Author’s response to reviews

Title: Mobile Phone Intervention for Increasing Adherence to Treatment for Type 2 Diabetes in an Urban Area of Bangladesh: Protocol for a Randomized Controlled Trial

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Version: 2

Date: August 24, 2014

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Dear Editor:

We are resubmitting a revised paper entitled "Mobile Phone Intervention for Increasing Adherence to Treatment for Type 2 Diabetes in an Urban Area of Bangladesh: Protocol for a Randomized Controlled Trial” according to the editor’s suggestion. We have followed the reviewers’ comments to adjust or correct our manuscript.

The following pages are our replies to reviewers’ comments. We have marked with red color for our any changes or adjustment in the revised manuscript.

Our manuscript has not previously been published in print or in electronic format and has not under consideration elsewhere. Besides, none of the authors has any conflict of interest in connection with this paper. We hope that you will consider our article for publication and look forward to hearing from you. Please let us know if any revisions are needed.

Sincerely yours,

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Response to reviewer's comments:

Reviewer 1: Omar F El-Gayar

Reviewer's report: The article describes a study protocol that aims to evaluate the efficacy of mobile phone intervention to the management of diabetes in Bangladesh. Overall, the protocol should provide a detailed description of the hypothesis, rationale and methodology of the study. The study design adequately tests the hypothesis. However, the details pertaining to the mobile intervention may not be enough to allow replication of the work or comparison with related analyses. The article will need provide additional details such as a list of SMS messages (space permitting), criteria for selecting messages, any personalization of the messages, e.g., matching the message to a specific patient-related event, etc. The manuscript adheres to the relevant standards for reporting and data deposition and the writing acceptable.

Minor Essential Revisions
Provide additional details such as a list of SMS messages (space permitting), criteria for selecting messages, and any personalization of the messages, e.g., matching the message to a specific patient-related event, etc.

Responses: Thank you for the valuable advice. We have now included a few examples of the SMS messages (Page-8; line-23-24, Page-9; line-1-17). We understand that personalization of SMS messages would be a better option, but due to lack of resources we sent the same messages to all participants in the intervention group. Also, this study will provide us with additional information about how the participants feel about receiving the messages which will help us to match messages in future studies.

Reviewer 2: Marcia Vervloet

Reviewer's report: This is a protocol for an interesting study, which can provide useful answers in the issue of improving adherence and control in diabetes patients in Bangladesh. A large amount of very interesting data are collected. The minimization of risk of bias is very well described in all sections. However, I do have some comments that need clarification.

Minor Essential Revisions
1. Only two hypotheses are given (for two of four objectives of the study). Maybe the authors want to think about providing hypotheses for the other two objectives as well?

Response: Thank you for the valuable suggestion. We have now included the third and forth hypotheses as follows: The third hypothesis is participants in the mobile phone SMS group will have a better quality of life than participants in the control group. The fourth hypothesis is that mobile phone SMS will be a cost-effective measure for glycaemic control (Page 5; line 20-23).

2. I would like to suggest to provide more details on the methods in the abstract, e.g. on the randomization methods, measurements and in/exclusion criteria. The background can be shortened to gain space.
Response: Thank you for your suggestions. The background section has been shortened and more details on the methods for inclusion criteria, randomization and measurements have been described (Page-2-3).

3. The randomization described in the discussion (p.16) is slightly different from what is described in the methods (p.6). In the discussion, income is also mentioned as variable. And a typo: sex and gender are synonyms.

Response: Thank you for your valuable suggestions. We have made corrections in the randomization mentioned in the discussion in line with descriptions in the methods section (Page 17; line 3-7). Also, the line 3-4 on income, sex and gender have now been removed.

4. Please clarify the abbreviation icddr,b in the data analysis section (first sentence, p.11).

Response: We have included the abbreviation of icddr,b- International Center for Diarrhoeal Diseases Research, Bangladesh. (Page -12; line-10)

**Major Compulsory Revisions**

5. The background needs more literature references as now statements are made without evidence. One example is the second sentence of the Background “More than 80% of diabetes related deaths occur in developing countries”. The authors may also want to find a more recent and fitting reference for the burden non-adherence rates pose on health systems (now a paper published in 1980(!), ref 3).

Response: Thank you for your valuable comments. We now have provided the reference for statements in the background and updated the reference with newer evidence (Page 4; line 10-13).

6. Do the authors base their power calculation on the literature? A reduction of 1% (control group) and 1.5% (intervention group) in HbA1c level with an SD of 1 is assumed. On what are these assumptions based?

