2. Brain Reorganization, Recovery and Organized Care

Robert Teasell MD, Norhayati Hussein MBBS MRehabMed, Mitchell Longval BSc

Table of Contents

2.1 Important Principles of Recovery

2.1.1 Neurological Recovery

Recovery after a stroke is associated with cortical reorganization. Motor recovery is a complex process combining:

1. **Neurological or Spontaneous Recovery.** Recovery of impairment or normal way of moving as measured by Fugl-Meyer score or 3D Kinematics (restoration of normal movement patterns).
2. **Functional Recovery.** Recovery of tasks or activities often through learned compensatory movements (new movement patterns) as measured by the ARAT, Barthel Index or even the FIM.

Both involve changes to the remaining motor cortex and this relationship is not fully understood.

Spontaneous or Intrinsic Neurological Recovery

Neurological recovery is defined as recovery of neurological impairments. These are determined primarily by the site and extent of the stroke. As a general rule, *the severity of the initial deficit is inversely proportional to the prognosis for recovery.* The majority of neurological recovery occurs within the first 1-3 months. Afterwards recovery may occur much more slowly for up to one year. The course of recovery is a predictable phenomenon; it *is initially very rapid and then negatively accelerates as a function of time* (Skilbeck et al. 1983). Skilbeck et al. (1983) studied 92 stroke survivors with a mean age of 67.5 years (range= 36-89) at final assessment, either 2 or 3 years after stroke. The majority of recovery was reported within the first 6 months, with continued but non-statistically significant recovery after 6 months. This type of recovery is still largely if not completely independent of rehabilitationand is discussed further later on.

Functional or Adaptive Recovery

Functional deficits are often referred to as *disabilities* and are measured in terms of functions such as activities of daily living. Functional recovery is defined as improvement in mobility and activities of daily living; it has long been known that it is influenced by rehabilitation. This recovery depends on the patient's motivation, ability to learn and family supports as well as the quality and intensity of therapy. Functional recovery is highly influenced by neurological recovery but is not dependent on it.

2.1.2 Time Course of Recovery

Peak neurological recovery from stroke occurs within the first one to three months. A number of studies have shown that recovery may continue at a slower pace for at least 6 months; with up to 5% of patients continuing to recover for up to one-year. This is especially true with patients who are severely disabled at the time of initial examination (Bonita & Beaglehole 1988, Duncan et al. 1992, Ferrucci et al. 1993, Kelly-Hayes et al. 1989, Wade et al. 1983, Wade et al. 1987).

Progress towards recovery may plateau at any stage of recovery with only a very small percentage of those with moderate to severe strokes (about 10%) achieving “full recovery”. The return of motor power is not synonymous with recovery of function; function may be hampered by the inability to perform skilled coordinated movements, apraxias, sensory deficits, communication disorders as well as cognitive impairment. Functional improvements may occur in the absence of neurological recovery (Duncan & Min

Lai 1997, Nakayama et al. 1994). Functional recovery (the ability to do activities despite limitations) and improvement in communication may continue for months after neurological recovery is complete.

2.2 Mechanisms of Neurological Recovery

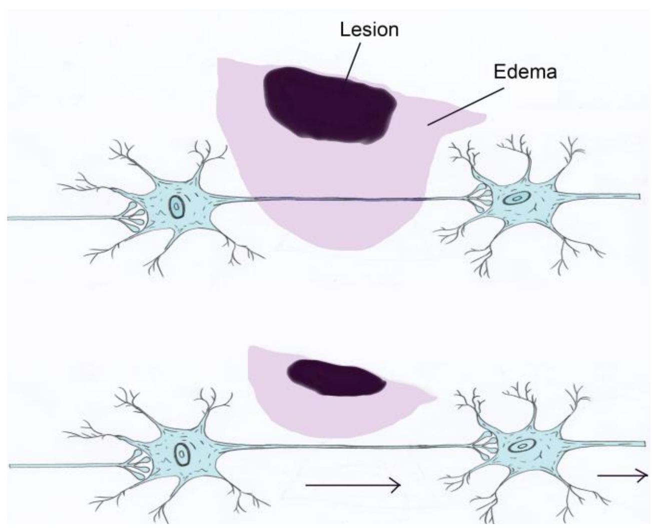
Neurological recovery is defined as recovery of neurological impairments and is often the result of a number of factors listed below.

2.2.1 Processes of Neurological Recovery

Processes leading to initial clinical improvement occur independent of behaviour or stimuli, although there is some concern about too aggressive very early mobilization (Bernhardt 2015). Processes which may account for neurological recovery include: 1) Resolution of post-stroke edema; 2) Reperfusion of the ischemic penumbra; 3) Resolution of diaschesis.

Post-Stroke Edema

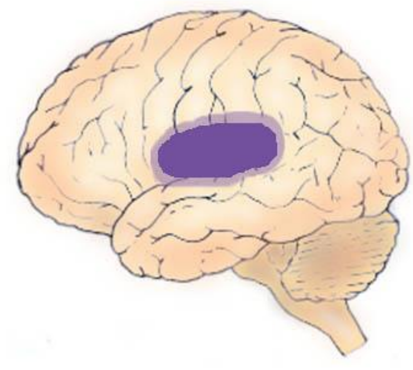
Edema surrounding the lesion may disrupt nearby neuronal functioning. Some of the early recovery may be due to resolution of edema surrounding the area of the infarct (Lo 1986) and as the edema subsides, these neurons may regain function. This process may continue for up to 8 weeks but is generally completed much earlier (Inoue et al. 1980). Cerebral hemorrhages tend to be associated with more edema, which take longer to subside, but which may in turn be associated with a more dramatic recovery.



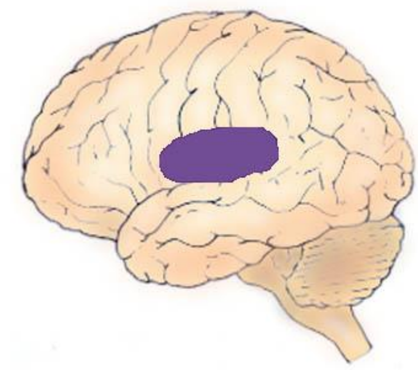
Reperfusion of the Ischemic Penumbra

Reperfusion of the ischemic penumbra is another local process which can facilitate early recovery. A focal ischemic injury consists of a core of low blood flow which eventually infarcts (Astrup et al. 1981, Lyden & Zivin 2000), surrounded by a region of moderate blood flow, known as the ischemic penumbra (Astrup et al. 1981, Lyden & Zivin 2000), which is at risk of infarction but is still salvageable. Reperfusion of this area causes affected and previously non-functioning neurons to resume functioning with subsequent clinical improvement.

The AVERT (2015) trial, looking at very early mobilization of the acute stroke patient, raised concerns about the penumbra and worsening or extension of the stroke.



Lesion with Ischemic Penumbra



Reperfusion of Ischemic Penumbra

Diaschesis
Diaschesis is a *state of low reactivity or depressed function as a result of a sudden interruption of major input to a part of the brain remote from the site of brain damage*. With injury to one area of the brain, other areas of brain tissue are suddenly deprived of a major source of stimulation. Nudo et al. (2001) noted that diaschesis occurs early after injury and is an inhibition or suppression of surrounding cortical tissue or of cortical regions at a distance that are interconnected with the injury core. The reversibility may be partially due to the resolution of edema, which may account for a portion of spontaneous recovery (Nudo et al. 2001). Neuronal function may return following the resolution of diaschisis, particularly if the connected area of the brain is left intact. This is particularly true of non-cortical structures after cortical injury (Lo 1986).

Proportional Recovery of Upper Limb Impairment
One recent controversial concept has been that within 6 months after a stroke, upper limb impairment resolves by **fixed proportion**. Fixed proportion argues that 70% of each patient's maximum possible improvement occurs regardless of the initial impairment (for instance, as measured by the Fugl-Meyer score), but only for those with relatively intact corticospinal (motor) tract functioning (Prabhakaran et al. 2008). This holds true for patients across all ages and countries with different rehabilitation services (Byblow et al. 2015).

