Author’s response to reviews

Title: Exploring the Feasibility and Acceptability of a Mixed-Methods Pilot Randomized Controlled Trial Testing a 12-Week Physical Activity Intervention with Adolescent and Young Adult Cancer Survivors

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Pilot and Feasibility Studies Editors in Chief
Professor Gillian Lancaster, Keele University, UK
Professor Lehana Thabane, St. Joseph’s Healthcare Hamilton, Canada

Dear Professor Gillian Lancaster and Professor Lehana Thabane,

Thank you for your consideration of our manuscript entitled: “Exploring the Feasibility and Acceptability of a Mixed-Methods Pilot Randomized Controlled Trial Testing a 12-Week Physical Activity Intervention with Adolescent and Young Adult Cancer Survivors”. We are pleased that you have provided us with an opportunity to revise our manuscript.

We have made every attempt to address the comments from the reviewers as we revised our manuscript. In doing so, we have prepared point-by-point responses. Any additions or changes made in response to comments appear in green in the manuscript to help you locate the revisions we have made. We have also uploaded a clean version of the manuscript.

We hope you will agree that the additional information requested by the reviewers has improved our manuscript by ensuring it is of utmost quality in terms of content. We would like to thank you again for inviting us to revise and resubmit our manuscript to the journal of Pilot and Feasibility Studies. We hope you will consider the revised version suitable for publication.

Warm regards,

Jennifer Brunet, PhD (on behalf of both authors)
Associate Professor
School of Human Kinetics
University of Ottawa
RESPONSES TO REVIEWERS’ COMMENTS

REVIEWER 1 COMMENTS

COMMENT 1:
I would like to thank the journal for giving me the opportunity to review this paper.

RESPONSE 1:
Thank you for your review of our manuscript, feedback, and suggestions for improvement.

COMMENT 2:
The trial used two strategies to recruit participants. The first relied upon participants being referred by their healthcare provider, after giving consent to have their details passed to the researchers. The second strategy involved participants contacting the author themselves. The authors reported a recruitment rate of 100%. One issue I have with this estimate is that it doesn't appear to take into account the participants who were screened eligible by their healthcare provider, but did not give consent to be contacted by the researchers. In my opinion these participants should be considered as eligible but non-consenting, which would decrease the estimate of the recruitment rate. Another issue I have is that the second recruitment strategy is likely to lead highly motivated participants to approach the researchers, and as a result these participants were likely to consent to be in the trial. The authors themselves state that 'it is likely that highly motivated survivors consented to be contacted and subsequently enrolled in the trial'. It seems to me that if a larger RCT is to be carried out, survivors less motivated that those recruited in this study would need to be approached to participate in the main trial. It may then be the case that these survivors would be less likely to consent to participate in the trial, and would also be less likely to complete follow-up. As a result I believe the recruitment and retention rate estimates presented in this paper are unlikely to be accurate estimates of the rates that would be observed in a larger RCT, and for this paper to be published I would like to see this discussed as a major limitation of the study. This also applies to the estimates of the amount of missing data.

RESPONSE 2:
We agree with the reviewer. As with all physical activity trials, our recruitment, retention, and missing data rates likely reflect the highly motivated AYA cancer survivors who participated. We have revised our limitations section in an attempt to underscore the limitations inherent with our recruitment strategy (i.e., healthcare provider referral and self-referral). Pages 26-27 now reads:

Limitations and Considerations
Although this pilot RCT provides useful feasibility and acceptability data for researchers wishing to explore physical activity with AYA cancer survivors, there are some major and minor limitations that should be considered. With regards to the major limitations, the recruitment strategy used in the study (i.e., healthcare provider referral and self-referral) did not provide data on the number or characteristics of AYA cancer survivors who were eligible but not interested, and therefore did not consent to be contacted or self-refer. Thus, the recruitment rate presented herein likely reflects only those AYA cancer survivors who were motivated enough to contact the researchers themselves.
survivors who intended to participate, and as a result may be higher than if alternative recruitment strategies and/or tracking systems were used. Relatedly, it is possible that the retention and missing data estimates would be lower and higher, respectively, if less motivated AYA cancer survivors were recruited. Despite our efforts to identify inactive or insufficiently active AYA cancer survivors (to limit ceiling effects in a definitive RCT and to explore whether inactive/insufficiently active AYA cancer survivors could be recruited), baseline assessments showed some participants were engaging in physical activity, with one participant meeting current physical activity recommendations. Revisions to this pilot RCT’s protocol should incorporate strategies to collect data on eligible but not interested AYA cancer survivors and test targeted strategies to recruit less motivated AYA cancer survivors. At the same time, concerted efforts to recruit a more heterogeneous sample comprised of AYA cancer survivors with different types of cancer, who are younger (i.e., adolescents at time of diagnosis and study), and self-identify as male will be required in advance of a future definitive RCT to ensure generalizability.

In addressing this comment, we have also amended text in several places throughout the revised manuscript. For example, the conclusions presented within the abstract on pages 2-3 now reads:

Conclusions: The methods and intervention piloted require modification and further pilot testing in advance of a definitive RCT. Recruitment strategies identifying a greater number of younger AYA cancer survivors who have different types of cancers and who lack motivation to participate in physical activity-based studies should be explored. Refining the assessments of directly-measured physical activity behaviour and aerobic capacity and incorporating behavioural support into the intervention may improve feasibility and acceptability. This study highlights the value of doing pilot work and provides critically useful data that can be used to refine studies seeking to assess causation and optimize physical activity interventions for AYA cancer survivors.

