PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Effect of wheelchair-modified rowing exercise on cardiometabolic risk factors in spinal cord injured wheelchair users – Protocol for a randomized controlled trial
AUTHORS	Hansen, Rasmus; Samani, Afshin; Laessoe, Uffe; Handberg, Aase; Larsen, Ryan

VERSION 1 – REVIEW

REVIEWER	Christof Leicht Loughborough University United Kingdom
REVIEW RETURNED	04-Jun-2020

GENERAL COMMENTS	General feedback This is a manuscript describing the protocol design of an exercise intervention in spinal cord injury. The intervention is clearly described, and a very strong scientific foundation is presented to justify the approach taken. Please see some comments below, I hope you will find them useful. - Stratification. I would suggest that SCI level should be included in the stratification process - cardiovascular risk is heavily influenced by this (to be honest, most factors you propose to measure are). If possible, it may be good to consider some measure of body composition (e.g. BMI) in the stratification process. It would also be good to balance physical activity levels between groups. - Intervention duration. What about a half-way (6-week) assessment period? If participants drop out anytime between weeks 6 and 12 then at least you'd have a 6 week point to analyse. - Exclusion criteria relating to physical activity (PA). This criterion is too loose in my view. If a participant's normal regular exercise is 150 min per week, the proposed intervention would add significantly less than this on top (only 90 min in total!). The danger is that these well-trained participants then simply reduce their habitual PA, meaning that the intervention will not have an effect as their total PA would not change. I would suggest to reduce this criterion to ~60 min. - Exercise test. If breath by breath analysis are available, I would recommend to analyse ventilatory thresholds, which are expected to be more sensitive to the training intervention than peak

	measures. Also, I was wondering why the exercise test is done in the arm cranking modality given this is a rowing intervention? You'd certainly find better improvements in a rowing exercise test. - Physical activity monitoring. I would recommend to monitor physical activity throughout the study (not only in the weeks leading up to the tests). Wearing accelerometers throughout is hardly an option, but what about a training diary throughout study? - Autonomic nervous system function. Based on what software / analysis / procedure? You are implying that this is an outcome measure sensitive to your training intervention - is there any evidence for this? The sit-up tilt test may give better understanding of autonomic function, and is just as easy to administer. check: Med Sci Sports Exerc. 2013 Feb;45(2):261-7. doi: 10.1249/MSS.0b013e31826f5099. - The instructions given to me by BMJ open indicate that I should check whether the dates of the study have been included. I don't think they are. Specific comments Abstract - Line 101: no example for "inflammatory" markers is given – you may consider this Introduction - Line 153: the mobility "of"… - Line 166: "traditional": indicate what these are, to make them distinctive from vascular measures introduced later - Line 172: able-bodied "individuals"… - Line 186: "earlier": make clearer what is meant with this. "2011" guidelines? - Line 189: "Recent": again, make distinction between guidelines clearer! - Line 195: "effects" Methods - Line 270: is a drop out in the exercise group not more likely? so better to have a 16/14 split? - Line 325: for glucose, insulin etc. it would be advisable to have a testing session after an overnight fast (as you say later on line 336) - Line 343: "months" - Line 352: "lowest values": what if values differ substantially? any maximum deviation you'd accept (e.g., 5%) for which you'd decide to take a third measure? - Line 402: "represents" Reference 23 – check author name

REVIEWER	Chelsea Pelletier University of Northern British Columbia, Canada
REVIEW RETURNED	12-Aug-2020

