Author’s response to reviews

Title: Effectiveness of pharmaceutical care at discharge in the emergency department: study protocol of a randomized controlled trial

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Author’s response to reviews:

Dear Editor,

We are resubmitting the manuscript entitled “Effectiveness of pharmaceutical care at discharge in the emergency department: study protocol of a randomized controlled trial” for your consideration for publication in Trials.

We appreciate the received suggestions and comments. Please, check in the next page the point-by-point response to the concerns.

Sincerely yours,

Regina Kuhmmer Notti

Reviewer’s report

Title: Effectiveness of pharmaceutical care at discharge in the emergency department: study protocol of a randomized controlled trial

Version: 4
Date: 17 September 2014
Reviewer: Johnson George

Reviewer's report: Major Compulsory Revisions

1. The title should have 'controlled' instead of 'clinical' to match the info in the text.

Answer: Thank you for the comment; we modified this part in the manuscript.

2. "Inadequate blood pressure (BP) control (systolic BP # 160 mmHg or diastolic BP # 100 mmHg)" - what is the basis for these targets? If patients have CVD risks these targets are high.

Answer: Systolic blood pressure of 160mmHg or higher or diastolic blood pressure of 100mmHg or higher represent Stage 2 hypertension according to the categories defined by the American Heart Association and by the Brazilian Cardiology Society. In our study, the inclusion criteria was the blood pressure at the emergency department triage, with a single measurement, and we judged that the use of lower cut-offs (such as 140/90) may include a larger proportion of patients with elevated blood pressure due to chance. Thank you for the comment, we agree that pharmacological care may be beneficial for patients presenting in the ER with lower blood pressure, and the use of these cut-offs are a potential limitation of our study; we will point out these concerns in the discussion of the final publication of the study.

3. How can the study be a double-blinded study? Participants will know if they received the pharmacist intervention.

Answer: Thank you for the comment. The control group received written recommendations about lifestyle modifications. We agree with your comment and, after discussion, we decided that it is not enough to be confident about the blinding of patients. We modified the manuscript, describing the study as with blinding only for outcome assessors.

4. "For the primary outcome, we will initially consider in the analysis patients with complete follow-up." - Why you are considering only patients with complete follow-up, when you have proposed doing an ITT? Can you use some imputation methods to have the complete data (e.g., use a last observation carry forward method)?

Answer: Thank you for the comment. There is a lot of discussion in the medical literature about the definition of intention to treat. What we mean by intention to treat is that participants should be analyzed according to the group allocated for, even if they did not fully adhere to the protocol or if contamination occurred. We will have only one follow-up visit, thus, we would have only the baseline data for patients without complete follow up. We think that it is not adequate to use
imputation methods for the primary outcome in this case. However, we will perform a sensitivity analysis with data imputation considering that among people with lost to follow-up only 29% would have good adherence, based on a previous study in the same population (see “data analysis”) and any discrepancy in the results will be discussed. Of note, currently we enrolled about 3/4 of the estimate sample size, with less than 10% of losses to follow-up.

5. The Discussion requires rewriting. It should be mainly about your study. It is unusual to have the hypothesis as the last sentence. This should have come up much earlier.

Answer: Unfortunately, we were not able to find any guideline about how to publish a study protocol for a Randomized Controlled Trial (RCT). The discussion sections in similar articles published in the same journal were very heterogeneous. Some authors mainly discuss the methodology of the study and its limitations – moreover, others comment mainly about the potential impact of the study, contrasting with existent data available in the literature. Thank you for your comment. We agree that we should discuss more about the study we are proposing. Please, see the modifications in the manuscript.

6. Fig 1 has no numbers. Use the CONSORT diagram for RCTs.

Answer: As this manuscript is the study protocol, we cannot use the CONSORT flow diagram, neither provide numbers in the Figure 1. We were not able to find a CONSORT statement for protocol, thus our Figure 1 was based on other articles published in the same journal. Thank you for your comment, in special for reminding us to use the CONSORT checklist and diagram in the final publication.

Minor Essential Revisions

1. Page 6 - is the aim to measure adherence or 'change in adherence’?

Answer: Thank you for the comment, our aim is to assess the adherence in the follow-up, not change in adherence. As it is a randomized trial, we expect that the adherence in the baseline will be similar among groups and we will present these data when we publish the RCT results.

2. "Behavioral variables" - what is listed here are demographic variables

Answer: Thank you, we modified this part in the manuscript.

3. Randomisation - will the authors use stratification to have a particular proportion or numbers of patients with high BP and high blood sugar levels?

Answer: No, we stratified the randomization only for the number of medications in use, as described in the methods section: “Randomization and participants allocation”.
4. "A secondary analysis will be performed with data of all patients initially randomized, considering, as the worst plausible scenario, that 29% of the losses to follow-up, in both groups, are nonadherent." - What is the source of this number? Include the reference.

Answer: The study is not published yet as article; however, it was recently presented as doctorate thesis. The study evaluated medication adherence (according to the same instrument – Morisky Green test) of 256 people with hypertension attending in primary care clinics in the same community of the present clinical trial. In this study, 34.5% (95% CI 29% to 40%) were adherent. We added the reference of the PhD thesis to the reference list.

Discretionary Revisions

1. Can 'with admission due to any cause' be deleted from the inclusion/exclusion criteria?

Answer: Thank you, we modified this part in the manuscript.

2. "Since most of outcome measures are continuous variables, for the secondary outcomes we will include only those patients who attended the follow-up visit." – I don’t get this....

Answer: We mean that we will not use any imputation methods for outcomes and losses to follow up will be treated as missing data. Of note, we expect that more than 90% of patients will have complete follow-up data.