As another example, pages 23-24 states:

The higher than anticipated recruitment and retention rates observed are promising for those seeking to deliver physical activity interventions to AYA cancer survivors. Findings re-affirm reports that some AYA cancer survivors are eager to participate in lifestyle interventions [44, 68] and want access to health promoting services during this time (i.e., &lt;5 years post-treatment; [69]) – widely considered a ‘teachable moment’ in the general cancer literature [70, 71]. However, the rates reported are associated with significant limitations (described in greater detail in the ‘Limitations and Considerations’ section) and do little to extend knowledge regarding those AYA cancer survivors who may lack motivation to participate in physical activity-based research.

COMMENT 3:
I do believe this paper can offer some useful information on the acceptability of the intervention to participants, as it appears that despite the participants being highly motivated, they still appeared to struggle to complete all of the sessions. To achieve this I think the paper needs to be rewritten as a feasibility study looking at the acceptability of the intervention, and perhaps laying the groundwork for a future pilot trial looking at whether the additional recruitment strategies the authors propose lead to adequate recruitment and retention rates.

RESPONSE 3:
We agree with the reviewer that the results from this mixed-methods pilot randomized controlled trial testing a 12-week physical activity intervention with adolescent and young adult cancer survivors offers useful information related to the acceptability of the intervention. However, we differ in opinion with regards to re-framing the study as a feasibility trial. This is because we conceived of this study and conducted it as a pilot trial. Thus, we believe it should be presented as such. Through piloting our methods and intervention, we learned important information with regards to our recruitment, measurement, and intervention strategies and hope the modifications made in response to COMMENT
1/RESPONSE 1 better clarify that each require refinement and further piloting prior to proceeding with a definitive RCT. To this end, we have tempered statements throughout our manuscript to better iterate that the findings from this pilot RCT lay the groundwork for a future pilot RCT exploring additional recruitment strategies (to see if they lead to adequate recruitment and retention rates), different measurements (i.e., accelerometers, 6-minute walk test), and modifying intervention techniques (i.e., including behaviour change techniques). For example, page 22 reads:

Modifications to recruitment strategies, trial methods, and intervention components are warranted and require additional piloting before a sufficiently powered definitive RCT can be considered.

As well, we now conclude our manuscript with the following statement on page 29:

This study provides critically useful data that can be used to inform future pilot trials seeking to establish feasibility and acceptability, with the ultimate goal of proving causation and optimizing physical activity interventions to enhance physical and psychological health for AYA cancer survivors – a population that has been underrepresented in the literature.

We hope that with these revisions the necessity of future pilot work is more transparent to readers.

COMMENT 4:
'Afterwards, participants were randomly assigned to either to the intervention group or to a wait-list control group by an independent researcher using a random number generator without an established allocation ratio.' I'm not sure how the randomisation could have been done without an allocation ratio?
RESPONSE 4:
Thank you for this comment we agree that this statement is misleading. As such, we have deleted the text: ‘…without an established allocation ratio’ and have added additional information to clarify our randomization process. Pages 8-9 now state:

Afterwards, participants were randomly assigned to either the intervention or wait-list control group by an independent researcher who used a web-based random number generator. Participants…

The reviewer may be interested to know that we used the random number generator found at: www.graphpad.com/quickcalcs/index.cfm. This random number generator first assigns each subject to a group non-randomly. Then the assignment of each subject is swapped with the group assignment of a randomly chosen subject. This entire process is repeated twice and a list with the subject numbers and group assignment is provided. Assigning random numbers this way has been deemed appropriate for studies with a small number of subjects (see Suresh, 2011. An overview of randomization techniques: an unbiased assessment of outcome in clinical research). Of note, the process of generating random assignment was done in groups of 5 and the lists were saved by an independent researcher who only revealed group allocation to the first author after participants had worn the accelerometer for 7 consecutive days. These two aspects (i.e., an unpredictable allocation sequence and allocation concealment) are particularly important to prevent correct anticipation of future assignments by those involved with the trial (Hecksteden et al., 2018. How to construct, conduct and analyze an exercise training study? and Moher et al., 2010. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials).

COMMENT 5:
'most had been diagnosed with breast cancer (n=7), and 50% reported managing at least one other physical or…'. It would be useful if when giving the number diagnosed with breast cancer you also gave the percentage, and when stating the number managing at least one other health condition you gave the number of participants.
RESPONSE 5:
This information has been added as requested. Page 15 now reads:

On average, participants were diagnosed with cancer at 29.64 (SD=7.73) years of age and most had received a diagnosis of breast cancer (n=7; 44%). Others had received a diagnosis of ovarian cancer (n=2; 13%), rhabdomyosarcoma (n=1; 6%), biphasic peritoneal mesothelioma (n=1; 6%), gastric cancer (n=1; 6%), osteosarcoma (n=1; 6%), soft tissue sarcoma (n=1; 6%), colorectal cancer (n=1; 6%), and Hodgkin’s lymphoma (n=1; 6%). Half of the sample (n=8; 50%) reported managing at least one other physical or psychological health condition (e.g., asthma, neurofibromatosis, blood clots, hypothyroidism, anxiety, depression).

COMMENT 6:
'On average, participants were 32.84 years', I think the word old needs to be added after years.
RESPONSE 6:
The word 'old' has been added as requested. Page 15 now reads:
At the time of the study, participants were 32.84 (SD=7.93) years old and had completed treatment for cancer 2.23 (SD=1.15) years prior…

REVIEWER 2 COMMENTS

COMMENT 1:
Thank you to the authors for a well written article. I think the trial is reported acceptably, but more work is needed to motivate and reflect on the limitations for future trials etc.
RESPONSE 1:
Thank you for your review of our manuscript, positive feedback, points of reflection, and detailed suggestions for improvement.

