Author’s response to reviews

Title: Trial to Incentivise Adherence for Diabetes (TRIAD): study protocol for a randomised controlled trial

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Author’s response to reviews:

Dear Professor Mader,

We are very grateful for the opportunity to revise and resubmit our manuscript. We also would like to thank the Reviewer for her careful reading and helpful suggestions on how to improve our work.

Sincerely yours,

The Authors
Reviewer 1

Overall, the article is interesting but unnecessarily long. It is also very judgemental yet fails in any way to acknowledge that the care delivered by healthcare professionals may contribute to non-adherence through lack of clarity of instructions, conflicting instructions from different HCPs, poor communication skills on both sides and low health literacy.

Response: It was certainly not our intent to appear judgemental. In our amendments presented below, we follow the more careful wording suggested by the Reviewer in efforts to correct this impression. We also address the role played by healthcare professionals in our response to Comment 8, and respond to the point regarding the length of the manuscript in our response to Comment 18.

Specific points:

Comment 1: Please replace 'patients with diabetes' to 'people with diabetes' throughout. People are people first and are only patients when they are in clinic or other medical setting.

Response: Amended as per the Reviewer’s suggestion.

Comment 2: Please replace 'poor glycaemic control' with 'sub-optimal glycaemic control' as currently worded it infers a judgement that is inappropriate.

Response: Amended as per the Reviewer’s suggestion.

Comment 3: Please replace 'uncontrolled diabetes' throughout with 'suboptimally controlled diabetes' as this infers a judgement that is inappropriate.

Response: Amended as per the Reviewer’s suggestion.

Comment 4: Please define 'normal' range.

Response: Normal range is defined as a glucose concentration between 4 to 7mmol/L. This information was already included in Table 1 and mentioned in Section “Arm 3: Outcome
Incentive” on page 10. We have clarified Section “Arm 3: Outcome Incentive” by adding the range in brackets following the first use of the term “normal range”:

[p. 10, l. 36] “Specifically, these participants will earn financial incentives for recording glucose readings within the normal range (between 4 to 7 mmols/L) before a meal on 3 non-consecutive days within the week as stated below.”

Further, we have added the glucose range in the Methods/Design sub-section of the abstract:

[Abstract] “Secondary outcomes (at Month 6) include the number of blood glucose testing days, glucose readings within normal range (between 4 to 7 mmols/L), medication-adherent days, physically-active days, and average incentives earned and time spent administrating the incentives.”

Comment 5: 'costly' to whom and in what terms? Costly in terms of financial burden of delivery of care/treatment or costly in terms of negative impact on quality of life of the individual and their families? Please clarify. If financial, please quantify as this is a subjective judgement that may mean different things to different people.

Response: We opted to refer to an estimate of direct economic burden of diabetes in terms of health care cost as this is well-documented. We have revised the manuscript as follows:

[p. 2, l. 28] “In 2014, there were 422 million adults with diabetes worldwide(1). Diabetes is associated with a host of adverse complications, including heart attacks, strokes, blindness, kidney failure and severe neuropathy that may result in amputations(2). The global direct health care cost of diabetes and its complications was estimated to exceed USD827 billion in 2014 (3,4).”

Comment 6: Please specify more clearly the participant group i.e. type 1 diabetes, type 2 diabetes, both? I assume type 2 however please clarify for the readership.

Response: The Reviewer’s assumption is right as patients on insulin are excluded. We now explicitly mention that the participant group has diabetes type 2 in the background section:

[p. 3, l. 46] “The first primary objective of this trial is to determine whether adding financial incentives to usual care can improve HbA1c levels among people with suboptimally controlled type 2 diabetes in the primary care setting.”
Comment 7: In the background (para 2), the data presented is 5 and 7 years old. Please present latest data.

Response: We double-checked carefully and the citations we present are the most recent available. Singapore being a small country, burden studies are not frequently conducted, which is why our reference is 7 years old. While it is true that there are more recent figures regarding global diabetes burden in general, the number of deaths specifically caused by higher-than-optimal blood glucose was assessed last for 2012 and reported in the 2016 WHO report on diabetes.