GENERAL COMMENTS	Thank you for the opportunity to review this important study to evaluate 12-weeks of adapted rowing on cardiometabolic risk factors in individuals with SCI. The evidence on the impacts of exercise training on cardiometabolic health for people with SCI is limited and I believe this project will make a strong contribution to the knowledge base. Conducting RCTs with this population is challenging so I commend the authors on a well-designed study and clear considerations for exercise training among people with SCI. Comments: 1. Consider the language used throughout the manuscript and switching to person-first language. For example, SCI individuals would be individuals with SCI 2. The introduction includes a statement that “Interventions on body composition are generally lacking (page 6, line 161).” This statement is quite vague - are you referring to muscle mass, fat mass, bone mass? What kind of exercise interventions? Since body composition is an outcome of your project, further discussion is warranted here, particularly links between muscle mass and visceral adiposity. 3. I suggest some additional information and considerations are provided on cardiovascular risk factors and fitness and how they differ between people with paraplegia or tetraplegia. The term ‘wheelchair users’ is commonly used in the introduction, but no definition is provided. I would also note that not everyone with an SCI uses a wheelchair for mobility. This is also relevant to the paragraph describing adapted rowing in the introduction. 4. Inclusion criteria. How will the sparing of arm function be determined? Will all individuals with an injury above C5 be excluded? Are there any inclusion or exclusion criteria based on level or completeness of injury? Since there are different cardiovascular consequences of paraplegia and tetraplegia, how will you account for this in the study design and outcomes? My recommendation would be to clarify the level and completeness of injury for inclusion/exclusion and consider splitting groups based on level or completeness of injury for analysis (although I realize this will depend on recruitment). 5. The intervention will be terminated after 12 weeks, even if participants have missed sessions. Is there a % adherence rate where you would exclude a participant from analysis? 6. The only limitation stated is the lack of control of food intake. I would suggest expanding on why this is expected to be a limitation and how you may minimize the impact.

VERSION 1 – AUTHOR RESPONSE

Reviewers' Comments to Author:

Reviewer: 1
Reviewer Name: Christof Leicht
Institution and Country: Loughborough University, United Kingdom Please state any competing interests or state ‘None declared’: none declared

General feedback

This is a manuscript describing the protocol design of an exercise intervention in spinal cord injury. The intervention is clearly described, and a very strong scientific foundation is presented to justify the approach taken. Please see some comments below, I hope you will find them useful.
Response: Thank you for your insightful comments that have improved our manuscript.

- Stratification. I would suggest that SCI level should be included in the stratification process - cardiovascular risk is heavily influenced by this (to be honest, most factors you propose to measure are). If possible, it may be good to consider some measure of body composition (e.g. BMI) in the stratification process. It would also be good to balance physical activity levels between groups.
Response: Thank you for the considerations related to the stratification process. We agree that SCI level influences the proposed outcome measures, and possibly also the exercise response. We also agree with the reviewer that it would be good to balance the groups based on BMI and physical activity level.
However, a relatively small sample size complicates stratification of several participant characteristics, a challenge common to studies within this field (e.g. (1)). That is, adding more participant characteristics to the stratification process will increase the predictability of the allocation, thereby potentially violating the aim of maintaining randomness to the allocation process (2). Accordingly and consistent with the reviewer's suggestion, we have added SCI level and physical activity level (line 259), and maintained age (but not gender) as factors in the stratification process.

References:
(1) Totosy de Zepetnek, J. O., Pelletier, C. A., Hicks, A. L. & MacDonald, M. J. Following the Physical Activity Guidelines for Adults With Spinal Cord Injury for 16 Weeks Does Not Improve Vascular Health: A Randomized Controlled Trial. *Arch. Phys. Med. Rehabil.* **96**, 1566–1575 (2015)

(2) Saghaei, M. An Overview of Randomization and Minimization Programs for Randomized Clinical Trials J Med Signals Sens. 2011 Jan-Apr; 1(1): 55–61.

- Intervention duration. What about a half-way (6-week) assessment period? If participants drop out anytime between weeks 6 and 12 then at least you'd have a 6 week point to analyse.
Response: Thanks for the suggestion. We have now included a half-way (6-week) measurement to the design (lines 102, 262, 379, 528, 573, 583).

- Exclusion criteria relating to physical activity (PA). This criterion is too loose in my view. If a participant's normal regular exercise is 150 min per week, the proposed intervention would add significantly less than this on top (only 90 min in total!). The danger is that these well-trained participants then simply reduce their habitual PA, meaning that the intervention will not have an effect as their total PA would not change. I would suggest to reduce this criterion to ~60 min.
Response: Thank you for raising an important consideration. While the current guidelines (2018) recommend 90 min of regular exercise per week, there may very well be beneficial effects of physical activity beyond these recommendations. Therefore, we now set the inclusion criteria to <90 min per week (line 280), and include physical activity level in the stratification process (as described earlier). In addition, using <90 min per week (compared with <60 min per week) as criterion will increase the number of eligible individuals for the study. This is relevant considering the relative low number of estimated SCI individuals in Denmark (3), and that the intervention will be conducted in a restricted part of Denmark (Northern region), limiting the number of eligible participants.

References:
(3) Regionshuset, Viborg . *[Spinal cord injury treatment and rehabilitation in West Denmark. Investigation of the future organization of the paraplegic function and its professional connection to Aarhus University Hospital]*. Regionmidtjylland; 2010. 65p.

- Exercise test. If breath by breath analysis are available, I would recommend to analyse ventilatory thresholds, which are expected to be more sensitive to the training intervention than peak measures. Also, I was wondering why the exercise test is done in the arm cranking modality given this is a rowing intervention? You'd certainly find better improvements in a rowing exercise test.
Response: Thanks for the suggestion. Based on the reviewer's suggestion, we have now included analyses of ventilatory thresholds (line 477, 494-504).

The reviewer raises a good point about the modality choice for the VO_{2peak} test. In fact, our group has discussed the choice of modality extensively. Indeed, there are pros and cons for both choices. Considering the type of intervention (rowing), we agree that an exercise test performed on the rowing ergometer would result in greater improvement in $VO_{2\ peak}$. This greater improvement in VO_{2peak}, however, would likely be influenced by a neuromuscular "learning effect", and thus reflect not only improved cardiorespiratory capacity but also familiarization to the rowing ergometer. By performing the exercise test on an arm-ergometer, both groups will experience the same degree of familiarity to the ergometer throughout all test sessions, which will allow us to evaluate changes in cardiorespiratory capacity specifically, and minimize the influence of a learning effect.
In addition, using the arm ergometer will allow us to control and standardize power output during the tests, which would be much more difficult on the rowing ergometer. Therefore, we maintain the assessment of cardiorespiratory capacity and ventilatory thresholds using the arm-crank exercise test.

- Physical activity monitoring. I would recommend to monitor physical activity throughout the study (not only in the weeks leading up to the tests). Wearing accelerometers throughout is hardly an option, but what about a training diary throughout study?
Response: Thanks for the suggestion. We agree with the reviewer that it is relevant to monitor physical activity throughout the intervention and not only during the weeks leading up to the tests. Based on the reviewer's suggestion, we have added The Leisure Time Physical Activity Questionnaire for People with Spinal Cord Injury (LTPAQ-SCI) to the protocol. In brief, the LTPAQ-SCI provides a valid and reliable self-reported measure of leisure time physical activity (LTPA), assessing minutes of mild, moderate, and heavy intensity LTPA performed over the previous 7 days (4). Compared to the PARA-SCI (which assesses the previous 3-days), the LTPA-SCI only takes 5-min to complete and can be self-administered instead of requiring a trained interviewer. To accommodate the reviewer's suggestion about implementing a training log, we therefore include the LTPA-SCI. Specifically, participants will be asked to complete the questionnaire once every week throughout the study period (i.e. 12 assessments for each participant) and again before 6 months follow up. This addition will allow us to monitor LTPA throughout the study. Description of self-reported LTPA has been added to the manuscript (lines 248, 265, 527, 529-538).
The individual calibration of accelerometer output via daily activity tasks and concurrent measurements of oxygen consumption has proven difficult to implement in this study. Therefore, we have removed the assessment of physical activity level via accelerometry.

References:
(4) Martin Ginis KA, Phang SH, Latimer AE, Arbour-Nicitopoulos KP. Reliability and validity tests of the
Leisure Time Physical Activity Questionnaire for People with Spinal Cord Injury. Arch Phys Med Rehabil 2012;93: 677-82.

- Autonomic nervous system function. Based on what software / analysis / procedure? You are implying that this is an outcome measure sensitive to your training intervention - is there any evidence for this? The sit-up tilt test may give better understanding of autonomic function, and is just as easy to administer. check: Med Sci Sports Exerc. 2013 Feb;45(2):261-7. doi: 10.1249/MSS.0b013e31826f5099.
Response: Autonomic regulation of heart rate can be evaluated through analysis of resting heart rate variability (HRV), a measure that is responsive to exercise training in able-bodied individuals (5). Yet, as the reviewer correctly indicates, no previous studies have investigated changes in HRV in response to exercise training in individuals with SCI. Therefore, we will investigate the effects of exercise on HRV as an explorative aim. We have now explicitly stated that HRV will be assessed as an exploratory aim, and provided a rationale for this approach (line 409-417).
For HRV measurements, participants will be equipped with a 4-lead surface electrodes on their chest and have their electrocardiogram (ECG) recorded (LabScribe v4, iWorx, Dover, NH, US) during 5 min of quiet rest. Data will be exported to dedicated software (Kubios HRV Standard 3.2.0; Kuopio, Finland) for analyses of frequency-domain parameters (low frequency power, high frequency power and total power) and time-domain parameters (HR and the root mean square of successive RR interval differences) in accordance with guidelines from The European Society of Cardiology and Heart Rhythm Society (6,7). We have now added this information to the manuscript (line 420-425).

We thank the reviewer for suggesting the sit-up tilt test and we appreciate the insight this kind of orthostatic challenge can provide into autonomic nervous system function. Accordingly, we have now included a sit-up test to the protocol (line 418, 425-432). Participants will be equipped with a finger plethysmograph (Finometer, Finapres Medical Systems BV, Enschede, the Nederlands) for continuous and non-invasive measurement of arterial blood pressure and heart rate during a 10 min orthostatic challenge (sit-up test) (8). Briefly, after 10-15 min of supine rest, participants will be moved (i.e. without assistance from the participant) to an upright seating position with their legs hanging free of the bed at an angle of 90°. Change in systolic and diastolic blood pressures will be calculated as the difference between mean seated and supine blood pressures (9). Orthostatic hypotension will be defined as a ≥20 mm Hg drop in systolic blood pressure or a ≥10 mm Hg drop in diastolic blood pressure when moving to an upright position (10).

References:
(5) Bellenger, CR., Fuller, JT, Thomson, RL., et al. Monitoring Athletic Training Status Through Autonomic Heart Rate Regulation: A Systematic Review and Meta-Analysis Sports Med (2016) 46:1461–1486.

(6) Malik, M. *et al.* (1996) 'Heart rate variability. Standards of measurement, physiological interpretation, and clinical use', *European Heart Journal*. Narnia, pp. 354–381

(7) Shaffer, F. and Ginsberg, J. P. (2017) 'An Overview of Heart Rate Variability Metrics and Norms', *Frontiers in Public Health*. Frontiers Media SA, 5

(8) West, CR., Romer, LM., Krassioukov, A. Autonomic Function and Exercise Performance in Elite Athletes with Cervical Spinal Cord Injury. Med Sci Sports Exerc. 2013 Feb;45(2):261-7

(9) Pelletier et al. Aerobic Capacity, Orthostatic Tolerance, and Exercise Perceptions at Discharge from Inpatient Spinal Cord Injury Rehabilitation. *Arch. Phys. Med. Rehabil.* **94**, 2013-9 (2013).

(10) Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American
Autonomic Society and the American Academy of Neurology. *Clinical Autonomic Research* 6, 125-126 (1996)

- The instructions given to me by BMJ open indicate that I should check whether the dates of the study have been included. I don't think they are.

Response: Thanks. We have now added the key dates of the study to the manuscript (line 12-13, line 109, 255, 286, 633-634).

Specific comments

Abstract

- Line 101: no example for "inflammatory" markers is given – you may consider this

Response: Thank you for your suggestion. We have now added C-reactive protein as an example of an inflammatory marker (line 103-104).

Introduction

- Line 153: the mobility "of"…

Response: Thank you. We have now added 'of' to the sentence (line 169).

- Line 166: "traditional": indicate what these are, to make them distinctive from vascular measures introduced later

Response: Examples of such traditional risk factors have now been added (line 187).

- Line 172: able-bodied "individuals"…

Response: Thank you. We have now added 'individuals' to the sentence (line 194).

- Line 186: "earlier": make clearer what is meant with this. "2011" guidelines?

Response: Thank you for suggesting this clarification. Correct, we are referring to the 2011 guidelines. We have now added 2011 to the sentence (line 209).

- Line 189: "Recent": again, make distinction between guidelines clearer!

Response: Thanks. We have revised, as suggested (line 212).

- Line 195: "effects"

Response: Thank you. We have now changed 'effect' to 'effects' (line 218).

Methods

- Line 270: is a drop out in the exercise group not more likely? so better to have a 16/14 split?

Response: Thank you for your suggestion. We are aware that some training studies conducted in individuals with SCI have shown greater drop out in the exercise group compared to the control group (e.g. (11)): However, contrary to this observation, other studies (e.g. (1)) have shown the opposite, i.e. a larger drop out in the control group. Therefore, we maintain the equal allocation number (15/15), as originally proposed (line 298-299).

References:

(1) Totosy de Zepetnek, J. O., Pelletier, C. A., Hicks, A. L. & MacDonald, M. J. Following the Physical Activity Guidelines for Adults With Spinal Cord Injury for 16 Weeks Does Not Improve Vascular Health: A Randomized Controlled Trial. *Arch. Phys. Med. Rehabil.* **96**, 1566–1575 (2015).

(11) Nightingale, T. E., Walhin, J. P., Thompson, D. & Bilzon, J. L. J. Impact of Exercise on Cardiometabolic Component Risks in Spinal Cord-injured Humans. *Med. Sci. Sports Exerc.* **49**, 2469–2477 (2017).

- Line 325: for glucose, insulin etc. it would be advisable to have a testing session after an overnight fast (as you say later on line 336)

Response: We agree with the reviewer that blood samples should be obtained after an overnight fast. This procedure (fasting blood samples) is described in the paragraph 'blood collection procedure' (line 373). The line the reviewer is referring to (line 325 – now line 362) refers to the testing session at the university laboratory, where no blood samples are collected. To avoid confusion, we have now explicitly stated that the blood measurements occur on a separate day (line 373).

- Line 343: "months"

Response: Thank you. We have now changed 'month' to 'months' (line 380).

- Line 352: "lowest values": what if values differ substantially? any maximum deviation you'd accept (e.g., 5%) for which you'd decide to take a third measure?

Response: Thank you for the suggestion. Based on the reviewer's suggestion, we have now added a sentence about a maximum acceptable deviation, for which a third measurement will be performed (line 390-391).

- Line 402: "represents"

Response: Thank you. We have now changed 'represent' to 'represents' (line 460).

Reference 23 – check author name

Response: Thank you. We have now corrected the author name (line 748).