As mentioned, proportional recovery or resolution of upper extremity impairment post stroke is dependent on corticomotor tract integrity. Motor evoked potentials (MEPs) early post stroke is associated with recovery outcomes (Stinear 2010). Irreversible structural damage to the corticospinal tract severely limits recovery of upper limb movement (Stinear 2010, Stinear et al. 2007). **This recovery is unaffected or minimally affected by rehabilitation therapy.** 3D kinematics in subacute and chronic stroke survivors have shown that motor recovery associated with rehabilitation is driven more by adaptive or compensatory learning strategies. Most of the tests that we use clinically only assess a patient's ability to accomplish a certain function or task; we do not tend to measure function.

2.2.2 CNS Reorganization (Later Recovery)
Neurological reorganization plays an important role in the restoration of function. It can extend for a much longer period of time than local processes, such as the resolution of edema or reperfusion of the

penumbra, and is of particular interest because it can be *influenced by rehabilitation training.* Nudo (2003), based on animal research, has suggested that changes occurring during motor learning (i.e. synaptogenesis and increases in synaptic strength), are likely the same type of changes that occur during this part of recovery from stroke. This has been well shown after small, focal lesions in the motor cortex where the same principles of motor learning and development of functional connections are occurring in adjacent, undamaged tissue.

In Normal Individuals

Cramer (2003) notes that*, "in normal right-handed persons, performance of a unilateral motor task by the right hand is associated with activation that is largely contralateral, with brain activity ipsilateral to the active hand being small by comparison (Kim et al. 1993). In contrast, there is greater ipsilateral activation for movements by the left hand."*

In Individuals Post Stroke

Nudo (2003) reports that *neuroplasticity post-stroke (with damage to the motor cortex as an example) is based on three main concepts:*

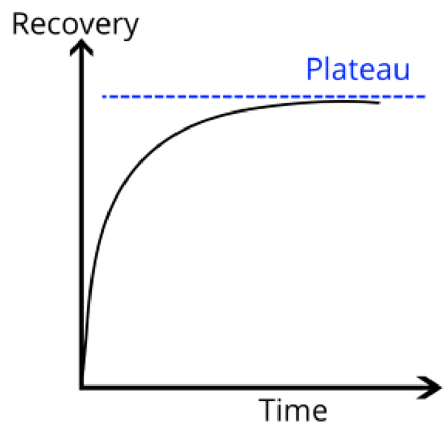
1. In normal (non-stroke) brains, acquisition of skilled movements is associated with predictable functional changes within the motor cortex.
2. Injury to the motor cortex post-stroke results in functional changes in the remaining cortical tissue.
3. After a cortical stroke, these two observations interact so that *reacquiring motor skills is associated with functional neurological reorganization occurring in the undamaged cortex* (Nudo 2003).

Mechanism of Reorganization

Cramer (2003) noted that after a stroke in humans, movement of the affected hand resulted in three patterns of cortical reorganization that were not mutually exclusive of each other and which may occur concomitantly:

1. A greater degree of bilateral motor cortex activity was seen with recruitment of the motor network of the ipsilateral (unaffected hemisphere; (Cramer 2003). In fact, there is widespread areas of cortical hyperactivity occurring days post stroke and dimishing within months of the stroke onset. Non-stroke (less affected) hemisphere cortical activity decreases over months post stroke in those patients who show a good motor recovery but not in those who do not show a good motor recovery.
2. There was increased recruitment of secondary cortical areas such as supplementary motor area (SMA) and pre-motor cortex in the contralateral (affected) hemisphere (Cramer 2003). Recruitment along the cortical rim of the infarct was seen (Cramer 2003). Reorganization of the brain after a stroke is dependent not only on the lesion site, but also on the surrounding brain tissue and on remote locations that have structural connections with the injured area. Following a stroke, brain reorganization in response to relearning motor activities, involves primarily the contralateral (affected) hemisphere. Reorganization in response to training occurs along the cortical rim of the infarction with increased recruitment of secondary cortical areas such as supplementary motor area and pre-motor cortex in the contralateral (affected) hemisphere.
3. Ipsilateral cortical involvement is more prominent early on; however, persistence of ipsilateral cortical involvement is generally associated with larger strokes and a poorer recovery.

Therefore, we can note that reorganization of cortex post stroke is dependent on the lesion site but also on remote brain areas with structural connections with the damaged area of the brain. Motor recovery is largely dependent on intact cortex adjacent to the infarct pointing out the importance of preserving penumbral areas.



2.3 Predictors of Stroke Recovery

Alexander (1994) noted the two most powerful predictors of functional recovery were **initial stroke severity** and **age**. Stroke severity is by far the most predictive factor.

2.3.1 Stroke Severity as Predictor

The best predictor of stroke outcome is initial clinical assessment of stroke severity. This correlates with the length of time to maximal neurological and functional recovery.

Garraway et al. (1985, 1981) first proposed the concept of 3 bands of stroke patients based upon stroke severity during the acute phase:

1. **Mild Strokes:** Few deficits, early FIM score (1st 5-7 days) > 80**,** Stineman et al. (1998) defined as motor FIM > 62***;*** rehab gains limited by "ceiling" effect.
2. **Moderately Severe Strokes:** Moderate deficits, conscious with significant hemiparesis***,*** early FIM 40-80 or motor FIM 38-62***;*** make marked gains in rehab and 85% discharged to community.
3. **Severe Strokes*:*** Severe deficits, unconscious at onset with severe paresis or serious medical comorbidity***,*** early FIM < 40 or motor FIM < 37***;*** slower improvement, unlikely to achieve functional independence (unless young) and smallest likelihood of community discharge.

Time Course for Recovery Depends on Initial Severity of Impairments
Jorgensen et al. (1995c, 1995d) studied 1,197 acute stroke patients in what is referred to as the Copenhagen Stroke Study. Impairments were classified using the Scandinavian Neurological Stroke Scale (SSS) and functional disability was defined according to the Barthel Index (BI). Neurological recovery occurred on average two weeks earlier than functional recovery. In surviving patients, the best neurological recovery occurred within 4.5 weeks in 80% of the patients, while best ADL function was achieved by 6 weeks. For 95% of the patients, best neurological recovery was reached by 11 weeks and best ADL function within 12.5 weeks. Jorgensen and associates (1995b) reported that best walking function was reached within four weeks for patients with mild paresis of the affected lower extremity, six

weeks for those with moderate paresis and 11 weeks for severe paralysis. Consequently, the time course of both neurological and functional recovery was strongly related to both initial stroke severity and functional disability. Jorgensen et al. (1995a, 1995b, 1995c), found two-thirds of all stroke survivors have mild to moderate strokes and are able to achieve independence in ADL.

Impairment and Neurological Recovery of Stroke Patients in the Copenhagen Stroke Study

Category (SSS)	Admission [1]	Discharge [2]	Survival (%)	Weeks to 80% Best Neurological Recovery [3]	Weeks to 95% Best Neurological Recovery [3]
Very Severe (0-14)	19%	4%	38%	10	13
Severe (15-29)	14%	7%	67%	9	15
Moderate (30-44)	26%	11%	89%	5.5	10.5
Mild/No (45-58)	41%	78%	97%	2.5	6.5

[1] Percentage patient distribution on admission, grouped by stroke severity sub groups, as measured by SSS (scores range from 0-58 points).
[2] Percentage distribution of survivors (79% of initial group) after completion of stroke rehabilitation.
[3] Neurological recovery as measured by SSS.