Comment 8: Statement: 'The effectiveness of diabetes treatment crucially depends on patient adherence'. This is partially true. It also depends on the provision of best medical advice and support from healthcare professionals. Please rephrase to reflect this.

Response: We fully agree with the Reviewer that healthcare professionals play a key role in diabetes management. We replaced the aforementioned sentence by what follows:

[p. 2, l. 45] “While treatment effectiveness crucially depends on the quality of care provided by health professionals (e.g. efficacious medications, clear and appropriate advice, relevant health education, and support), patient engagement is especially important to chronic disease management as most of the treatment takes place outside the healthcare system.”

Comment 9: Please delete 'were greatly undermined by non-adherence' as this is inappropriate.

Response: We rephrased as follows:

[p. 2, l. 52] “Regarding diabetes, all aspects of treatment (glucose monitoring, administration of medication, diet, and physical activity) were affected by non-adherence.”

Comment 10: Please rephrase 'behavioural economic theory provides an explanation for lack of adherence …' with 'behavioural economic theory may provide …'

Response: Amended as per the Reviewer’s suggestion.

Comment 11: Which survey questionnaires will be completed? Are these validated measures in English and Mandarin?

Response: We already describe the survey questionnaires in the “Data collection” section:
“Paper-based survey questionnaires will be administered at Baseline and Month 6 by the CRC. Both questionnaires include the EQ-5D-5L, BIPQ and BMQ survey instruments. The Baseline survey also includes patient socioeconomic characteristics while the Month 6 questionnaire contains questions on compliance with the medication tracker and medication purchasing habits during the intervention period.”

To clarify, we now refer to this section the first time survey questionnaires are mentioned:

“At the Baseline and Month 6 Assessments, the participants will fill out survey questionnaires (see the section on data collection below) and take HbA1c blood tests.”

Regarding measure validation, we now specify in the “Outcome measures” section which measures are validated in English and/or Mandarin. Section “Explanatory Outcomes” (pp. 11-12) now reads as follows:

- Mean change from baseline in EQ-5D(21) score at Month 6 as a measure of functional health status. This scale has been validated in people with type 2 diabetes(22). In Singapore, both the English and Mandarin versions have been validated in people with cancer(23).

- Mean change from baseline in Brief Illness Perception Questionnaire(24) (BIPQ) score at Month 6. This scale has been validated in English for multiple health conditions including diabetes(25). The Mandarin version has been validated in Taiwan in people with coronary heart disease(26).

- Mean change from baseline in Self-Monitoring of Blood Glucose(27) (SMBG) score at Month 6. This scale has been validated in English in people with type 2 diabetes but has yet to be validated in Mandarin and in Singapore.

- Mean change from baseline in general and specific scores of the Beliefs about Medication Questionnaire(28) (BMQ) at Month 6. The English version of the scale has been validated for several chronic diseases including diabetes(29) while the Mandarin version has been validated in other settings such as after mechanical heart-valve...
replacement(30) and depression(31). Validity in Singapore has not been established for this scale.

- Mean change from baseline in the exercise sub-scale of the Diabetes Self-Care Activities(32) (DSCA) at Month 6. The English version of the scale has been pretested for acceptability and comprehensibility in a study involving people with type 2 diabetes(32) but has neither been pretested in Mandarin nor in Singapore.

Comment 12: How has the financial incentive been calculated? How do these payments relate to the socio-economic status of potential participants?

Response: We first calculated the incentive amount for the Process Incentive arm and then applied the same incentive amount to the Outcome Incentive arm to control for incentive size. We added the following explanations in the “Arm 2: Process Incentive” section:

[pp. 9-10]

- “SGD3.50 weekly for blood glucose testing: measuring blood glucose on three non-consecutive days each week. This will be assessed via timestamps logged by the glucometer. For the Process Incentive arm, testing counts towards the goal even when readings fall outside the recommended range. The incentive amount approximately offsets the cost of the required glucometer strips and lancets.

- SGD0.50 daily for medication adherence: taking all medications as prescribed during the day, which will be monitored by the medication tracker. This will be assessed based on medication-taking times within specified time windows. For instance, if a participant’s specified timing is 4am to 11am (breakfast) and 5pm to 12am (dinner), a reading has to be logged within both windows for the participant to be considered adherent on that day. For the sake of simplicity, the incentive amount was set at the same level as for glucose testing.
• SGD1.00 daily for regular physical activity: taking 8,000 steps during the day as recorded by the pedometer. The incentive amount is the double of that for glucose testing and medication adherence to account for the relative difficulty of the goal to achieve.”

We also added the following explanation at the end of the “Arm 3: Outcome Incentive” section:

[p. 11, l. 7] “Note that the incentive amount was set at the same level as for the Process Incentive arm so that to control for incentive size.”

Finally note that the financial incentives are not set according to socioeconomic status. Whether lower-income participants will benefit less (for instance due to the monetary cost of adherence) or more (for instance due to the greater size of the incentive relative to their income) is an interesting research question with important policy implications. Our manuscript already notes the following at the end of the “Explanatory analysis” section:

[p. 20, l. 16] “In particular, this analysis will be used to determine the benefit incidence of the intervention according to socioeconomic factors.”

We now better highlight this fact at the end of the “Background” section:

[p. 4, l. 11] “Finally, explanatory analysis will aim at determining whether patient perception about diabetes management is altered by the interventions, uncovering factors that might moderate the effect of financial incentives, and identifying socioeconomic groups that may benefit more from the interventions.”

Comment 13: For those participants who will be using their own meter, how will you ensure accuracy of that meter?

Response: Glucose testing is recommended to all patients at SingHealth Polyclinics and the use of glucometers supported as part of usual care. The patients who already have a glucometer will continue using the model they are accustomed to while those patients without a glucometer will receive one for the trial (and beyond). In both cases, glucometer usage will be supported throughout the trial as part of usual care.

We added the following note in the “Data collection” section:
“As glucose testing is part of usual care, all patients receive support for adequate usage of their glucometer.”

Comment 14: What is a ‘fairness payment’?
Response: It is an amount paid to control group participants to compensate them for not being eligible for contingent financial incentives. To clarify, we now refer to this payment as “non-contingent payment” in Table 1. This new term is also more consistent with the presentation of our incentive scheme:

“Participants in the UC arm will not receive any financial incentives for meeting the recommended goals, but they will receive a non-contingent payment at the end of the intervention.”

Comment 15: Explanatory outcomes - why is 6 months HbA1c not included here?
Response: HbA1c at Month 6 is not listed as an explanatory outcome but as primary outcome in the “Primary outcome” subsection:

“The primary outcome is mean change from baseline in glycated haemoglobin HbA1c at Month 6.”

Comment 16: The EQ5D is not a measure of quality of life. It is a measure of functional health status and used as part of the QALY calculation. Please rephrase to accurately reflect.
Response: The Reviewer is right. We rephrased the presentation of this explanatory outcome as follows:

“Mean change from baseline in EQ-5D score at Month 6 as a measure of functional health status.”

Comment 17: How will you know that it is the financial incentive that is effective (if it works) and not the several text messages that will be sent to participants?
Response: All participants will receive the same number of text messages irrespective of study arm (see Table 2). Further, the messages are strictly identical except for the description of the financial incentive which is arm-specific (see Table 3). Consequently, any difference in outcome
between the study arms must, by design of this randomised controlled trial, be caused by the financial incentive.

We added the following explanation in the manuscript:

[p. 14, l. 15] “To avoid any bias, all participants will receive the same number of text messages and the messages will be strictly identical except for the description of the financial incentive which is arm-specific.”

Comment 18: The article is repetitive and could be shortened considerably if duplication were deleted.