Reviewer: 2

Reviewer Name: Chelsea Pelletier

Institution and Country: University of Northern British Columbia, Canada Please state any competing interests or state 'None declared': None declared

Thank you for the opportunity to review this important study to evaluate 12-weeks of adapted rowing on cardiometabolic risk factors in individuals with SCI. The evidence on the impacts of exercise training on cardiometabolic health for people with SCI is limited and I believe this project will make a strong contribution to the knowledge base. Conducting RCTs with this population is challenging so I commend the authors on a well-designed study and clear considerations for exercise training among people with SCI.

Response: Thank you for your praise of our study, and for the insightful comments that have improved our manuscript.

Comments:

1. Consider the language used throughout the manuscript and switching to person-first language. For example, SCI individuals would be individuals with SCI

Response: Thank you. We have now revised the manuscript, as suggested.

2. The introduction includes a statement that "Interventions on body composition are generally lacking (page 6, line 161)." This statement is quite vague - are you referring to muscle mass, fat

mass, bone mass? What kind of exercise interventions? Since body composition is an outcome of your project, further discussion is warranted here, particularly links between muscle mass and visceral adiposity.
Response: As suggested by the reviewer, we have now provided more information with respect to description of body composition. In addition, we have now expanded the discussion of body composition as an outcome measure by including discussion of changes in (visceral) adipose tissue ((line 178-183).
We have also emphasized that we refer to upper-body aerobic exercise interventions (line 181).

3. I suggest some additional information and considerations are provided on cardiovascular risk factors and fitness and how they differ between people with paraplegia or tetraplegia. The term 'wheelchair users' is commonly used in the introduction, but no definition is provided. I would also note that not everyone with an SCI uses a wheelchair for mobility. This is also relevant to the paragraph describing adapted rowing in the introduction.
Response: Thank you. Considerations on fitness and cardiovascular risk and differences between individuals with paraplegia and tetraplegia have now been added to the manuscript (line 153-161, 409-413). Also see the original text (lines 598-610 and 624-626).
We have now defined 'manual wheelchair users' as those wheelchair users with sufficient strength and movement control in their arms allowing them to use a manual wheelchair (i.e. a wheelchair that can be propelled by the user) for mobility (12) (line 162-164). As suggested by the reviewer, we have also added a note clarifying that not everyone with an SCI uses a manual wheelchair for mobility (line 220-221, 238).

References:
(12) SCIRE Community, *Manual Wheelchairs*. *Practitioner* (2020).
www.scireproject.com/community/topic/manual-wheelchairs/

4. Inclusion criteria. How will the sparing of arm function be determined? Will all individuals with an injury above C5 be excluded? Are there any inclusion or exclusion criteria based on level or completeness of injury? Since there are different cardiovascular consequences of paraplegia and tetraplegia, how will you account for this in the study design and outcomes? My recommendation would be to clarify the level and completeness of injury for inclusion/exclusion and consider splitting groups based on level or completeness of injury for analysis (although I realize this will depend on recruitment).
Response: Thank you for the comments. Although manual muscle testing could be a solution to determine arm muscle functioning (13), we choose to determine the sparing of arm functioning using a pragmatic approach. Firstly, volunteers will be asked if they possess sufficient arm functioning to perform an upper-body rowing motion. Secondly, volunteers will be asked to practice the rowing exercise on the ergometer during the first laboratory visit. If a volunteer is unable to perform the exercise due to insufficient arm functioning (as determined by the first author of this study), this individual will be excluded for participation in the study (line 274-276).
In order to perform voluntary upper-body rowing, at least partial innervation of the elbow flexor muscles (biceps, brachialis) are required (13): We have made this point clearer by adding 'flexor' to the sentence (line 270, 605). Therefore, as already mentioned on line 270-271, individuals with a complete SCI at or above C5 will not be included in the study. In contrast, due to the large variation that can be observed in motor function in response to an incomplete SCI (13), it may be possible for some individuals with incomplete SCI above C5 to perform the pull motion during rowing, whereas for others this may not be possible. We therefore choose not to exclude individuals based on an isolated neurological lesion level or completeness.
We agree with the reviewer that there are different cardiovascular consequences of paraplegia and tetraplegia, which could influence the proposed outcome measures, and possibly also the exercise response. As the reviewer suggests, we have therefore now included lesion level in the stratification process, so that the groups will be balanced on this characteristic (line 259). As described (line 271-274), participants will be asked to provide a copy of their medical records to confirm SCI level and American Spinal Injury Association Impairment Scale (AIS) classification. This classification will provide the basis for the SCI level stratification.