Disability and Outcome of Stroke Patients in the Copenhagen Stroke Study

Category (BI)	Discharge [1]	Survival (%)	Weeks to 80% Best Functional Recovery [2]	Weeks to 95% Best Functional Recovery [2]
Very Severe (0-20)	14%	50	11	17
Severe (25-45)	6%	92	15	16
Moderate (50-70)	8%	97	6	9
Mild (75-95)	26%	98	2.5	5
No (100)	46%	-	-	-

[1] Percentage patient distribution on discharge, grouped by stroke severity sub groups, as measured by Barthel Index.
[2] Functional recovery as measured by Barthel Index.

Based on these observations one can safely conclude that *the initial severity of the stroke is inversely proportional to the final functional outcome*, with the majority of patients who suffer mild strokes demonstrating no or only mild disabilities, while the majority of patients suffering very severe strokes still experience severe or very severe deficits even after the completion of rehabilitation.

2.3.2 Impact of Age on Recovery/Rehabilitation

Recovery is more rapid and occurs to a greater extent in younger individuals with a stroke. This correlates with decline in ability to form neurological connections with aging. There is also a small but significant effect of age on functional recovery.

Impact of Age in Animal Studies

In rats, the duration of motor impairment post brain lesion increases with age (Brown et al. 2003). The regenerative response of neurons and glial cells, though largely preserved with age, appears to be delayed or occurs at a diminished rate the older the animal (Popa-Wagner et al. 1999, Whittemore et al. 1985). Reactive neuronal synaptogenesis declines (Scheff et al. 1978), sprouting responses are less robust

(Schauwecker et al. 1995, Whittemore et al. 1985) and synaptic replacement rates diminish (Cotman & Anderson 1988). Generally recovery is more rapid and occurs to a greater extent in a younger animal. This correlates with a decline in the rate of formation of new neuronal connections or synaptogenesis in older animals. Older animals do improve post-stroke but it takes longer and occurs to a lesser extent.

Impact of Age in Clinical Studies

In a cohort study of 2219 patients, Kugler et al. (2003) studied the effect of patient age on early stroke recovery. The authors found that relative improvement decreased with increasing age: patients younger than 55 years achieved 67% of the maximum possible improvement compared with only 50% for patients above 55 years ($p< 0.001$). They also found that age had a significant but relatively small impact on the speed of recovery with younger patients demonstrating a slightly faster functional recovery ($p< 0.001$). The authors concluded that although age had a significant impact it nevertheless was a poor predictor of individual functional recovery after stroke and could not be regarded as a limiting factor in the rehabilitation of stroke patients. However, younger patients did demonstrate a more complete recovery.

In conclusion, in humans, age has a small but significant effect on the speed and completeness of recovery. However, because older stroke patients do recover, albeit at a slower rate, and the overall impact of age is relatively small, age in and of itself is a poor predictor of functional recovery after stroke.

2.3.3 Hemorrhagic versus Ischemic Stroke

Approximately 10% of all strokes are due to intra-cerebral hemorrhage (Andersen et al. 2009, Kelly et al. 2003, Paolucci et al. 2000). Hemorrhagic strokes have been associated with more severe neurological deficits and are generally thought to have a higher mortality rate. The apparent poorer outcome among patients with hemorrhagic stroke was attributed to greater initial stroke severity compared to patients with ischemic stroke (Jørgensen et al. 1995a). Patients with hemorrhagic strokes have lower functional score upon admission to rehabilitation but tend to fare better in terms of functional gains and achieve higher outcome efficiency scores when compared to those with ischemic strokes. Hemorrhagic strokes are usually admitted to rehabilitation later than ischemic strokes because of greater initial severity.

Lipson et al (2005) studied medical records of 819 consecutive patients with strokes and found that those with a hemorrhagic stroke were admitted to rehabilitation at a significantly later date post stroke with median of 30 days (IQR 15-77) compared to ischemic stroke with median of 18 days (IQR 10.39; $p<0.0001$). Kelly et al (2003) reported that although the total admission FIM score was lower in patients with hemorrhagic compared to ischemic (51 vs 59, $p=0.0001$), there was no significant difference in total discharge FIM score between the two groups (79.1 hemorrhagic vs 82.3 ischemic, $p=0.2$). Patients with ICH gained more FIM points during rehabilitation then ischemic strokes (28 vs 23.3, $p=0.002$). Hemorrhagic stroke patients with the most severely disabling strokes had significantly greater recovery than ischemic strokes of similar severity.

Paolucci et al (2003) matched patients on the basis of initial stroke severity, age and onset to admission time and found that patients with hemorrhagic strokes demonstrated higher outcome scores at discharge when compared to ischemic strokes. Hemorrhagic patients showed a probability of high therapeutic response on the BI at approximately 2.5 times greater than that of ischemic stroke. The authors attributed the greater gains in hemorrhagic strokes to better neurological recovery associated with resolving brain compression.

2.4 Measures of Functional Outcome

Category	Rationale	Individual Assessment Tools
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.	• Canadian Neurological Scale (CNS) • Modified Rankin Scale (MRS) • National Institutes of Health Stroke Scale (NIHSS) • Oxford Handicap Scale • Scandinavian Stroke Scale (SSS)
Activities of Daily Living	These outcome measures assessed performance and level of independence in various everyday tasks.	• Adelaide Activities Profile • 4-point ADL Scale • Assessment of Motor and Process Skills (AMPS) • Barthel Index (BI) • Canadian Occupational Performance Measure (COPM) • Frenchay Arm Test (FAT) • Frenchay Activities Index (FAI) • Functional Independence Measure (FIM) • Hamrin Activity Index • Instrumental Activity Measure • Katz Index of Independence in Activities of Daily Living • Lawton Instrumental Activities of Daily Life Scale • London Handicap Scale • Motor Assessment Scale (MAS) • Nottingham Extended Activities of Daily Living • Nottingham Leisure Questionnaire • Nottingham Stroke Dressing Assessment (NSDA) • Older Adults Resources and Services – Activities of Daily Living Scale • Rivermead Activities of Daily Living • Stroke Impact Scale (SIS)
Motor function	These outcome measures covered gross motor movements and a series of general impairment measures when using the upper extremities.	• Action Research Arm Test (ARAT) • B. Lindmark Motor Assessment • Fugl-Meyer Assessment (FMA) • Jebsen-Taylor Hand Function Test (JTHFT) • Motor Club Assessment (MCA) • Motor Status Scale (MSS) • Motricity Index (MI) • Nine Hole Peg Test (9HPT) • Profiles of Recovery • Rivermead Motor Assessment (RMA) • Rivermead Mobility Index (RMI) • Rivermead Motor Assessment (RMA) • Stroke Rehabilitation Assessment of Movement (STREAM) • Wolf Motor Function Test (WMFT)

Ambulation and mobility	These outcomes measures assessed ambulatory abilities during distance-based or timed walking exercises commonly.	• 10-Metre Walk Test • 5-Meter Walk Test • 6-Minute Walk Test • Functional Ambulation Category • Gait Speed • Dynamic Gait Index • Rivermead Mobility Index (RMI) • Step Length (SL) • Walking Speed (WS)
Balance	These outcome measures assessed postural stability, and both static and dynamic balance.	• Berg Balance Scale • Trunk Impairment Scale (TIS) • Activities-Specific Balance Confidence Scale • Functional Reach Test • Postural Assessment Stroke Scale (PASS) • Timed Up & Go Test (TUG) • Stair Climb Test (SCT) • Dizziness Handicap Inventory
Cognition	These outcome measures assessed an individual's overall cognitive processing capability factoring in multiple domains.	• The Barrow Neurological Institute Screen for Higher Cerebral Functions • Short Portable Mental Status Questionnaire • Mini Mental Status Examination (MMSE) • Cognitive Test 50
Speech and language	These outcome measures assessed speech and language outcome measures.	• Aachen Aphasia Test • Action Communication Test • Frenchay Aphasia Screening Test • Functional Communication Profile • Reinvang's Aphasia Test • Western Aphasia Battery
Spasticity	These outcome measures assessed changes in muscle tone, stiffness, and contractures.	• Modified Ashworth Scale (MAS)
Mental Health	These outcome measures assess psychiatric dysfunction in a number of mental health related dimensions.	• General Health Questionnaire • Beck Depression Inventory (BDI) • Geriatric Depression Scale (GDS) • Hospital Anxiety and Depression Scale (HADS) • Montgomery-Asberg Depression Rating Scale
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.	• Australian Quality of Life • Dartmouth co-op charts • EuroQol Quality of Life (EQ-5D) • Life Satisfaction Index • Medical Outcome Trusts' Short Form Health Survey (SF-36 or SF-12) • Nottingham Health Profile

		• Pearlman's Quality of Life Scale • Satisfaction with stroke care questionnaire • Sickness Impact Profile
Community Reintegration 	These outcome measures assess an individual's ability to reintegrate into their community and social behaviours.	• Brief Assessment of Social Engagement McMaster Family Assessment Device • Reintegration to Normal Living Index (RNLI) • Subjective Index of Physical and Social Outcome
Caregiver Burden 	These outcome measures assess the level of burden for caretakers of stroke survivors.	• Caregiver Strain Index
Length of stay 	Assessed how long a patient was admitted to a stroke unit or outpatient service.	
Mortality 	Assessed a patient's mortality.	

