Reviewer's report

Title: Predicting OptimaL cAncer Rhabllitation and Supportive care (POLARIS); Rationale and design for meta-analyses of individual patient data of randomized controlled trials evaluating the effect of exercise and psychosocial interventions on health-related quality of life in cancer survivors.

Version: 2 Date: 10 July 2013

Reviewer: Devan Kansagara

Reviewer's report:

This is a well-written manuscript detailing the study protocol for an individual patient data level meta-analysis examining the effects - and mediators of effects - of physical activity and psychosocial interventions on quality of life in patients with cancer. The study design is robust and appears well-suited to answer the important research questions posed. I have a few suggestions which may further improve the manuscript:

1) The description of moderators and mediators may be confusing for readers (page 5). As currently written, it is not entirely clear what the difference between moderators and mediators is. I think this can be easily remedied by modifying the language in these two paragraphs. For example, clarify that moderating factors are factors present at baseline that may impact responsiveness to an intervention, but are not changed by the intervention. On the other hand, mediating factors (as I understand it) are those factors that the intervention changes and, by changing these factors, impacts the outcome of interest. In your examples, then, physical activity might improve HRQoL by reducing fatigue (or by reducing psychologic distress).

2) I'm not sure I understand the difference between physical activity and exercise interventions - please clarify.

3) page 7 - inclusion criteria - how did you arrive at these exclusions? How is mindfulness different from a coping skill?

4) page 11 - statistical analysis - it seems that there might be important "clustering" effects from study to study - ie - there are similarities among patients within a given study based on site/treatment team characteristics. How do you account for these effects?

5) predictive model - will there be different models for each different intervention type? It seems that the type of model constructed would depend on the question being asked and the end user needs. For example, one might want to know given a patient with ___ characteristic (metastatic cancer or elderly), what type of intervention might work best. Or, people designing and implementing interventions might want to understand the implementation characteristics that are associated with success. It would be helpful to more clearly identify the
potential uses of such models and whether or not you will be designing different models based on intervention type.

6) page 15 - you identify lack of willingness to participate as a potential issue. Even if the results are not biased by non-participation, high rates of non-participation will threaten the ability to carry out many of the analyses you propose simply from lack of power. It would also threaten the generalizability of results. Please describe any incentives you have in place to mitigate this issue, or any plans for repeated contact etc to help decrease non-response. As the methods are currently written, it sounds like there will simply be an e-mail sent out to PIs - as we all know, it is incredibly easy to ignore e-mails and I am concerned that non-response could be a very real issue without a clear plan in place to reduce this risk.

Minor issues:
- page 8 - core data set section, first sentence - "...measured [by] such..."
- page 9, bottom - "Before transferring..." - this is redundant with bottom of page 10
- page 11 - last sentence - data confidentiality - redundant with top of page 7