

Effectiveness of Increased Intensity of Rehabilitation in Post-Stroke Patients: A Rapid Review

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Rapid Review Methodology

Clinical questions are developed by the Division of Evidence Development and Standards 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; if none are located, the search is expanded to include randomized controlled trials (RCTs), and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. 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 included in the systematic review are retrieved and a maximum of two outcomes are graded. If no well-conducted systematic reviews are available, RCTs and/or guidelines are evaluated. Because rapid reviews are completed in very short timeframes, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. Health Quality Ontario works with clinical experts, scientific collaborators, and field evaluation partners to develop and publish research that evaluates the effectiveness and cost-effectiveness of health technologies and services in Ontario.

Based on the research conducted by Health Quality Ontario and its partners, the Ontario Health Technology Advisory Committee (OHTAC)—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.

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In addition, Health Quality Ontario 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 can 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.

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List of Abbreviations

FIM Functional Independence Measure

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 Funding (QBF) 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 Funding initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis is to investigate whether increasing the intensity of rehabilitation for the first few weeks after stroke can improve functional independency in terms of activities of daily living in patients with stroke.

Clinical Need and Target Population

Stroke is a leading cause of disability, and patients who have had a stroke often have long-term difficulties in performing activities of daily living such as personal care, sitting, or getting out of a chair. Rehabilitation helps stroke survivors regain skills that are lost when part of the brain is affected. It is a major part of patient care and can help to maximize physical function and independence.

In June 2012, the Expert Panel on Episode of Care for Stroke suggested that the Evidence Development and Standards unit of Health Quality Ontario (HQP) conduct a "rapid review" to provide the evidence for the effectiveness of 2 elements in stroke rehabilitation: the timing and the intensity of rehabilitation. The Expert Panel selected 2 measures, the Barthel Index of Activities of Daily Living and the Functional Independence Measure (FIM), to use in this rapid review.

Members of the Expert Panel included physicians specialized in physical medicine and rehabilitation, members of the Ontario Stroke Network, physicians treating stroke patients, experts from academic health economic centres, and personnel from the Ministry of Health and Long-Term Care. However, the statements, conclusions, and views expressed in this rapid review are the work of the Evidence Development and Standards unit of HQO and do not necessarily represent the views of members of the Stroke Expert Panel.

Rapid Review

Research Questions

Does increasing the intensity of rehabilitation enhance the motor and functional recovery of patients following stroke?

Do the observed benefits (if any) continue in the longer term if the intensive rehabilitation is removed?

Research Methods

Literature Search

A literature search was performed on May 23, 2012, using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2000, until May 23, 2012. 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

- studies published between January 1, 2000, and May 23, 2012
- studies compared 2 or more levels of intensity of rehabilitation
- randomized controlled trials (RCTs) and non-randomized trials
- English language full-text reports

Exclusion Criteria

- studies that compared 1 dose of therapy with no treatment
- studies in which experimental and control groups were not treated in the same setting
- studies that included patients with other neurological conditions (e.g., traumatic brain injury)
- studies that compared results between different centres
- studies in which therapy involved using drugs (e.g., vasoactive drugs, levodopa, botulinum toxin) in combination with physical therapy
- studies in which therapy involved using somatosensory stimulation
- studies that used constraint-induced movement therapy
- studies that used repetitive transcranial magnetic stimulation
- studies that used adjunctive therapy (e.g., acupuncture)
- studies on the treatment of contractures or shoulder pain following stroke

Outcomes of Interest

- Score on Barthel index or Functional Independence Measure (FIM)

Results of Literature Search

The database search yielded 1,713 citations published between January 1, 2000, and May 23, 2012 (with duplicates removed). Articles were excluded based on information in the title and abstract. Systematic reviews and any major review article on the topic of intensity of rehabilitation were identified within the Reference Manager database. The full texts of these articles were reviewed to identify and compile a list of studies published since January 2000 for further assessment.

