Reviewer's report

Title: Effects of Cardiovascular Exercise Early After Stroke: A Meta-Analysis

Version: 2 Date: 20 February 2012

Reviewer: Ada Tang

Reviewer's report:

Discretionary revisions

1. Throughout manuscript, suggest use of person-first language, e.g. individual with stroke, rather than stroke patient
2. Suggest referring to ‘person/participant’, rather than ‘patient’, since they are participants enrolled in research studies
3. Page 3 para 1: Replace ‘new stroke patients’ with ‘new cases of stroke’
4. Page 3 para 2: Remove ‘due to the traumatic event and’
5. Throughout manuscript, spell out number when beginning a sentence with a number. Some specific examples:
   a. Page 8 para 2: Replace ‘10 studies …’ with ‘Ten studies …’
   b. Page 9 para 4: Replace ‘2 studies …’ with ‘Two studies …’
6. Page 7 para 2: Delete ‘included’ in first sentence
7. Page 10 para 2: Replace ‘yield’ with ‘yielded’
8. Page 11 para 2: Replace ‘;’ with ‘:’
9. Page 16 para 2: Remove ‘However,’ from last sentence
10. Throughout manuscript, change ‘minor affected’ to ‘mildly affected’

Minor essential revisions

1. Readers may have different perspectives on what is the ‘acute’ phase of stroke, so it would be helpful to clarify this. I suspect that the majority of the studies included in this meta-analysis refer to the sub-acute phase after stroke. That is, participants are medically stable and are participating in rehabilitation programs, and not in acute care settings. To avoid confusion, perhaps an operational definition would be helpful.

2. The authors did note on page 9 para 1 that one study (which one? No reference was provided) did include a participant as early as 5 days post-stroke, but were they in acute care or rehabilitation?

3. Correct units for VO2, should be ml/kg/min or ml#kg#-1#min#-1 (not ml/kg/min#-1)

4. Page 9 para 4: second sentence is redundant of data provided in Table 2
5. Page 12 para 1: VO2peak data was available in 3 studies, but authors cited 4 (references 35, 37, 42, 44). Please clarify this discrepancy.

6. Page 14 para 1: specify which studies did not use same modalities for testing and training

7. Page 15 para 4: Since there are many forms of bias, are the authors referring to potential intervention bias that may result from inconsistency of exercise protocols employed?

8. Page 17 para 2: The authors should acknowledge that the paucity of evidence regarding exercise testing and training among individuals with severe stroke is not unique to those in the early post-stroke phase, but is also a gap in knowledge in the later (chronic) stages after stroke

Major compulsory revisions

1. Page 5 para 3 indicates ‘Participants of any age …’ but in the search strategy description earlier, studies including participants > age 18 years were included. Please clarify.

2. The manuscript seemed disjointed in many places, and would benefit from some re-structuring for continuity and flow. For example:
   a. It would be helpful for the Methods to be mirrored in the Results, and to be consistent between these 2 sections
   b. Some sections in Results are missing from Methods, e.g. explanation for Risk of bias across studies
   c. In the Results, Synthesis of results (page 12) can be moved earlier, perhaps before Primary outcomes (page 10), as these are the main results of this meta-analysis and crux of the paper
   d. On that note, what is difference between these 2 sections? Are VO2peak and 6MWT distance not the primary outcomes (as outlined on page 9 para 2)? Is gait speed not a secondary outcome, yet why was it reported in Synthesis of results along with VO2peak and 6MWT?
   e. Page 10 para 2: Please report the ES, MD, 95%CI for change in VO2peak
   f. Subsections on Risk of bias within studies and Risk of bias across studies could follow one another

3. Page 14 para 2 has some inconsistencies. At first, the authors refer to the ‘large effect size’ for VO2peak outcome, yet later attributed the short intervention lengths for the ‘small effects were to be expected’

4. Also on page 14 para 2, how did the authors conclude that individuals in the sub-acute phase of stroke have a larger potential for increasing VO2peak compared to chronic stroke?

5. Page 14 para 2: The authors report that the ES for 6MWT distance was lower
among studies that did not use walking training in the exercise intervention relative to studies that did, but this sub-analysis was not reported in the Results. Can the authors report the different ES for 6MWT distance among studies that did / did not utilize walking training as part of the intervention?

6. Page 15 para 1 “… stair walking tests should last until fatigue”: It is possible that changes in stair climbing may be seen even without continuing until fatigue. Perhaps a timed test might still provide an indication of aerobic capacity (over a longer duration than climbing 1 flight of stairs). For example, a test that is analogous to the 6MWT (meant to reflect durations of daily functional activities but does not take the subject to the point of fatigue) might be appropriate and may still be responsive to change. The primary limitation is that no such test currently exists.

7. From a practice standpoint, considering the potential impact of this manuscript on clinical practice, it is important for the readers to be fully aware of the procedures and protocols that were used in these studies to ensure participant safety. It would be helpful for the authors to provide some commentary or discussion in this regard. This will have important implications for knowledge translation, as health professionals who wish to implement exercise training for their clients may look to this research evidence to inform their practice. For example:

8. Page 16 para 1: Can the authors provide more details regarding the screening procedures used by these studies to ensure safety of participants? Why were potential subjects excluded, e.g. unstable cardiovascular status or other reasons? Are these criteria different from standard criteria recommended by ACSM?

9. Page 16 para 2: It would be helpful to include some details on how the exercise tests were performed, specifically how the subjects were monitored for safety (HR, ECG etc) and what criteria for test termination were employed (if different from ACSM guidelines)

10. Page 17 para 2: clarify what are ‘brain changes’, are the authors referring to cortical activation or re-organization? Or other structural or functional changes?

11. Table 1: Why is the Time since stroke (days) ‘N/A’ for Katz-Leurer et al?

12. Overall, this paper would benefit from careful editing for grammar and language. Some specific examples:

   a. Page 3 para 1: Replace ‘population aged over 65’ with ‘population over the age of 65’
   b. Page 6 para 1: Replace ‘medically deemed stable’ to ‘deemed medically stable’
   c. Page 14 para 2: The sentence ‘Whether this is due to a lack of training intensity …’ seems incomplete? Or, should the last word be ‘here’, rather than ‘where’?
d. Page 15 para 4: Unclear of intended meaning of ‘… falsify the outcomes regarding true effects …’ Do they mean that the heterogeneity of the exercise protocols limits the clinical applicability? Or that we are left unclear of the optimal training protocol to be used in this population?

e. Page 17 para 1: ‘It is well known, e.g. …’ is an incomplete sentence

f. Page 17 para 2: ‘… these concepts are not feasible …’ is not grammatically correct. Do the authors intend to convey that the findings are not applicable or relevant to individuals with severe functional limitations after stroke?

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

No competing interests