2.4.1 Motor Function

Fugl-Meyer Assessment (FMA)
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 (Nilsson et al. 2001, Sanford et al. 1993).

Walking Speed (WS)
Walking speed 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 nonstroke patients. This measure has been shown to have good reliability and validity (Himann et al. 1988, Jordan et al. 2007).

2.4.2 Balance

Berg Balance Scale

The 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 (Blum & Korner-Bitensky 2008).

Timed Up & Go Test (TUG)
TUG is a measure of the ability of a stroke patient to perform sequential motor tasks. This measure consists of 1 functional task which involves the patient standing up from a chair, walking 3 metres, turning around and sitting back down again. This task is then evaluated on a scale from 1 to 5 (1=normal function, 5=severely abnormal function). This measure has been shown to have good reliability and validity (Shumway-Cook et al. 2000, Steffen et al. 2002).

Activities of Daily Living

Barthel Index (BI)
The Barthel Index 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).

Barthel Index

Questions	Answer
What does it measure?	The BI is an index of independence that is used to quantify the ability of a patient with a neuromuscular or musculoskeletal disorder to care for him/ herself (regardless of particular diagnostic designations).
What is the scale?	The index consists of 10 common ADLs, 8 of which represent activities related to personal care while 2 are related to mobility.
What are the key scores?	The index yields a total score out of 100 with higher scores indicating greater degrees of functional independence (McDowell & Newell 1996).
What are its strengths?	Easy to administer and does not require formal training. Takes little time to complete, which may reduce patient burden. Widespread familiarity contributes to its interpretability.
What are its limitations?	Relatively insensitive. A lack of comprehensiveness may result in problems with ceiling/floor effects (Duncan & Min Lai 1997). Although many scoring cut-offs have been suggested, there remains a lack of consensus regarding the categorization of BI scores (Roberts & Counsell 1998).

Functional Independence Measure (FIM)
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 18 items which make up the FIM are listed below:

- Bladder management
- Bowel management
- Social interaction
- Problem solving
- Memory
- Comprehension
- Bed-to-chair and wheelchair-to-chair transfer
- Toilet transfer
- Tub and shower transfer

- Locomotion (walking or wheelchair)
- Climbing stairs
- Eating
- Grooming
- Bathing
- Dressing (upper body)
- Dressing (lower body)
- Toileting

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. 1998).

Functional Independence Measure

Questions	Answer
What does it measure?	Physical and cognitive disability in terms of burden of care – that is, the FIM score is intended to measure the burden of caring.
What is the scale?	The FIM is a composite measure consisting of 18 items assessing 6 areas of function. These fall into 2 basic domains; physical and cognitive. Each item is scored indicating of the amount of assistance required to perform each item. A simple summed score is obtained determining the level of dependence of the individual. Subscale scores may yield more useful information than combining them (Linacre et al. 1994).
What are the key scores?	Beninato et al. (2006) determined that 22, 17 and 3 were the change scores for the total FIM, motor FIM and cognitive FIM, respectively, which best separated those patients who had demonstrated clinically important change from those who had not. Each item is scored on a 7-point scale (1=total assistance, 7 = total independence). A simple summed score of 18 – 126 is obtained where 18 represents complete dependence/total assistance and 126 represents complete independence.
What are its strengths?	The FIM has been well studied for its validity and reliability. FIM is widely used and has one scoring system increasing the opportunity for comparison.
What are its limitations?	Training and education in administration of the test is necessary (Cavanagh et al. 2000). The use of a single summed raw score may be misleading. Training and education of persons to administer the FIM may represent a significant cost.

Stroke Impact Scale (SIS)

The 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).

2.4.3 Cognition

Mini Mental Status Examination (MMSE)

The MMSE is a brief screening tool and quantitative assessment of cognitive impairment. It is one of the most commonly used instruments for this purpose. The exam consists of 11 questions/tasks in 7 cognitive domains: 1) orientation to time; 2) orientation to place; 3) registration of 3 words; 4) attention and calculation; 5) recall of 3 words; 6) language; and 7) visual construction. The test is scored out of 30 possible points, with a score between18 to24 denoting mild impairment and a score between 0 to17 denoting severe impairment. The test has been found to be valid as a screening tool, and is sensitive for detecting moderate/severe impairment, but not mild impairment. It has good interrater reliability. The MMSE is appropriate for screening for post-stroke cognitive impairment (Bour et al. 2010, Dick et al. 1984, Tombaugh & McIntyre 1992).

Quality of Life

EuroQol Quality of Life (EQ-5D)
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)
The 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 (Bugge et al. 2001, Guilfoyle et al. 2010).

2.4.4 Stroke Severity

Canadian Neurological Scale (CNS)
The CNS is a measure used to assess neurological status of acute phase stroke patients. Ten clinical domains including ,motor rehabilitations, both weakness and response of arm, face and legs are measured along with mentation (speech, orientation and level of consciousness). The scale has demonstrated reliability and concurrent validity (Bushnell et al. 2001).

Modified Rankin Scale (MRS)
The Rankin scale is a global outcomes rating scale for patients post stroke (Rankin 1957). The 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).

Modified Rankin Handicap Scale

Rankin Grade	Description
0	No Symptoms
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability: unable to carry out all previous activities but able to look after own affairs without assistance.
3	Moderate disability: requiring some help, but able to walk without assistance
4	Moderately severe disability: unable to walk without assistance, and unable to attend to own bodily needs without assistance
5	Severe disability: bedridden, incontinent, and requiring constant nursing care and attention

(Van Swieten et al. 1988)

Modified Rankin Handicap Scale as an Outcome Measure

Questions	Answer
What does it measure?	The Rankin scale is a global outcomes rating scale for patients post stroke (Rankin 1957).
What is the scale?	The scale assigned a subjective grade from 1 – 5 based on level of independence with reference to prestroke activities rather than on observed performance of specific tasks.
What are the key scores?	An original Rankin score of 1 indicated no significant disability and 5 the most severe level of disability. Van Swieten et al. (1988) expanded the ranking system to include 0; no symptoms.
What are its strengths?	The Modified Rankin Scale is an extremely simple, time efficient measure. Feasible for use in large centers or large trials (de Haan et al. 1995, Wade et al. 1992). The MRS requires no special tools or training.
What are its limitations?	The categories within the scale are broad and poorly defined (Wilson et al. 2002). The use of dichotomization to classify global outcome may be associated with a loss of information with regard to benefits derived from any rehabilitation intervention.

National Institutes of Health Stroke Scale (NIHSS)

The 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).

2.4.5 Community Reintegration

Reintegration to Normal Living Index (RNLI)
The RNLI assesses the degree to which individuals who had experienced traumatic or incapacitating illness achieve reintegration into normal social activities. It consists of 11 items with domains of: daily functioning, recreational and social activities, family roles, personal relationships and perception of self. Each statement is rate on a visual analogue scale (1-minimal reintegration, 10-maximum reintegration). The tool has been validated for self-administration in stroke survivors (McKellar et al. 2015).

