section of the manuscript, but do not report on any of these in the Results section. The consort diagram includes this information, but it was not discussed in the text itself. According to the diagram, 85 were not eligible but the reason for ineligibility was not known. It is unclear how the reason can be unknown.

RESPONSE: Thank you for raising this. Staff promoting the study did not consistently record data on those excluded. We have added a sentence acknowledging this in the Strengths and limitations section (as above): “Thirty six percent of people assessed for eligibility (328/908) were excluded from the study. The reason for ineligibility was not recorded for 85 people, which could limit the generalizability of the trial findings. While the recording of this information was not complete, of those that are known, the majority appear to have been excluded because they either did not have an Android phone (n = 99).

We have changed the two ‘not knows’ to ‘not recorded’ in the CONSORT diagram ‘Excluded’ box.
Specific comments:

Page 4 line 28: Are instant messages the same thing as text messages? Or, did participants receive instant messages through the app itself?

RESPONSE: (p4 Study design and participants). We have changed this sentence to the following to make it clearer: “Participants must also have been willing to download a mobile phone app and receive instant messages about contraception through the app.”

Page 4 line 32: Can you specify what is meant by 'the normal care that a young person would receive if they attended a service in Tajikistan'? Does this refer to a medical service?

RESPONSE: (p4 Study design and participants), we have added ‘sexual and reproductive health service’: “All participants received usual care (the normal care that a young person would receive if they attended a sexual and reproductive health service in Tajikistan) and were free to seek any other support.”

Page 5 line 37: Did men answer the question 'The [method] insertion would not be a problem for me'?

RESPONSE: Yes, men also answer this item. However, there was a typo, it should read “…would not be a problem”. We have changed this in the text (p5 Primary outcome).

Page 6 line 2: The sentence states that the primary outcome was assessed at baseline, which is confusing as the actual primary outcome was collected 4 months after baseline. Rather, participants' baseline view of the acceptability of at least one method of effective contraception was collected after providing informed consent.

RESPONSE: We agree that this could be confusing. We have changed it to the following, (p6): “At baseline, we collected personal and demographic data and acceptability of at least one method of effective contraception (using the same scales as the primary outcome measure).”

Page 13 line 25: The authors note that a potential explanation for why they did not observe a difference between groups for the secondary outcomes is that the BCMs may have been altered when adapted by mobile phone. Can the authors provide an example of this? How were they altered when adapted? Can the authors recommend how these might be better adapted in the future?

RESPONSE: We have expanded upon this on p14 Implications of the findings: “In addition, because a large proportion of meaning comes from visual cues in face-to-face interaction (46), some of the meaning of the BCMs may have been lost when delivered by mobile phone. For example, the BCM ‘guided practice’ requires skill demonstration, enactment and individual feedback. While the intervention messages demonstrated and provided instruction, we were not able to observe the participant enacting the behavior or to provide individual feedback. This may have resulted in a loss of effectiveness of the BCM.”
Consort diagram: The reporting of randomization frequency vs. participant frequency is a bit confusing. There were 580 randomizations across 575 participants. Two participants and 7 records were excluded leaving 573 participants and 573 records. It seems like the 908 at the top of the diagram describes 908 people, not 908 records, however 908-328 (people excluded) = 580, not 573. Can you clarify this in the diagram and the text (page 7 line 50)?

RESPONSE: Thank you for pointing this out. We have changed the CONSORT diagram so that it is clearer how the duplicate randomisations were dealt with.

Table 1: 93% of the population was unmarried. The footnote to Table 1 states that not married was used as a proxy for not being sexually active. It seems that the validity of marital status as a proxy for sexual activity status would differ across cultures. For readers unfamiliar with Tajik culture, is this a reasonable assumption? Secondly, 537/573 (93%) are unmarried according to the marital status question, 495/573 (86%) of the participants are unmarried according to the current pregnancy intention question, and only 384/573 (67%) are unmarried according to the baseline method question. Can the authors please comment on the inconsistency of marital status reporting?

RESPONSE: Our local partner advised that marital status is a good proxy for sexual activity (and pragmatic as it would be unacceptable to ask about sexual activity directly) in Tajikistan.

Yes, the proportion that responded ‘not married’ to the current pregnancy intention and baseline method questions is inconsistent with the proportion that responded ‘not married’ when asked directly about their marital status. We added the following to p13 Strengths and limitations: “There were inconsistencies in participants’ self-reporting of marital status. The proportion that responded ‘not married’ to the current pregnancy intention (495/573, 86%) and the baseline method question (384/573, 67%) is lower than the proportion that responded ‘not married’ when asked directly about their marital status (537/573, 94%). We cannot say why these inconsistencies occurred. However, we can speculate that some participants who responded ‘not married’ to the marital status question were sexually active and responded to the other two questions with responses other than ‘not married’.”