The literature search identified 3 systematic reviews, 1 evidence-based review, and 1 review of the guidelines on stroke rehabilitation (Table 1) From a list of studies included in these 5 citations, 8 studies that met the inclusion criteria were identified and included in this rapid review (Table 2). For each included study, the study design was identified and is summarized in Table 3, which is a modified version of a hierarchy of study design by Goodman. (1)

Table 1: Review Studies on Stroke Rehabilitation Identified Through Literature Search

Included Studies	Study Type	Design of Included Studies	Search Period	Objective
Veerbeek et al, 2011 (2)	Systematic review	RCTs	1990 to Oct 13, 2010	To determine the effects of augmented exercise therapy on gait, gait-related activities, and basic and extended ADL
Cooke et al, 2010 (3)	Systematic review	RCTs and quasi-RCTs	From induction of databases to Oct 2009	To determine the strength of current evidence for provision of a higher dose of the same types of exercise-based therapy to enhance motor recovery after stroke
Galvin et al, 2008 (4)	Systematic review	RCTs	From 1985 onward	To determine whether increased duration of exercise therapy is associated with improvement in ADL in stroke patients
Teasell et al, 2009 (5)	Evidence-based review	RCTs and non-RCTs	From 1980	To determine whether patients who receive post-stroke rehabilitation for longer period of time or at a higher level of intensity benefit more than those who receive conventional dosage of rehabilitation
Foley et al, 2012 (6)	Review of guidelines	Practice guidelines	N/A	To examine the related literature to determine whether a specific evidence-based recommendation could be supported

Abbreviations: ADL, activities of daily living; N/A, not applicable; RCT, randomized controlled trial.

Of the 8 studies identified, 7 used the Barthel Index as a measure of results and only 1 used the Functional Independence Measure (FIM); 5 provided mean scores with standard deviation (SD) and 3 provided median and interquartile ranges for the scores at the baseline and follow-up times.

Table 2: Studies on Stroke Rehabilitation Included in the Rapid Review

Study, Year	Study design Focus	Sample size, N Sample	Comparison Groups	Scale scores (Barthel or FIM) Mean (SD)
Askim et al, 2010 (7)	RCT Lower limb	62 Patients admitted to stroke unit with mild/moderate stroke within 14 days of stroke	<p>Intensive motor training (IMT) group: received lower limb motor training in addition to standard treatment: 3 additional sessions of motor training/week for the first 4 weeks after discharge from the stroke unit, plus one additional session/week for the next 8 weeks. Each session was intended to be 30–50 minutes. Patients were also encouraged to receive home exercise training (10 repetitions of 4 tasks twice per day, 6 days/week)</p> <p>Standard therapy (ST) group: received 2 daily sessions of training focusing on ADL, 30 minutes, 5 days/week</p>	<p>Barthel index <u>Baseline:</u> IMT = 72.7 (20.0); ST = 70.8 (16.2) <u>4 weeks:</u> IMT = 88 (NR); ST = 86.3 (NR) <u>12 weeks:</u> IMT = 91.0 (NR); ST: 92.0 (NR) <u>26 weeks:</u> IMT: 92.5 (9.7); ST: 91.4 (16.9); <i>P</i> = 0.48</p>
GAPS, 2004 (8)	RCT Lower limb	70 Patients admitted to stroke rehabilitation facilities within 6 weeks of having stroke and able to tolerate and benefit from mobility rehabilitation	<p>Augmented PT group: received double the amount of PT (60–80 minutes/day, 5 times/week), for a total of 34 hours (9 hours on lower limb, 10 hours on upper limb, 15 hours other work)</p> <p>Standard PT group: received the regular amount of PT (30–40 minutes/day, 5 times/week, total of 21 hours (5 hours on lower limb, 5 hours on upper limb, 11 hours on other work)</p>	<p>Barthel index <u>Baseline:</u> Augmented PT = 11.8 (3.3); Standard PT = 10.3 (3.1) <u>4 weeks:</u> Augmented PT = 14.6 (3.4); Standard PT = 14.1 (3.7); <i>P</i> = 0.55 <u>3 months:</u> Augmented PT = 16.6 (2.8); Standard PT = 16.1 (3.3); <i>P</i> = 0.39 <u>6 months:</u> Augmented PT = 16.9 (2.7); Standard treatment = 16.2 (4.2); <i>P</i> = 0.45</p>
Sonoda et al, 2004 (9)	Non-RCT Gait and exercise related ADL	104 Patients admitted to hospital within 30–80 days of stroke	<p>Full-time integrated therapy (FIT): 40 minutes PT and 40 minutes OT/day for 7 days/week</p> <p>Conventional therapy: 40 minutes PT and 40 minutes OT/day for 5 days/week</p>	<p>FIM scores <u>Baseline:</u> FIT: 92.9 (15.9); Conventional: 95.3 (14.9); nonsignificant <u>6 weeks:</u> FIT: 110.1 (12.1); Conventional: 106.9 (10.4); nonsignificant</p>