COMMENT 2:
Addressing age: I find it very surprising that adolescents (from 15) and young adults (up to 39!) are included as one group - I would have considered them quite different groups. I don't think I will be the only reader to think this, so I think the authors need to defend/motivate why this group can be treated as one (homogenous?) group. Also, make clear /early/ what the age range includes (add to abstract and early in the background).
RESPONSE 2:
Thank you for this comment. First, we would like to acknowledge that defining and describing AYA cancer survivors is a source of discussion in the literature (e.g., https://www.ncbi.nlm.nih.gov/pubmed/26812562). In this manuscript, we have chosen to use the term ‘AYA cancer survivor’ as experts in the field have advocated for AYA to be defined as those individuals diagnosed with cancer between the ages of 15 to 39 years (see Bleyer et al. 2017. Cancer in Adolescents and Young Adults, 2nd Edition). To clarify our definition for readers, we have added this information to our abstract, which now states:
Background: Adolescent and young adult (AYA) cancer survivors (i.e., individuals diagnosed with cancer between 15-39 years and completed treatment; [1]) may benefit from physical activity…

As well, we have added a paragraph to our background to better define and describe this population. Page 4 now reads:
Adolescent and young adult (AYA) cancer survivors (i.e., individuals diagnosed with cancer between the ages of 15-39 years who have completed treatment; [1]) face a range of negative physical (e.g., body composition changes, disfigurement, tissue damage, morbidity, premature mortality) and
psychological effects (e.g., reduced self-esteem, lowered quality of life, anxiety; [2-4]). Though these adverse effects are reported regardless of age at diagnosis, researchers have found AYA cancer survivors experience a greater symptom burden than their older counterparts diagnosed with similar cancers [5-7]. This is due, in part, to the transitional period AYA cancer survivors are in when diagnosed that necessitates managing cancer and its effects while navigating critical developmental milestones (e.g., moving from childhood to adulthood physically, psychologically, socially, financially, and educationally; [8]). Given AYA cancer survivors’ age at diagnosis and the subsequent number of life-years affected by cancer-related sequelae, minimizing the negative impact for this population while promoting longevity has been identified as a priority [9, 10]. Despite this, few interventions that have the potential to promote length and quality of life have been developed, implemented, and evaluated with AYA cancer survivors.

COMMENT 3:
Given the nature of the pilot work, I would like to see more detail about the types of cancer involved - not just about the number of breast cancer survivors. Please list the other types of cancers.
RESPONSE 3:
A table has been added that provides details on each unique participant. The revised table includes information on the diagnoses for each participant (see page 16). As well, we have expanded on the other types diagnosed within the body of the text. Page 15 now reads:

On average, participants were diagnosed with cancer at 29.64 (SD=7.73) years of age and most had received a diagnosis of breast cancer (n=7; 44%). Others had received a diagnosis of ovarian cancer (n=2; 13%), rhabdomyosarcoma (n=1; 6%), biphasic peritoneal mesothelioma (n=1; 6%), gastric cancer (n=1; 6%), osteosarcoma (n=1; 6%), soft tissue sarcoma (n=1; 6%), colorectal cancer (n=1; 6%), and Hodgkin’s lymphoma (n=1; 6%).

COMMENT 4:
Given the small numbers, and my comments about age above, I would like more details on the age of participants recruited. Given only 16 participants, could you just report the individual ages? How many were adolescent? How many in the 20s? Etc.
RESPONSE 4:
As per COMMENT/RESPONSE 3 above, we have added a table providing details for each unique participant. The revised table contains information related to the age, age at diagnosis, etc. of each participant (see page 16).

COMMENT 5:
Linked with my previous points: I would like more reflection on the participants recruited: they are predominantly female and seem to be in the older end of AYA. How does this impact on the researchers’ findings? I don't know the literature, but do men and women engage with physical activity differently? I suspect they do. Does this differ by cancer type? Are there some cancers that more directly impact on ability to be active? Do some cancer that impact self-esteem more directly (eg breast cancer?)? The recruited sample is small, so the strength of conclusions need to be moderated, but I think more reflection is justified (perhaps less detail on missing data).
RESPONSE 5:
Thank you for this comment. First, the reviewer may be interested in knowing that our sample ranged in age from 15 to 37 years at time of diagnosis, consistent with the way in which we are defining AYA cancer survivors. However, we also recognize the point that the reviewer is making in terms of the skew of our participants towards the upper limit of our age range. Second, we agree that the overrepresentation of females could be problematic, especially when looking forward to a definitive RCT. Thus, we have added statements to our limitations section. For example, page 13 now reads:
Further, using recruitment strategies beyond those used herein may increase the number of AYA cancer survivors referred or who self-refer and ensure greater diversity (e.g., younger AYA cancer survivors, different types of cancers).

We have also added the following statement on page 27: At the same time, concerted efforts to recruit a more heterogeneous sample comprised of AYA cancer survivors with different types of cancer, who are younger (i.e., adolescents at time of diagnosis and study), and self-identify as male will be required in advance of a future definitive RCT to ensure generalizability.

We have also made several minor edits throughout our discussion in an attempt to temper our conclusions. That said, we have elected to keep the details regarding missing data as we feel it is important information.

