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HEART & STROKE FOUNDATION
Canadian Partnership
for Stroke Recovery

Chapter 6: The elements of stroke rehabilitation

Abstract

The primary goals of stroke rehabilitation are to encourage and foster functional improvement and neurological recovery. Organised stroke care, processes of care, early timing of rehabilitation and high intensity of rehabilitation therapies are important factors which have been identified as promoting better overall outcomes for individuals with stroke. This chapter examines the evidence for those elements which have been proven to be important in the effectiveness of stroke rehabilitation.

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Key points

Stroke unit care appears to improve activities of daily living, length of stay and overall mortality compared to general medical ward care.

Integrated care pathways may not be beneficial for improving activities of daily living or mortality, but the evidence is conflicting with respect to length of stay or quality of life.

Early mobilization may be beneficial for improving motor function and ambulation and mobility, but not stroke severity, length of stay or mortality. The evidence is mixed concerning activities of daily living.

Higher intensity physiotherapy may not be more beneficial than standard intensity for improving outcomes post stroke.

Higher intensity speech and language may not be more beneficial than standard intensity for improving speech and language.

There is level 1a evidence that additional caregiver-supported therapy results in improved functional outcomes compared to conventional therapy alone.

Greater intensities of therapy with caregiver support may result in improved functional outcomes. More research is needed to strengthen the current evidence.

There is level 1a evidence that relatively greater functional improvements are made by patients rehabilitated on specialized stroke units when compared to general medical units in the long term.

There is level 1a evidence that functional outcomes achieved through stroke rehabilitation are maintained for up to one year post stroke.

There is level 1b evidence that by five years post-stroke functional outcomes plateau and may decline. By ten years, overall functional outcome scores significantly decline although it is unclear to what extent the natural aging process and comorbidity may contribute to these declines.

Greater functional improvements made on interdisciplinary stroke rehabilitation units are maintained over the long-term.

Modified Sackett Scale

Level of evidence	Study design	Description
Level 1a	Randomized controlled trial (RCT)	More than 1 higher quality RCT (PEDro score ≥6).
Level 1b	RCT	1 higher quality RCT (PEDro score ≥6).
Level 2	RCT	Lower quality RCT (PEDro score <6).
	Prospective controlled trial (PCT)	PCT (not randomized).
	Cohort	Prospective longitudinal study using at least 2 similar groups with one exposed to a particular condition.
Level 3	Case Control	A retrospective study comparing conditions, including historical cohorts.
Level 4	Pre-Post	A prospective trial with a baseline measure, intervention, and a post-test using a single group of subjects.
	Post-test	A prospective post-test with two or more groups (intervention followed by post-test and no re-test or baseline measurement) using a single group of subjects
	Case Series	A retrospective study usually collecting variables from a chart review.
Level 5	Observational	Study using cross-sectional analysis to interpret relations. Expert opinion without explicit critical appraisal, or based on physiology, biomechanics or "first principles".
	Case Report	Pre-post or case series involving one subject.

New to the 19th edition of the Evidence-based Review of Stroke Rehabilitation

1) PICO conclusion statements

This edition of Chapter 14: Aphasia and Apraxia rehabilitation synthesizes study results from only randomized controlled trials (RCTs), all levels of evidence (LoE) and conclusion statements are now presented in the Population Intervention Comparator Outcome (PICO) format.

For example:

Population: Stroke survivors

Intervention **Comparator**

SPASTICITY			
LoE	Conclusion Statement	RCTs	References
1b	**Bilateral arm training** may not have a difference in efficacy when compared to **TENS** for improving spasticity.	1	Stinear et al. 2014

Outcome

New to these statements is also the use of colours where the levels of evidence are written.

Red statements like above, indicate that the majority of study results when grouped together show no significant differences between intervention and comparator groups.

Green statements indicate that the majority of study results when grouped together show a significant between group difference in favour of the intervention group.

For example:

Population: Stroke survivors

Intervention

MOTOR FUNCTION			
LoE	Conclusion Statement	RCTs	References
1a	**Bilateral arm training** may produce greater improvements in motor function than **conventional therapy**.	4	Meng et al. 2018; Lee et al. 2017; Stinear et al. 2008; Desrosiers et al. 2005

Outcome **Comparator**

Yellow statements indicate that the study results when grouped together are mixed or conflicting, some studies show benefit in favour of the intervention group, while others show no difference between groups.

For example:

Population: Stroke survivors

Outcome **Intervention**

DEXTERITY			
LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **CIMT** to improve dexterity when compared to **conventional therapy or motor relearning programmes** during the acute/subacute phase poststroke.	4	Shah et al. 2016; Yoon et al. 2014; Boake et al. 2007; Ro et al. 2006

Comparator

2) Aphasia and apraxia rehabilitation outcome measures

Outcome measures were classified into the following broad categories:

Motor function: These outcome measures covered gross motor movements and a series of general impairment measures when using the upper extremities.

Ambulation and mobility: These outcomes measures assessed ambulatory abilities during distance-based or timed walking exercises commonly.

Balance: These outcome measures assessed postural stability, and both static and dynamic balance.

Speech and language: These outcome measures assessed speech and language outcome measures.

Spasticity: These outcome measures assessed changes in muscle tone, stiffness, and contractures.

Mental Health: These outcome measures assess psychiatric dysfunction in a number of mental health related dimensions.

Activities of Daily Living: These outcome measures assessed performance and level of independence in various everyday tasks.

Quality of Life: These outcome measures assessed an individual's overall quality of life and their perception of it, generally compared to their preinjury status.

Stroke severity: These outcome measures assessed the severity of one's stroke through a global assessment of a multitude of deficits a stroke survivor may experience.

Caregiver Burden: These outcome measures assess the level of burden for caretakers of stroke survivors.

Length of stay: Assessed how long a patient was admitted to a stroke unit or outpatient service.

Mortality: Assessed a patient's mortality.

Outcome measure definitions

Motor Function

Action Research Arm Test (ARAT): Is an arm-specific measure of activity limitation that assesses a patient's ability to handle objects differing in size, weight and shape. The test evaluates 19 tests of arm motor function, both distally and proximally. Each test is given an ordinal score of 0, 1, 2, or 3, with higher values indicating better arm motor status. The total ARAT score is the sum of the 19 tests, and thus the maximum score is 57. This measure has been shown to have good test-retest reliability and internal validity when used to assess motor function in chronic stroke patients (Ward et al. 2019; Nomikos et al. 2018)

B. Lindmark Motor Assessment: is a measure used to evaluate motor outcomes in patients post-stoke. The measure is based on the Fugl-Meyer assessment. It has seven domains; active selective movement (31 items), rapid movement changes and coordination (4 items), mobility (8 items), balance (7 items), sensation (13 items), joint pain (9 items), and passive range of motion (26 items). The majority of the items are scored from 0-3, with higher numbers indicating better outcomes. The measure has shown good intra- and inter-rater reliability in acute stroke settings (Kierkegaard & Tollback, 2005).

Fugl-Meyer Assessment (FMA): is an impairment measure used to assess locomotor function and control, including balance, sensation, and joint pain in patients post-stroke. It consists of 155 items, with each item rated on a three-point ordinal scale. The maximum motor performance score is 66 points for the upper extremity, 34 points for the lower extremity, 14 points for balance, 24 points for sensation, and 44 points each for passive joint motion and joint pain, for a maximum of 266 points that can be attained. The measure is shown to have good reliability and construct validity (Nillson et al. 2001; Sanford et al. 1993).

Motricity Index (MI): Is a measure of the overall strength of joints in both the upper and lower extremities in stroke survivors. The measure consists of 6 functional movements (e.g. shoulder abduction, elbow flexion, pinch grip, hip flexion, knee extension and ankle dorsiflexion). These movements are subdivided into upper extremity movements and lower extremity movements. Each task is scored on an ordinal 6-point scale (0=cannot complete movement, 5=can complete movement as well as the unaffected side). This measure has been shown to have good test/retest reliability and validity (Fayazi et al. 2012).

Profiles of Recovery: is a measure deigned to assess gross motor function and recovery in stroke patients. It is based on a larger database of recovery profiles from stroke patients. It consists of 12 different items, each comprising of a different motor related tasks (eg. sitting balance for 1 minute). Scoring is a binary decision of whether or not the activity could be completed (Partridge et al., 2000).

Rivermead Motor Assessment (RMA): Is a multi-faced measure that assesses gross motor function, leg and trunk movements and arm movements in post-stroke patients. The arm movements section consists of 15 items ranging from specific isolated movements (e.g. protracting shoulder girdle in supine position) to complex tasks (e.g. placing a string around the head and tying a bow at the back). Patients perform all movements actively, and dichotomous scores indicate either success (score 1) or failure (score 0). The measure is shown to have good test-retest reliability, content validity, and construct validity (Dong et al. 2018, Van de Winckel et al. 2007).

Wolf Motor Function Test (WMFT): Is a measure that quantifies upper extremity motor ability in stroke survivors. The measure consists of 17 tasks (e.g. lifting arm up using only shoulder abduction, picking up a pencil, picking up a paperclip). These tasks are then subdivided into 3 areas: functional tasks, measures of strength, and quality of movement. Patients are scored on a 6-point scale (1=cannot complete task, 6=completes task as well as the unaffected side. This measure has been shown to have good reliability and validity (Wolf et al. 2005; Wolf et al. 2001).

Ambulation and Mobility

10-Metre Walk Test: Is a measure used to assess walking speed, in which participants are asked to walk a distance of 10m in a straight line at maximum walking speed. The time taken to perform the task is recorded, and maximum walking speed is reported in m/s. The test is shown to have high interrater and intrarater reliability in stroke (Druzbicki et al. 2018).

5-Meter Walk Test: Is a measure of ambulation in which the time to walk five meters is taken. It has been shown to be more responsive than the 10-Meter Walk Test for assessing ambulation at a comfortable speed after stroke (Salbach et al. 2001).

6-Minute Walk Test: Is a measure of walking endurance, in which the distance walked by participants in a straight line within 6 minutes is reported. The test is proven to be valid and reliable in stroke (Kwong et al. 2019; Fulk et al. 2008).

Functional Ambulation Category: Is a measure of functional mobility in which participants are ranked on their walking ability with categories ranging from zero, indicating the inability to walk or the requirement of two people assisting, to a 5, corresponding to the ability to walk anywhere independently. This measure has demonstrated excellent test-retest reliability, interrater reliability, and excellent concurrent validity in an acute stroke population (Mehrholz et al. 2007).

Gait Speed: Is a measure that is influenced by stride length and cadence and can be used to assess hemiparesis or motor recovery post-stroke (Olney & Richards 1996).

Rivermead Mobility Index (RMI): Is a self-reported measure of the ability of a stroke patient to complete functional tasks. This measure consists of 15 functional tasks (e.g. turning over in bed, stairs, walking outside) which are then rated on 2-point scale completed by the patient in the form of a questionnaire (0=cannot complete task, 1=can complete task). This measure is has been shown to have good reliability and validity (Lennon et al. 2000; Colleen et al. 1991).

Step Length (SL): Is the distance between the heel print of one foot to the heel print of the second foot. The higher the distance, the better the score. This measure has been shown to have good reliability and validity. (Kuo 2001).

Walking Speed (WS): Is a measure that simply evaluates how quickly a stroke patient can walk and compares that to an age-matched baseline score. This measure consists of the patient walking a set distance (usually 10-15m) with a trained clinician timing them. The patient's time is then compared to the average age-matched score in non-stroke patients. This measure has been shown to have good reliability and validity (Jordan et al. 2007; Himann et al. 1988).

Balance

Berg Balance Scale: Is a 14-item scale that measures balance ability and control while sitting and standing. Each item is ranked on a 4-point scale for a total score of 56. The measure is shown to have high interrater, intrarater, and test-retest reliability (Reinkensmeyer et al. 2019; Blum et al. 2008).

Speech and Language

Aachen Aphasia Test: Is a speech rating scale that includes 6 subscales. Spontaneous language, the Token Test, repetition, written language, naming, and comprehension. Each subscale is made up of multiple subtests, each examining various aspects of language comprehension, processing and production. The test originally developed in german has been translated to multiple different languages, ad has shown good validity and reliability (Miller, Willmes & De Bleser, 2000).

Action Communication Test: Is a diagnostic test of aphasia that assesses the ability of utterance-centered object naming and communicative pragmatic social interaction upon verbal request. When naming or requesting objects, two points are given for a correct response, 1 for a correct response after error, or a related utterance, and 0 points for any further errors or omissions. The measure has shown good reliability and sensitivity (Stahl et al. 2017).

Functional Communication Profile: Is a measure of a patient's communication abilities, mode of communication, and degree of independence. Subtests include sensory/motor, attentiveness, receptive language, expressive language, pragmatic/social language, speech, voice, oral, fluency, non-oral communication (Sarno, 1970).

Western Aphasia Battery: Is an assessment of linguistic and nonlinguistic skills of individuals with aphasia. It characterizes strengths and weaknesses in fluency, comprehension, repetition, and naming (Pritchard & Dipper 2018). This measure has three composite scores consisting of the language quotient, the cortical quotient, and the aphasia quotient (Shewan & Kertesz 1980). This measures has been demonstrated to be valid, with excellent reliability (Shewan & Kertesz 1980).