Study, Year	Study design Focus	Sample size, N Sample	Comparison Groups	Scale scores (Barthel or FIM)
				Mean (SD)
Fang et al, 2003 (10)	RCT General	156 Patients admitted to stroke centre. Therapy started during the first week after stroke	Additional early PT (AEP): 45 minutes, 5 days/week for 4 weeks, started first week after stroke Routine therapy (RT): no professional rehabilitation therapy	Modified Barthel index <u>Baseline:</u> AEP = 25.70 (19.56); RT = 33.53 (31.04) <u>4 weeks:</u> AEP = 47.67 (28.75); RT = 47.16 (28.73); nonsignificant <u>6 months:</u> AEP = 83.93 (19.63); RT = 80.0 (32.96); nonsignificant
Di Lauro et al, 2003 (11)	Non-RCT General	60 Patients admitted to hospital with very severe stroke	Intensive therapy: 2 hours/day with an interval of 6 hours between the 2 hours, duration of 14 days Ordinary therapy: 45 minutes/day, duration of 14 days	Barthel index <u>Baseline:</u> intensive = 1.4 (1.4); ordinary = 1.5 (1.5) <u>2 weeks:</u> intensive = 3.2 (2.0); ordinary = 3.2 (2.6) <u>6 months:</u> intensive = 8.0 (2.8); ordinary = 7.7 (3.0); nonsignificant
Rodgers et al, 2003 (12)	RCT Upper limb	123 Patients admitted to stroke unit with upper limb dysfunction within 10 days of onset of stroke	Enhanced upper limb rehabilitation (EUR) group: 30 minutes per day/ 5 days a week of EUR for 6 weeks plus stroke unit care, median of 52 minutes/working day Control group: median of 38 minutes/ working day plus stroke unit care	Barthel index Median (IQR) <u>Baseline:</u> EUR = 8 (6–13); control = 9 (6–14); $P = 0.7$ <u>3 months:</u> EUR = 17 (8–19); control = 17 (10–19); $P = 0.96$ <u>6 months:</u> EUR: 18 (11–20); control: 17 (14–18); $P = 0.28$