COMMENT 6:
If you go to a multi-site trial you are going to need substantial funding. I would be surprised by any grant funding panel approving such funding with no long term follow-up (I'd have thought at minimum outcomes at 6 months, or, more ideally, one year). Will your controls be willing to wait this long? Your trial only provides evidence on a waiting list control of 12 weeks - this is an unknown that your trial does not address. I would like this point to be explored in the limitations. Can you point to other successful trials in this area where a long waiting list control has been successful?
RESPONSE 6:
With regards to the first point, we agree that long-term follow-up is important when exploring the feasibility and acceptability of physical activity interventions and agree that our lack of follow-up is a limitation. With regards to the second point, this two-arm, mixed-methods pilot RCT was conducted to inform a future definitive RCT that would test the effects of a 12-week physical activity intervention on a range of physical and psychological outcomes and explore potential mediators and moderators (to determine the processes underlying any beneficial effects). To achieve these aims, we do not feel it is necessary to ask the wait-list control group participants to wait for 6-12 months. This is based on the ‘overwhelming’ amount of research evidence showing the benefits of physical activity for cancer patients and survivors (see Santa Mina et al. 2018. Connecting people with cancer to physical activity and exercise programs: a pathway to create accessibility and engagement) and due to the fact that cancer-specific exercise guidelines have been released (see Schmitz et al., 2010. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors). We believe that adding long-term follow-up measures could be more appropriate to explore physical activity maintenance and factors that may be implicated in long-term behaviour change following the intervention period (for both intervention group and wait-list control group participants). A statement to this effect has been added to page 28, which now reads:
As well, the feasibility and acceptability of including follow-up assessments remains unknown. To better prepare for a fundable definitive RCT and enable examination of physical activity behaviour change maintenance, piloting follow-up assessments will be necessary.

COMMENT 7:
Data analysis: Is the mean and SD appropriate for all variables? None are skew? If some are skew, it would be more appropriate to report them as median and interquartile range etc. I would like some consideration of this. Also, as per item 17 in the CONSORT checklist: I am unclear why this item is marked as "not applicable" - please explain. Also, why can 95% CIs not be reported?
RESPONSE 7:
Thank you for this comment. With regards to the first portion of the comment, only self-reported and
directly-assessed physical activity behaviour (for full sample and intervention group) were non-normally distributed. As such, we have reported the median and and interquartile range for these variables. The reviewer may be interested to know that we defined non-normal distribution as less than -2 or greater than +2 (see acceptable cut-offs for normal univariate distribution; George & Mallery, 2010. SPSS: a simple guide and reference; Fields, 2013. Discovering statistics using IBM SPSS statistics). All other variables were normally distributed and were within -1 and +1 for skewness and kurtosis. We have revised Table 3 to include medians and interquartile ranges (where appropriate) and 95% confidence intervals for all variables.

We have also amended the data analysis section to reflect this change. Page 14 now reads: We conducted quantitative and qualitative analyses. Descriptive statistics consisted of frequencies, means and standard deviations [SD], and 95% confidence intervals for normally distributed data, whereas medians, interquartile ranges, and 95% confidence intervals were computed for non-normally distributed data. All descriptive statistics were estimated using IBM SPSS (Version 25; [60]).

With regards to the second portion of this comment referring to the CONSORT checklist, we did not provide estimates of change pre- to post-intervention. The numbers reported in Table 3 are scores at baseline only. However, we recognize the value of including 95% confidence intervals alongside these estimates. As per our response above, we have included 95% confidence intervals in Table 3 and have updated the CONSORT checklist accordingly.

COMMENT 8: L404: Here, or in the discussion - I wanted to know how the intervention proposed in refs 51 and 52 compared to the intervention of this study - how does this study's intervention contribute to and fit in with other literature?
RESPONSE 8: The other interventions conducted with AYA cancer survivors were distance based, using either Facebook (Valle et al., 2013) or telephone counselling (Rabin et al., 2016). To our knowledge, this is the first pilot RCT designed to assess the effects of a face-to-face physical activity intervention on physical and psychological outcomes with AYA cancer survivors. This information has been added where the literature is referenced. Page 22 now states: Though recruitment, retention, and missing data rates were better than targets set a priori and superior to other trials testing distance-based physical activity interventions (e.g., telephone counselling, Facebook; [47, 48]), the number of AYA cancer survivors referred/self-referred and participants’…

COMMENT 9: L467-470: Point about BCTs: I have sat on funding panels which have rejected applications due to insufficient consideration of behavioural change - this point deserves much stronger emphasis.
RESPONSE 9: Thank you for this comment. We agree with the importance of BCTs and focus heavily on them within our own research program. We have amended the text in this section to emphasize the importance of BCTs. Pages 25-26 now reads:
BCTs are the “observable, replicable, and irreducible component” of interventions designed to increase physical activity behaviour [77]. Trials including BCTs have reported greater adherence and behaviour change compared to those that do not [78-80]. Given the critical role BCTs can play in promoting physical activity [81], examining the feasibility and acceptability of integrating BCTs into physical activity interventions for AYA cancer survivors is warranted.
COMMENT 10:
L557-558: I think the authors need to revisit their funding statement assertion. How was this work funded? While perhaps not getting explicit funding in particular for this project, L561 notes that the first author "received donations" and L571 notes that the first author was supported by a "Vanier Canada Graduate scholarship" - I would expect such information to be given in the funding section. In short, I do not believe "Not applicable" is appropriate for CONSORT item 25.
RESPONSE 10:
As requested, we have amended CONSORT item 25.