Spasticity

Modified Ashworth Scale (MAS): Is a measure of muscle spasticity for stroke survivors. The measure contains 20 functional movements which are done with the guidance of a trained clinician. These movements are evenly divided into 2 sections: upper extremity and lower extremity. Each movement is then rated on a 6-point scale (0=no increase in muscle tone, 1=barely discernible increase in muscle tone 1+=slight increase in muscle tone, 2=moderate increase in muscle tone 3=profound increase in muscle tone (movement of affected limb is difficult) 4=complete limb flexion/rigidity (nearly impossible to move affected limb)). This measure has been shown to have good reliability and validity (Merholz et al. 2005; Blackburn et al. 2002).

Mental Health

General Health Questionnaire: has many different versions of various sizes, but the 28-item one in the most popular. The tool is meant to identify minor psychiatric disorders and mental health problems. The 28 item version consists of 4 subclasses (somatic symptoms, anxiety/insomnia, social dysfunction and severe depression) each with 7 items. It has been validated and found reliable in 38 different languages (Jackson, 2007).

Activities of Daily Living

4-point ADL Scale: is measure designed to assess activities of daily living. It consists of 8 different tasks, each rated on a 4-point Likert scale. A score of one on a task indicates 'total need for help' and four indicates 'no assistance needed'. The maximum score is 27, with higher scores indicating greater levels of independence (Sivenius et al., 1985)

Barthel Index (BI): Is a measure of one's ability to perform activities of daily living. The scale consists of 10 items: personal hygiene, bathing, feeding, toilet use, stair climbing, dressing, bowel control, bladder control, ambulation or wheelchair mobility and chair/bed transfers. Each item has a five-stage scoring system and a maximum score of 100 points, where higher scores indicate better performance. The scale is suitable for monitoring on the phone, and is shown to have a high inter-rater reliability (Park, 2018).

Functional Independence Measure (FIM): Is an 18-item outcome measure composed of both cognitive (5-items) and motor (13-items) subscales. Each item assesses the level of assistance required to complete an activity of daily living on a 7-point scale. The summation of all the item scores ranges from 18 to 126, with higher scores being indicative of greater functional independence. This measure has been shown to have excellent reliability and concurrent validity in its full form (Stineman et al. 1996).

Hamrin Activity Index: was developed to assess functional capacity in stroke survivors. The index consists of 16 variables that are divided into three parts; mental capacity, motor activity and ADLs. The maximum score is 92. The test has been validated and found to be reliable within a stroke population (Hamrin & Lindmark, 1990).

Katz Index of Independence in Activities of Daily Living: is a short questionnaire that consists of 6 different activities of daily living. Each activity is scored either 1 (independent) or 0 (dependent), and the points are summed to provide a number between 0-6 which would indicate an individual's overall independence everyday tasks. It has shown good reliability and validity measures (Wallace & Shelkey, 2008).

Motor Assessment Scale (MAS): Is a performance-based measure that assesses everyday motor function. The measure consists of 8 motor-function based tasks (e.g. www.ebrsr.com Page 15 supine lying, balanced sitting, walking). Each task is then measured on a 7-point scale (0=suboptimal motor performance, 6=optimal motor performance). This measure has been shown to have good reliability and concurrent validity (Simondson et al. 2003).

Nottingham Extended Activities of Daily Living: is a measure of activities of daily living specifically designed to assess stroke survivors. It consists of 22 questions, each with a 4-point Likert scale assessing varying levels of dependence on the task described in the item. There are four subscales (mobility, kitchen, domestic, leisure), with higher scores indicating greater independence in each area, and overall. Conclusions on its reliability and validity have been mixed (Green & Young, 2001).

Nottingham Stroke Dressing Assessment (NSDA): Is a measure of a stroke survivor's ability to successfully dress themselves. The measure consists of 25 functional dressing tasks (e.g. buttoning up a shirt, buckling a belt/watch, putting on pants). These tasks are then measured on a 4-point scale (0=cannot complete task, 3=completes task as well as the unaffected side). This measure has been shown to have good reliability and validity (Walker et al. 2012).

Rivermead Activities of Daily Living: is a an assessment of independence in activities of daily living. It contains two subscales (domestic and community activities) that each contain 6 items. Each item is scored on a scale from 0-3, with higher scores indicating greater independence. It has shown good reliability and sensitivity (Rossier, Wade & Murphy, 2001).

Stroke Impact Scale (SIS): Is a patient-reported measure of multi-dimensional stroke outcomes. The measure consists of 59 functional tasks (e.g. dynamometer, reach and grab, walking, reading out loud, rating emotional regulation, word recall, number of tasks completed, and shoe tying). These tasks are then divided into 8 distinct subscales which include: strength, hand function, mobility, communication, emotion, memory, participation and activities of daily living (ADL). Each task is measured on a 5-point scale (1=an inability to complete the task, 5=not difficult at all). The measure has been shown to have good reliability and validity (Mulder & Nijland. 2016; Richardson et al. 2016).

Quality of Life

Australian Quality of Life: is a measure designed to assess an individual's quality of life. It consists of four dimensions (independent living, relationships, mental health and senses) each with three items. Each item is scored on a 5-point Likert scale, with higher scores indicating a greater quality of life. The measure has been shown to have good reliability and validity in chronically ill populations (Hawthorne & Richardson, 1997; Hawthorne et al., 1997).

EuroQol Quality of Life (EQ-5D): Is a widely-used measure of quality of life. It is a brief, self-reported scale covering 5 dimensions: 1) mobility; 2) self-care; 3) usual activities; 4) pain/discomfort; and 5) anxiety/depression. There are two different versions of the scale, one with 3 levels (EQ-5D-3L) and one with 5 levels (EQ-5D-5L) in which subjects rate each dimension from 1 to 3 or 1 to 5, respectively. A "health state" is generated from the score on each dimension, generating a state of 11111 to 33333 in the EQ-5D-3L or 11111 to 55555 in the EQ-5D-5L, with lower numbers representing better health-related quality of life. A summary value can be calculated from each health state to generate a value from 0 to 1. In the second part of the test, subjects rate their current state of health from 0 (worst imaginable) to 100 (best possible) on a visual analogue scale (EQ VAS). The EuroQol scale has been extensively validated in many populations, including stroke survivors. The scale has also been shown to have good reliability (Golicki et al. 2015; Janssen et al. 2013).

Medical Outcome Trusts' Short Form Health Survey (SF-36 or SF-12): Is a commonly used measure of health-related quality of life and overall health status. The test contains 36 items (or 12) encompassing 8 subscales: 1) physical functioning; 2) role limitations – physical; 3) bodily pain; 4) general health; 5) vitality; 6) social functioning; 7) role limitations – emotional;

and 8) mental health. The result of each subscale is transformed to a score from 0-100 representing the lowest and highest possible scores, respectively. Two summary measures, physical and mental health, are generated by weighting the relevant subscales. The test has been validated in a wide range of populations, including stroke and traumatic brain injury patients. In stroke, the survey has demonstrated convergent validity and has high reliability (Guilfoyle et al. 2010; Hagen, Bugge & Alexander, 2003).

Satisfaction with stroke care questionnaire: Is a 20-item questionnaire that is comprised of 8 items measuring satisfaction with inpatient stroke care, 12 items measuring satisfaction with stroke care after discharge. Items are scored on a 4-point rating scale (0-strongly disagree, 3-strongly agree). The higher the sum score, the greater their satisfaction with inpatient care or care after discharge (Boter et al. 2003).

Stroke Severity

Modified Rankin Scale (MRS): Is a measure of functional independence for stroke survivors. The measure contains 1 item. This item is an interview that lasts approximately 30-45 minutes and is done by a trained clinician. The clinician asks the patient questions about their overall health, their ease in carrying out ADLs (cooking, eating, dressing) and other factors about their life. At the end of the interview the patient is assessed on a 6-point scale (0=bedridden, needs assistance with basic ADLs, 5=functioning at the same level as prior to stroke). This measure has been shown to have good reliability and validity (Quinn et al. 2009; Wilson et al. 2002).

National Institutes of Health Stroke Scale (NIHSS): Is a measure of somatosensory function in stroke survivors during the acute phase of stroke. This measure contains 11 items and 2 of the 11 items are passive range of motion (PROM) assessments delivered by a clinician to the upper and lower extremity of the patient. The other 9 items are visual exams conducted by the clinician (e.g. gaze, facial palsy dysarthria, level of consciousness). Each item is then scored on a 3-point scale (0=normal, 2=minimal function/awareness). This measure has been shown to have good reliability and validity (Heldner et al. 2013; Weimar et al. 2004).

Caregiver Strain

Caregiver Strain Index: is a measure designed to assess caregiver burden. It consists of 13 items in the form of a statement, which is answered with a binary yes or no. Yes answers are counted as one point, and the total score is the number of yes'. Higher scores indicate greater levels of burden, with scores of seven or greater considered 'high burden'. It is one of the most widely used measures for assessing caregiver burden (Post et al., 2007).

Length of Stay

Length of Stay: can be quantified in different ways but is generally reported as the duration of time from admission into the hospital until discharge.

Mortality

Mortality: is the proportion of individuals who have died at a given time point post-injury.

Elements of Care Associated with Improved Outcomes

Why specialized stroke unit care improves patient outcomes remains unclear. It is likely that the processes of care and the structures that support these processes contribute to their success; however, the issue is complex. In the case of stroke rehabilitation, the unit of study is broad and involves the examination of complex care delivery systems. Furthermore, comparisons of studies which appear to provide similar interventions, can be quite different. Several features associated with organised stroke unit care have been identified to contribute to the better outcomes:

- Co-ordinated multidisciplinary staff
- Regularly scheduled meetings
- Routine involvement of carers
- Staff specialization
- Standardized and early assessments
- Better diagnostic procedures
- Early mobilization
- Prevention of complications
- Better application of "best-evidence"
- Attention to secondary prevention measures

Evans et al. (2001) suggested specific components of acute stroke care that might be associated with decreased mortality and dependence, including: thrombolysis, physiological homeostasis, anticoagulation among patients with atrial fibrillation, early aspirin use and early mobilization. Processes of care were evaluated between a dedicated stroke unit, which included both acute and rehabilitative services and less organized stroke team, located on a general medical ward. Within the first seven days of admission, patients on the stroke unit were more closely monitored neurologically. A greater percentage of patients received oxygen therapy, nasogastric feeding and measures to prevent aspiration.

Within the first four weeks of stroke, a greater percentage of stroke unit patients received a formal bedside swallowing assessment, a social work and occupational therapy assessment within 7 days, written evidence of rehabilitation goals and discharge/rehabilitation plans (Evans et al., 2001). Although both groups were comprehensively assessed and investigated, greater attention was paid to evaluations of consciousness, swallowing and communication among patients treated on the stroke unit. Medical complications were more common among patients admitted to the general medical ward and appeared to be the factor most strongly associated with improved outcome among patients receiving care on the stroke unit. However, to what extent this factor and other unidentified factors contributed to the better outcome is unknown.

Indredavik et al. (1999) found that aggressive medical management including the use of intravenous saline solutions, oxygen therapy, heparin and Paracetamol to reduce fever was more frequent among patients managed on a stroke unit, compared to treatment received by patients on a general medical ward. Early mobilization was the most significant factor associated with discharge home at six weeks, although it remains unclear whether the benefit resulted from a decrease in medical complications such as deep vein thrombosis and pneumonia or was due to positive psychological benefits. There were no differences in either the total mean hours of both occupational and physical therapy the groups received, which further highlights the intangible elements of a stroke unit that could account for the better outcomes.

In a retrospective study, Ang et al. (2003) reported that patients treated within the integrated stroke unit had a shorter LOS and better functional outcome. The authors speculated that the main reasons for the improved outcome was due to the seamless nature of care since patients did not have to be physically transferred to a different facility or wait have to wait for a bed to become available, before intensive rehabilitation therapies could begin. However, the report contained insufficient detail of the interventions provided within the two groups to assess the differences in care processes, which may have been responsible for the observed differences.

Strasser et al. (2008) investigated the role of education within existing interdisciplinary rehabilitation units. A multiphase, staff training program compared training and information provision delivered over six-month period with information provision only. The group that received additional training discharged patients with a significantly greater gain in mean motor FIM score (+13.6). The authors speculated that *"the intervention taught the necessary skills and provided a useful conceptual model to positively impact on team dynamics".*

Barber et al. (2004) examined the changes in stroke care at an Auckland Hospital between 1996 (prior to the establishment of a stroke unit) and 2001 (following the establishment of a mobile stroke team), and reported that while there were changes in the processes of stroke care since the implementation of the new stroke services, there had been no corresponding decrease in mortality (14% in 2001 vs. 17% in 1996). However, greater proportions of patients were treated with aspirin within 24 hours of admission, and were discharged on anticoagulation therapy. Only 24% of patients were kept nil by mouth for 24 hours, compared to 46% in 1996.

Using data from the 2001-2002 National Stroke Audit (including England, Wales and Northern Ireland), Rudd et al. (2005) evaluated the organization, processes of care and outcomes for stroke. The authors found that better processes of care, were more frequently associated with stroke unit care and decreased the risk of death considerably. The risk of death for patients who received care on a stroke unit was estimated to be 75% that of the risk for those receiving treatment on a non-stroke unit.