Study, Year	Study design Focus	Sample size, N Sample	Comparison Groups	Scale scores (Barthel or FIM) Mean (SD)
Kwakkel et al, 2002 (13)	RCT	101 Severely disabled patients during the first 2 weeks after stroke admitted to hospital (Barthel index of 9 or lower)	<p>Arm training group: received arm training for 30 minutes per day/ 5 days per week for 20 weeks</p> <p>Leg training group: received leg training for 30 minutes per day/ 5 days per week for 20 weeks</p> <p>Control group: arm and leg were immobilized for 30 minutes, 5 days per week, 20 weeks</p> <p>All 3 groups received 15 minutes of lower limb rehabilitation, 15 minutes of upper limb rehabilitation, and 1.5 hour of ADL training</p>	<p>Barthel index Median (IQR)</p> <p><u>Baseline:</u> arm training = 5 (3–7); leg training = 6 (3–8); control = 5.5 (3–7)</p> <p><u>6 weeks:</u> arm training = 10 (5–13); leg training = 13 (8.8–19.0); immobilized = 8.5 (7–13); arm vs. leg training = $P < 0.01$</p> <p><u>12 weeks:</u> arm training = 14 (10.8–18); leg training = 17 (13–20); immobilized = 11 (8–18); leg training vs. immobilized = $P < 0.05$</p> <p><u>20 weeks:</u> arm training = 17 (14.3–20); leg training = 19 (16–20); immobilized = 16 (10–19); leg training vs. immobilized = $P < 0.05$ for difference between leg training and immobilized</p> <p><u>26 weeks:</u> arm training = 17 (11.8–20); leg training = 19 (15–20); control = 17 (10.5–19); nonsignificant</p> <p><u>38 weeks:</u> arm training = 17 (10.5–20); leg training = 17.5 (15.25–20.0); control = 17 (12.5–18.25); nonsignificant</p> <p><u>1 year:</u> arm training = 15 (12.5–20); leg training = 18 (14.5–20); control = 17 (14–20); nonsignificant</p>
Gilbertson et al, 2000 (14)	RCT	138 Patients admitted to hospital with a definite plan for discharge from hospital (median days after stroke 23–31 days)	<p>Domiciliary OT group: for 6 weeks</p> <p>Routine follow-up group: receive routine services</p>	<p>Barthel index Median (IQR)</p> <p><u>Baseline:</u> domiciliary OT = 17 (15–18); routine = 18 (16–19)</p> <p><u>8 weeks:</u> domiciliary OT = 18 (16–20); routine: 17 (14–19); $P = 0.06$</p> <p><u>6 months:</u> domiciliary OT = 17 (15–19); routine: 17 (13–18); $P = 0.25$</p>

Abbreviations: AEP, additional early physiotherapy; ADL, activities of daily living; EUR, enhanced upper limb rehabilitation; FIM, Functional Independence Measure; FIT, full time integrated treatment; IMT, intensive motor training; IQR, interquartile range; NR, not reported; OT, occupational therapy; PT physiotherapy; RCT, randomized controlled trial; RT, routine therapy; ST, standard therapy.

Table 3: Body of Evidence Examined According to Study Design

Study Design	Number of Eligible Studies
RCT Studies	
Systematic review of RCTs	
Large RCT	
Small RCT	6
Observational Studies	
Systematic review of non-RCTs with contemporaneous controls	
Non-RCT with non-contemporaneous controls	
Systematic review of non-RCTs with historical controls	
Non-RCT with historical controls	2
Database, registry, or cross-sectional study	
Case series	
Retrospective review, modelling	
Studies presented at an international conference	
Expert opinion	
Total	8

Abbreviation: RCT, randomized controlled trial.

Results from 4 studies that reported the mean and SD (7;8;10;11) were used for pooling data and providing a summary effect size for the intervention under the study. Figure 1 shows the effect size with respect to improvement in Barthel Index 2 to 6 weeks after intensive rehabilitation. The improvement in each study was minimal and nonsignificant and the summary effect size was also nonsignificant (see Figure 1). A result from 1 study in which the FIM was reported was consistent with this finding. There was no significant difference between the intensive and the standard groups at the 6-week follow-up (Table 3).