Caregiver Burden

Caregiver Strain Index
The Cagiver 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).

Organized Stroke Care – Interdisciplinary Care/Team

2.5 Efficacy of Stroke Rehabilitation Organized Care

Stroke rehabilitation improves functional outcomes (especially in moderately severe strokes) and reduces mortality (especially in more severe strokes).

Stroke rehabilitation is challenging for a number of reasons:
- Multiple impairments, several domains
- Interaction between impairments
- Different speed of recovery
- Several disciplines and agencies involved
- Staged interventions, therapy input
- Personal, environment and support
- Complex interdisciplinary process

2.5.1 Stroke Rehabilitation Programs

Stroke rehabilitation is characterised by an interdisciplinary team working cohesively and closely to provide a comprehensive program for each patient. They are inevitably found in rehabilitation centres or acute care hospitals. Weekly team conferences are held to establish or revise rehabilitation goals and plans, assess patient progress, identify barriers or complications, and develop a plan for discharge or transfer to another type of rehabilitation program. These programs may vary in the types of therapies offered as well as their intensity, frequency, and duration. Brandstater and Basmajian (1987) identified common features of comprehensive stroke rehabilitation programs (Table 2.5.1).

Table 2.5.1 Common Elements of Comprehensive Stroke Rehabilitation Programs

- Commitment to continuity of care from the acute phase of the stroke through long-term follow-up.
- Use of an interdisciplinary team of professionals experienced in and dedicated to the care of the patient with stroke.
- Careful attention to the prevention, recognition, and treatment of comorbid illnesses and medical complications.
- Early initiation of goal-directed treatment that takes maximal advantage of the patient's abilities and minimizes disabilities.
- Systematic assessment of the patient's progress during rehabilitation, with adjustment of treatment to maximize benefits.
- Emphasis on patient and family/caregiver education, with attention to psychological and social issues affecting both the patient and family/caregiver.
- Early and comprehensive discharge planning aimed at a smooth transition to the community, promoting social reintegration and resumption of roles in the home, family, recreational, and vocational domains.

Clinical practice guidelines for adult stroke care (Duncan et al. 2005) endorsed by the American Heart Association recommend that stroke rehabilitation care be provided by a multidisciplinary team and delivered in a setting that is formally coordinated and organized. The authors also acknowledged the need for a flexible approach and were unable to identify a universally applicable “best practice” approach applicable to all stroke patients. The authors noted the heterogeneity of the literature on which their recommendations were based, the inability to identify the nature of the intervention(s) under study, and the inability to elucidate the distinctively unique aspects of care that enabled superior outcomes when compared to standard care.

2.5.2 Reviews of Stroke Rehabilitation Unit Efficacy

The Stroke Unit Trialists’ Collaboration (2013) was a Cochrane review that systematically reviewed a total of 28 randomized trials that compared services provided along a continuum of care from 'more organized' to 'less organized' stroke unit care. Primary outcome measures included death, dependency, and requirement for institutionalized care at follow-up. At a median of one-year follow-up, stroke unit care was associated with a significant reduction in death (OR 0.87, 95% CI 0.69-0.94, p=0.005). Stroke unit care was also associated with a reduction in the combined outcomes of death or institutional care (OR 0.78, 95% CI 0.68-0.89, p=0.0030) and death or dependency (OR 0.79, 95% CI 0.68-0.90, p=0.0007). There was no indication that organised stroke unit care resulted in longer hospital stay. The benefits of specialized stroke care were independent of age, sex, stroke severity, or stroke type.

Subacute Stroke Rehab Units (Foley et al. 2007) result in:
- 10 day reduction in inpatient stay
- 1 in 27 patients treated will not need institutionalization
- Increased functional outcomes with decrease in informal care costs

Stroke units improve outcomes by:
- Greater attention to stroke specific medical, nursing and therapy processes
- Greater involvement of caregivers
- Fewer stroke related complications
- Greater and earlier functional recovery

- Expedited hospital discharges
- Specialized interdisciplinary care

Table 2.5.2 Type of Stroke Unit

Type	Admission	Discharge	Features	Efficacy
Acute, intensive	Acute (hours)	Days	High nurse staffing Life support facilities	No trials
Acute, semi-intensive	Acute (hours)	Days	Close physiological monitoring	Better than non-specific stroke care
Combined Acute-Subacute	Acute (hours)	Days–weeks	Acute care/rehabilitation Conventional staffing	Better than non-specific stroke care and rehab
Subacute Rehab	Delayed	Weeks	Rehabilitation	Better than non-specific stroke rehab
Mobile Rehab (SWAT) team	Variable	Days-weeks	Medical / rehabilitation advice	No better than non-specific stroke rehab
Mixed Neuro-rehabilitation	Variable	Weeks	Mixed patient group Rehabilitation	Better than non-specific stroke rehab

Given that this review examined studies that assessed all types of the stroke care along the continuum, from "super-acute" to subacute, studies were categorized in an effort to compare the effectiveness of similar interventions:

i. Acute stroke unit care: patients randomized within 24 hours and remained for a period of two weeks or less (n=7)
ii. Units combining both acute and rehabilitative care (n=7)
iii. Rehabilitation units with transfer from another service or facility after a delay, usually within two weeks of stroke (subacute) (n=7)

Mobile stroke teams (n=4)

Table 2.5.3 Randomized Controlled Trials Evaluating All Stroke Care Models

Acute Stroke Care (n=7)	Combined Acute/Rehabilitation (n=7)	Subacute Rehabilitation (n=7)	Mobile Stroke Teams (n=4)
Ronning & Guldvog (1998b) Cabral et al. (2003) Sulter et al. (2003) DiLauro et al. (2003) Cavallini et al. (2003) Silva et al. (2005) Langhorne et al. (2010b)	Garraway et al. (1981) Sivenius et al. (1985) Indredavik et al. (1991) Kaste et al. (1995b) Fagerberg et al. (2000) Ma et al. (2004a) Chan et al. (2014)	Peacock et al. (1972) Stevens et al. (1984) Kalra et al. (1993) Kalra & Eade (1995) Juby et al. (1996) Ronning & Guldvog (1998b) Yagura et al. (2005)	Dey et al. (2005) Wood-Dauphinee et al. (1984a) Kalra et al. 2000, (2005) Hamrin et al. (1982)

2.5.3 Acute Stroke Rehabilitation Units

Seven RCTs evaluating the benefit of acute stroke care were identified, which assessed the following interventions (Table 5.4.1):

1. Stroke unit with continuous monitoring vs. Conventional stroke unit (Cavallini et al. 2003, Langhorne et al. 2010b, Silva et al. 2005, Sulter et al. 2003)
2. Early, intensive rehabilitation vs. Conventional rehabilitation (Di Lauro et al. 2003, Langhorne et al. 2010b)
3. Acute stroke unit vs. General medical ward (Cabral et al. 2003, Ronning & Guldvog 1998b)

A Cochrane review regarding continuous monitoring of patients post stroke (Ciccone et al. 2013) examined the results of only three articles, all of which were previously discussed (Cavallini et al. 2003, Langhorne et al. 2010a, Sulter et al. 2003). The authors concluded that continuous monitoring provided no significant reduction in dependency, death from vascular causes, neurological complications, or length of hospital stay.

