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Cardiovascular and Aerobic Exercise in Postacute Stroke Patients: A Rapid Review

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February 2015

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Suggested Citation

This report should be cited as follows:

Ghazipura M. Cardiovascular and aerobic exercise in postacute stroke patients: a rapid review. Toronto, ON: Health Quality Ontario; 2015 February. 17 p. Available from: http://www.hqontario.ca/evidence/evidence-process/episodes-of-care#community-stroke.

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews must be completed in a 2- to 4-week time frame. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, the Evidence Development and Standards branch and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

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List of Abbreviations

ADL	Activities of daily living
AMSTAR	Assessment of Multiple Systematic Reviews
GRADE	Grading of Recommendations Assessment, Development and Evaluation
RCT	Randomized controlled trial
SR	Systematic review

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this rapid review is to determine whether stroke patients should receive aerobic training and/or cardiovascular exercise post-discharge to improve functional ability and walking endurance.

Clinical Need and Target Population

In Ontario, there is an aim to improve home care and community-based services, particularly during a patient's early stages of recovery. For stroke rehabilitation, significant literature exists describing the beneficial effects of cardiovascular exercise and aerobic training. However, little is known about the early effects of cardiovascular exercise in stroke survivors. (1) Thus, this rapid review aims to assess the effectiveness of aerobic/cardiovascular exercise during the early stages of stroke rehabilitation, such that a detailed evidence-based recommendation can be derived and applied in the Ontario context.

Rapid Review

Research Question

Should postacute stroke patients receive aerobic training and or cardiovascular exercise to improve functional ability and walking endurance?

Research Methods

Literature Search

A literature search was performed on January 6, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2008, until January 6, 2014. Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full reports
- Published between January 1, 2008, and January 6, 2014
- Health technology assessments, systematic reviews (SRs), and meta-analyses
- Stroke patients in the community
- Studies reporting a measure of functional ability and walking endurance

Exclusion Criteria

- Primary studies (randomized controlled trials [RCTs], observational studies, case series, etc.)
- Children (patients < 18 years of age)
- Acute stroke patients not yet discharged into the community
- Studies where outcomes of interest cannot be extracted

Outcomes of Interest

- Walking endurance
- Functional ability

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for Stroke Patients was struck. Members of the panel included physicians, nurses, allied health professionals, and personnel from the Ministry of Health and Long-Term Care.

The role of the expert advisory panel was to provide advice on primary stroke patient groupings; to review the evidence, guidance, and publications related to defined stroke patient populations; to identify and prioritize interventions and areas of community-based care; to advise on the development of a care

pathway model; and to develop recommendations to inform funding mechanisms. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) tool was used to assess the quality of the final selection of the systematic review (SR). (2) Details on the outcomes of interest were abstracted from the selected review, and primary studies were referenced as needed.

The quality of the body of evidence for each outcome was examined according to the GRADE Working Group criteria. (3) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural method.

Study design was the first consideration; the starting assumption was that RCTs are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: the large magnitude of effect, the dose response gradient, and any residual confounding factors. (3) For more detailed information, please refer to the latest series of GRADE articles. (3)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	Very confident that the true effect lies close to the estimate of the effect;
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different;
Low	Confidence in the effect estimate is limited—the true effect could be substantially different from the estimate of the effect;
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect.

Results of Literature Search

The database search yielded 266 citations published between January 1, 2008, and January 6, 2014 (with duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

One SR by Stoller et al (4), met the inclusion criteria for both outcomes of functional ability and walking endurance. The SR received an AMSTAR score of 9, and the details of the score are shown in Appendix 2, Table A1. Table 1 below provides a summary of the SR.

Table 1: Summary of Systematic Review Included

Author, Year	Review Type	Search Dates	Inclusion Criteria	No. of Studies	AMSTAR Score
Stoller et al, 2012 (4)	SR/MA	To February 2009	RCTs Non-randomized prospective controlled trials Adults >18 years of age Sub-acute phase of stroke (7 days to 6 months post-discharge) Only studies with cardiovascular, cardiopulmonary, or aerobic training interventions	11	9

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; SR, systematic review; MA, meta-analysis; RCT, randomized control trial
[a]Only outcomes that are relevant to this review are included.

Results for Outcomes of Interest

Functional Ability: Activities of Daily Living

Stoller et al (4) identified 4 RCTs that report on the outcome of functional ability through activities of daily living (ADL) measures for postacute stroke patients receiving cardiovascular and/or aerobic exercise in the early stages of rehabilitation. The individual RCTs use different instruments to measure and report on functional ability and ADLs; therefore, the results could not be pooled or meta-analyzed. The results from the individual RCTs are summarized below in Table 2.

Table 2: Results on Functional Ability From Stoller et al (4) Systematic Review

RCT	No. of Participants	Instrument	Between-Group Difference
Duncan et al, 2003 (5)	20	Barthel index	No difference
		Lawton Instrument	No difference
Eich et al, 2004 (6)	50	Rivermead Motor Assessment Score	No difference
Katz-Leurer et al, 2007 (7)	92	Functional Independence Measure	No difference
		Frenchay Activities Index	No difference
Letombe et al, 2010 (8)	18	Barthel index	Favours intervention

Abbreviations: No., number; RCT, randomized control trial.

When comparing the individual RCTs from Table 2, there are mixed results for the outcome of functional ability based on functional independence scores. The majority of studies did not find a significant difference in ADL between the intervention and control group, but the exact scores were not provided in the SR.

Based on the information provided by Stoller et al (4) about the individual studies, as well as their assessed PEDro score to detect risk of bias, this outcome received a low GRADE quality of evidence. (Appendix 2, Table A2)

Functional Ability: Aerobic Capacity

Evidence suggests that VO_2max is reduced to 10-17 ml/kg/min during the first 30 days post-stroke. This is 25-45% lower than the VO_2max in age-matched healthy patients. (9-11) Any decline in aerobic capacity has the ability to inhibit participation in exercise programs and limits a patient's ability to perform functional activities independently. Therefore, aerobic capacity has the potential to inform level of dependency in ADL. (4)

Stoller et al (4) conducted a meta-analysis on 3 RCTs that report on aerobic capacity. The results of the meta-analysis are summarized below in Table 3.

Table 3: Results of Meta-Analysis on Aerobic Capacity From the Stoller et al (4) Systematic Review

No. of Participants in Intervention	No. of Participants in Control	Std. Mean Difference[a] (95% CI)	I^2	P-heterogeneity
76	79	0.83 (0.50, 1.16)	0%	0.90

Abbreviations: CI, confidence interval; No., number; Std., standardized.

[a]The standardized mean difference is in addition to the 16.9% increase that occurs as part of the natural recovery process during the first 6 months in the postacute stage. (4)

Generally, 10 ml/kg/min is required for light instrumental activities during all activities of daily living. (4) However, since the data was synthesized using standardized mean differences, the exact difference in ml/kg/min is unknown. Nonetheless, the results of the meta-analysis suggest that the results are in favour of the intervention group. Based on the authors' overview of the individual studies and their reported PEDro score to detect risk of bias (4), this outcome received a high GRADE quality of evidence. (Appendix 2, Table A2)

Walking Endurance

The Stoller et al (4) SR identified 6 RCTs that report on the 6-Minute Walk Test as a measure of walking endurance. The authors conducted a meta-analysis on the individual studies, and a summary of the meta-analysis is provided below in Table 4.

Table 4: Results of Meta-Analysis on Walking Endurance Based on 6-Minute Walk Test from the Stoller et al (4) Systematic Review

No. of Participants in Intervention	No. of Participants in Control	Std. Mean Difference[a] (95% CI)	I^2	P-heterogeneity
138	140	0.69 (0.45, 0.94)	0%	0.83

Abbreviations: CI, confidence interval; No., number; Std., standardized.

[a]The standardized mean difference is in addition to the 16.9% increase that occurs as part of the natural recovery process during the first 6 months in the postacute stage. (4)

The results of the meta-analysis suggest that the results are in favour of the intervention group. Based on the authors' overview of the individual studies and their reported PEDro score to detect risk of bias (4), this outcome received a moderate GRADE quality of evidence (Appendix 2, Table A2).

Conclusions

On the basis of 1 SR evaluating the effectiveness of aerobic training and cardiovascular exercise, the following conclusions were reached:

- Low quality evidence shows an inconsistent improvement in functional ability with cardiovascular and aerobic exercise.

- High quality evidence suggests that individuals in the early stages of post-acute stroke rehabilitation have a high potential to increase peak oxygen uptake following aerobic training and/or cardiovascular exercise.

- Moderate quality evidence indicates that aerobic and/or cardiovascular exercise improves walking endurance.

Acknowledgements

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Health Quality Ontario's Expert Advisory Panel on Post-Acute, Community-Based Care for Stroke Patients

Name	Affiliation(s)	Appointment(s)
Panel Co-Chairs		
Dr Mark Bayley	Toronto Rehabilitation Institute; University of Toronto	Medical Director of the Neuro-rehabilitation Program; Associate Professor
Karyn Lumsden	Central West Community Care Access Centre (CCAC)	Vice President of Client Services
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Dr Leanne Casaubon	Toronto Western Hospital; University of Toronto	Assistant Professor-Division of Neurology, Stroke Program
Physical Medicine and Rehabilitation		
Dr Robert Teasell	Stroke Rehabilitation Program at Parkwood Hospital; Western University	Medical Director; Professor
Family Medicine		
Dr Adam Stacy	Ontario Medical Association	Board Member
Nursing		
Connie McCallum	Niagara Health System	Nurse Practitioner, TIA/Stroke Prevention Clinic
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Arms Armesto	Sunnybrook Health Sciences Centre	Clinical Nurse Specialist
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Rebecca Fleck	Hamilton Health Sciences Centre	Regional Stroke Educator and Research Coordinator
Physiotherapy		
Sara McEwen	Sunnybrook Research Institute, St. John's Rehab	Research Scientist