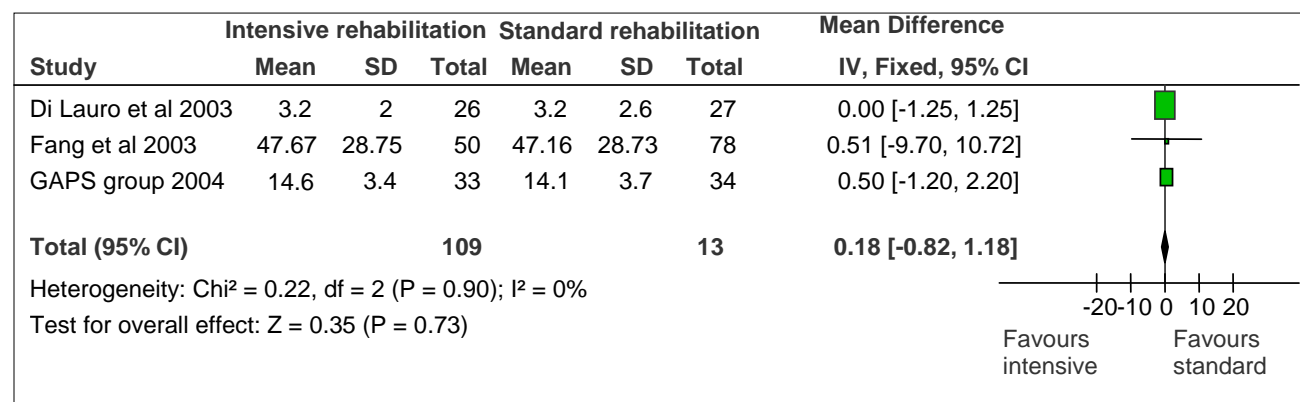


Figure 1: Comparison Between Intensive Rehabilitation and Standard Rehabilitation: Mean Barthel Index Scores at 2–6 Weeks Postintervention

Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation,

All 4 studies that reported the mean scores for Barthel Index at 6 months reported a minimal and nonsignificant improvement in scores. The pooled summary effect size and 95% confidence interval (CI)

was 0.53 (95% CI: -0.65 to 1.70) indicating no significant improvement. In addition, the confidence intervals for summary effect size included negative scores (Figure 2). The effect of higher intensity of rehabilitation on the Barthel Index appeared to be no greater than that of standard physiotherapy.

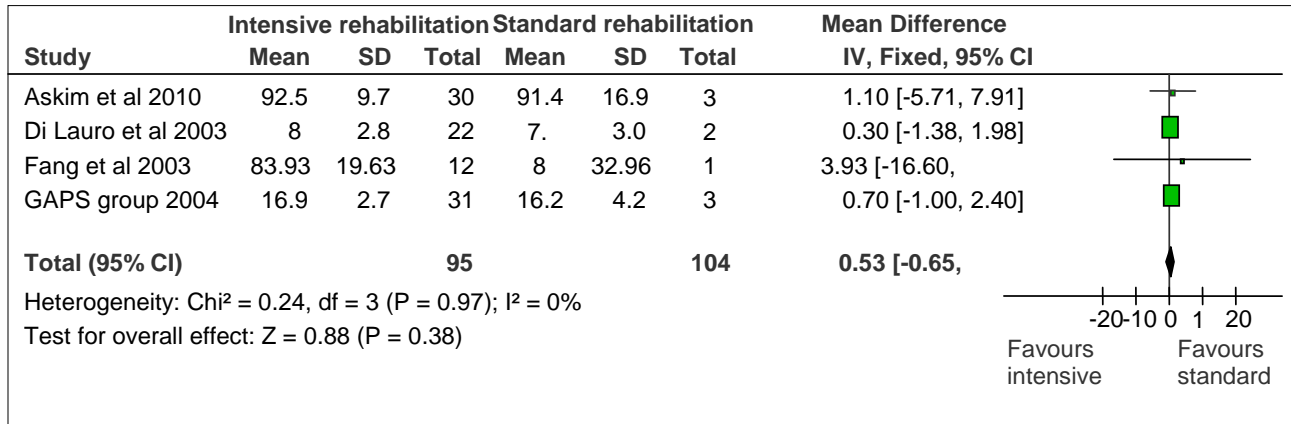


Figure 2: Comparison Between Intensive Rehabilitation and Standard Rehabilitation: Mean Barthel Index Scores at 6 Months Postintervention

Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation.

Results from 3 studies (12-14) on hospitalized patients that reported the median scores are consistent with the pooled summary effect size drawn from the mean scores. None of these studies found a significant difference between intensive therapy and standard therapy groups at different time points (see Table 3).

When the scores at baseline and at 6 months after the start of therapy were compared, a significant improvement was observed for both the intensive therapy group and the standard therapy group (see Figures 3–4). (7;8;10;11)