While all of the above mentioned studies have focused on identifying the individual contributions of a variety of therapies or interventions, associated with a good outcome, Wade (2001) warns against the risk of committing a "type III error" (falsely rejecting the experimental hypothesis of the interactive effects of complex interventions are not considered), by pursuing such a course. He suggests that attempting to deconstruct the elements of specialized stroke rehabilitation therapies, in an effort to establish which isolated component(s) are effective may be flawed, by failing to recognise the interdisciplinary and complementary nature of the stroke rehabilitation. Ballinger et al. (1999) concluded that the types and duration of therapies provided by 13 physical and occupational therapists at four rehabilitation facilities treating stroke patients were heterogeneous and varied between institutions and individuals.

It can be difficult to realize the same benefits associated with processes of care from clinical trials when they are translated into usual practice. As Kalra & Langhorne (2007) noted, "*most stroke units evolve in response to local patients' needs, priorities and service arrangements, which may not be replicated in other settings*".

One of the elements of stoke unit care that has been associated with improved outcome is the prevention of complications. Complications are known to be common following acute stroke. Indredavik et al. (2008) followed 489 acute stroke patients who were admitted to a comprehensive stroke unit and subsequently enrolled in an early supported discharge service. Despite the benefit of the best model of care, medical complications were still common. During the first seven days following stroke, 64% of patients experienced at least one complication. The most common complications were pain, elevated temperature, stroke progression and urinary tract infections. Increasing stroke severity, advancing age and female gender were the strongest predictors of complications.

Sorbello et al. (2009) also reported a high frequency of medical complications during the acute period following stroke, with or without early mobilization. 82% of patients experienced at least one complication, the most common being falls and urinary tract infections. These findings suggest that some complications experienced following stroke are difficult or impossible to prevent. Furthermore, it suggests that complications may not impact on stroke outcome as much as previously believed. In contrast to this finding, Govan et al. (2007), using a subset of data from the SUTC, found that patients receiving specialized stroke care had a lower incidence of chest infections, other infections and pressure sores. The prevention and treatment of complications was believed to be a contributing factor in improved outcomes.

Kinoshita et al. (2015) revealed a significant association between patients who received early rehabilitation from a board-certified physiatrist (BCP) and FIM effectiveness ([discharge FIM – admission FIM]/[maximum FIM – admission FIM]). A significant association was also reported with FIM Motor subscale effectiveness. Further, a logistic regression revealed that receiving care from a BCP was also a significant predictor for patients to be discharged home. A subgroup analysis showed that the involvement of a BCP was a significant factor for FIM effectiveness in patients with an admission FIM score of $\geq$53. Although the study did not specifically look at the reasons as to why rehabilitation lead by a BCP would be efficacious, Kinoshita et al. (2015) note that the duration of daily exercise was longer and regular meetings were significantly more frequent compared to patients who did received rehabilitation from non-BCP specialists. The authors also speculate that BCPs may have been better able to coordinate a multidisciplinary rehabilitation team. However, as there was no data after discharge from hospital it is unclear whether these gains were maintained in the long-term.

Whyte and Hart (2003) identified some factors which contribute to the difficulties encountered in attempting to unveil the effective elements of stroke rehabilitation:

- The broad range of treatments provided, as well as the poor definitions of treatments often described in published reports, means that reproducibility and dissemination of proven therapies may be difficult.
- The intensities of treatments provided and the composition of therapy can vary across studies, even when evaluating similar therapies.
- The importance of patient participation, motivation and engagement is difficult to capture and can influence the result, when other factors may be constant between studies.
- Variations between individual therapists can occur as therapists respond to the responses and cues from patients they are treating. This effect can also result in subtle differences between like therapies and affect the study result.
- The therapist effect which refers to “non-specific treatment effects brought about by the therapists’ personality, verbal communication skill or degree of warmth and empathy.”

Conclusions Regarding Elements of Stroke Units Associated with Improved Outcomes:

Many elements contribute to the success of stroke rehabilitation unit. Although improved outcomes have been reported among trials evaluating stroke units, no causal mechanism(s) has been identified and verified.

Type of Stroke Units Associated with Improved Outcomes

What Form of Stroke Unit is Best?

Specialized stroke rehabilitation units are associated with better outcomes, compared with mixed rehabilitation wards, general medicine, and mobile stroke teams:

The Stroke Unit Trialists' Collaboration (SUTC) systematic review (2013) has described the hierarchical service organization in stroke care, moving along a continuum from more to less organised care:

1. Stroke ward:

Wards where a multidisciplinary team including specialist nursing staff based in a discrete ward cares exclusively for stroke patients. This category included the following subdivisions:

a) Acute stroke units

Patients are accepted acutely but discharged early (usually within seven days). These units are further subcategorised into:

i) 'intensive' model of care with continuous monitoring, high nurse staffing levels, and the potential for life support

ii) 'semi-intensive' model of care with continuous monitoring high nurse staffing but no life support facilities

iii) 'non-intensive' model of care with no high nurse staffing or life support facilities

b) Rehabilitation stroke units

Patients are accepted after a period of five to seven days or more, and the focus is on rehabilitation.

c) Comprehensive stroke units (i.e. combined acute and rehabilitation)

Patients are accepted acutely but are also provided with rehabilitation for at least several weeks if necessary.

Both the rehabilitation unit and comprehensive unit models offer prolonged periods of rehabilitation.

2. Mixed rehabilitation ward: where a multidisciplinary team including specialist nursing staff in a ward provides a generic rehabilitation service but not exclusively caring for stroke patients.

3. Mobile stroke team: where a peripatetic multidisciplinary team (excluding specialist nursing staff) provides care in a variety of settings.

4. General medical ward: where care is provided in an acute medical or neurology ward without routine multidisciplinary input.

The SUTC (2013) reported that more organised stroke care was consistently associated with improved outcomes, and with decreased mortality, institutionalised care, and dependency. Based on 21 trials, stroke unit care showed reductions in the odds of death recorded at final (median one year) follow-up (OR 0.87, 95% CI 0.69-0.94; p=0.005), the odds of death or institutionalised care (OR 0.78, 95% CI 0.68-0.89; p=0.0003), and the odds of death or dependency (OR 0.79, 95% CI 0.68-0.90; p=0.0007) compared to care provided on a general medical ward.

Outcomes were independent of age, sex, initial stroke severity or stroke type, and appeared to be better in stroke units based in a discrete ward. There was no indication that organised stroke unit care resulted in a longer hospital stay.

Subgroup analyses from the SUTC (2013) indicated that the observed benefits of organized stroke unit care are not limited to any one models of stroke unit organisation that were examined. Comprehensive units and mixed assessment/rehabilitation units tended to be more effective than care in a general medical ward. There were also trends towards better outcomes within the dedicated stroke rehabilitation ward setting as opposed to the mixed rehabilitation ward, and within the acute (semi-intensive) ward as opposed to the comprehensive ward. Further analyses indicated that the observed benefits of organized stroke unit care were not limited to any subgroup of patients. Apparent benefits were seen in people of both sexes, aged under and over 75 years, with ischemic or hemorrhagic stroke, and across a range of stroke severities.

Foley et al. (2007) compared three models of stroke care (acute, rehabilitation and comprehensive units) and found that all models stroke units were associated with significant reductions in mortality, combined death and dependency, and length of stay. However not every model was associated with equal benefit (See Table 1)

Table 1. Mortality and dependency rates for different models of stroke

Models of stroke care	Mortality Odds Ratio (95% CI)	Death/dependency Odds Ratio (95% CI)
Acute stroke care	0.80 (0.61-1.03)	0.70 (0.56-86)
Combined acute and rehabilitation	0.71 (0.54-0.94)	0.50 (0.39-0.65)
Post acute rehabilitation	0.60 (0.44-0.81)	0.63 (0.48-0.83)
Overall	0.71 (0.60-0.83)	0.62 (0.53-0.71)

Further analyses in the SUTC (2013) indicate that the observed benefits of organised stroke unit care are not limited to any of the subgroup of patients. Apparent benefits were seen in people of both sexes, aged under and over 75 years, with ischemic or hemorrhagic stroke and across a range of stroke severities.

In a meta-analysis, O'Rourke and Walsh (2010) examined 17 multicentre studies with a total of 42,000 patients. The authors reported that stroke units were associated with reduced mortality compared to general medical wards (OR 0.79, 95% CI 0.73-0.86), although there was significant heterogeneity between the studies (I^2=45.5%, p=0.02). More recently, large-scale multicentre studies from Canada (Saposnik et al., 2009a; Yanagawa et al., 2016), Australia (Gattellari et al., 2009), Germany (Nimptsch & Mansky, 2014), Japan (Inoue & Fushimi, 2013), the UK (Langhorne et al., 2010a; Turner et al., 2015) have found similar results.

Similarly, Langhorne et al. (2013) noted that there whilst stroke unit care reduced death or dependency (RR 0.81; 95% CI: 0.47–0.92; *p*=0.0009; *I*2=60%) there were no difference in benefits for stroke patients with intracerebral hemorrhage (RR, 0.79; 95% CI, 0.61–1.00) when compared to patients with ischemic stroke (RR, 0.82; 95% CI, 0.70–0.97; $p_{interaction}$=0.77). Table 6.3.1.2 evaluates the differences between various rehabilitation models.

13 RCTs were found that evaluated stroke units compared to general wards (Table 2), and 10 non-randomized studies (Table 3).

Table 2. Summary of RCTs evaluating stroke units compared to general wards

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Indredavik et al. (2000) Fjaertoft et al. (2003) Fjaertoft et al. (2004) Fjaertoft et al. (2011) RCT (8) N_{Start}=320 N_{End}=320 TPS= Acute	E: Stroke unit with early supported discharge (until discharge) C: Conventional stroke unit services Duration: 6wks	• Modified Rankin Scale (+exp) • Barthel Index (-) • Discharge destination (+exp) • LOS (+exp) • Mortality 6mo (-)
Fagerberg et al. (2000) Claesson et al. (2000) Claesson et al. (2003) RCT (6) N_{Start}=249 N_{End}=249 TPS= Acute	E: Acute stroke unit (until discharge) C: General ward Duration: 3mo	• Mortality (+exp) • Barthel Index (+exp) • LOS (+exp) • Mean annual cost per patient (-)
Chan et al. (2014) RCT (7) N_{Start}=41 N_{End}=41 TPS= Acute	E: Co-located acute/rehabilitation stroke care (stroke unit) C: Separated acute/rehabilitation stroke care (general ward) Duration: 3mo	• Functional Independence Measure (-) • LOS (-)
Donnelly et al (2004) RCT (7) N_{Start}=113 N_{End}=97 TPS=Acute	E: Community-based rehabilitation with early discharge C: Conventional care (stroke unit) Duration: 12mo	• Barthel Index (-) • Nottingham ADL (-) • 10m timed walk (-) • EuroQoL (-) • SF-36 (-) • Patient satisfaction (+exp) • Carer Strain Index (-)
Sulter et al. (2003) RCT (6) N_{start}=54 N_{end}=54 TPS= Acute	E: Stroke monitoring unit (until discharge) C: Conventional stroke unit Duration: 3mo	• Mortality (+exp) • Modified Rankin Scale (-) • Barthel Index (-)
Kalra et al. (1994) RCT (5) N_{Start}=146 N_{End}=141 TPS=Acute	E: Stroke rehabilitation unit C: General medical ward Duration: 3mo	• Barthel Index (+exp) • LOS (+exp)

Sivenius et al. (1985) RCT (5) N_{Start}=95 N_{End}=77 TPS= Acute	E: Intensive physiotherapy in stroke unit C: Conventional physiotherapy in general medical unit Duration: 3mo	• Motor Function 4-Point Scale (+exp) • ADL 4-Point Scale (+exp) • LOS (-) • Recurrence of stroke (-)
Garraway et al. (1980) RCT (5) N_{Start}=311 N_{End}=307 TPS= Acute	E: Received care in stroke unit C: Received care in one of 12 medical units on call for emergency admissions Duration: 4mo	• Classified as independent on ADLs (+exp) • Mortality (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Table 3. Summary of non-randomized studies evaluating stroke units compared to general wards

Authors (Year) Study Design Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Jorgenen et al. (1999) PCT N_{Start}=1241 N_{End}=1241	E: Stroke unit C: General medical ward	Mortality: • 1mo (+exp) • 6mo (+exp) • 1yr (+exp) • 5yr (+exp)
West et al. (2013) PCT N_{start}=232 N_{end}=232	E1: Acute stroke care unit E2: Comprehensive stroke unit	• Time spent on moderate-high activity (+exp) • Less time physically inactive (+exp) • Discharge home (+exp)
Di Carlo et al. (2011a) Retrospective N_{Start}=355 N_{End}=355	E: Acute stroke unit C: Geriatric ward	• Resource use (+exp) • LOS (-) • Discharge destination: Home (+exp) • Rehabilitation Hospitals (+exp) • Long-term Care Institutions (-) • Mortality: 3mo (+exp), 1yr (+exp) • Death/dependency: 3mo (+exp), 1yr (+exp)
Schnitzler et al. (2014) Retrospective N_{Start}=28201 N_{End}=28201	E: Neurological rehabilitation centre C: General/geriatric rehabilitation centre	• Dependency (+exp)
Saposnik et al. (2009b) Case Control N=3161	E: Hospital with stroke unit C: Hospital without stroke unit	Mortality: • 7d (+exp) • 1mo (+exp)
Gatterllari et al. (2009) Case Control N=17,659	E: Hospital with stroke unit C: Hospital without stroke unit	• Mortality: non-principal referral hospital (+exp) • Mortality: principal referral hospital (-)

Langhorne et al. (2010b) Case Control N=157,639	E: Hospital with stroke unit C: Hospital without stroke unit	• Mortality (+exp) • Discharge destination: home (+exp)
Inoue & Fushimi (2013) (2013) Case Control N=6997	E: Stroke unit C: General medical ward	• Mortality (+exp)
Nimptsch et al. (2014) Case Control N=1,445,357	E: Hospital with stroke unit C: Hospital without stroke unit	• Mortality (+exp)
Turner et al. (2015) Case Control N=41,692	E: Stroke unit C: General medical ward	Mortality: • 7d (+exp) • 1mo (+exp) • 2mo (+exp) • 3mo (+exp) • 1yr (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Discussion

Di Carlo et al. (2011b) and Schnitzler et al. (2014), which found reduced death and dependency in an acute stroke unit. However, Di Carlo et al. (2011b) also reported that more patients from the acute stroke unit were discharged home, and that there were no differences in length of stay. When comparing a stroke rehabilitation unit to a general medical ward, Kalra et al. (1994) and Jorgensen et al. (1999) found that the stroke unit was associated with improved independence and reduced mortality.

