Author’s response to reviews

Title: INTEGRA study protocol: Primary Care Intervention in Type 2 Diabetes Patients with Poor Glycaemic Control

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Author’s response to reviews:

Tovah Honor Aronin, Ph.D.
Editor-in-Chief
BMC Family Practice
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Dear Dr. Tovah,

We are pleased to return a revised version of the manuscript with MS Number FAMP-D-17-00014R1 entitled “INTEGRA study protocol: Primary Care Intervention in Type 2 Diabetes Patients with Poor Glycaemic Control”. We appreciate the comments provided, which enabled us to improve the quality of our manuscript. We have attached a point-by-point response to each of the comments and noted the changes made.

We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in BMC Family Practice.
Thank you for the attention to our manuscript and the interest expressed by the Reviewers. We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

Dídac Mauricio, on behalf of all co-authors

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We appreciate the input given by the Editor and the Reviewers. Below, you will find a point-by-point description of how each comment has been addressed. Original Editor’s and Reviewers’ comments are written in boldface, and responses in regular typeface. Please note that, in the revised version of the manuscript that we are submitting, changes are highlighted in yellow so that they can be easily tracked.

Editor Comments:

1. Please include a summary of the informed consent procedure in your Ethics approval and consent to participate statement in the Declarations.

As suggested by the Editor, in the revised version of the Manuscript we have added details on the written informed consent procedures as a new subsection in the Declarations statement (Page 26; lines 667-678):

“Summary of the informed consent procedure:
We used the final study protocol to prepare the patient information sheet (PIS) and the written informed consent signature form (ICF) in accordance with the current Spanish applicable legislation. The PIS included all the procedures, visits, risks and inconveniences for the participant in the study. A properly qualified site investigator provided the information to the potential study participants during a personal interview prior to the subject’s inclusion and before performing any procedures of the study. During the interview, all subjects had an adequate period of time to reflect before making the decision to participate in the study, and had the opportunity to ask any questions or concerns about the study procedures. Once they agreed to participate, each study subject signed and dated the ICF, and included information regarding the complete name of the investigator and the date of the interview. All the procedures of informed consent acquisition were adequately reflected in the patient’s clinical history.

2. Please remove figure title and legend from the figure file and list them at the end of the manuscript. Full guidelines are here: https://bmcfampract.biomedcentral.com/submission-guidelines/preparing-your-manuscript#preparing+figures

Following the Editor’s recommendation, we made the suggested changes in the manuscript.

3. If you would like to publish your additional file as supplemental information, please include a List of additional files according to the guidelines here:

https://bmcfampract.biomedcentral.com/submission-guidelines/preparing-your-manuscript#preparing+additional+files

The following additional files have been listed as supplementary information at the end of the Manuscript (Page 37):

Additional file

Additional file 1: Monitoring plan.pdf

The monitoring plan include process for monitoring activities of the study, definition of the key information concerning the realization of the study, the verification of data sources, essential documents of the study.
Márcio Flávio Moura de Araújo (Reviewer #1)

1. In the methodology item, authors have commented about pragmatic clinical trial (design), but I think in relation to intervention mixed method study.

1. We thank the Reviewer for this comment, as we agree that the INTEGRA study includes a phase 1 qualitative study and a phase 2 quantitative study, which entirely fit in a mixed method intervention study design. The pragmatic clinical trial design refers to the phase 2 quantitative study, primarily conducted because of the complex nature of our intervention. As recently reviewed (Ford and Norrie, 2016), a pragmatic trial may include multiple strategies like those implemented in our phase 2 study. These strategies can involve clinical practice training, coaching, interventions based on patients’ SMS phone messages, and may require skills and experience from different healthcare professionals (e.g., endocrinologists, psychologist, and primary health care physicians) to deliver the intervention. To clarify this point, we made changes in the sentences in the Study design section in page 8; line 231 and page 9; line 255:

“A mixed method study, (…)”

Reference:


2. I could not observe statistical test that measure homogeneity groups study base on glycated haemoglobin, for example. It important to me ensures the similarity both groups before the intervention. Based on this methodological failure, many results can be predictable since the intervention. So I suggest authors do it this time in article essay.