COMMENT 11:
While accepting I am suggesting a fair amount of new material - if space permits - I think it would be useful to reflect on the health economic/resource implications of your intervention. Could a future trial benefit from an economic evaluation? Is it practical/feasible to deliver a tailored program to each cancer survivor? I'd suggest a future trial explores the economic implications.
RESPONSE 11:
We very much agree with the importance of considering the health economic/resource implications of this intervention and think that a future trial would certainly benefit from an economic evaluation. We have integrated text discussing this on page 26:
Considering current resource constraints (e.g., personnel, infrastructure) and limited funding available, such approaches may also lower costs needed to translate successful models into care. Moving forward, refining, piloting and testing different study designs (e.g., preference-based trials) and triaged approaches with AYA cancer survivors could answer important research questions, ultimately ensuring this population receives individualized interventions and care. If these and other changes are made, cost description analyses for participants (i.e., time, costs) and researchers (e.g., personnel time and costs, materials/equipment) will be necessary to inform future trials and scalability initiatives.

COMMENT 12:
L76-79: I feel there is a strong need here to define terms of "adolescent" and "young adult"
RESPONSE 12:
As per COMMENT/RESPONSE 2, we have defined and described adolescent and young adult cancer survivors in the abstract and background to our manuscript. Specifically, our abstract now states:
Background: Adolescent and young adult (AYA) cancer survivors (i.e., individuals diagnosed with cancer between 15-39 years and completed treatment) may benefit from physical activity…
As well, the opening paragraph of the background section of our revised manuscript now reads:
Adolescent and young adult (AYA) cancer survivors (i.e., individuals diagnosed with cancer between the ages of 15-39 years who have completed treatment; [1]) face a range of negative physical (e.g., body composition changes, disfigurement, tissue damage, morbidity, premature mortality) and psychological effects (e.g., reduced self-esteem, lowered quality of life, anxiety; [2-4]). Though these adverse effects are reported regardless of age at diagnosis, researchers have found AYA cancer survivors experience a greater symptom burden than their older counterparts diagnosed with similar cancers [5-7]. This is due, in part, to the transitional period AYA cancer survivors are in when diagnosed that necessitates managing cancer and its effects while navigating critical developmental milestones (e.g., moving from childhood to adulthood physically, psychologically, socially, financially, and educationally; [8]). Given AYA cancer survivors’ age at diagnosis and the subsequent number of life-years affected by cancer-related sequelae, minimizing the negative impact for this population while promoting longevity has been identified as a priority [9, 10]. Despite this, few interventions that have the potential to promote length and quality of life have been developed, implemented, and evaluated with AYA cancer survivors.
COMMENT 13:
L82-99: "Need for a trial": I find it odd that little literature is referenced in this section in the Background. I particularly wanted some evidence/justification about the lack of RCTs in this area (L85-86)
RESPONSE 13:
References have been added as appropriate throughout this section.

COMMENT 14:
RESPONSE 14:
The first author screened all potential participants to ensure they were able to safely participate in physical activity. To do this, a series of ‘physical activity readiness questions’ were administered:
1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?
2. Do you feel pain in your chest when you do physical activity?
3. In the past month, have you had chest pain when you were not doing physical activity?
4. Do you lose your balance because of dizziness or do you ever lose consciousness?
5. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity pattern?
6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
7. Do you know of any other reason why you should not do physical activity?
If a potential participant answered ‘yes’ to any of the ‘physical activity readiness questions’ their healthcare provider was required to complete a Physical Activity Readiness Medical Examination Form (PARmed-X).

A footnote to describe this has been added on page 8:
bDetermined based on potential participants’ responses to a series of physical activity readiness screening questions. If a participant’s responses to screening questions indicated cause for concern, they were required to obtain medical clearance from their healthcare provider using the Physical Activity Readiness Medical Examination Form (PARmed-X) prior to participating in the study.

COMMENT 15:
L176: Relating to my point with respect to age above: what were the ages of the AYA cancer survivors?
RESPONSE 15:
Thank you for this comment. We did not formally collect data on the ages of the AYA cancer survivor advisory board members. However, at the time of collecting feedback (May 2016), each AYA cancer survivor confirmed they met the eligibility criteria as outlined on page 8. A statement to this effect has been added on page 9:
This was augmented by eliciting opinions from an advisory board comprised of three AYA cancer survivors (who met the eligibility criteria outlined above), three allied healthcare providers (n=1 Kinesiologist; n=2 Certified Exercise Physiologists), and two oncologists.

Though we agree with the reviewer that including information relating to basic personal (e.g., age, sex) and medical factors (e.g., cancer diagnosis) would be beneficial, we are choosing not to do so. This is because two of the three advisory board members experienced relapses and passed away shortly after participating in this project and we do not feel it appropriate to contact their family members/significant others to obtain this information. We hope the reviewer will respect and understand our decision.
COMMENT 16:
L255-261: Somewhere - here or in the results etc - please indicate the "direction" of the scales eg do higher esteem scores indicate higher esteem? Needed for psychological outcomes where the "orientation" is not so clear.
RESPONSE 16:
As requested, information related to the direction of the scales has been added. Page 13 now reads: Across all surveys used to assess psychological outcomes, higher scores reflect more positive outcomes.

COMMENT 17:
L274: It is appropriate that a formal size calculation is not completed/calculated, given hypothesis testing is not appropriate in the pilot/feasibility study context; however, can any justification be given for the recruited/approached sample size? Why only 30?
RESPONSE 17:
Thank you for this comment. With regards to the latter portion, we recruited AYA cancer survivors across a 12-month period. This was because we wanted to see how many would be referred and eligible within this time frame. This information is contained on page 8:
AYA cancer survivors were recruited across a 12-month period starting in September 2017 through healthcare provider referral (wherein eligible AYA cancer survivors were first screened and then approached by their healthcare provider to obtain consent for the first author to contact) and snowball sampling (wherein potentially eligible AYA cancer survivors self-screened and then contacted the first author). A 12-month period was specified a priori so as to capture seasonal variation that may affect trial and intervention feasibility and/or acceptability, and thus better inform the timeline for a definitive RCT.