Both Indredavik et al. (2000) and Sulter et al. (2003) compared a conventional stroke unit to an extended stroke unit or a stroke care monitoring unit respectively. Neither study reported a significant difference between groups concerning ADL performance according to the Barthel Index. However, independence as measured by the Modified Rankin Scale was found to be significant higher among those who received extended stroke unit care compared to conventional stroke care in Indredavik et al. (2000); conversely, the results from Sulter et al. (2003) did not reflect the findings from Indredavik et al. (2000). Although Indredavik et al. (2000) were unsure as to why the extended stroke unit service was efficacious in improving independence, they propose that inclusion soon after stroke onset, a sample population with greater functional impairment, and a large participant pool may have contributed. Conversely, Sulter et al. (2003) reported a significantly lower mortality rate among patients who received care in a stroke unit compared to a conventional stroke unit while Indredavik et al. (2000) reported no differences. Monitoring patients for potential complications may have allowed for greater prevention and therefore fewer cases of mortality.

In comparing two differing models of care (acute care followed by rehabilitation vs. combined acute and rehabilitation), Chan et al. (2014) did not report any significant differences on the FIM. However, this study revealed that an early comprehensive approach can provide effective and efficient care within one location. Although length of stay did not differ significantly between groups, patients in the comprehensive group experienced a mean of 5.28 days less in total which increased to 7.7 days for moderate stroke patients. FIM efficiency (FIM ÷ LOS) was found to be significantly higher in the comprehensive group. These findings suggest that early rehabilitation may prove to be more efficacious in achieving functional improvements and earlier discharge home (D. K. Y. Chan et al., 2014). In a similar study, West et al. (2013) found that more patients in a comprehensive stroke unit received physical activity and were discharged home than those in an acute stroke unit. However, future research is required to evaluate the cost of such a model.

Donnelly et al. (2004) did not report any significant differences in ADL performance, gait, or quality of life between community and hospital rehabilitation approaches at 1-year follow-up. The cost of the community program was non-significantly less, and as the program had limited staff, the authors suggested that increased capacity could lead to faster response times, higher savings in bed days, and lower care costs overall. At 1-year follow-up from their initial study, Claesson et al. (2003) revealed no significant long-term differences in re-admission rates, length of stay, and discharge destination between patients treated in a stroke unit or a general hospital ward. The authors suggested that management of cardiovascular diseases and risk factors improved, and that knowledge of stroke care improved in general with the development of stroke units. Further, previous research suggested that stroke has become less severe within the Swedish population and so Claesson et al. (2003) suggested that this may have been reflected in their results.

Conclusions about stroke units vs general medical wards

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Stroke unit care** may produce greater improvements in motor function than **general medical ward care.**	1	Sivenius et al., 1985

AMBULATION AND MOBILITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Stroke unit care** may not have a difference in efficacy compared **general medical ward care** for improving ambulation and mobility.	1	Donnelly et al., 2004

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Stroke unit care** may produce greater improvements in activities of daily living than **general medical ward care.**	6	Donnelly et al., 2004; Sulter et al., 2003; Fagerberg et al., 2000; Kalra et al., 1994; Sivenius et al., 1985; Garraway et al., 1980

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Stroke unit care** may not have a difference in efficacy compared **general medical ward care** for improving quality of life.	1	Donnelly et al., 2004

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Modified wheelchair arm support** may not have a difference in efficacy compared **to traditional wheelchair arm support** for improving pain.	1	Sivenius et al., 1985

CAREGIVER STRAIN			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Stroke unit care** may not have a difference in efficacy compared **general medical ward care** for improving caregiver strain.	1	Donnelly et al., 2004

LENGTH OF STAY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Stroke unit care** may produce greater improvements in length of stay than **general medical ward care.**	3	Fagerberg et al., 2000; Kalra et al., 1994; Sivenius et al., 1985

MORTALITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Stroke unit care** may produce greater improvements in mortality than **general medical ward care.**	3	Sulter et al., 2003; Fagerberg et al., 2000; Garraway et al., 1980

Key Points

Stroke unit care appears to improve activities of daily living, length of stay and overall mortality compared to general medical ward care.

Impact of Care Pathways and Guidelines

Integrated Care Pathways (ICP) has been introduced in an attempt to improve the quality and consistency of stroke rehabilitation care. ICP have been seen as a means to translate the recommendations from national guidelines to a local setting. In some centres, ICPs have been developed to reduce lengths of hospital stay in an effort to reduce costs. ICPs can also be referred to as "care mapping" (Falconer et al., 1993).

The definition of a care pathway may vary from one institution to another, although there are several common elements and include: being patient focused, the management is evidence-based, is multidisciplinary, documents in detail the clinical process and is constructed in a manner that facilitates an audit of outcomes (Edwards et al., 2004). However, the development and successful implementation of an ICP is time consuming and expensive and raises concerns over their associated opportunity costs. Sulch et al. (2000) described the development of an ICP as "*an organized, goal-defined and time management plan that has the potential of facilitating timely interdisciplinary coordination, improving discharge planning and reducing length of hospital stay*." Other, less formal systems may include checklists of processes of care (Cadilhac et al., 2004). Kwan et al. (2007) suggested that the development of care pathways might be more appropriate for acute stroke management where they have the greatest potential to alter the highly complex processes of care, rather than in the rehabilitative phase of stroke when well-coordinated service is usually provided by an interdisciplinary team. See Table 4 for a summary of RCTs evaluating the impact of care pathways on stroke outcomes, and table 5 for a summary of non-randomized studies.

Table 4. Summary of RCTs evaluating the impact of care pathways

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Middleton et al. (2011) RCT (8) N_{Start}=19 N_{End}=31 TPS= Acute	E: Care in an acute stroke unit following standard treatment protocols C: Care in an acute stroke unit following an abridged version of the guidelines Duration: 3mo	• Death/dependence (Modified Rankin > 2) (+exp) • SF-36 - physical component (+exp) • SF-36 - mental component (-) • Barthel Index (-)
Sulch et al. (2002b) RCT (6) N_{Start}=152 N_{End}=121 TPS= Acute	E: Integrated care pathway (based on evidence based practice) C: Conventional multidisciplinary care Duration: 6mo	• EuroQOL5d – mobility (-) • EuroQOL5d – self-care (+exp) • EuroQOL5d – social participation (+exp) • EuroQOL5d – pain (-) • EuroQOL5d – psychological functioning (-) • Mortality (-)
Panella et al. (2012) RCT (6) N_{Start}=476 N_{End}=476 TPS= Acute	E: Clinical pathway C: Usual care pathway Duration: 1mo	• Risk of mortality (-) • Mortality 1mo (-) • LOS (-) • Functional Independence Measure (+exp) • Readmission/institutionalization (-)
Falconer et al. (1993) RCT (5) N_{Start}=121 N_{End}=121 TPS= Acute	E: Critical Path Method of care C: Usual care method (Multidisciplinary rehab team) Duration: discharge (~1mo)	• Functional Independence Measure – motor function (-) • Functional Independence Measure – cognitive function (-) • LOS (-) • Cost (-)
Deng et al. (2014)	E: Integrated acute care pathway	• LOS (+exp)

RCT (5) N_{Start} =379 N_{End} =370 TPS= Acute	C: Conventional acute care Duration: 3mo	• Hospitalization cost (+exp) • Barthel Index (-) • Mortality (-) • NIHSS (-)
Hamrin & Lindmark.. (1990) RCT (4) N_{Start} =280 N_{End} =280 TPS= Acute	E: Systematized care pathway C: Conventional care pathway Duration: discharge (~2wks)	• Activity Index (-) • Katz Activities of Daily Living (-) • Fugl-Meyer Assessment (-) • B Lindmark Motor Assessment (-) • LOS (+exp) • Mortality (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Table 5. Summary of non-randomized studies evaluating the impact of care pathways

Authors (Year) Study Design Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Brusco et al. (2015) PCT N_{Start}=996 N_{End}=996	E: Monday-Saturday rehab C: Monday-Friday rehab	• FIM: 6mo (+exp), 1yr (-) • QOL: 1 yr (-)
Cadilhac et al. (2004) PCT N=468	E: Acute stroke unit with higher adherence to care processes C: Conventional acute care with lower adherence to care processes	• Mortality (+exp) • Independence (-) • Discharge destination (-)
Rai et al. (2016) PCT N=157	E: Integrated acute care pathway C: Conventional acute care	• Mortality: 3mo (+exp) • Barthel Index (-) • Modified Rankin Scale (-) • Complications (-)
Ganesh et al. (2016) Case Control N=319,972	E: Integrated acute care pathway C: Conventional acute care	• Mortality: 1mo (+exp)
Kwan et al. (2004) Case Control N=351	E: Integrated acute care pathway C: Conventional acute care	• Mortality (-) • Complications (-) • Discharge destination (-)
Taylor et al. (2006) Case Control N=153	E: Acute clinical pathway C: Conventional acute care	• LOS (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Discussion

A Cochrane review (Kwan & Sandercock, 2009) which included 3 randomized and 12 non-randomized trials, reported no significant difference between care pathway and control groups in terms of death or alter the eventual discharge destination. In fact, patients managed with a care pathway were more likely to be dependent at discharge ($p=0.04$); less likely to suffer a urinary tract infection [(OR) 0.51, 95% (CI) 0.34-0.79], less likely to be readmitted (OR 0.11, 95% CI 0.03-0.39); and more likely to have neuroimaging (OR 2.42, 95% CI 1.12-5.25). Evidence from randomised trials suggested that patients' satisfaction and quality of life were significantly lower in the care pathway group ($p=0.02$ and $p<0.005$ respectively).

This finding was confirmed by Hoenig et al. (2002) who found the structure of care (systematic organization, staffing expertise and technological sophistication) was not associated with better functional outcomes whereas interestingly, compliance with AHCPR post stroke rehabilitation guidelines improved those same outcomes. The apparent paradox may signify the importance of using evidence or guidelines to assist rehabilitation clinicians in individualizing the rehabilitation of stroke patients as opposed to a "one size fits all" approach.

In contrast, a cluster-randomized controlled trial (Panella et al., 2012) reported that an evidence-based care pathway that was developed with the input from a multidisciplinary team resulted in a reduction in the odds of 7-day mortality, and increased the odds of return to pre-stroke function. Another cluster randomized controlled trial (Middleton et al. 2011) demonstrated that patients who were allocated to a stroke unit with standardized evidence-based nursing protocols designed to improve the management of dysphagia, hyperglycemia and fever had better outcomes compared to patients who were randomized to a stroke unit without similar protocol.

Sulch et al. (2002a; 2000) randomized 152 stroke patients to a rehabilitation program of integrated care pathways (ICP), characterized as an organized, goal-defined and time managed plan with the potential to improve discharge planning and reduce length of hospital stay, or to a conventional multidisciplinary team (MDT) program of conventional rehabilitation. Patients receiving MDT care improved significantly faster between weeks 4 and 12 (median change in Barthel Index 6 vs. 2, $p<0.01$) and had higher Quality of Life scores, assessed by the EuroQol Visual Analogue Scale (EQ-VAS) at 6 months (72 vs. 63, $p<0.005$).

Although intuitively care pathways should improve the quality of stroke care, the evidence does not support this conclusion. Although organized interdisciplinary stroke rehabilitation units have been shown to improve outcomes, care pathways do not appear to be a contributing component to their success. There is evidence that the use of care pathways may actually be associated with poorer patient satisfaction and quality of life.