Thanks for bringing this to our attention. To overcome this limitation, we will conduct a comparative analysis adjusted by baseline characteristics. The Statistical Analysis Plan of the revised Manuscript has been modified accordingly to include this additional step (Pages 20-21; lines 529-534):

“Initially, baseline characteristics of all groups will be evaluated to establish homogeneity in terms of age, socio-demographic characteristics, comorbidities, laboratory parameters, concomitant medication, and diabetes complications. For this, an initial descriptive comparison of all variables between groups will be performed to evaluate whether they are balanced at baseline, and statistical significance will be assessed by the Chi-square or t-test between the groups.”
3. Authors didn't worry about cognitive evaluation from diabetic patients before data collection.

We believe that this is indeed a very good suggestion to improve the quality of our research work. Unfortunately, we cannot include this in the trial at this stage. However, this is something that we will definitely consider for future projects.

4. Put in your method item what was considered as poor glycaemic control (specific point value of glycated haemoglobin or serum blood glucose).

We thank the reviewer raising this point, as it is certainly important to clarify this in the Methods section. In the new version of the Manuscript, we added the following sentence (Study design; Page 8; lines 232-233):

“Poor glycaemic control was defined as an HbA1C value ≥ 9% in the last test performed in the 12 months prior to study inclusion”.

Reviewer #2 (Reviewer 2):

Overall, this study has already been running since 2015 and there is very little that we can do to address in terms of study design. This i feel should have been sent earlier to a journal for review since it would appear that there are some limitations into the design. Firstly, one issue I would think would be the controls, since it would appear that there are differences in practice so it would be better to have control in each practice.

Nevertheless, the study has already been long underway and thus only important issue to address now would be trying to improve the article

We thank the reviewer for this comment regarding the control group. In order to clarify this issue, we revised the manuscript and reworded the Study design section, and we have included details of the rationale for control selection (Study design, Page 9, lines 240-252):
“We designed this study considering that the Intervention group 2 will be the control group for Intervention group 1, where the specific monographic consultation is implemented. Group Intervention 1 includes the main intervention for which we will test the effectiveness to improve glycaemic control. In parallel to Intervention group 2, we decided to include an additional comparison group consisting of type 2 diabetic subjects attending Primary Care Centres (PCCs) managed by our institution in our region, with subjects selected according to the same study criteria. To select this latter group, we describe the use of the SIDIAP database, which contains anonymised electronic health records of patients attended at PCCs of the same health care districts not participating in the study.

This study is non-randomized because it would be difficult to give a different treatment to an individual in the same PCC treated by the same professional without it affecting the outcome in the standard care arm of the study.”

1. I think from the article the authors suggest that treatment intensification and inertia is important from the introduction but the methods don't portray such a message. This I think should be made clear

Following the reviewer’s suggestion, we have reworded the description of the intervention design to clarify that one of the main aims of the intervention was to reduce inertia and appropriately intensify treatment to improve glycaemic control and to reduce complications associated with type 2 diabetes mellitus. The new paragraph reads as follows (Phase 2: Interventional study; Intervention design; Page 13, lines 347-352):

“In each basic health area, two intervention groups and one control group were included. Two different interventions focused on treatment intensification, namely reducing inertia by professionals and reducing the possible barriers to treatment adherence, have been implemented, one in each intervention group. In order to reduce inertia by PC professionals, to get closer to the objectives of health control, and to allow reproducibility in the current context of PCCs, the intervention was carried out through multiple integrated strategies. (…)”

2. In addition, the MRC framework suggests that a pilot study be conducted, so this I believe is not in line with the MRC framework.”

The Reviewer is right that we did not actually follow the MRC stepwise approach and conduct a pilot or feasibility study. Our study consists of 2 phases: a 6 month phase 1 qualitative study
(already published in Berenguera et al., 2016) and a phase 2 quantitative study immediately prior to the initiation of the proposed final intervention study (phase 2). The phase 1 study contributed to the design and included additional measures, such as training sessions to health professionals of the participating centres or automated messaging to patients with reminders and motivational objectives. Thus, we did actually use a mixed method research in order to examine a complex intervention. Please note that, as a response to question #1 from Reviewer #1 (see our complete response to this point), we have modified the description of design to reflect the mixed nature of the study.

Reference: