Author’s response to reviews

Title: Feasibility of a Tapering Opioids Prescription Program for Trauma Patients at High Risk of Chronic Consumption (TOPP-Trauma): Protocol for a Pilot Randomized Controlled Trial

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Author’s response to reviews:

We would like to thank the reviewers for their in-depth analysis which, we believe, helped greatly improve the quality of this manuscript.

Reviewer # 1:

Comment 1 - The manuscript needs better clarification and justification for the study. The background/introduction needs more information on the justification for this specific study rather than the broad review of characteristics of the opioid crisis, and the broad overview of interventions. Presentation of the closely related studies using iPACT-E-Trauma would be useful given that the content is stated to be the same as TOPP-Trauma. Justification for face-to-face counseling is needed and why the iPACT-E-Trauma is not sufficient. In addition, justification for a pilot trial rather than a full randomized clinical trial should be clearly stated.

Answers:
- We now provide more information on the links between iPACT-E-Trauma and TOPP-Trauma in the introduction. We described the components of iPACT-E-Trauma and we specified that similar self-management behaviors will be taught in TOPP-Trauma, in addition to the counseling on opioid tapering. We also detailed what justified evaluating the feasibility of TOPP-Trauma and its research methods. We believe iPACT-Trauma is not sufficient considering that it was not pilot tested in patients at high risk for chronic consumption of opioids, and that the feasibility of measuring the reduction in opioid consumption was not its main objective.

- The rational for using a pilot RCT was added in the design section. Patients who are psychologically vulnerable and have a lower socio-economic status are known to be at higher risk for the chronic consumption of opioids, which may impact their willingness to be involved in counseling sessions and adhere to them over time. Hence, we believe that we need to randomize patients in an intervention (TOPP-Trauma) and a control group (educational pamphlet) to document 1) the acceptance of randomization and 2) the attrition rate in both groups at the end of the study.

- Justification for face-to-face counseling was provided at the end of the Program structure section. We could only provide counseling over the phone after hospital discharge. However, patients usually have a few follow-up appointments at the outpatient clinic. Clinicians who will carry out the intervention would need to inform treating physicians on the tapering plan during patients’ follow-up visits. Hence, we thought it would be more convenient to conduct the counseling sessions at that time.

Comment 2 - Similarly, there is confusion in presentation of the purpose of the study. The title states that the focus is on the feasibility, while the methods include section on primary and secondary outcomes, with the focus being that the primary outcome will be morphine equivalent dose. There is discussion of research methods feasibility, but limited discussion of feasibility of delivery of the intervention. How will the outcome of the study determine whether a larger-scale trial is truly feasible? Because the control group does not have counseling sessions, feasibility for variables such as session attendance cannot be compared across condition and thus need to be established a priori. Justifiable a priori levels can also be set for patient acceptability, engagement, and treatment completion. These measures can be informed by the prior studies with the same content delivery (iPACT-E). Feasibility could be established by addressing whether patient engagement is at or above the level of those prior trials or some other justifiable level.

Answers:

- We removed the primary and secondary outcomes in order to underscore the feasibility aspect of this study. Moreover, we added a table (Table 3), which provides details on criteria to
determine the feasibility of the intervention and of the research methods, as per recommended guidelines and findings from the pilot RCT on iPACT-E-Trauma.

Comment 3- If feasibility is the study focus, justification for the use of a randomized clinical trial is needed. Most evaluations of feasibility of behavioral interventions can be evaluated in a single arm trial, so additional justification is needed.

Answers: 
- As previously mentioned, the rational for using a pilot RCT was added in the design section. Patients who are psychologically vulnerable and have a lower socio-economic status are known to be at higher risk for the chronic consumption of opioids which may impact their willingness to be involved in counseling sessions and to adhere to them over time. Hence, we believe that we need to randomize patients in an intervention (TOPP-Trauma) and control group (educational pamphlet) to document the acceptance of randomization and the attrition rate in both groups at the end of the study.

Comment 4 - It is odd that patient acceptability is not evaluated as a potential indicator of study feasibility.

Answer:
- Specifications on how the acceptability will be assessed, based on feasibility assessment, were added at the end of the feasibility section.

Comment 5 -The use of a treatment-as-usual control group should be justified for the pilot RCT. The study has the potential for a clear time-and-attention bias which generally inflates the estimated effect size, particularly in a small-scale trial. Was there a rationale for not including a time-and-attention control condition?

Answers:
- We justified the use of an educational pamphlet for the control group in the intervention section. Distributing a pamphlet right before hospital discharge was selected because it reflects what is most commonly implemented in clinical practice. Furthermore, we hoped to determine if patients receiving only an educational pamphlet are more likely to drop out than patients with follow-up and to explore if education at hospital discharge is sufficient to reduce long-term consumption of this type of analgesic.
Comment 6 - Although there is general information on the assessments included, and the program broadly, there's insufficient detail on what will actually occur in the counseling sessions. How will the 15-minute sessions be structured, what content will be covered in each of them, and what will be the goal of each session? Is there a level of counseling engagement that corresponds to a sufficient dose of the intervention? How will fidelity of counseling delivery be measured. Fidelity is commonly examined in pilot studies of counseling interventions. How will you know that the counseling is being delivered competently?