Table 2.5.4 Acute Continuous Monitoring Compared to an Alternative Intervention

Study (PEDro Score)	Mortality	Dependency	Length of Stay	Institutionalization
Silva et al. (2005) (3)	-	-	NA	NA
Cavallini et al. (2003) (5)	-	-	+	+
Sulter et al. (2003) (7)	+	-	+	-
Langhorne et al. (2010) (8)	NA	+	-	NA

Table 2.5.5 Acute Intensive Rehabilitation Compared to Alternative Intervention

Study (PEDro Score)	Mortality	Dependency	Length of Stay	Institutionalization
Di Lauro et al. (2003) (7)	NA	-	NA	NA
Langhorne et al. (2010a) (8)	NA	+	-	NA

Table 2.5.6 Acute Stroke Unit Care Compared to General Medical Ward Care

Study (PEDro Score)	Mortality	Dependency	Length of Stay	Institutionalization
Ronning & Guldvog (1998b) (6)	-	-	-	-
Cabral et al. (2003) (5)	-	-	-	NA

Figure 2.5.1 Mortality in Acute Stroke Unit Care vs. Alterative Care

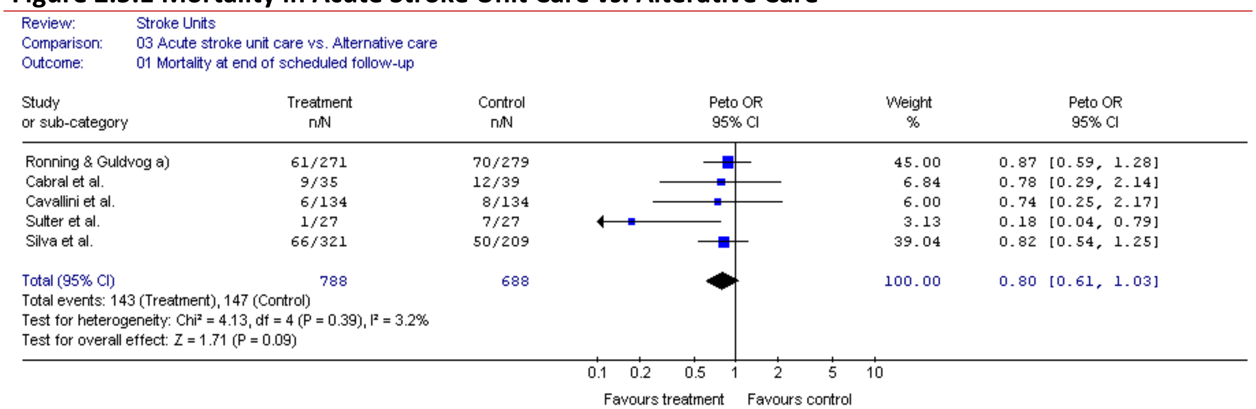


Figure 2.5.2 Combined Death/Dependency in Acute Stroke Unit Care vs. Alterative Care

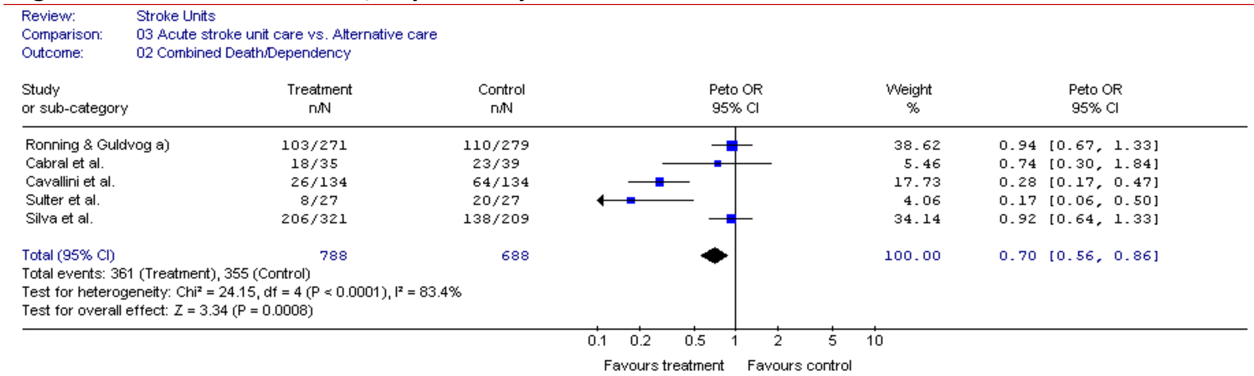


Figure 2.5.3 Need for Institutionalization in Acute Stroke Unit Care vs. Alterative Care

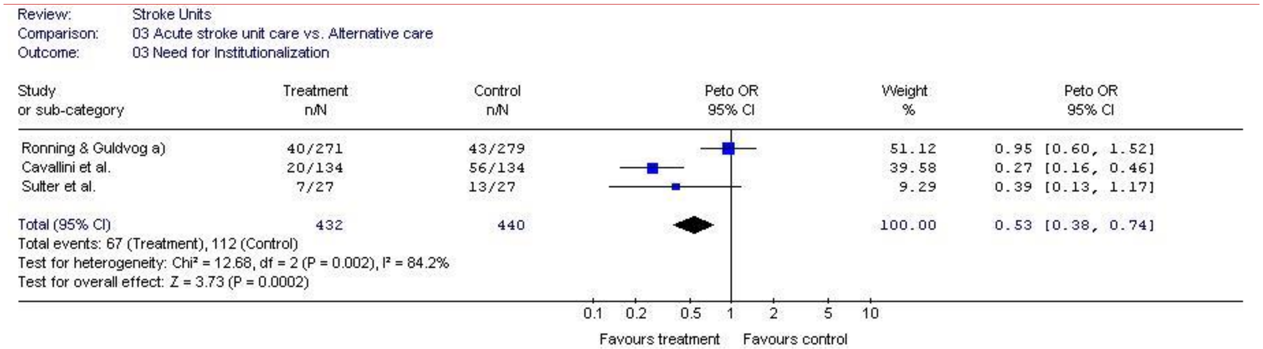
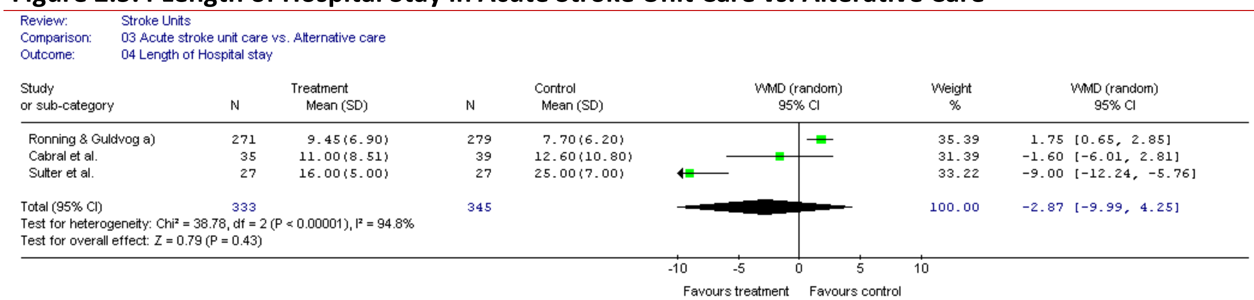


Figure 2.5.4 Length of Hospital Stay in Acute Stroke Unit Care vs. Alterative Care



<u>Conclusions</u>

Acute stroke care, characterized by intensive monitoring and treatment for medical complications, is associated with reductions in combined death/disability and the need for institutionalization, but not reductions in mortality, length of hospital stay, or functional disability.

2.5.4 Combined Acute and Rehabilitation Units

Seven studies evaluating combined acute/rehabilitation stroke units were identified. All these studies admitted patients acutely and offered both acute and rehabilitative care (Table 5.5.1). A single intervention was assessed:

1. Combined stroke unit or neurology ward vs. General medical ward (Chan et al. 2014, Fagerberg et al. 2000, Garraway et al. 1980, Indredavik et al. 1991, Kaste et al. 1995a, Ma et al. 2004b, Sivenius et al. 1985).