In contrast, there appears to be strong evidence that adherence to clinical guidelines, which involves application of evidence-based practices at an individual patient level, does improve outcomes. Despite this observation, it is important to understand however, the quality of the guideline.

Conclusions about integrated care pathways

MOTOR FUNCTION			
LoE	Conclusion Statement	RCTs	References
2	**Integrated care pathways** may not have a difference in efficacy compared **standard care** for improving motor function.	1	Hamrin & Lindmark, 1990

ACTIVITIES OF DAILY LIVING			
LoE	Conclusion Statement	RCTs	References
1a	**Integrated care pathways** may not have a difference in efficacy compared **standard care** for improving activities of daily living.	5	Deng et al., 2014; Panella et al., 2012; Middleton et al., 2011; Falconer et al., 1993; Hamrin & Lindmark, 1990

QUALITY OF LIFE			
LoE	Conclusion Statement	RCTs	References
1b	There is conflicting evidence about the effect of **integrated care pathways** to improve quality of life when compared to **standard care.**	4	Middleton et al., 2011; Sulch et al., 2002

STROKE SEVERITY			
LoE	Conclusion Statement	RCTs	References
1b	**Integrated care pathways** may not have a difference in efficacy compared **standard care** for improving stroke severity.	1	Sulch et al., 2002

LENGTH OF STAY			
LoE	Conclusion Statement	RCTs	References
1b	There is conflicting evidence about the effect of **integrated care pathways** to improve length of stay when compared to **standard care.**	4	Deng et al., 2014; Panella et al., 2012; Falconer et al., 1993; Hamrin & Lindmark, 1990

MORTALITY			
LoE	Conclusion Statement	RCTs	References
1a	**Integrated care pathways** may not have a difference in efficacy compared **standard care** for improving mortality.	5	Deng et al., 2014; Panella et al., 2012; Middleton et al., 2011; Sulch et al., 2002; Hamrin & Lindmark, 1990

Key Points

Integrated care pathways may not be beneficial for improving activities of daily living or mortality, but the evidence is conflicting with respect to length of stay or quality of life.

Timing of Stroke Rehabilitation

Early Admission to Rehabilitation

Animal studies suggest that there is a time window when the brain is “primed” for maximal response to rehabilitation therapies, such that any delays are detrimental to recovery (Biernaskie et al., 2004). The brain appears to be “primed” to “recover” early in post stroke period. The results of several studies in humans have suggested that stroke rehabilitation should be initiated soon after stroke to achieve optimal results (Feigenson et al., 1977; Hayes & Carroll, 1986; Shah et al., 1990; Wertz, 1990). Ottenbacher and Jannell (1993) conducted a meta-analysis including 36 studies with 3,717 stroke survivors, and demonstrated a positive correlation between early intervention of rehabilitation and improved functional outcome. In their review, Cifu and Stewart (1999) reported that there were four studies of moderate quality that demonstrated a positive correlation between early onset of rehabilitation interventions following stroke and improved functional outcomes. These authors noted that *“Overall, the available literature demonstrates that early onset of rehabilitation interventions – within 3 to 30 days post stroke – is strongly associated with improved functional outcome”*. Ottenbacher and Jannell (1993) conducted a meta-analysis including 36 studies with 3,717 stroke survivors, and demonstrated a positive correlation between early intervention of rehabilitation and improved functional outcome.

The results from individual studies are difficult to compare owing to the variations in inclusion criteria and cohort characteristics. Studies by Paolucci et al. (2000) and Gagnon et al. (2006) were similar with respect to their categorization of time from stroke onset (within 20 days), although the results were conflicting. Patients in the early onset cohort showed a greater rate of recovery in one study (Paolucci et al., 2000), but not in the other (Gagnon et al., 2006). Yagura et al. (2003) reported that patients who were admitted within 90 days of stroke achieved greater gains in independence, ambulation, and upper extremity function compared to patients who had been admitted either 91-180 days or >180 days following stroke. However, all patients significantly benefited from rehabilitation regardless of their onset to admission time. Salter et al. (2006) found that earlier admission was associated with greater improvements in independence at discharge from rehabilitation, while Musicco et al. (2003) reported that patients admitted within seven days of stroke had significantly better outcomes at six months than those admitted after 15 days. In a longitudinal study by Huang et al. (2009), greater time to admission was found to be negatively associated with improvements in independence for up to one year.

The Post-Stroke Rehabilitation Outcomes Project (PSROP), was a prospective observational study, which enrolled 1,291 patients from six inpatients rehabilitation facilities in the US (Maulden et al., 2005). Increases in the length of time from stroke onset to admission to rehabilitation were associated with lower discharge FIM scores and increased LOS for patients with both moderate and severe strokes. Days from stroke onset to admission was also a significant predictor of discharge total FIM score, discharge motor FIM score, discharge mobility FIM score and rehabilitation LOS in regression analysis. The strongest relationship between early admission to rehabilitation and improved functional outcome was among the most severely impaired patients.

Large-scale retrospective studies similar to PSROP have emerged over the recent years. In a study of 1,908 patients, Wang et al. (2011) reported that those with severe impairment showed significant improvements in motor and cognition FIM scores when admitted earlier, especially within 30 days. However, time to admission was only associated with motor FIM score in those with moderate impairment. As well, each additional day from stroke to admission was associated with a significant decrease in potential FIM score gains. A later study of 5,224 patients by Wang et al. (2015) supported the results of the previous study, but also found that time to admission was not associated with FIM score in patients with mild impairment. Most recently, Yagi et al. (2017) examined data collected from multiple rehabilitation centres across Japan with a total of 100,791 patients. The authors concluded that early rehabilitation (within three days) was a significant predictor of ADL improvement upon discharge.

While there is a strong correlation between early admission to stroke rehabilitation and improved functional outcomes, demonstrated in both individual studies and based on the results of meta-analysis, this relationship may not be one of cause and effect. Patients with severe strokes (and higher levels of impairment) are also more likely to experience medical complications, or be too impaired to participate in rehabilitation that may delay their admission to a stroke rehabilitation unit. In contrast, mild to moderate stroke patients with fewer medical complicating factors are more likely to be admitted sooner than later to a stroke rehab unit. Several studies have eluded to factors influencing time to admission including: age, stroke severity, stroke type, history of stroke, level of impairment, and the presence of complications (H. Wang et al., 2015; Wang et al., 2011; Yagi et al., 2017).

The impact of timing to rehabilitation on overall functional outcome was not limited to patients transferred from acute care to rehabilitation. Early initiation of rehabilitation predicted better functional outcome on patients with severe strokes in a stroke intensive care unit with a multidisciplinary stroke care team (Hu et al., 2010). After adjusting for stroke severity and age, patients who started earlier rehabilitation had higher Barthel Index scores at discharge. Commencing rehabilitation one day earlier in the stroke ICU resulted in an increase of the Barthel Index score by 0.65 points (Hu et al., 2010).

Overall, there is a clinical association between early admission to rehabilitation and better functional outcomes (Bai et al., 2012; Paolucci et al., 2000; Salter et al., 2006). The effects of training after stroke are generally greater when started early after stroke, perhaps because of a "sensitive period" of enhanced neuroplasticity.

Very Early Mobilization

Given the importance of early initiation of rehabilitation, there has been increasing interest in very early mobilization (VEM). VEM has been defined as any intervention delivered with the aim of reducing the time from stroke onset to first mobilization (first out of bed episode) and increasing the amount of out-of-bed physical activity post stroke (J. Bernhardt et al., 2008a). There is considerable evidence regarding the effect of VEM on clinical outcomes when compared with delayed mobilization (see Table 6).

Table 6. Summary of RCTs evaluating timing of stroke rehabilitation and mobilization

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Bernhardt et al. (2015) Bernhardt et al. (2016) RCT (8) N=2104 N=2083 TPS= Acute	E: Very Early Mobilization (within 24hr) C: Standard Care Duration: 14 days or until discharged (3mo)	• Good Outcome (mRS≤2) (+exp) • Death (-) • Ambulation (-) • Complications (-)
Bernhardt et al. (2008b) Sorbello et al. (2009) Cumming et al. (2011) RCT (8) N_{Start}=71 N_{End}=71 TPS= Acute	E: Very Early Mobilization (within 24hr) (14d or until discharge) C: Standard Care Duration: 3mo	• Barthel Index (+exp), • Rivermead Motor Assessment (+exp) • Ambulation (+exp) • Mortality (-) • Complications (-) • Fatigue (-) • Falls (-)
Langhorne et al. (2010b) RCT (7) N_{Start}=32 N_{End}=31 TPS= Acute	E1: Early Mobilization (EM) (within 24hr) E2: Automated physiological monitoring (AM) E3: Combined EM + AM C: standard stroke unit care Duration: 3mo	• Modified Rankin Scale (-) • Barthel Index (-)
Chippala & Sharma (2016) RCT (7) N_{Start}=86 N_{End}=80 TPS= Acute	E: Very Early Mobilization (within 24hr) (7d or until discharge) C: Standard Care Duration: 7d	• Barthel Index (+exp)
Diserens et al. (2012) RCT (7) N_{Start}=50 N_{End}=42 TPS= Acute	E: Early Mobilization (after 48hr) C: Mobilization (after 7d) Duration: 7d or discharge	• Severe complications (+exp) • Minor complications (-) • LOS (-) • NIHSS (-)
Sundseth et al. (2012) Sundseth et al. (2014) RCT (7) N_{Start}=65 N_{End}=44 TPS= Acute	E: Very Early Mobilization (within 24hr) C: Control mobilization (between 24hr and 48hr) Duration: 3mo	• Modified Rankin Scale < 2 (-) • Mortality (-) • NIHSS (+con) • Barthel Index (-)
Poletto et al. (2015) RCT (7) N_{Start}=39 N_{End}=29 TPS= Acute	E: Very Early Mobilization (within 48hr) C: Standard Care Duration: 3mo	• Modified Barthel Index (-) • Modified Rankin Scale (-) • National Institutes of Health Stroke Scale (-) • Length of Stay (-) • Complications (-) • Mortality (-)
Morreale et al. (2016) RCT (7) N_{Start}=340 N_{End}=302 TPS= Acute	E1: Proprioceptive Neuromuscular Facilitation (PNF), early (within 24hr) E2: Cognitive Therapeutic Exercise (CTE), early (within 24hr) C1: PNF, late (after 4d) C2: CTE, late (after 4d) Duration: 38 weeks	E1/2 vs C1/2 • Modified Rankin Scale (-) • Barthel Index (+exp) • Motricity Index (+exp) • Ambulation (+exp) • Complications
Bai et al. (2014) RCT (6) N_{Start}=165 N_{End}=156	E: Standardized 3-stage rehabilitation (began therapy within 24hr of admission)	• Modified Ashworth Scale – fingers, elbow and ankle (+exp)

TPS= Acute	C: Standard hospital ward/Internal medical intervention Duration: 6mo	
Bai et al. (2012) RCT (4) N_{Start}=364 N_{End}=345 TPS= Acute	E: Standardized 3-stage rehabilitation (began therapy within 24hr of admission) (45 min/day, 5 days/week) C: Standard hospital ward/Internal medical intervention Duration: 6mo	• Fugl Meyer Scores (+exp) • Modified Barthel Index (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Discussion

The AVERT trial was a large international randomized controlled trial examining the benefit of very early mobilization (VEM) of stroke patients initiated within the first 24 hours of the stroke. The AVERT trial initially produced three publications examining the early findings of the study (J. Bernhardt et al., 2008b; Cumming et al., 2011; Sorbello et al., 2009). In the first presentation of results, there were no reported differences between the early mobilization and conventional groups in death or the number and severity of complications at 3 months. The authors attributed the lack of statistically significant between study groups to a small sample size. In the second publication, there was no reported difference between groups in the frequency of medical complications between groups (Sorbello et al. 2009). Finally, in a last publication, Cumming et al. (2011), reported that patients randomized to the early group were able to walk 50 meters unassisted, were discharged from hospital slightly earlier (median 6 vs. 7 days) and a greater percentage were discharged home (32% vs. 24%).

Results from the phase II of AVERT showed that the VEM resulted in delivery of more and earlier therapy (van Wijk et al., 2012)**.** Schedule (hours to first mobilization, dose per day, frequency and session duration) and nature (percentage out-of-bed activity) of therapy differed significantly between the VEM and standard care (SC) groups. Mobilization was earlier, happened on average 3 times per day in those receiving VEM, with the higher median proportion of out-of-bed activity in VEM session (85.5%) compared to median 42.5% in the standard care (van Wijk et al., 2012). In addition to VEM being effective in improving mobility and independence, economic evaluation suggested that VEM is potentially cost effective (Tay-Teo et al., 2008). Patients receiving VEM incurred significantly less costs at 3 months compared to standard care; and the difference in mean per patient total cost persisted at the 12-month assessment (Tay-Teo et al., 2008).