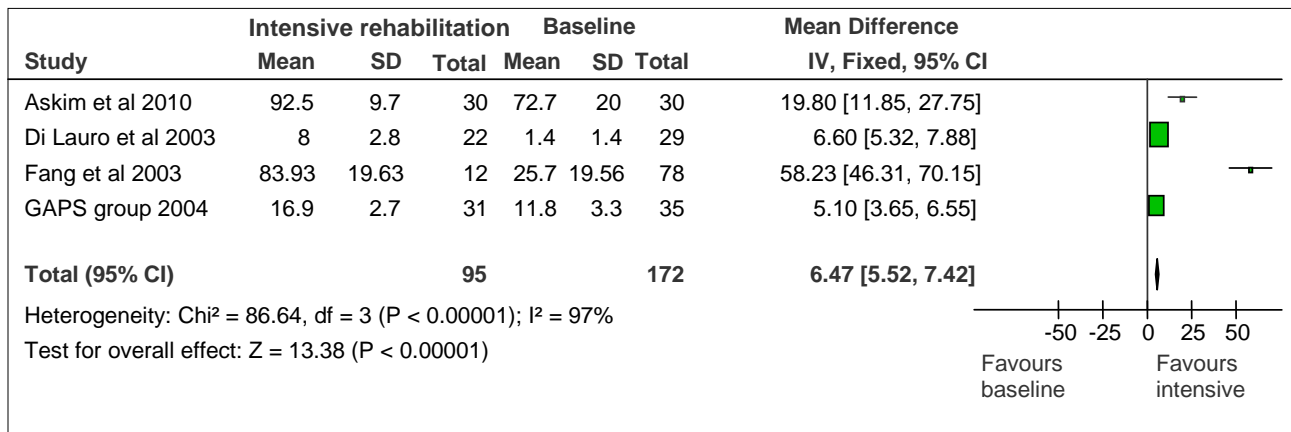


Figure 3: Comparison Between Baseline and 6 Month Barthel Index Scores: Intensive therapy Group

Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation,

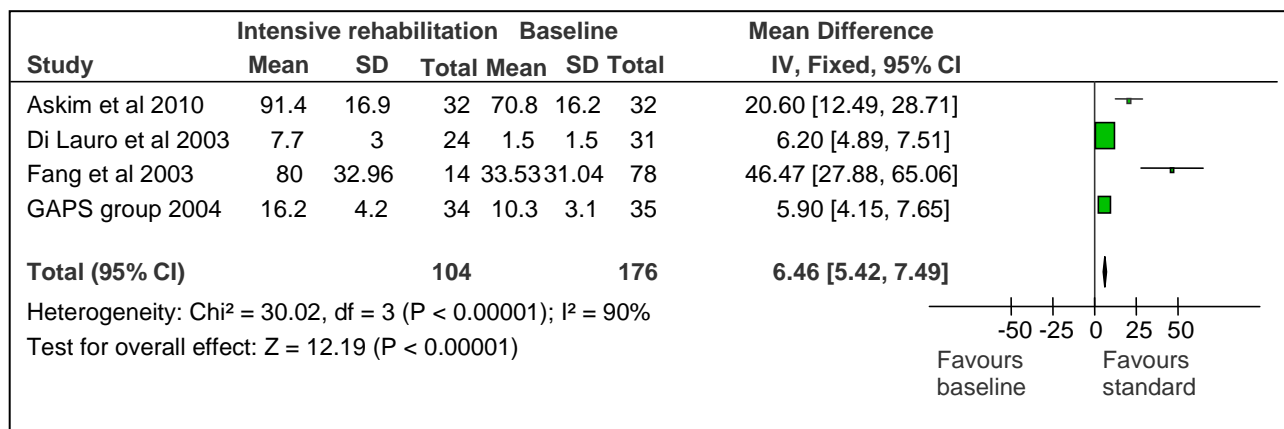


Figure 4: Comparison Between Baseline and 6 Month Barthel Index Scores: Standard Therapy Group

Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation.

Conclusions

The majority of the studies analyzed were randomized controlled trials (RCTs) and included patients hospitalized for stroke. These studies compared 1 level of intensity of rehabilitation with another. The summary score of the studies that reported mean scores as well as the results of individual studies are consistent. In conclusion, the present finding suggests that functional recovery in patients hospitalized for stroke, as measured using the Barthel Index or Functional Independence Measure (FIM) scores, is not greater with higher intensity rehabilitation compared with the standard rehabilitation.

Significant improvements in scores from baseline to 6 months were observed regardless of the intensity of rehabilitation. This improvement may also be due to spontaneous natural neurological recovery or through other interventions that may enhance neurological recovery.