Highlighted Study

Garraway WM, Akhar AJ, Prescott RJ, Hockey L. Management of acute stroke in the elderly: preliminary results of a controlled trial. BMJ 1980; 280:1040-1043.		
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 (-)
Prospective RCT of 311 consecutive moderately severe acute stroke patients, admitted within 7 days of stroke onset and randomized to either stroke unit or general medical unit. A greater proportion of stroke unit patients were classified as independent when compared to medical unit patients, 50% vs. 32% at 60 days; when comparing survivors the proportion of independent patients rose to 62%. Follow-up at one year found no longer significant differences in proportion of patients deemed independent between groups. Also see Garraway et al. (1980b) and Smith et al. (1982). This was the first trial to demonstrate the benefit of a stroke rehabilitation unit over standard medical care.		

Highlighted Study

Indredavik B, Bakke F, Solberg R, Rokseth R, Haaheim LL, Holme I. Benefit of a stroke unit: a randomized controlled trial. Stroke 1991; 22:1026-1031.		
Norway 7 (RCT) N=220	Patients within 7 days post stroke were randomized to a combined acute/rehabilitation stroke unit or a general medical unit.	1. Patients who were treated on the combined stroke unit were more likely to have been discharged home, were less likely to have been institutionalized, and were more likely to have higher Barthel Index scores at both 6 weeks and 1 year. 2. The 6-week mortality rate was lower for patients treated on the combined stroke unit.
Indredavik B, Slordahl SA, Bakke F, Rokseth R, Haheim LL. Stroke unit treatment. Long-term effects. Stroke 1997; 28:1861-1866.		
Norway 7 (RCT) N=220	5-year follow-up study of Indredavik et al. 1991.	1. At 5 years post stroke, a greater proportion of patients originally treated on the stroke unit were alive and residing at home with higher Barthel Index scores when compared to patients treated on the general medical ward.
Indredavik et al. (1999b)		
Norway 7 (RCT) N=220	5-year follow-up study of Indredavik et al. 1991.	1. 5-year mortality rate for patients initially treated on a stroke unit was lower. 2. A greater proportion of patients treated on the stroke unit were classified as independent.
Indredavik B, Slordahl SA, Bakke F, Rokseth R, Haheim LL. Stroke unit care improves long-term survival and function. Cardiology Review 1999; 16:24-27(a).		
Norway 7 (RCT) N=220	10-year follow-up study of Indredavik et al. 1991.	1. At 10 years post stroke, a greater proportion of patients initially treated on the stroke unit were alive (25 vs. 13%), residing in their homes (20 vs. 8%), and had Barthel Index scores ≥ 60 (20 vs. 8%) compared to patients

		treated on a general medical ward.

220 acute (within 7 days) stroke patients were randomized to either a combined acute/rehabilitation stroke unit or a general medical unit. Patients who were treated on the combined stroke unit were more likely to have been discharged home, were less likely to have been institutionalized and were more likely to have higher Barthel Index scores at 6 weeks and 1 year. The 6 week mortality for patients treated on the combined stroke unit was lower. 5 and 10 year follow-up found a greater proportion of patients originally treated on the stroke unit were alive, residing at home with higher Barthel Index scores. Significant benefit was still seen at 10 years.
This study showed the benefits of stroke units could be determined by 6 weeks and continued through for 10 years after the study.

Highlighted Study

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 (-)

Table 2.5.7 Combined Stroke Unit Care Compared to General Medical Ward Care

Study (PEDro Score)	Mortality	Dependency	Length of Stay	Institutionalization
Garraway et al. (1980) (5)	-	+	+*	NA
Sivenius et al. (1985) (6)	-	+	-	NA
Indredavik et al. (1991) (7)	+ (6 weeks)	+	+	+
	- (52 weeks)	+	NA	+
Indredavik et al. (1997) (7)	+	+	NA	-
Indredavik et al. (1999a) (7)	+	+	NA	-
Kaste et al. (1995a) (8)	-	+	+	NA
Fagerberg et al. (2000) (8)	-	-	-	-
Ma et al. (2004b) (5)	NA	+	NA	NA
Chan et al. (2014) (9)	NA	-	-	NA

** No test of statistical significance was performed*

Figure 2.5.5 Combined Death/Dependency in Combined Stroke Unit Care Compared to General Medical Ward Care

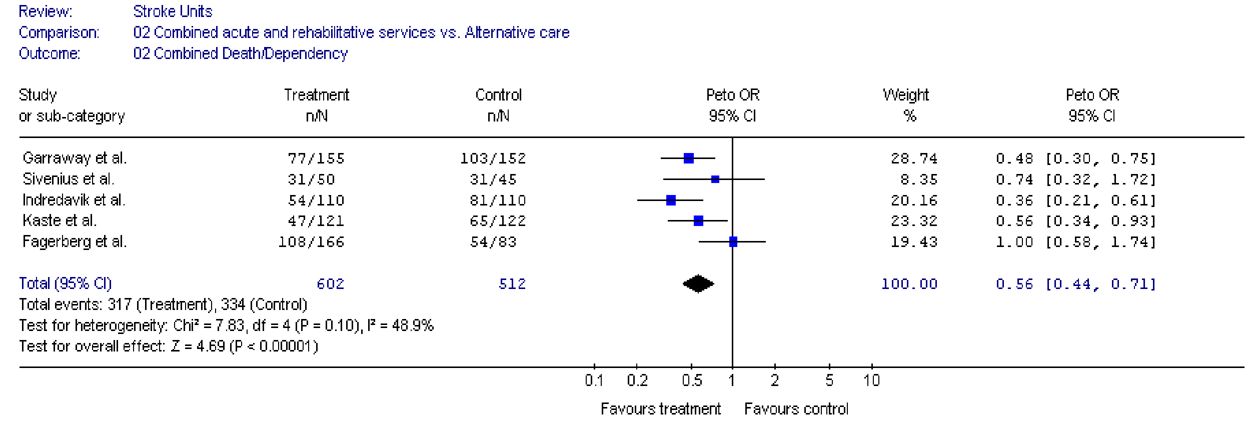


Figure 2.5.6 Need for Institutionalization in Combined Stroke Unit Care Compared to General Medical Ward Care

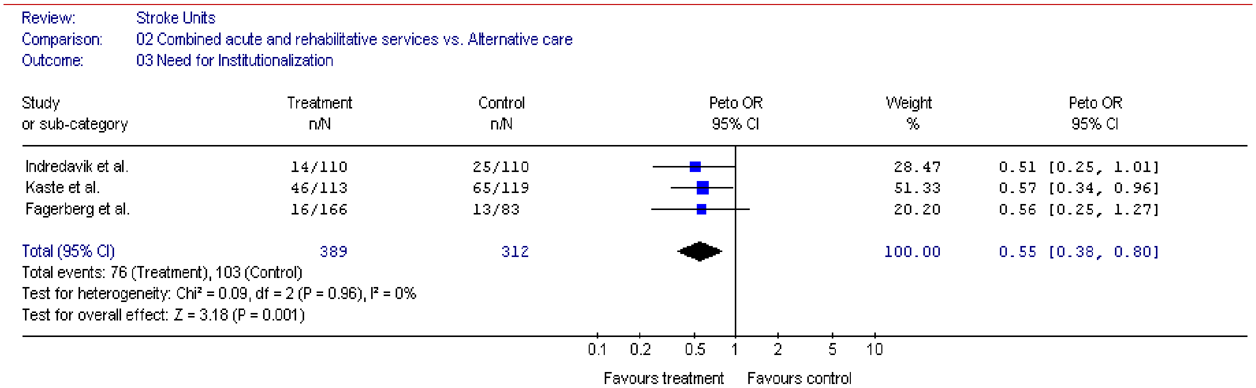
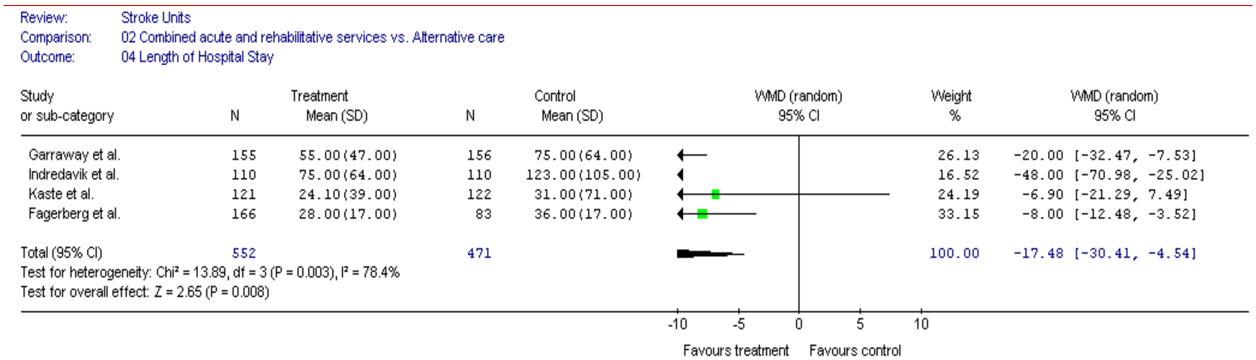