The benefit of early mobilization was also investigated in an observer-blinded, pilot randomised controlled trial studying the key aspects of early stroke unit care, the Very Early Rehabilitation or Intensive Telemetry After Stroke (VERITAS) trial, where early mobilization and intensive monitoring was incorporated within a 2x2 factorial study design (Langhorne et al., 2010b). The early mobilization intervention arm utilized protocol based on the AVERT trial with respect to the timing, nature, and frequency of the intervention (Langhorne et al., 2010b). Degree of mobilization activity, defined as the mean time spent upright per working day, was 61 (SD, 54) minutes in the early mobilization group compared with 42 (SD, 57) minutes with standard care. By Day 5, 74% of patients in the early mobilization group were independent in walking, compared to 44% of patients with standard care. There was also a trend to more patients on the early mobilization protocol being independent at 3 months (Langhorne et al., 2010b). Although there was no difference in good outcome at 3 months (defined as modified Rankin Scale score of 0-2) between groups, the odds of medical complications were lower among subjects in the early mobilization group (OR 0.1, 95% CI: 0.001 to 0.9, p=0.04), after adjusting for age and severity of stroke.

Pooling of individual patients' data from some of the initial AVERT research and VERITAS showed that time to first mobilization from symptom onset was significantly shorter among VEM patients (median, 21 hours; IQR: 15.8-27.8 hours) compared with standard care patients (median, 31 hours; IQR: 23.0-41.2 hours) (Craig et al. 2010). VEM patients had significantly greater odds of independence at 3 months compared with standard care patients (adjusted OR, 3.11; 95%CI 1.03-9.33) (Craig et al., 2010).

Diserens et al. (2012) also investigated whether early mobilization was safe and effective in preventing serious complications. While patients receiving early mobilization had a lower rate of severe complications, there were dropouts from the standard care group and the overall sample size was small. In another trial, Sundseth et al. (2012, 2014) found that VEM (within 24 hours) and early mobilization (between 24-48 hours) were similar in terms of death, dependency, and outcome on the Modified Rankin Scale. However, the authors noted a positive trend toward VEM and reported a large number of dropouts. Similarly, a small pilot trial with a significant dropout rate found no difference between VEM (within 48 hours) and standard care in improving independence and impairment, or reducing length of stay, complications, and mortality (Poletto et al., 2015). Comparisons with other studies of early mobilization are difficult to make since the criteria used to define "early" were different.

Larger trials of early rehabilitation have yielded more clear and consistent findings. Liu et al. (2014) found that earlier rehabilitation (within 48 hours) was associated with greater independence at six months compared to later rehabilitation (after seven days). In two trials, Bai et al. (2012; 2014) (2012, 2014) evaluated a three-stage rehabilitation program that was provided within 24 hours of admission. The authors reported that the program was associated with greater improvements in independence and impairment (Bai et al., 2012), as well as spasticity (Y. Bai et al., 2014) when compared to standard care. In terms of VEM, Chippala and Sharma (2016) showed that patients who received VEM (within 24 hours) had greater levels of independence at discharge and three months than those who received standard care. As well, a trial by Morreale et al. (2016) examined VEM using two different rehabilitation techniques: proprioceptive neuromuscular facilitation and cognitive therapeutic exercise. While the two techniques achieved similar outcomes, patients who received VEM had greater independence, motricity, and ambulation at one year compared to those who were mobilized later.

Given that most of the evidence has seemingly supported VEM, the final results of the AVERT came as a surprise. The authors reported that a greater proportion of patients who received standard care had a favourable outcome (Modified Rankin Scale score of 0-2) at three months post stroke than those who received VEM (Bernhardt, 2015). The full study was conducted over eight years at 56 sites around the world and included a total of 2104 patients admitted less than 24 hours post stroke. The VEM group received earlier mobilization, more out-of-bed sessions, and more therapy (per day and in total). Later analysis of AVERT found that increased daily frequency of out-of-bed sessions was associated with improved odds of favourable outcome (Bernhardt et al., 2016). It was also revealed that increased time to first mobilization and daily amount of rehabilitation were both associated with reduced odds of favourable outcome. Overall, more frequent and shorter VEM improved the chance of regaining independence, while higher doses of long-term VEM worsened outcomes.

Conclusions about early mobilization

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Early mobilization** may produce greater improvements in ambulation and mobility than **standard care**	3	Morreale et al., 2016; Bai et al., 2012; Bernhardt et al., 2008

AMBULATION AND MOBILITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Early mobilization** may produce greater improvements in ambulation and mobility than **standard care**	3	Morreale et al., 2016; Bernhardt et al., 2015; Bernhardt et al., 2008

BALANCE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Early mobilization** may not have a difference in efficacy compared to **standard care** for improving balance.	1	Bernhardt et al., 2008

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Early mobilization** may produce greater improvements in spasticity than **standard care**	1	Bai et al., 2014

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **early mobilization** to improve activities of daily living when compared to **standard care.**	7	Chippla & Sharma, 2016; Morreale et al., 2016; Poletto et al., 2015; Bai et al., 2012; Sundseth et al., 2012; Langhorne et al., 2010; Bernhardt et al., 2008

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Early mobilization** may not have a difference in efficacy compared to **standard care** for improving stroke severity.	6	Morreale et al., 2016; Bernhardt et al., 2015; Poletto et al., 2015; Disernes et al., 2012; Sundseth et al., 2012; Langhorne et al., 2010;

LENGTH OF STAY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Early mobilization** may not have a difference in efficacy compared to **standard care** for improving length of stay.	2	Poletto et al., 2015; Disernes et al., 2012

MORTALITY			
LoE	Conclusion Statement	RCTs	References
1a	**Early mobilization** may not have a difference in efficacy compared to **standard care** for improving mortality.	4	Bernhardt et al., 2015; Poletto et al., 2015; Sundseth et al., 2012; Bernhardt et al., 2008

Key Points

Early mobilization may be beneficial for improving motor function and ambulation and mobility, but not stroke severity, length of stay or mortality. The evidence is mixed concerning activities of daily living.

Intensity of Therapy

Intensity of Physical and Occupational Therapy

When attempting to determine factors that contribute to the improved functional outcomes that are associated with specialized stroke rehabilitation, the intensity of rehabilitation therapies is often cited as an important element. Do patients who receive therapy for longer periods of time or at a higher level of intensity realize greater benefits compared to patients who receive conventional care? This hypothesis has been investigated extensively although these studies have found that intensity of therapy was only weakly correlated with improved functional outcome. However, Kalra and Langhorne (2007) have noted that "*there is evidence from neuroimaging studies showing that increased intensity of rehabilitation therapies results in greater activation of areas associated with the function towards which this therapy is directed*".

Overall greater intensity of therapy practice results in better outcomes. Research with animals that have shown the benefit of increased intensity of therapies have involved thousands of repetitions. Lang et al. (2009) found that in monitoring occupational therapists involved in inpatient stroke rehabilitation noted that task-specific, functional upper extremity movements occurred in about half the upper extremity rehabilitation sessions; the average number of upper extremity repetitions was only 32, a fraction of the thousands of repetitions seen in animal research. Kwakkel et al. (2004) noted additional therapy time of at least 16 hours in the first 6 months post stroke was necessary to see the positive effects from the increased intensity of therapy. This was affirmed by Verbeek et al. (2014). The Canadian Stroke Guidelines recommend that stroke rehabilitation patients should receive a minimum of three hours of direct task-specific therapy, five days per week delivered by an interprofessional team. A number of innovative approaches have been initiated in an attempt to increase intensity including group therapy (Renner et al., 2016), non-immersive virtual reality (gaming) and altering the therapy skill mix, taking advantage of less expensive alternatives to increase the overall intensity of therapy.

Definition of Intensity

The definition of intensity or 'dosage' has been an unresolved issue in studies investigating the dose-response relationship in rehabilitation therapies (Kwakkel et al., 2006). Restrictions in measuring energy expenditure as a measure of activity intensity have resulted in estimates of therapy intensity in rehabilitation, measures such as the number of repetitions (frequency), the overall time spent in therapy or frequency of treatment sessions (Kwakkel, 2006).

While a universally accepted definition of the term "intensity" does not exist, it is usually defined as number of minutes per day of therapy or the number of hours of consecutive therapy. Studies evaluating the effects of increased intensity of therapy usually provide "more" therapy over a given course of total treatment time compared to the alternative, which receive a lesser amount. This weak association may be explained by differences in the time, duration and composition of therapies provided and/or the characteristics of the stroke patients under study.

The American Congress of Rehabilitation Medicine Stroke Movement Interventions Subcommittee have recommended operational definitions for concepts that are common in stroke motor rehabilitation (Page et al., 2012). The recommendations focused on those terms regarded as often mislabelled, terms such as intensity and dosing (duration and frequency). The recommended definition for intensity is *"the amount of physical or mental work put forth by the client during a particular movement or series of movements, exercise or activity during a defined period of time"* (Page et al., 2012). Duration is defined as *"length of time during which a single session is administered"* and frequency is defined as *"how often during a fixed period the regimen is administered"* (Page et al., 2012). In addition, the delivery method and window of therapy have been identified as areas for further refinement (Page et al., 2012).

Amount of Time Spent in Rehabilitation Therapies

The total amount of time that a patient spends engaged in rehabilitation activities vary considerably, between units, institutions and countries. Lincoln et al. (1996) observed that patients on a stroke rehabilitation unit were engaged in interactive behaviours for only 25% of their time. De Weerdt et al. (2000) used behavioural mapping to quantify the amount of time patients spent in therapeutic activities on two rehabilitation units, one in Belgium and one in Switzerland. Patients were engaged in rehabilitation for a larger percentage of the day than those from Switzerland (45% vs. 27%). De Wit et al. (2005) also observed significant differences in the amount of time patients spent in rehabilitation activities among four European countries (Belgium, UK, Switzerland and Germany) Patients from Germany spent a larger percentage of the day in therapy time (23.4%), while those from the UK spent the least (10.1%). Therapy time ranged from 1 hour per day in the UK to about 3 hours per day in Switzerland. In all of the units, patients spent 72% of their time in non-therapeutic activities.

Even more discouraging are the results from A Very Early Rehabilitation Trial (AVERT) (Bernhardt et al., 2007; Bernhardt et al., 2004) in which a cohort of 58 patients in 5 acute stroke units in Australia were observed. Patients engaged in moderate or high levels of activity for only 12.8% of their therapeutic day. 53% of the time, patients spent their time in bed and were alone 60% of the time. Although there was a direct relationship between stroke severity and activity, even patients with only mild stroke spent only 11% of their active day walking. Patients' affected upper limbs were observed to be moving only 33% of the time, regardless of whether the patient was with a therapist or alone.

A comparison between Australian patients and those in Norway (J. Bernhardt et al., 2008a) revealed that patients admitted to acute stroke units in Trondheim spent an average of 21% less time in bed and 10% more time engaged in either sitting out of bed or in standing/walking activities compared with patients in Melbourne hospitals. There were differences between these two systems in terms of staffing ratios, policies and in the rehabilitation programs themselves.

Randomized Controlled Studies Examining Intensity of Therapies

Many trials have evaluated the efficacy of increased intensity of therapy and the relationship to improved functional outcomes. The results are presented in Table 7.

Table 7. Summary of RCTs evaluating the intensity of physiotherapy and occupational therapy post-stroke

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
High Intensity Physiotherapy vs Standard Physiotherapy		
Askim et al. (2010) RCT (8) N_{Start}=62 N_{End}=60 TPS= Acute	E: 3 extra sessions/wk of physiotherapy and structured home exercise program C: Standard treatment Duration: 4wks post discharge	• Berg Balance scale (-) • Motor Assessment Scale (+exp) • Barthel Index (-) • Step test (-) • 5m walk (-) • Stroke impact scale (-)
Partridge et al. (2000) RCT (8) N_{Start}=114 N_{End}=93 TPS= Acute	E: Physiotherapy for 60min/d (until discharged) C: Physiotherapy 30 min/d (until discharged) Duration: 6wks	• Profiles of Recovery (-)
Kwakkel et al. (1999) Kwakkel et al. (2002) RCT (8) N_{Start}=101 N_{End}=89 TPS= Acute	E1: Arm training (extra 30min 5d/wk) E2: leg training (extra 30min 5d/wk) C: control Duration: 30 min, 5 days/week for 30 weeks	• Barthel Index (-) • Walking ability (-) • Dexterity (ARAT) (+exp)
Di Lauro et al. (2003) RCT (7) N_{Start}=60 N_{End}=46 TPS= Acute	E: Intensive rehabilitative treatment (1h, 2x/d) C: Ordinary rehabilitative treatment (45min/d) Duration: 2 wks	• Barthel Index (-) • NIHSS (-)
English et al. (2015) RCT (7) N_{Start}=283 N_{End}=261 (CIRCIT) TPS= Acute	E1: Physical Therapy 7d/wk E2: Circuit Training 3hr/d C: Standard Physical Therapy 5d/wk Duration: 4 weeks	• 6-Minute Walk Test (-) • Gait Speed (-) • Functional Ambulation Classification (-) • Functional Independence Measure (-) • Wolf Motor Function Test (-) • Stroke Impact Scale (-) • Australian Quality of Life (-) • Length of Stay (-)
GAPS. (2004) RCT (7) N_{Start}=70 N_{End}=66 (GAPS) TPS= Acute	E: Twice regular Physiotherapy (60-80 min per day, 5 days/week) C: Physiotherapy (30-40 min per day, 5 days/week Duration: 1mo	• Mobility Index (-) • Rivermead Mobility Index (-) • Walking speed (-) • Barthel index (-)