Note: Since there is some discrepancy between the findings in this rapid review and the opinions of experts in the field of stroke rehabilitation, Health Quality Ontario will undertake a full analysis on this topic. The effectiveness of increasing the intensity of rehabilitation following stroke on key outcomes, including changes in functional status, the impact on hospital length of stay, the rate of discharge to home or other living settings, and the hospital readmission rate, will be analyzed in greater detail.

Acknowledgements

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Appendices

Appendix 1: Literature Search Strategies

- 1 exp Stroke/ or exp brain ischemia/
- 2 exp intracranial hemorrhages/ use mesz
- 3 exp brain hemorrhage/ use emez
- 4 exp stroke patient/ use emez
(stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or
- 5 cerebrovascular infarct* or brain infarct* or CVA or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 hemorrhag*) or (brain adj2 hemorrhag*)).ti,ab.
- 6 or/1-5
- 7 exp Rehabilitation/ or exp Rehabilitation Nursing/
- 8 exp Rehabilitation Centers/ use mesz
- 9 exp rehabilitation center/ use emez
- 10 exp rehabilitation medicine/ or exp rehabilitation research/ use emez
- 11 exp rehabilitation care/ use emez
- 12 exp Stroke/rh [Rehabilitation]
- 13 exp Physical Therapy Modalities/ use mesz
- 14 exp physical medicine/ use emez
- 15 exp mobilization/ use emez
(rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational
- 16 therap* or mobilization or mobilisation or strength train*).ti,ab.
- 17 or/7-16
- 18 exp Time/ or exp early diagnosis/
- 19 exp Early Ambulation/ use mesz
- 20 exp dose response/ use emez
- 21 exp early intervention/ use emez
- 22 exp treatment duration/ or exp exercise intensity/ use emez
((time* or timing or interval* or delay* or early or initiation or onset or intens* or duration or augment* or dose-
- 23 response or dose or dosing or dosage or frequency or enhance* or amount* or quantit*) adj4 (rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*)).ti,ab.
- 24 or/18-23
- 25 6 and 17 and 24
- 26 limit 25 to english language
- 27 limit 26 to yr="2000 -Current"
- 28 limit 27 to (controlled clinical trial or meta analysis or randomized controlled trial)
- 29 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ use mesz
- 30 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ use emez
- 31 (health technology adj2 assess\$).ti,ab.
- 32 exp Random Allocation/ or exp Double-Blind Method/ or exp Control Groups/ or exp Placebos/ use mesz
- 33 Randomized Controlled Trial/ or exp Randomization/ or exp RANDOM SAMPLE/ or Double Blind Procedure/

- or exp Triple Blind Procedure/ or exp Control Group/ or exp PLACEBO/ use emez
- 34 (random* or RCT).ti,ab.
- 35 (placebo* or sham*).ti,ab.
- 36 (control* adj2 clinical trial*).ti,ab.
- 37 meta analysis/ use emez
- 38 (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.
- 39 or/28-38
- 40 27 and 39
- 41 remove duplicates from 40

CINAHL

#	Query
S1	(MH "Stroke")
S2	(MH "Cerebral Ischemia+")
S3	(MH "Intracranial Hemorrhage+")
S4	(stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA or (brain N2 isch?emia) or (cerebral N2 isch?emia) or (intracranial N2 hemorrhag*) or (brain N2 hemorrhag*))
S5	(MH "Stroke Patients")
S6	S1 OR S2 OR S3 OR S4 OR S5
S7	(MH "Rehabilitation+") OR (MH "Rehabilitation Centers+") OR (MH "Rehabilitation Patients")
S8	(MH "Rehabilitation Nursing") or (MH "Stroke/RH")
S9	(rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*)
S10	S7 or S8 or S9
S11	(MH "Time+")
S12	(MH "Early Ambulation") OR (MH "Early Intervention+")
S13	(MH "Dose-Response Relationship")
S14	(MH "Treatment Duration") OR (MH "Treatment Delay")
S15	(MH "Exercise Intensity")
S16	((time* or timing or interval* or delay* or early or initiation or onset or intens* or duration or augment* or dose-response or dose or dosing or dosage or frequency or enhance* or amount* or quantit*) N4 (rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*))
S17	S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	S6 AND S10 AND S17
S19	(MH "Random Assignment") or (MH "Random Sample+") or (MH "Meta Analysis") or (MH "Systematic Review") or (MH "Double-Blind Studies") or (MH "Single-Blind Studies") or (MH "Triple-Blind Studies") or (MH "Placebos") or (MH "Control (Research)")
S20	(random* or sham* or rct* or (health technology N2 assess*) or meta analy* or metaanaly* or pooled analysis