Answers:

- We added details on the structure of the 15-minute counseling session in the Program content section. We also created a table (Table 1) describing the content of each teaching and counseling session.

- We added the rationale for the intervention dose in the Program structure section. In fact, the dose of the intervention (6 sessions) was determined based on interventions tested in other high-risk populations which showed positive outcomes. We therefore believe that this dose represents the level of counseling engagement required for stopping opioids or reducing them to the target maintenance dose in chronic user.

- We added details with regard to the experience of clinicians who will provide the intervention in the Program content section. Also, we specified that to ensure constancy in the intervention delivery, meetings will be held every two weeks between the PI and clinicians who will provide TOPP-Trauma (i.e., operational-skills fidelity). Furthermore, as explained in the feasibility part of the Variables and measurement tools section, a logbook detailing the components that need to be delivered will guide clinicians who will provide the intervention. Moreover, clinicians will need to document challenges when providing the interventions in order to adjust its features after the feasibility assessment. We added that according to Sidani & Braden (2011) gathering data on the intervention components provided and on challenges in the application of the intervention activities, in the selected mode, and the selected dose, allow to demonstrate the fidelity with which the intervention can be delivered in a feasibility study (i.e., content fidelity).

Comment 7 - The assessments include evaluation of opioids at community pharmacies and non-opioid analgesics but stated components of the intervention are the use of non-pharmacological strategies for pain management, health promotion strategies, and return to preferred activities. It is unclear why these are not being assessed.

Answers:

- The ability of participants to apply other pain management strategies, rather than taking opioids including returning to preferred activities, will be evaluated as part of the intervention’s
feasibility, and is described in the feasibility section. To this end, we defined intervention feasibility in the objectives, to highlight that feasibility includes the ability to deliver the intervention and of participants to complete pre-established activities, such as the implementation of recommended pain self-management strategies. Moreover, the pain interference with a variety of daily life activities will be evaluated with the Brief Pain Inventory.

Comment 8 - The sample size justification should not only focus on collecting data for effect size estimation, but also on whether there will be sufficient data to determine feasibility.

Answers:
- The section on sample size calculation was reformulated to emphasize the need to collect sufficient data to determine feasibility.

Comment 9 - The paper could use some additional editing and proofreading.

1. It is odd to see p values in a background/introduction, and unclear how they are informative given the citation to published work.

2. The subheadings do not add sufficient information to the background section.

3. There are a number of typos in the manuscript. (e.g., line 131, 343)

4. Inclusion of the number of patients in the pilot study should be provided in the last paragraph of the introduction.

5. Given that many readers may be focused on opioid use disorders, and have psychiatric backgrounds, clarification that trauma is physical traumatic injury could be helpful to differentiate from psychological traumatic injury. In the inclusion criteria, examples of traumatic injury would be useful.

Answers:
1. P values were removed as requested.

2. We reformulated the background subheadings to highlight the issue of chronic opioid consumption.

3. The manuscript was edited and proofed again by a native English-speaking medical editor.
4. We added the number of patients to be recruited in the methods section of the abstract to promptly inform readers on the sample size needed.

5. We specified, in the background and methods sections, that the study will be conducted in patients with traumatic injuries. We also provided examples of traumatic injuries in the inclusion criteria section.

Reviewer #2:

Comment 1- The introduction does not provide background on the development of the TOPP-Trauma protocol and on its relationship with the iPACT-E-Trauma protocol. It is unclear which the intervention components are and why they were chosen.

Answers:

- As mentioned when answering reviewer # 1, we provided more information on the links between iPACT-E-Trauma and TOPP-Trauma in the Background section. We described the components of iPACT-E-Trauma and we specified that similar self-management behaviors will be taught in TOPP-Trauma, in addition to the counseling on opioid tapering.

- We added details on the structure of the 15-minute counseling session in the Program content section. We also created a table (Table 1) describing the content of each teaching and counseling session.

Comment 2 -It is unclear on which phase of development the TOPP-trauma protocol is. Has it been tested in other populations? Is it in its final format or there is still room for improvements in its format that may be altered after the results of a feasibility trial?

Answers:

- We specified in the discussion section that data collected with regard to the intervention feasibility will serve to adjust its feature before conducting any further studies.

Comment 3 -Methodology is based on efficacy clinical trials. The aim of using an underpowered comparator at this point is unclear.

Answer:
- As previously explained, we removed details pertaining to an efficacy trial including the identification of primary and secondary outcomes and sample size calculation based on the estimated effect size of the main trial.