Parry et al. (1999) RCT (7) N_{Start}=282 N_{End}=282 TPS= Acute	E: 10 hours of additional physiotherapy over 5 weeks C: Regular amounts of physiotherapy Duration: 5 weeks	• Barthel Index (-) • Rivermead Motor Assessment Arm score (-) • Extended Activities of Daily Living (-) • Action Research Arm Test (-)
Slade et al. (2002) RCT (7) N_{Start}=161 N_{End}=126 TPS= Subacute	E: 67% increase in the amount of routine inpatient physio/occupational therapy per week C: Regular amount of physiotherapy Duration: discharge (mean 84.6d)	• Length of stay (+exp) • Barthel Index (-)
Smith et al. (1981) RCT (5) N_{Start}=133 N_{End}=89 TPS= Subacute	E1: Intensive outpatient rehabilitation therapy E2: Conventional outpatient therapy C: Home visits by a nurse with no therapy Duration: 3mo	• ADL Index deterioration (+exp)
Ruff et al. (1999) RCT (3) N_{Start}=113 N_{End}=113 TPS= Acute	E: received therapy 7 days/wk C: therapy 6 days/wk Duration: Mean LOS for E: 20.11 d; mean LOS for C: 20.14 d	• Functional Independence Measure (-) • LOS (-)
High Intensity Speech and Language Therapy vs Standard Speech and Language Therapy		
Stahl et al. (2018) RCT (6) N_{Start}=30 N_{End}=30 TPS=Chronic	E: Highly Intensive Language-action Therapy (4hrs/d) C: Moderately Intensive Language-action Therapy (2hrs/d) Duration: 3x/wk, 4wks	• Action Communication Test (-) • Aachen Aphasia Test (-)
Martins et al. (2013) RCT (7) N=30 N=25 TPS= Subacute	E: Intensive Speech and Language Therapy (2h/d, 5d/wk, 10wks) C: Conventional Speech and Language Therapy (2h/wk, 50wks) Duration: 50wks	• Functional Communication Profile (-) • Aphasia Quotient (-)
Godecke et. al. (2012) RCT (7) N_{Start}=60 N_{End}=52 TPS=Acute	E: Daily Semantic Therapy C: Usual Frequency of Therapy Duration: 5d/wk, 4wks	• Western Aphasia Battery (+exp) • Functional Communication Profile (+exp)
Bakheit et al. (2007) RCT (7) N=116 N=90 TPS= Acute	E: Intensive Speech and Language Therapy (1hr/d, 5d/wk) C: Conventional Speech and Language Therapy (1h/d, 2d/wk) Duration: 12wks	• The Western Aphasia Battery (-) -
Denes et al. (1996) RCT (4) N_{Start}=17 N_{End}=17 TPS=Subacute	E: Intensive Language Therapy (range of 94-160 sessions) (45-60min) C: Standard Language Therapy (range of 56-70 session) Duration: 6mo	Aachen Aphasia Test • Written Language (+exp) • Token Test (-) • Repetition (-) • Naming (-) • Comprehension (-) • Profile Level (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Discussion

The nature of specialized stroke rehabilitation services implies a greater intensity of therapy although this fact is not always documented. Several studies have attempted to determine the contribution of therapy intensity in stroke rehabilitation. However, illuminating the effect of greater intensity of therapy on functional outcome is difficult due to the variability of treatments provided, the timing and duration of their delivery and the outcomes that were assessed. Additionally, self-report of actual duration of therapy provided by physical therapists has been shown to be overestimated, compared with video recording (mean time 32 vs. 25 min) (Bagley et al., 2009). Intensity of treatment is also dependent on the ability and the willingness on the part of the patient. The mechanism through which improved outcomes are achieved has not been well described. Fang et al. (2003) suggested that a program of greater intensity physiotherapy simply enabled patients to improve or achieve independence in ADL faster through compensation of the non-paretic limb, rather than necessarily through neurological improvements.

Of the studies outlined above, many demonstrated a benefit on at least one testing but failed to demonstrate a difference when compared to conventional treatment at another point in time or among different stroke sub-types. A significant improvement was found on initial assessment however, the benefit disappeared at a later date. The highest quality studies were associated with no benefit when compared to the control condition.

Reviews and Meta-Analyses

The results of three meta-analyses, suggest that increased intensity of therapy is beneficial. Langhorne et al. (1996) examined the effects of differing intensities of physical therapy and showed significant improvements in activities of daily, living (ADL) function and reduction of impairments with higher intensities of treatment. Kwakkel et al. (1997) included 8 RCTs and one non-randomized experiment and found a small but statistically significant intensity-effect on ADL and functional outcome parameters. However, Cifu and Stewart (1999) identified only 3 moderate quality studies and one meta-analysis which examined the intensity of rehabilitation services, and reported that the intensity of rehabilitation services was only weakly associated with improved functional outcomes after stroke.

Kwakkel et al. (2004) conducted an extension of previous meta-analysis and evaluated the benefit of augmented physical therapy which included 20 studies on several interventions: occupational (upper extremity), physiotherapy (lower extremity), leisure therapy, home care and sensorimotor training. After adjusting for differences in treatment intensity contrasts, augmented therapy was associated with statistically significant treatment effects for the outcomes of ADL and walking speed, although not for upper extremity therapy assessed using the Action Research Arm test. A 16-hour increase in therapy time during the first six-months following stroke was associated with a favourable outcome.

Chen et al. (2002) examined the relationship between intensity of therapy and functional gains in a retrospective study of 20 sub-acute rehabilitation facilities in the USA. Stroke patients made larger self-care gains if they had lower self-care, higher mobility and cognition function at admission, longer, uninterrupted stays, received more intensive therapies and weren't admitted to a rehabilitation facility initially. Determinants of improvement in mobility included younger age, admission soon after impairment, higher self-care and cognition measures. Although admission function, length of stay and therapy intensity collectively contributed to greater functional gains, length of stay and therapy intensity did not always predict those gains. There was an interdependency between the domains of self-care, mobility and cognition, such that patients with deficits in self-care on admission made the greatest improvements if mobility or cognitively remained intact or relatively intact.

Wodchis et al. (2005) studied a large cohort of stroke survivors (n=23,824) admitted to skilled nursing facilities in Ohio, Michigan and Ontario. For patients with an uncertain prognosis on admission the intensity of rehabilitation therapies was positively associated with an increased likelihood of going home. However, it should be noted that the weekly therapy time would not generally be considered to be intensive (The maximum category was 500+ min/week).

Duncan et al. (2005) reviewed all RCTs and meta-analyses published to date examining the effect of intensity on improved functional outcome and concluded that there was weak evidence of a dose-response relationship. The authors suggest that all subsets of patients may not benefit equally and could not recommend specific guidelines about the intensity or duration of rehabilitation therapies.

Galvin et al. (2008) examined the effect of increased duration of exercise therapy on functional recovery post stroke. The results of the meta-analysis which included the results from 10 studies demonstrated that increased duration of exercise therapy time had a small but positive effect on activities of daily living as measured by the Barthel Index. The improvements were maintained over a 6-month period.

Cooke et al. (2010) included the results from 9 RCTs representing 7 individual studies examining varying doses of the same exercise-based interventions. The authors meta-analyzed the studies on the basis of individual outcomes (ARAT scores, Motricity Index, handgrip strength, and comfortable walking speed) at the end of treatment and at follow-up. Most of the analyses contained the results from only 2-3 studies. Some small, but statistically significant treatment effects were reported. The authors concluded that there was some, but limited support in favour of greater therapy intensity.

In a meta-analysis, Lohse et al. (2014) explored the relationship between rehabilitation dosage and motor improvements to discern whether additional therapy is beneficial. The study defined therapy “dose” as the amount of time spent during therapy. A total of 34 RCTs were included in the analysis with a population group consisting of 1750 chronic stroke patients. The average therapy duration was virtually the same in both the treatment group and the control group (49.56±68.12 days vs. 49.60±68.10 days); however, the time scheduled for therapy averaged to just under 60 hours (57.41±44.88 hours) for the treatment group while the control group received only 24.08±36.39 hours of therapy. The resultant effect of the meta-analysis revealed an overall benefit favouring more time spent for therapy compared with less. Moreover, the effect of time was found to be a significant predictor of functional improvement.

A recent Cochrane review by French et al. (2016) focused on repetitive task training following stroke and highlights differences between upper and lower limb rehabilitation. While repetitive training is effective for both upper limb (arm function: 11 studies, $p=0.045$; hand function: 8 studies, $p=0.05$) and lower limb (walking distance: 9 studies, $p<0.0001$; functional ambulation: 8 studies, $p=0.026$; sit to stand: 7 studies, $p=0.0018$; balance: 9 studies, $p=0.0071$) recovery, there are notable differences in the optimal approach.

Evidence suggests upper limb repetitive task training rehabilitation is most optimal with less than 20 hours of training (9 studies, $p=0.046$); however, training sessions over 20 hours trended towards significance (6 studies, p=0.072). Additionally, improved upper limb function following repetitive task training favoured the experimental when focusing on single task training (4 studies, p=0.019) compared to mixed (8 studies, p=0.11) or whole therapy (3 studies, p=0.16) (French et al. 2016). There is also evidence that upper limb repetitive task training is more effective in improving outcomes for patients 16 days to 6 months post-stroke (7 studies, p=0.026) compared to patients within 16 days (4 studies, p=0.1) or over 6 months (4 studies, p=0.31) post-stroke (French et al. 2016).

Conversely, lower limb repetitive task training rehabilitation is more effective with greater than 20 hours of training (8 studies, p<0.0001) compared to less than 20 hours of training, although less than 20 hours of lower limb repetitive task training still favoured the experimental groups (16 studies, p=0.018). A meta-analysis by Kendall et al. (2016) reported significant improvements in walking endurance (8 studies, p<0.001) and speed (6 studies, p=0.002) with increased dose of aerobic training. Contrary to upper limb rehabilitation, lower limb repetitive task training rehabilitation is more effective using a mixed training protocol (11 studies, p=0.00088) and in a stroke population that is greater than 6 months post-stroke (10 studies, p<0.0001) (French et al., 2016). The results suggest that a different approach to upper versus lower limb rehabilitation using repetitive task training is necessary to achieve optimal functional recovery.

Intensity of Aphasia Therapy Post Stroke

The impact of the intensity of aphasia therapy post-stroke has also been studied. The most effective means of treating aphasia post stroke has yet to be determined, and studies investigating the efficacy of speech and language therapy for patients suffering aphasia post stroke have yielded conflicting results. One possible explanation for the observed heterogeneity of findings across studies is a difference in intensity of therapy. We have noted that the failure to identify a consistent benefit might have been due to the low intensity of speech-language therapy applied in the negative studies while higher intensities of therapy was present in positive studies (Poeck et al., 1989).

The RCT conducted by Bakheit et al. (2007) failed to uncover a benefit of intensive aphasia therapy as assessed using the Western Aphasia Battery. The average length of stroke onset was one-month. The authors reported that the majority of patients receiving intensive treatment weren't able to tolerate it. Patients were either too ill or refused therapy and actually had lower WAB scores compared with patients who received less intensive, standard therapy (68.6 vs. 71.4). While this study was considered to be negative, patients who received an average of 1.6 hours of therapy (standard group) per week had significantly higher scores than those who received only .57 hours of therapy (NHS group). Patients in the highest intensity therapy group received an average of 4 hours of therapy per week. Therefore, depending on how" intensive" is defined, this trial could be considered positive.

More recently, several studies have demonstrated that greater intensity of therapy does not improve outcomes when provided over an extended period of time (Dignam et al., 2015; Martins et al., 2013). In Dignam et al. (2015) and Martins et al. (2013), groups received the same total hours of therapy, but the therapy was provided over a condensed time frame for the experimental group, while the participants in the control group received the therapy distributed over a longer time frame. All groups showed significant improvement regardless of the frequency of therapy (Dignam et al., 2015; Martins et al., 2013). These results suggest that an increase in total duration of therapy may be more effective than increasing intensity of individual therapy sessions.

Bhogal et al. (2003) investigated the effects of both frequency and the amount of therapy provided and found that a significant treatment effect was achieved among studies which provided a mean of 8.8 hours of therapy per week for 11.2 weeks compared to trials that only provided approximately 2 hours per week for 22.9 weeks. On average, positive studies provided a total of 98.4 hours of therapy while negative studies provided a total of 43.6 hours of therapy. Consequently, total length of therapy was significantly inversely correlated with mean change in Porch Index of Communicative Abilities (PICA) scores. The hours of therapy provided in a week was significantly correlated to greater improvement on the PICA and on the Token Test. And finally, total hours of therapy were significantly correlated with greater improvement on the PICA and the Token Test. The authors concluded that intense therapy over a short amount of time could improve outcomes of speech and language therapy for stroke patients with aphasia (Bhogal et al., 2003).

Cherney et al. (2011) performed a systematic review of treatment studies which directly compares conditions of higher and lower intensity treatment for aphasia. Results were described based on International Classification of Functioning, Disability and Health-ICF (WHO 2001). Results at the ICF's language impairment and communication activity/ participation levels tend to be equivocal for both acute and chronic aphasia; with no clear differences between intensive and non-intensive treatment across studies.