	or (systematic* N2 review*) or published studies or medline or embase or data synthesis or data extraction or cochrane or (control* N2 clinical trial*))
S21	S19 OR S20
S22	S18 AND S21
S23	S18 AND S21 Limiters - Published Date from: 20000101-20131231; English Language

Cochrane

ID	Search
#1	MeSH descriptor: [Stroke] explode all trees
#2	MeSH descriptor: [Brain Ischemia] explode all trees
#3	MeSH descriptor: [Intracranial Hemorrhages] explode all trees
#4	(stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA or (brain near/2 isch?emia) or (cerebral near/2 isch?emia) or (intracranial near/2 hemorrhag*) or (brain near/2 hemorrhag*)):ti or (stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA or (brain near/2 isch?emia) or (cerebral near/2 isch?emia) or (intracranial near/2 hemorrhag*) or (brain near/2 hemorrhag*)):ab
#5	#1 or #2 or #3 or #4
#6	MeSH descriptor: [Rehabilitation] explode all trees
#7	MeSH descriptor: [Rehabilitation Nursing] explode all trees
#8	MeSH descriptor: [Rehabilitation Centers] explode all trees
#9	MeSH descriptor: [Stroke] explode all trees and with qualifiers: [Rehabilitation - RH]
#10	MeSH descriptor: [Physical Therapy Modalities] explode all trees
#11	(rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*)
#12	#6 or #7 or #8 or #9 or #10 or #11
#13	MeSH descriptor: [Time] explode all trees
#14	MeSH descriptor: [Early Diagnosis] explode all trees
#15	MeSH descriptor: [Early Ambulation] explode all trees
#16	((time* or timing or interval* or delay* or early or initiation or onset or intens* or duration or augment* or dose-response or dose or dosing or dosage or frequency or enhance* or amount* or quantit*) near/4 (rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*))
#17	#13 or #14 or #15 or #16
#18	#5 and #12 and #17 from 2000 to 2013

CRD

Line	Search
1	MeSH DESCRIPTOR stroke EXPLODE ALL TREES
2	MeSH DESCRIPTOR brain ischemia EXPLODE ALL TREES
3	MeSH DESCRIPTOR intracranial hemorrhages EXPLODE ALL TREES
4	((stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 hemorrhag*) or (brain adj2 hemorrhag*)))
5	#1 OR #2 OR #3 OR #4
6	MeSH DESCRIPTOR Rehabilitation EXPLODE ALL TREES
7	MeSH DESCRIPTOR Rehabilitation Nursing EXPLODE ALL TREES
8	MeSH DESCRIPTOR Rehabilitation Centers EXPLODE ALL TREES
9	MeSH DESCRIPTOR Stroke EXPLODE ALL TREES WITH QUALIFIER RH
10	MeSH DESCRIPTOR Physical Therapy Modalities EXPLODE ALL TREES
11	(rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*)
12	#6 OR #7 OR #8 OR #9 OR #10 OR #11
13	MeSH DESCRIPTOR time EXPLODE ALL TREES
14	MeSH DESCRIPTOR Early Ambulation EXPLODE ALL TREES
15	MeSH DESCRIPTOR Early diagnosis EXPLODE ALL TREES
16	((time* or timing or interval* or delay* or early or initiation or onset or intens* or duration or augment* or dose-response or dose or dosing or dosage or frequency or enhance* or amount* or quantit*) adj4 (rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*))
17	#13 OR #14 OR #15 OR #16
18	#5 AND #12 AND #17
19	(#18) FROM 2000 TO 2013

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