References:
(13) Kirshblum, S. C. *et al.* International standards for neurological classification of spinal cord injury (Revised 2011). *J. Spinal Cord Med.* **34**, 535–546 (2011).

5. The intervention will be terminated after 12 weeks, even if participants have missed sessions. Is there a % adherence rate where you would exclude a participant from analysis?
Response: As a starting point, we will use an adherence rate threshold of 75%, as proposed in a similar study (14). Notably, there are no previous reports of adherence rates with this type of exercise intervention (12 weeks of wheelchair-modified rowing) in individuals with SCI. Therefore, if some participants show low (<75%) adherence rates, we intend to do a sensitivity analysis in order to determine how sensitive the exercise responses are to reaching (≥75%) or not reaching (< 75%) the *a priori* set adherence rate. If adherence rate influences the exercise response, we will consider to include adherence rate as a covariate in the statistical analyses (line 343-346). In addition, considering that low adherence rate is a general issue in exercise studies performed on individuals with SCI (15), adherence to the exercise intervention will be a relevant outcome by itself.

References:
(14) Krassioukov AV, Currie KD, Hubli M, *et al*. Effects of exercise interventions on cardiovascular health in
individuals with chronic, motor complete spinal cord injury: protocol for a randomized controlled trial [Cardiovascular Health/Outcomes: Improvements Created by Exercise and education in SCI (CHOICES) Study]. *BMJ Open* 2019;9:e023540.

(15) Ginis KAM, Hicks AL. Exercise research issues in the spinal cord injured population. *Exerc Sport Sci Rev*. 2005;33:49-53

6. The only limitation stated is the lack of control of food intake. I would suggest expanding on why this is expected to be a limitation and how you may minimize the impact.
Response: Thank you for the comment. Because energy intake influences energy balance, differences in energy intake between groups could influence outcome measures such as body mass and body composition. Also, it cannot be excluded that a compensatory increase in energy intake, due to increased energy expenditure from the exercise intervention, could mask changes in body mass and body composition in the intervention group. As suggested, we have expanded on the lack of control of food intake as a limitation (line 125-126).
As this study uses a strict exercise intervention and not a nutrition or lifestyle intervention, there will be no dietary constraints imposed. A food diary could provide some information about energy intake, however this approach is time consuming and individuals tend to underreport their energy intake (16), especially those who are obese (17). As a feasible attempt to minimize the impact of not controlling food intake, participants will be asked to continue their normal eating habits throughout the study period (line 265-266).

References:

(16) Champagne et al., 2002. Energy intake and energy expenditure: a controlled study comparing dietitians and non-dietitians. J Am Diet Assoc 2002; 102: 1428-1438

(17) Pietila¨inen1 et al. Inaccuracies in food and physical activity diaries of obese subjects: complementary evidence from doubly labeled water and co-twin assessments. International Journal of Obesity (2010) 34, 437–445

VERSION 2 – REVIEW

REVIEWER	Christof Leicht Loughborough University, UK
REVIEW RETURNED	11-Sep-2020

GENERAL COMMENTS	The authors have done a very thorough job with this review, and have addressed all my queries to my satisfact

REVIEWER	Chelsea Pelletier University of Northern British Columbia, Canada
REVIEW RETURNED	10-Sep-2020

GENERAL COMMENTS	I wish the authors luck with this project and look forward to reading about the findings.