In a Cochrane Review by Brady et al. (2016), intensive speech language therapy (SLT) was compared to conventional SLT. Findings suggest that the intensive SLT approach generated greater improvements in aphasia post stroke (2 trials, 84 participants). Furthermore, participants who underwent long duration of SLT compared to short duration of therapy experienced significantly greater improvements (2 trials, 50 participants). However, the authors note that the included studies were limited by low methodological quality (Brady et al., 2016).

Conclusions about therapy intensity

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Higher intensity physiotherapy** may not have a difference in efficacy compared **standard intensity physiotherapy** for improving motor function.	6	English et al., 2015; Askim et al., 2010; GAPS, 2004; Partridge et al., 2000; Kwakkel et al., 1999; Parry et al., 1999

AMBULATION AND MOBILITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Higher intensity physiotherapy** may not have a difference in efficacy compared **standard intensity physiotherapy** for improving ambulation and mobility.	4	English et al., 2015; Askim et al., 2010; GAPS, 2004; Kwakkel et al., 1999

BALANCE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Higher intensity physiotherapy** may not have a difference in efficacy compared **standard intensity physiotherapy** for improving balance.	1	Askim et al., 2010

SPEECH AND LANGUAGE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Higher intensity speech and language therapy** may not have a difference in efficacy compared **standard intensity speech and language therapy** for improving speech and language.	5	Stahl et al., 2018; Martins et al., 2013; Godecke et al., 2012; Bakheit et al., 2007; Denes et al., 1996

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Higher intensity physiotherapy** may not have a difference in efficacy compared **standard intensity physiotherapy** for improving activities of daily living.	9	English et al., 2015; Askim et al., 2010; GAPS, 2004; Di Lauro et al., 2003; Slade et al., 2002; Kwakkel et al., 1999; Parry et al., 1999; Ruff et al., 1999; Smith et al., 1981

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Higher intensity physiotherapy** may not have a difference in efficacy compared **standard intensity physiotherapy** for improving stroke severity.	1	Di Lauro et al., 2003

LENGTH OF STAY			
LoE	Conclusion Statement	RCTs	References
1a	**Higher intensity physiotherapy** may not have a difference in efficacy compared **standard intensity physiotherapy** for improving length of stay.	3	English et al., 2015; Slade et al., 2002; Ruff et al., 1999

Key Points

Higher intensity physiotherapy may not be more beneficial than standard intensity for improving outcomes post stroke.

Higher intensity speech and language may not be more beneficial than standard intensity for improving speech and language.

Caregiver-Support of Intensive Therapy

When faced with the sudden disability of a family member as is the case post-stroke, the patient's immediate support group (i.e. family, close relatives, or friends), often take on the responsibility of a caregiver (Clark & Smith, 1999). The patient's recovery process has been suggested to be influenced by the availability of the primary caregiver which can provide emotional support, and facilitate family communication (Bleiberg, 1986; Palmer & Glass, 2003).

While increasing the intensity of therapy alone may improve outcomes, recent research has explored the influence of caregiver support during intensive therapy. Studies evaluating the outcomes of caregiver support during intensive therapy are listed in table 8.

Table 8. Studies evaluating caregiver-support of intensive therapy

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Galvin et al. (2011) RCT (8) N_{Start}=40 N_{End}=37 TPS= Acute	E: Additional caregiver-mediated fitness and mobility exercise program C: Conventional therapy alone Duration: 35 minute sessions daily for 8 weeks.	• Fugl-Meyer Assessment: 5mo (+exp), 8mo (-) • Motor Assessment Scale:5mo (+exp), 8mo (-) • Berg Balance Scale: 5mo (+exp), 8mo (-) • 6-Minute Walk Test: 5mo (+exp), 8mo (+exp) • Barthel Index: 5mo (+exp), 8mo (-) • Activities of Daily Living: 5mo (+exp), 8mo (-)
Barzel et al. (2015) RCT (7) N_{Start}=156 N_{End}=147 TPS= Chronic	E: Additional caregiver-coached constraint induced movement therapy C: Standard therapy alone Duration: 50-60 minute sessions, 37 sessions over 4 weeks	• Motor Activity Log: Quality of Movement (+exp) • Wolf Motor Function Test (-)
Wang et al. (2015) RCT (7) N_{Start}=51 N_{End}=51 TPS= Chronic	E: Additional caregiver-mediated home-based exercise program C: Usual care alone Duration: 90 minute sessions once per week for 12 weeks	• Free-Walking Velocity (+exp) • Max-Walking Velocity (-) • 6-Minute Walk Test (+exp) • Berg Balance Scale (+exp) • Barthel Index (+exp)

Dai et al. (2013) RCT (6) N_{Start}=55 N_{End}=48 TPS= Acute/subacute	E: Additional caregiver-assisted virtual reality therapy C: Conventional therapy alone Duration: 30 minute sessions, once per day for 10 sessions over 2 weeks.	• Behavioural Inattention Test Conventional (-) • Functional Independence Measure (-) • Postural Assessment Scale (-) • Falls (-)
Agrawal et al. (2013) RCT (5) N_{Start}=30 N_{End}=30 TPS= Subacute	E1: 90min Caregiver-supported Graded Repetitive Arm Supplementary Program E2: 60min Caregiver-supported Graded Repetitive Arm Supplementary Program C: Usual care alone Duration: 90 minute sessions, 5 days/week for 4 weeks	• Fugl-Meyer Assessment: E1 vs. E2/ C (+exp) • Chedoke Arm and Hand Activity Inventory: E1 vs. E2/ C (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

The impact of caregiver support during intense therapy has only recently been investigated, with some studies showing significant improvements in recovery when caregiver support was provided. Thus far, several studies have shown that participants who underwent additional caregiver-mediated exercise training and standard therapy compared to standard therapy alone had significantly greater improvements in walking ability, balance, and mobility (Galvin et al., 2011; T. C. Wang et al., 2015). Furthermore, participants who underwent additional repetitive arm training with caregiver support had significantly greater quality of movement (Agrawal et al., 2013; Barzel et al., 2015). These results suggest that caregiver support during greater intensity therapy may facilitate an additive beneficial effect to therapy for the recovery of both upper and lower limb function.

Although the evidence is positive, the findings are limited to only a few trials, with the majority having a small sample size. Furthermore, there is great variability between trials regarding the role of the caregiver, the identity of the caregiver, and the interventions provided for the stroke survivor, among many others. As such, these factors increase the complexity of synthesizing the evidence and establishing a strong foundation for the involvement of caregivers in the care and recovery of the stroke survivor. More research is encouraged to determine whether different caregiver roles and identities have differing effects on the patient's recovery.

Conclusions Regarding Caregiver-Mediated Intensity of Therapy

There is level 1a evidence that additional caregiver-supported therapy results in improved functional outcomes compared to conventional therapy alone.

Greater intensities of therapy with caregiver support may result in improved functional outcomes. More research is needed to strengthen the current evidence.

Durability of Rehabilitation Gains

Functional recovery (the ability to perform activities despite impairment) and improvement in communication may continue for months after neurological recovery is complete (Stineman & Granger, 1998). Between 6 months and 3 years post stroke the average level of functional ability is maintained (Borucki et al., 1992; Dombovy et al., 1987). Beyond 3-5 years, slight decreases were noted, most likely related to the effects of increasing age and comorbidity (Stineman & Granger, 1998). Therefore, in the absence of a new event, it has long been thought that stroke patients tend to maintain gains made in rehabilitation over the long-term.

Previous Reviews

Evans et al. (1995) reviewed 11 studies published between 1980 and 1993 that evaluated rehabilitation treatments, which included an untreated control group. The outcomes of mortality, discharge location and functional ability were assessed. Three of the papers evaluated the rehabilitation of individuals with disabilities other than stoke. Their analysis revealed that treatment on a rehabilitation unit resulted in greater odds of survival, higher rates of discharge to home, higher rates of remaining at home at 8-12 month follow-up, and higher levels of functional ability at discharge. However, the difference in survival and functional independence had disappeared at the 12-month follow-up period, suggesting that many patients who are discharged from rehabilitation may deteriorate medically, physically, and functionally.

Bagg (1998) stated that this finding accentuated the need to assess the effectiveness of outpatient and home- based therapies after discharge from inpatient rehabilitation programs, as well as the role of maintenance therapy for individuals with stroke requiring long-term institutionalization. This is discussed in greater detail in the last section on Community Reintegration.

Gresham et al. (1995) noted that studies examining long-term outcomes have reached mixed conclusions. Some studies found functional gains were maintained (Indredavik et al., 1991; Smith et al., 1981; Strand et al., 1985) while others did not (Garraway et al., 1980; Garraway et al., 1981; Sivenius et al., 1985; Stevens et al., 1984; Sunderland et al., 1994; Sunderland et al., 1992; Wade et al., 1992)

Five "good" (PEDro > 6) quality studies evaluated the durability of rehabilitation gains. The results are summarized in Table 6.8.1.1 below.

Table 6.8.1.1 Summary of outcome measures from RCTs with PEDro ≥ 6 evaluating the durability of rehabilitation gains

Author/Year PEDro score	Intervention	Outcome	Durability
Bernhardt et al. (2008b) Sorbello et al. (2009) Cumming et al. (2011) RCT (8) N_{Start}=71 N_{End}=71 TPS= Acute	E: Very Early Mobilization (within 24hr) (14 days or until discharge) C: Standard Care Duration: median LOS for E: 6 d; median LOS for C: 7 d (3mo)	3mo • mRs score 0-2 (+exp)	6 mo • mRS score 0-2 (-) 12 mo • mRS score 0-2 (+exp)
Kwakkel et al. (2002) RCT (8) N=101 N=86 TPS= Acute	E1: Upper extremity E2: lower extremity therapy C: control condition Duration: 30 min, 5 days/week for 30 weeks	6mo • Action Research Arm Test - Dexterity (+exp)	9mo • Action Research Arm Test - Dexterity (+exp)

			12mo • Action Research Arm Test - Dexterity (+exp)
Indredavik et al (1991) Indredavik et al. (1997) Indredavik et al. (1999) RCT (7) N=220 N=51 TPS= Acute	E: Rehabilitation stroke Unit C: General ward Duration: 10yrs	6wks • Barthel Index (+exp)	1yr • Barthel Index (+exp) 5yrs • Barthel Index (+exp) 10yrs • Barthel Index (+exp)
Stevens et al. (1984) RCT (6) N=228 TPS= Acute	E: Treatment in special ward C: Conventional treatment location Duration: Total therapy time for group E: 5750 hours; Total therapy time for group C: 1886 hours	4mo • Independence in dressing (-)	8mo • Independence in dressing (-) 12mo • Independence in dressing (+exp)
Juby et al. (1996) Lincoln et al. (2000) Drummond et al. (2005) RCT (6) N=315 TPS= Acute	E: Stroke unit C: Conventional ward Duration: Median of 7 sessions given with a median total duration of 369 therapy minutes.	3mo • Nottingham EADL (-) • General Health Questionnaire (-) • Barthel Index (+exp) • Rivermead ADL (+exp) • LOS (+exp)	6mo • Nottingham EADL (+exp) • General Health Questionnaire (-) • Barthel Index (+exp) • Rivermead ADL (+exp) 1yr • Nottingham EADL (+exp) • General Health Questionnaire (+exp) • Barthel Index (-) • Rivermead ADL (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

All of these studies reported improvement in the functional outcome of stroke rehabilitation patients compared to the control group (general medical ward) anywhere between 12 months and 10 years following stroke. The relative benefit attributed to stroke rehabilitation appears to be very robust. However, the absolute gains achieved through stroke rehabilitation appear to be less robust. Stevens et al. (1984) found selective continued improvement from four to 12 months. In contrast, patients in the control group actually declined in function. Indredavik et al. (1999; 1997) reported a decline in scores associated with functional outcome between five and 10 years post stroke, although the Barthel Index scores of patients treated on the stroke unit were higher compared to control group patients. Davidoff et al. (1991) reported a significant improvement in ADL scores between rehabilitation discharge and one year. Leonard et al. (1998) found that FIM scores improved for the first year and then plateaued, with a non-significant decline over the next four to five years.

Bernhardt et al. (2008) demonstrated that early mobilization during the first 2 weeks following stroke was associated with a good outcome at 12 months following stroke. The program was also found to be cost-effective. Mean total costs over the 12 month study period were AUD $13,559 for the AVERT group and AUD $21,860 for the standard care group (Tay-Teo et al., 2008). A large follow-up study, AVERT III, is planned to examine the effects of additional early mobilization (3x/day for 14 days) following acute stroke.

Conclusions Regarding the Durability of Rehabilitation Gains

There is level 1a evidence that relatively greater functional improvements are made by patients rehabilitated on specialized stroke units when compared to general medical units in the long term.

There is level 1a evidence that functional outcomes achieved through stroke rehabilitation are maintained for up to one year post stroke.

There is level 1b evidence that by five years post-stroke functional outcomes plateau and may decline. By ten years, overall functional outcome scores significantly decline although it is unclear to what extent the natural aging process and comorbidity may contribute to these declines.

Greater functional improvements made on interdisciplinary stroke rehabilitation units are maintained over the long-term.

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