

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A Telehealth Cancer-Related Fatigue Clinic Model for Cancer Survivors: a Pilot Randomized Controlled Trial Protocol (the T-CRF Trial)
AUTHORS	Ladwa, Rahul; Pinkham, Elizabeth; Teleni, Laisa; Hanley, Brigid; Lock, Gemma; Nixon, Jodie; Agbejule, Oluwaseyifunmi; Crawford-Williams, Fiona; Jones, Lee; Pinkham, Mark; Turner, Jane; Yates, Patsy; McPhail, Steven; Aitken, Joanne; Escalante, Carmen; Hart, Nicolas; Chan, Raymond

VERSION 1 – REVIEW

REVIEWER	Craig Underhill Border Medical Oncology, MEDICAL ONCOLOGY
REVIEW RETURNED	07-Jan-2022

GENERAL COMMENTS	This is a well written protocol, aimed at addressing an important unmet need in cancer care. One minor suggestion, if it is possible to amend the protocol after this open-review process, would be to add regionality (modified Monash Criteria) to the demographics and include that in your process to ensure balance across arms. In the past it may not have been possible for regional patients to participate in the intervention arm, due to travel needs. As this study is utilising tele-health methodology, it would be ideal to demonstrate if regional residents are able to be recruited and if they benefit in the same way as metropolitan participants. I look forward to reading the results and analysis in the time ahead.
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REVIEWER	Ronaldo Elkaddoum Saint Joseph University of Beirut
REVIEW RETURNED	15-Jan-2022

GENERAL COMMENTS	<p>Dear authors,</p> <p>I have enjoyed reading the protocols of your study, entitled A Telehealth Cancer-Related Fatigue Clinic Model for Cancer Survivors: a Pilot Randomized Controlled Trial Protocol (the T-CRF Trial).</p> <p>While telehealth is nothing new, the past two years have given us a lot of lessons concerning the importance of virtual clinics. Therefore your study comes at a very interesting time to discuss this matter. Let's discuss each part of the manuscript.</p> <p>I find the title and the abstract very informative towards the content of your paper. As for the summary, I am not sure if your study is the first of its kind. This here is a link towards a clinical trial on the same subject.</p> <p>https://clinicaltrials.gov/ct2/show/NCT04525183</p> <p>Nonetheless, this does not make your study any less original or of</p>
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	<p>any less value.</p> <p>Concerning the background, I have concerns with linguistics. I think that you ought to proof read it and correct some mistakes (line 10, line 11...). Otherwise, I find this part to be a great summary of the problem of cancer related fatigue.</p> <p>P7, L27, the authors state that nurses are the biggest workforce and are the key to lead CRF clinics. However, almost all countries are struggling with the lack of nurses in their health systems. Therefore, dedicated fatigue clinics will definitely face a human resources problem.</p> <p>Methods :</p> <p>I think that the idea of parallel group as done is the most suitable. Inclusion/Exclusion criteria are well defined, especially when it concerns unnecessary burden.</p> <p>However, when it comes to recruitment, how will the research team contact patients that will be screened for eligibility ? Through a telehealth method ? Than both arms will have experienced telehealth at a certain stage.</p> <p>I find it very interesting that you have decided to stratify the patients according to their BFI score.</p> <p>Concerning the main objective of the study :</p> <p>Is it to study the feasibility of T-CRF clinics or to compare it in terms of patient satisfaction to usual care ? Please state the main objective in a more up-front way.</p> <p>As for the method, I find it very interesting, and have no further comments on its presentation, I think that it is sufficiently detailed to be replicated and is worth being published.</p> <p>Thank you</p>
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VERSION 1 – AUTHOR RESPONSE

The authorship team thank the reviewers for their feedback. Please see our point-by-point responses below.

Reviewer 1

This is a well written protocol, aimed at addressing an important unmet need in cancer care. One minor suggestion, if it is possible to amend the protocol after this open-review process, would be to add regionality (modified Monash Criteria) to the demographics and include that in your process to ensure balance across arms. In the past it may not have been possible for regional patients to participate in the intervention arm, due to travel needs. As this study is utilising tele-health methodology, it would be ideal to demonstrate if regional residents are able to be recruited and if they benefit in the same way as metropolitan participants. I look forward to reading the results and analysis in the time ahead. **Author response:** Thank you for your positive appraisal of our manuscript, and your excellent suggestion. As the trial has commenced and has progressed substantially, we are unable to add the Monash Criteria – regionality, to our demographic questionnaire. However, we have noted this in the Strengths and Limitations of the study as an item that we have not evaluated, but that we acknowledge would be very beneficial for future research in this space. (page 2, Article Summary section, point 4: *“This study is not powered to examine intervention efficacy and does not assess regionality.”*)

Reviewer 2

Dear authors, I have enjoyed reading the protocol of your study, entitled A Telehealth Cancer-Related Fatigue Clinic Model for Cancer Survivors: a Pilot Randomized Controlled Trial Protocol (the T-CRF Trial). While telehealth is nothing new, the past two years have given us a lot of lessons concerning the importance of virtual clinics. Therefore, your study comes at a very interesting time to discuss this matter. **Author response:** Thank you for your comments.

Title & Abstract

1. I find the title and the abstract very informative towards the content of your paper. As for the summary, I am not sure if your study is the first of its kind. Here is a link of a clinical trial on the same

subject. <https://clinicaltrials.gov/ct2/show/NCT04525183> Nonetheless, this does not make your study any less original or of any less value. **Author Response:** While our study is not the first to investigate the effects a telehealth intervention on fatigue in a cancer population, it is one of the first in published literature to investigate a telehealth intervention that is embedded in a community setting. We note that this statement may be contentious – so we have removed any reference of our intervention being ‘the first’ in the manuscript.

Background

2. Concerning the background, I have concerns with linguistics. I think that you ought to proof read it and correct some mistakes (line 10, line 11...). Otherwise, I find this part to be a great summary of the problem of cancer related fatigue. **Author Response:** Thank you for highlighting this. We have reviewed the Background of the manuscript with minor adjustments to improve the flow and linguistics of the information.

3. P7, L27, the authors state that nurses are the biggest workforce and are the key to lead CRF clinics. However, almost all countries are struggling with the lack of nurses in their health systems. Therefore, dedicated fatigue clinics will definitely face a human resources problem. **Author Response:** Thank you for noting this. We agree that this might be a barrier in some countries or health systems and note that CRF clinics can be facilitated in partnership with allied health professionals which will most certainly assist to overcome this barrier, depending on where this TCRF clinic model will be implemented by others in the future. We have added some wording around this to help illustrate this (page 5, Background Section, lines 18-22).

Methods:

4. I think that the idea of parallel group as done is the most suitable. Inclusion/Exclusion criteria are well defined, especially when it concerns unnecessary burden. **Author Response:** Thank you for your comment.

5. However, when it comes to recruitment, how will the research team contact patients that will be screened for eligibility? Through a telehealth method? Then both arms will have experienced telehealth at a certain stage. **Author Response:** The trial is comparing a telehealth cancer-related fatigue clinic intervention **with** usual care (usual care may often involve telehealth depending on the treating clinician and participant circumstance). It is **not** comparing the use of telehealth vs non-telehealth. Thus, the use of telecommunications/ telehealth with participants in the usual care arm has no bearing on trial outcomes.

6. I find it very interesting that you have decided to stratify the patients according to their BFI score. Thank you for this comment. We believe it will be a suitable tool to understand the severity of their cancer-related fatigue that may link to outcomes measured.

7. Concerning the main objective of the study. Is it to study the feasibility of T-CRF clinics or to compare it in terms of patient satisfaction to usual care? Please state the main objective in a more up-front way **Author Response:** The main objective of the study is to determine the feasibility of the intervention. A secondary objective is to determine preliminary clinical efficacy.

The following sentence has been added to the abstract to make this distinction clear: *“The primary objective of this pilot RCT is to determine intervention feasibility, with a secondary objective to determine preliminary clinical efficacy”* (page 2, Abstract, lines 13-15).

Several lines in the main manuscript, including *“Primary outcomes include measurements relevant to the feasibility of conducting large-scale RCT. Secondary outcomes involve measurements of preliminary clinical efficacy intended for use in the full-scale trial.”* (page 13, Outcomes section, lines 10-12) and *“Feasibility of the T-CRF trial is the primary outcome of this pilot RCT and will be assessed using the following process outcomes: recruitment and uptake, attrition, adherence, fidelity, apathy, functionality, acceptability, and satisfaction with the intervention (see Table 4).”* (page 13, Outcomes section, lines 14-16) highlight feasibility as the main objective of the study.

8. As for the method, I find it very interesting, and have no further comments on its presentation, I think that it is sufficiently detailed to be replicated and is worth being published. Thank you. **Author Response:** Thank you for taking the time review our manuscript.