There was no reason that 31 participants were referred/self-referred; rather, this was simply the number who were referred/self-referred over the 12-month period.

COMMENT 18:
L292-293: Are there no norms for a more comparable age group? Seems odd to compare/place in context with over 60 year olds.
RESPONSE 18:
The reviewer is correct, there are no normative scores available for a more comparable age group. Normative data on this test are only available for older adult populations. Though other types of sit to stand tests are available (e.g., 5-repetition sit-to-stand test) and other tools exist by which to assess muscular strength and endurance (e.g., squat test), we chose the 30-second sit to stand test for two main reasons. First, the 30-second sit to stand test is a common assessment tool within both the pediatric and adult oncology and physical activity literature. Some examples are listed: Capozzi et al., 2016 (https://www.ncbi.nlm.nih.gov/pubmed/26828426), Eden et al., 2017 (https://www.ncbi.nlm.nih.gov/pubmed/29068767), Thorsteinsson et al., 2017 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5530132/#SP1), Nielsen et al., 2018 (https://www.ncbi.nlm.nih.gov/pubmed/29741279).
By including this assessment over others, the results from the future definitive RCT could enable researchers to compare AYA cancer survivors to their older and younger counterparts. Second, the 30-second sit to stand test is a cost-effective and implementable measure of lower body muscular strength and endurance. This is because it uses minimal equipment, has simple instructions, does not require extensive tester training, and can be performed in any setting (e.g., participants homes). Considering the pragmatic nature of this trial, we felt it was an ideal choice. This was only bolstered with literature showing that scores on the 30-second sit to stand test are reliable, valid, and highly correlated with
other exercise capacity tests (e.g., Bohannon 2012. Measurement of sit-to-stand among older adults; Ozalevli et al. 2007. Comparison of the sit-to-stand test with 6 min walk test in patients with chronic obstructive pulmonary disease). Further, it is used and endorsed by healthcare governing bodies such as the Canadian Society for Exercise Physiology and the Centres for Disease Control.

COMMENT 19:
L294: What is "normal' range"?
RESPONSE 19:
Normal blood pressure range was defined as systolic (mmHg) less than 120 and diastolic (mmHg) less than 80, which is recognized by the American Heart Association. This information as been added on page 17:
Blood pressure was considered normal (i.e., systolic less than 120 mmHg and diastolic less than 80 mmHg) for most participants (n=10; 63%)

COMMENT 20:
L315-371: There is a lot of switching between percentages of different denominators in this section (participants v. eligible v. sessions etc). I think it would be helpful for the reader and clearer to have the numbers relating to the percentages in parenthesis - eg: "100% (16/16)" etc.
RESPONSE 20:
Thank you for this comment. We have added numbers as requested throughout the section describing quantitative results. Page 20 now reads:

Adherence to physical activity program [intervention group only]. During weeks 1-6, a total of 12 supervised strength sessions were provided. Participants’ adherence to these supervised strength sessions varied from 58% (7/12 sessions) to 92% (11/12 sessions) with an average adherence rate of 82% (mean=9.83 [SD=1.60]/12 sessions). Five of six participants adhered to ≥75%, or ≥9 of the 12 sessions. Across all participants, 13 sessions were cancelled due to travel for holidays (n=5), illness (n=6), and work/appointment conflicts (n=2); however, in seven of these instances participants still completed strength sessions on their own unsupervised. During weeks 7-12, participants were instructed to participate in two unsupervised strength sessions per week to total 12 unsupervised strength sessions. Adherence to the unsupervised strength sessions ranged from 50% (6/12 sessions) to 92% (11/12 sessions) with an average adherence rate of 69% (mean=8.33 [SD=1.97]/12 sessions). Three of six participants adhered to ≥75%, or ≥9 of the 12 sessions. Most sessions during weeks 7-12 were missed due to being too busy, tired, or ‘lazy’ (n=21); one session was missed due to illness. Throughout weeks 1-12, participants were instructed to participate in two unsupervised aerobic sessions per week to total 24 unsupervised aerobic sessions. Adherence to the unsupervised aerobic sessions ranged from 54% (13/24 sessions) to 88% (21/24 sessions) with an average adherence rate of 76% (mean=18.17 [SD=2.93]/24 sessions). Four of six participants adhered to ≥75%, or ≥18 of the 24 sessions. The main reasons unsupervised aerobic sessions were missed were being too busy or tired (n=23), illness (n=7), work conflicts (n=2), holidays (n=2), and an unrelated injury (n=1).

COMMENT 21:
L327: Can more detail be given about ineligibility? What was the most common reason for people to be ineligible? Could this be relaxed going forward, to make the intervention more applicable?
RESPONSE 21:
Reasons for exclusion are provided in Figure 1 on page 19. The most common reasons for ineligibility was time since treatment (i.e., being &gt; 5 years post-treatment; n=5) and treatment status (i.e., being on-treatment; n=4). No further details regarding ineligibility were collected.
COMMENT 22:
L351: For ease of reference, give the total number of sessions somewhere around here.
RESPONSE 22:
As per COMMENT 20/RESPONSE 20, this section has been revised as requested.