Response: Thank you for point it out. We have now included the literature reference based on what we calculated our sample size (Page-7; line-2).

7. The first exclusion criterion is uncontrolled diabetes. What exactly do the authors define as ‘uncontrolled’ diabetes? And do the authors only wish to include patients who already have their diabetes under control, i.e. have a near optimal HbA1c level? In that case, the intervention is not aimed at the right patients, that is patients who need support in controlling their diabetes? The authors need to further clarify this criterion.

Response: Thank you for pointing out our mistake. We have now corrected the exclusion criteria. It now includes- patients with other types of diabetes, such as diagnosed as type-1 diabetes, gestational diabetes and those mental illness, other serious illness or co-morbidities requiring hospitalization.
8. It remains unclear what the content of the SMS can be. A total of 90 different messages were developed, with medication reminders, diabetes education, diabetes complications, diet and physical activity as topics. Maybe the authors can provide some examples. In addition, it is unclear whether patients receive all possible messages, or whether the messages will be tailored to the needs of the patients. E.g. patients forgetting to take their medication receive reminders, whereas patients not being forgetful do not receive reminders? In other words, will the SMS be send completely randomly to each patient?

Response: Thank you for your valued suggestions. In this study we did not match the SMS messages with the needs of the patients. Most of the 90 SMS were developed based on the principles of behavioural learning theory and transtheoretical model of behavioural change. All participants in the SMS intervention group received the 90 SMS randomly, once a day over the 6 months period. Some examples of the SMS have been provided (Page-8; line-23-24, Page-9; line-1-17)

9. Please provide more details about outcome variables: medical history, family history and medication history - are these extracted from medical files or self-reported by patients?

Response: We have now included the details of outcome variable measurements (Page-12; line 17-22). Medical history and family history will be obtained through a face-to-face interview using structured questionnaire. The medication use will be recorded from patient's medication book that is maintained by all registered patients. The duration of diabetes, duration of hypertension and complications will be collected from patient medical records maintained by BIHS physician, review of the patient’s file and investigations.

10. The authors may need to correct for baseline HbA1c level in their analyses of the effect of the intervention, as this can have an influence on the measured effect. When baseline HbA1c level is already near optimal in patients in the intervention group, there is little room for improvement, concealing the effect of the intervention.

Response: We have already mentioned in the data analysis section that adjustments will be made for baseline HbA1c levels in the analysis of effect of the intervention (Page-14; line-6-8).

11. In the discussion (as well as the background) it is stated that “lack of awareness and education about diabetes, its complications and optimal way to treatment” is one of the most significant barriers to effective treatment. And the second objective of the study is “Test the use of mobile phone SMS for … building awareness about diabetes and its complications”.

However, awareness and education about diabetes are not described as outcome measures: the primary outcome is change in HbA1c level, secondary outcomes are adherence, QoL and clinic attendance. When the awareness and knowledge of diabetes are such important factors, the influence of these factors on treatment adherence and treatment effect are not well investigated in this study? Or the path to effective treatment (the mechanism that the authors investigate) needs more clarification (or better explained in background and discussion): increasing awareness/knowledge leads to increased adherence, which leads to better glycemic control.
Response: Thank you for the valuable comment. We have now included knowledge about diabetes as a secondary outcome (Page-2, line-20 and page-10; line-2). We have now also included in the discussion the following point: Also, it is expected that the SMS intervention will possibly help to increase knowledge about diabetes and its complications, leading to better medication adherence which ultimately might lead to better glycaemic control. (Page-19; line-11-13).

12. In the discussion, the health literacy issue is not being well addressed, as patients may be able to read the message, but whether they also understand the message goes further than the ability to read.

Response: Thank you for raising the very important issue. We have included the following information in the methods section: However, as the literacy rate of Bangladesh has been reported to be only 62.5%, the ability to read the SMS messages were considered in the inclusion criteria which does not automatically translate into the ability to understand the contents of the SMS. To address this issue, the SMS messages were developed by a team comprising of general physicians, an endocrinologist, an epidemiologist, a nurse and an undergraduate student. After developing the SMS messages in Bengali, we sent these messages to several individuals in the pre-test stage including persons who can only read SMS and have no formal education qualifications. After receiving the feedback, we tried to make the contents of the SMS suitable for the general population. We will ensure that all our participants in the study can read the SMS messages by themselves or someone in the family who can describe the messages to them if they do not understand. At the end of the follow-up we will evaluate if they failed to understand any of the SMS.