Response: It is true that some trial design features might appear to have been presented multiple times. However, our primary objective while writing this manuscript was to comply with the SPIRIT Statement. We designed the various sections of the manuscript not merely to describe the features of the trial but primarily to describe how these meet the recommendations of the SPIRIT checklist (please also refer to the populated SPIRIT checklist that we submitted along with the manuscript).

Notwithstandingly, we agree with the Reviewer that unnecessary repetitions were present. After carefully reviewing the manuscript, we have removed more than 500 words without taking out critical information. The cuts we propose are the following:

[p. 6, l. 18] “Participants will be randomised to their study arm during the baseline visit upon enrollment in the study. To test whether financial incentives can improve diabetes outcomes there will be 3 study arms – the UC arm will serve as a control, and the Process Incentive and Outcome Incentive arms will complement UC with two different types of financial incentives.”

[p. 10, l. 20] “During the Months 3 and 6 visits at the polyclinic, the CRC will verify that the goals for the Process Incentive arm were achieved using the data stored on the study devices. The data will be imported to a trial application which will evaluate adherence and calculate the corresponding financial incentive earned for each device. The application will calculate the total financial incentives earned by the participants and the CRC will make the payments in supermarket vouchers.”
“During the Month 3 and 6 visits at the polyclinic, the CRC will verify that the goals for the Outcome Incentive arm were achieved using the data stored on the glucometer. As for the Process Incentive arm, adherence and incentive calculations will be performed using the trial application and the CRC will make the payments in supermarket vouchers.”

“Participants will be recruited from the SingHealth Polyclinic in Geylang through two approaches.”

“Participants in the UC arm will receive a non-contingent payment of SGD75 when they complete the study at Month 6, as they do not have the opportunity to earn contingent incentives.”

“Note that participants will have given informed consent for their data to be accessed for up to 2 years after they have completed the intervention. Study documents will be available to participants in English and Mandarin to ensure the study is open to a wide range of the patient population. The CRC will check for completeness of all study documents and questionnaires on-site and the Project Coordinator will perform checks during quarterly site visits and at the data entry point.”

“Key information from the checklists including the HbA1c readings at Baseline, Month 3 and 6, along with the participant’s diabetes medication regimen, study arm and scheduled study visits will be entered into the trial application by the CRC. The rest of the data will be digitized at Duke-NUS.”

“During the study all paper-based documents and used study devices will be stored in locked cabinets at the polyclinic and Duke-NUS. Upon study completion, the paper-based survey questionnaires and checklists will be scanned and saved in an encrypted and password protected digital format. Paper documents will be securely shredded and disposed of. The digital version of the survey questionnaires and checklists will then be stored on an external storage device which will be stored in a safe at Duke-NUS for 10 years, or 3 years after publication, whichever is later. Data will be securely destroyed once the stipulated time has passed. For audit purposes, Duke-NUS will maintain a record of the destruction.”
Comment 19: The participation oath is ridiculous. The inference that participants may be dishonest, in itself is offensive, however to suggest that by making them sign an 'oath' would have any impact is bizarre.

Response: We respectfully disagree with the Reviewer on this point. The participation oath we will administer is no more offensive than any declaration that self-reported statements are true, which is commonly encountered in real life. Such declarations can for instance be found when filing taxation, or reporting pre-existing conditions on an application form for health insurance. Furthermore, we used this oath in other studies(5,6) and never received any negative feedback from the participants. We have now added a reference to the TRIPPA trial(5) which involved 800 Singaporean employees into the manuscript to strengthen this point.

A rationale for using oaths is based on the psychological theory of self-concept maintenance(7). According to this theory, while dishonest actions provide a benefit they come at the expense of one’s honest self-concept. By increasing one’s attention to one’s moral standards and decreasing categorization malleability by clearly stating that specific actions are dishonest, oaths can theoretically reduce dishonest actions. The authors tested their theory and found that oaths reduced dishonest actions such as cheating when reporting test scores.

We would like to stress that the sole intent of the participation oath, along with other measures such as the verification of medication purchases and examination of step records, is to promote the integrity of the data collected, which we see as being a very important consideration in empirical research.

References