COMMENT 23:
L363: 29% of what? Might be clearer with my suggested change above.
RESPONSE 23:
Thank you for this comment. We can see how this percentage could be difficult to interpret in isolation. We have made several revisions to the section on missing data:
Missing data. There were no missing data on self-reported physical activity behaviour and psychological outcomes for study completers (n=15). For physical tests, participants completed all measures of body composition, musculoskeletal strength, muscular endurance, and resting blood pressure. However, there were missing data for aerobic capacity and directly-measured physical activity behaviour (as assessed using accelerometers). With regards to the former, there were 21 instances of missing aerobic capacity data (out of a possible 45 data points) as six participants could not complete the test at all three time-points due to high blood pressure (a skipping criteria for this assessment stipulated by the study protocol; n=18) and three participants elected to not complete the test of aerobic capacity at a single time-point due to weather (n=2)c or feeling unwell (n=1). With regards to the latter, there were 13 instances of missing accelerometer data (out of a possible 45 data points) due to insufficient wear time (i.e., &lt; 3 days of valid wear time; n=8), accelerometer dysfunction (n=1), and participant error (e.g., wearing the accelerometer incorrectly; n=4). Combined, there were &lt;10% missing quantitative data across all three time-points for the 15 participants who completed the study. All study completers (n=15) participated in both qualitative interviews.

COMMENT 24:
L413-414: Why should there be corroboration? Explicitly say what is sought to be overcome through this.
RESPONSE 24:
Lines 413-414 originally stated: Further, results suggest fostering collaborations, working across sites, and using multiple and varied sources of recruitment are necessary to increase the number of AYA cancer survivors referred, approached, and enrolled...We and others (e.g., Kremer et al., 2012 [https://www.ncbi.nlm.nih.gov/pubmed/23281199]) believe that collaboration is important to reduce duplication of effort, optimize use of expertise, and enhance research opportunities. Further, collaborations can facilitate knowledge transfer, enable the pooling of data across sites, and eventually promote multi-site trials. When conducting research with small, underserved, and under-researched populations, such as AYA cancer survivors, collaboration is a vital way to advance knowledge through adequately powered studies. We have added a statement to clarify this for readers. Page 23 now reads:
Moving forward, researchers interested in this line of work may wish to collaborate and conduct multi-site trials to increase sample sizes, ultimately ensuring adequately powered studies.

COMMENT 25:
L80: Replace "that" with "whether"
RESPONSE 25:
This statement was deleted in response to other modifications requested.

COMMENT 26:
L83-84: I would like the language softened here around the value of non-RCT evidence: there is a suggestion that RCT provide the /only/ definitive/useful evidence - other evidence sources have their
place and should not be completely disregarded.
RESPONSE 26:
Thank you for this comment. We agree with the reviewer regarding the value of other types of evidence. As requested, we have softened the language around the value of non-RCT evidence and have made several revisions to the introduction in terms of language and order of content. For example, pages 6-7 now state:
The Continuum of Evidence
Though a definitive randomized controlled trial (RCT) is warranted to address questions of causation and elucidate mechanisms, it is not indicated at this time [32]. This is because there is a lack of research exploring the effects of physical activity interventions delivered in-person (i.e., face-to-face) to AYA cancer survivors. As a result, markers of feasibility (e.g., recruitment, retention, adherence) and acceptability (e.g., satisfaction with trial methods and intervention components) remain unknown. Moreover, there is little information regarding recruitment, retention, and adherence metrics for physical activity research in this population. Collecting this information is vital to conserve valuable research resources and enhance the likelihood of successful definitive RCTs [32, 33]. Following from the continuum of evidence put forth by Campbell et al. [32], a pilot RCT is the necessary next step towards examining if and how physical activity improves physical and psychological outcomes among AYA cancer survivors.

We have also softened the way in which we speak about the limitations of the research that has been conducted to date. Pages 4-5 now read:
Physical Activity for AYA Cancer Survivors
There is considerable evidence from experimental studies showing that participation in physical activity yields numerous physical and psychological health benefits for adult cancer survivors [11-13]. Commonly reported benefits include improved muscular strength and endurance, aerobic capacity, physical functioning, mood, self-esteem, and quality of life [11-13]. As such, many researchers have begun to explore the role of physical activity for AYA cancer survivors. Early evidence suggests physical activity is associated with a range of physical and psychological benefits, similar to those reported among older adult cancer survivors [14, 15]. Notwithstanding the contributions from these studies, the collective body of research has limitations. Specifically, researchers have typically assessed a narrow range of outcomes with homogenous samples and have primarily used cross-sectional study designs grounded in the positivist paradigm [16]. There is a need for research that incorporates a range of physical and psychological outcomes, adopts longitudinal or intervention study designs, and utilizes different paradigms (e.g., interpretivist; [17-19]). As well, potential mediators and moderators of the relationship between physical activity and physical and psychological outcomes remain unexplored, which prevents an understanding of how physical activity might be beneficial and under what circumstances desired outcomes may be maximized in this population.

COMMENT 27:
L169: Drop the decimal places relating to the costs of the gift card.
RESPONSE 27:
The decimal places relating to the costs of the gift card have been dropped as suggested.