Name	Affiliation(s)	Appointment(s)
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Holly Sloan	Trillium Health Centre	
Social Work		
Joanne Avery	Providence Healthcare, Out-patient Stroke Clinic	Social Worker
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Christina O'Callaghan	Ontario Stroke Network (OSN)	Executive Director
Jim Lumsden	The Ottawa Hospital, LHIN-Champlain Regional Stroke Program	Director
Paula Gilmore	London Health Sciences Centre, Southwestern Ontario Stroke Strategy	Community and Long Term Care Coordinator
Mathew Meyer	Ontario Stroke Network (OSN)	
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Patient Representation		
Daniel Brouillard	Kingston Heart Clinic	Internist, Stroke Survivor
Nicole Martyn-Capobianco	University of Guelph-Humber	Program Head of Human Services

Appendices

Appendix 1: Literature Search Strategies

Search date: January 6, 2014
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, All EBM Databases (see below)

Q: Should stroke patients receive aerobic training/cardiovascular exercise to improve outcomes of functional ability and walking endurance?
Limits: 2008-current; English
Filters: Meta-analyses, systematic reviews, health technology assessments

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to November 2013>, EBM Reviews - ACP Journal Club <1991 to December 2013>, EBM Reviews - Database of Abstracts of Reviews of Effects <4th Quarter 2013>, EBM Reviews - Cochrane Central Register of Controlled Trials <November 2013>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <4th Quarter 2013>, EBM Reviews - NHS Economic Evaluation Database <4th Quarter 2013>, Ovid MEDLINE(R) <1946 to November Week 3 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <January 03, 2014>
Search Strategy:

#	Searches	Results
1	exp Patient Discharge/	20096
2	exp Aftercare/	7014
3	exp Convalescence/	3346
4	"Continuity of Patient Care"/	15215
5	exp "Recovery of Function"/	34907
6	((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab.	38106
7	exp Stroke/	90317
8	exp brain ischemia/	85085
9	exp intracranial hemorrhages/	56497
10	(stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) adj (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 h?emorrhag*) or (brain adj2 h?emorrhag*)).ti,ab.	202133
11	or/1-10	390527
12	exp Exercise/	128536
13	exp Exercise Therapy/	36002
14	exp Physical Exertion/	58341
15	exp Exercise Test/	57522
16	exp Physical Fitness/	24541
17	exp Physical Endurance/	29858
18	(exercis* or strength train* or aerobic* or (physical adj2 (fitness or condition*)) or ((cardio* or endurance or fitness) adj2 (train* or program*))).ti,ab.	300121
19	or/12-18	420279
20	11 and 19	16105
21	Meta Analysis.pt.	53853
22	Meta-Analysis/ or exp Technology Assessment, Biomedical/	63094
23	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	213477
24	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	2769
25	or/21-24	230465
26	20 and 25	527
27	limit 26 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	516
28	limit 27 to yr="2008 -Current" [Limit not valid in DARE; records were retained]	352
29	remove duplicates from 28	266

Appendix 2: Quality-Assessment Tables

Table A1: AMSTAR Score of Systematic Reviews[a]

Author, Year	AMSTAR Score[a]	1) Provided Study Design	2) Duplicate Study Selection	3) Broad Literature Search	4) Considered Status of Publication	5) Listed Excluded Studies	6) Provided Characteristics of Studies	7) Assessed Scientific Quality	8) Considered Quality in Report	9) Methods to Combine Appropriate	10) Assessed Publication Bias	11) Stated Conflict of Interest
Stoller et al, 2012 (4)	9	✓	✓	✓	✓		✓	✓	✓	✓	✓	

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews.
[a]Details of AMSTAR method are described in Shea et al. (2)

Table A2: GRADE Evidence Profile

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Functional Ability: Activities of Daily Living							
4 (RCTs)	No serious limitations[a]	No serious limitations	Very serious limitations[b] (−2)	No serious limitations	Undetermined	None	⊕⊕ Low
Functional Ability: Aerobic Capacity (Peak Oxygen Uptake)							
3 (RCTS)	No serious limitations[a]	No serious limitations	No serious limitations	No serious limitations	Undetermined	None	⊕⊕⊕⊕ High
Walking Endurance							
6 (RCTs)	No serious limitations[a]	No serious limitations	Serious limitations[b] (−1)	No serious limitations[c]	Undetermined	None	⊕⊕⊕ Moderate

[a]The risk of bias for this outcome was determined based on the details of individual studies provided in the Stoller et al SR. (4)
[b]The authors of the Stoller et al SR summarized the results of this outcome by comparing RCTs that used different instruments to measure ADL.
[c]The authors indirectly extracted the results from one of the RCTs to infer the individual results for the 6-Minute Walk Test.

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