COMMENT 28:
L224: What was the relevant literature? I would like to see some justification for these figures.
RESPONSE 28:
The relevant literature that informed our a priori targets for each feasibility outcome included studies conducted with AYA cancer survivors and older adult cancer survivors. Specifically, referral, recruitment, and missing data rates were informed by studies conducted with AYA cancer survivors on
the topic of physical activity and from our work conducting ongoing physical activity trials with this population. We also drew upon our own clinical experience and that of our collaborators to better understand estimates of the number of AYA cancer survivors seen by healthcare providers in the long-term follow-up clinics at the hospitals in Ottawa. The retention and intervention adherence rate estimates were selected based upon other intervention work conducted with AYA and older adult cancer survivors. For example, the reviewer may be interested to know that adherence rates for on-site supervised programs for cancer survivors generally range from 77% (Campbell et al., 2005 [https://www.ncbi.nlm.nih.gov/pubmed/15774341]) to 98% (Courneya et al., 2003 [https://www.ncbi.nlm.nih.gov/pubmed/12721239]); however, for home-based programs, adherence rates have ranged from 76% (Courneya et al., 2004 [https://www.ncbi.nlm.nih.gov/pubmed/15386794]) to 94% (Matthews et al., 2007 [https://www.ncbi.nlm.nih.gov/pubmed/17001492]). These findings have been summarized in a recent systematic review of factors influencing adherence for older adult cancer survivors (Ormel et al., 2018 [https://www.ncbi.nlm.nih.gov/pubmed/29247584]). As such, we have cited this source in our revised manuscript. As well, research collating evidence on adherence to lifestyle behaviour interventions delivered via technology among AYA cancer survivors (Kopp et al., 2016. [https://www.ncbi.nlm.nih.gov/pubmed/27468131]) was also used to inform our estimates. Being mindful of word count, we have not elaborated on this literature within the manuscript, however, citations have been added and interested readers may read the manuscripts referenced should they be interested. Page 12 now reads:

As recommended for pilot studies [46, 33], a priori targets for each feasibility outcome were set using relevant literature [47-50] and the authors’ own clinical experience…

COMMENT 29:
L270-272: Will the findings be published? Some indication for the reader would be useful.
RESPONSE 29:
The findings will be published and this information has been added to the text. Page 14 now states:

Data pertaining to perceived changes in EXSEM variables are not reported herein, but will be published in forthcoming work, as they are outside of the scope of the present study, which was to assess the feasibility and acceptability of our methods and intervention.

COMMENT 30:
L285: While appreciating the desire to maintain consistency, I think readability would be improved by reporting age to the nearer integer (keep the decimal points etc for the Table)
RESPONSE 30:
We have chosen to maintain consistency and have therefore reported age to the nearest hundredth.

COMMENT 31:
L295: "due to significant difference in the walking track measured" - I can't parse this. Are some words missing, or is the word order slightly wrong? I think this could also do with spelling out.
RESPONSE 31:
Thank you for this comment. There were no words missing in this statement, though we see how this may have been a difficult statement to interpret. Essentially, there is evidence to suggest that different testing conditions (i.e., different lengths of the walking track) can result in significant differences in scores that are not attributable to differing performance, but are merely a function of the different testing conditions (see Scivoletto et al., 2011). It is recommended that the walking track be standardized to ensure accurate estimates. We have revised this section in an attempt to clarify this for the reader. Page 17 states:

Aerobic capacity scores (i.e., 6MWT) were not computed due to the differences in the lengths of the walking track across participants, which can artificially increase/decrease participant scores [63].
As well, page 24 now reads:
Further, the distance of the walking track could not be standardized at any time-points across participants due to the location of assessments (e.g., home, apartment hallway). Discrepancies in length can artificially increase/decrease scores on this assessment [63]; thus, 6MWT data for those who could complete the assessment were not reported herein. In the future, researchers and practitioners may wish to omit this assessment or conduct it within a research/healthcare centre to ensure appropriate monitoring, supervision, and standardization.

COMMENT 32:
L412: "population specific barriers" - an example would be good for non-cancer experts etc
RESPONSE 32:
As requested examples have been provided. Page 23 reads:
…population-specific barriers to participating in trials (e.g., geographic mobility, small numbers; [66])
….

COMMENT 33:
L420: For clarity: perhaps insert "only" between "typically" and "provide"
RESPONSE 33:
This modification has been made. Page 23 reads:
Partnering with organizations that typically only include AYA cancer survivors in their network and using Internet and social networking are other low-/no-cost options [67].

COMMENT 34:
L424: Insert "in" between "participate" and "lifestyle"
RESPONSE 34:
This modification has been made as requested on page 23:
Findings re-affirm reports that some AYA cancer survivors are eager to participate in lifestyle interventions [44, 68] and want access to health promoting services during this time (i.e., <5 years post-treatment; [69]) – widely considered a ‘teachable moment’ in the general cancer literature [70, 71].

COMMENT 35:
L439: "not cleared" - language sounds odd to me - reword?
RESPONSE 35:
We have modified this statement. Page 24 now reads:
In terms of lessons learned with regards to assessment selection, there were missing data on the objective assessment of aerobic capacity. Specifically, the 6MWT (without appropriate monitoring and the supervision of a certified exercise physiologist) was contraindicated due to high blood pressure for six participants during at least one of their assessments, and there were three instances wherein participants chose not to complete an assessment.

COMMENT 36:
L440: Substitute "a" with "any"?
RESPONSE 36:
As above, this section was modified. Thus, this statement was removed entirely. Page 24 now reads:
In terms of lessons learned with regards to assessment selection, there were missing data on the objective assessment of aerobic capacity. Specifically, the 6MWT (without appropriate monitoring and the supervision of a certified exercise physiologist) was contraindicated due to high blood pressure for six participants during at least one of their assessments, and there were three instances wherein participants chose not to complete an assessment.
REVIEWER 3 COMMENTS

COMMENT 1:
This is a great piece of research and you have drawn lots of conclusions from your pilot study already of how to improve upon these processes for the (future planned) main RCT study. I look forward to reading your follow up work.

RESPONSE 1:
Thank you for your review of our manuscript.