Figure 2.5.7 Length of Hospital Stay in Combined Stroke Unit Care Compared to General Medical Ward Care



Conclusions

Interdisciplinary combined acute and rehabilitation stroke units reduce combined death/dependency, need for institutionalization, and length of hospital stay, but not overall mortality, when compared to general medical wards.

2.5.5 Subacute Rehabilitation

Thirteen RCTs evaluating subacute rehabilitation (i.e. following transfer from another unit or facility) were identified, which evaluated the following interventions (Table):

1. Stroke rehabilitation or Stroke unit vs. General medical ward (Juby et al. 1996, Kalra et al. 1993, Kalra & Eade 1995, Stevens et al. 1984, Yagura et al. 2005)
2. Inpatient rehabilitation vs. Ad hoc community care (Ronning & Guldvog 1998a)

Table 2.5.8 Stroke Rehabilitation Units Compared to General Medical Ward

Study (PEDro Score)	Mortality	Dependency	Length of Stay	Institutionalized
Peacock et al. (1972) (5)	NA	-	NA	NA
Stevens et al. (1984) (6)	-	+ (ADL: dressing) - (ADL: all others)	-	-
Kalra et al. (1994a, 1994b, 1993) (5)	+ (Severe) - (Mild/Moderate)	+ (Moderate) - (Mild/Severe)	+ (Moderate/ Severe) - (Mild)	+ (Moderate) - (Mild/ Severe)
Kalra & Eade (1995) (5)	+	-	+	-
Juby et al. (1996) (6)	-	+ (ADL at 3/6mo)	- at 1yr	- at 1yr
Drummond et al. (2005) (6)	+ (at 10yr)	- (ADL at 1yr)	NA at 10yr	NA at 10yr
Yagura et al. (2005) (6)	None	-	-	- + (Severe)

Highlighted Study

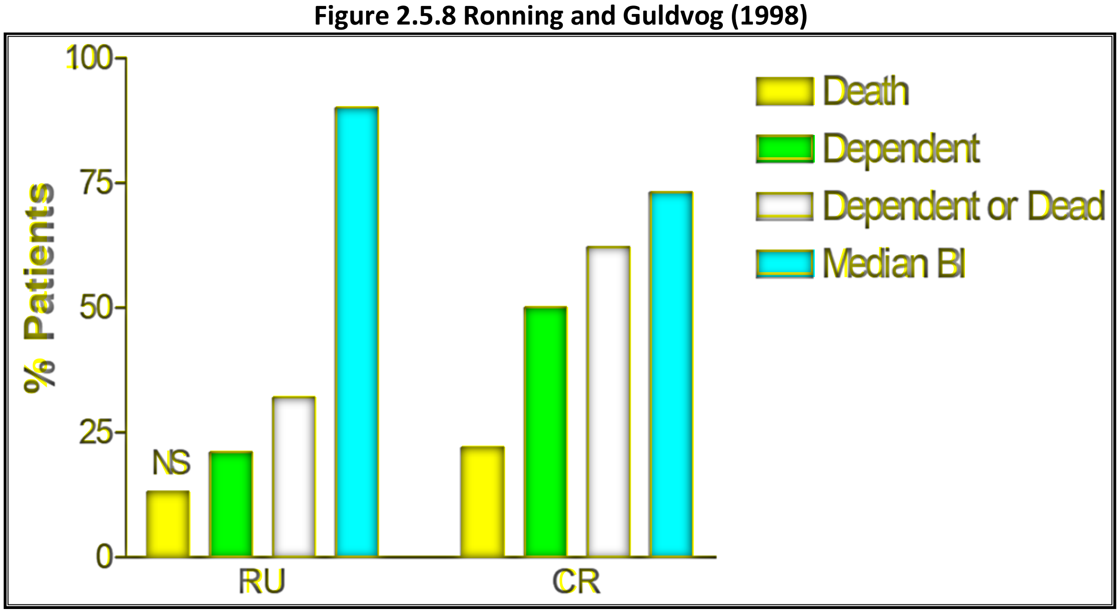
Kalra L, Dale P, Crome P. Improving stroke rehabilitation. A controlled study. Stroke 1993; 24:1462-1467.		
UK 5 (RCT) N=245	Patients admitted within 2 weeks of stroke were randomized to a rehabilitation unit or a general medical unit after stratification by stroke severity.	1. Patients with a poor prognosis treated on a general medical ward had higher mortality rates and longer hospital stays. 2. Patients in the stroke rehabilitation unit with moderate stroke severity had better discharge Barthel Index scores and shorter hospital stays.
245 stroke patients randomized at 2 weeks post stroke to a rehabilitation unit or a general medical unit after stratification by stroke severity. Patients with a poor prognosis treated on a general medical ward had higher mortality and longer hospital stays. Patients in the stroke rehab unit with intermediate severity of stroke had better discharge Barthel Index scores and shorter hospital stays. ***This RCT showed that patients in subacute stroke units had better outcomes with regard to mortality, average length of stay and discharge Barthel Index scores.***		

Highlighted Study

Ronning OM, Guldvog B. Outcome of subacute stroke rehabilitation: a randomized controlled trial. Stroke 1998; 29:779-784.

Norway 6 (Quasi RCT) N=251	Patients were randomized to subacute rehabilitation in a hospital-based stroke rehabilitation program or to a community-based program (nursing home 40%, outpatient rehabilitation 30% and no rehabilitation 30%) and followed for 7 months.	1. Greater proportion of community-based rehabilitation patients were dependent or dead compared to hospital rehabilitation patients; no difference in survival at 7 months. 2. Patients with moderate or severe stroke, treated in a hospital-based program, had higher median Barthel Index scores at 7 months (90 vs. 73) and lesser combined dependency and death (23% vs. 38%).
Stroke patients who were deemed in need of rehabilitation (n=251) were randomized to Rehab Unit (n=127) or Community Care (n=124) after an average of 10 days in acute care. Rehab Unit LOS was a mean of 27.8 days. Of those admitted to Community Care, 40% went to a nursing home, 30% to outpatient therapy and 30% to no formal rehab treatment. At 7 month follow-up for all stroke patients, 23% of the Rehab Unit patients vs. 38% of the Community Care patients were dependent (BI < 75) or dead (p=.01), a 39% reduction in worse outcomes with stroke rehab care. For moderate to severe stroke patients (Barthel Index <50 at time of admission; n=114), 32% of the Rehab Unit patients vs. 62% of the Community Care patients were dead or dependent 7 months post stroke (p=.002), a 48% reduction in worse outcomes with stroke rehab care for more severe stroke patients. Of all the stroke patients in the study, the Barthel Index score was 90 in the Stroke Rehab Unit group and 73 in the Community Care group. Milder stroke patients (Barthel Index >50 at time of admission; n=137) did not improve any more in the Stroke Rehab Unit than in the Community Care Unit indicating these patients can be rehabilitated in the community. ***Comparison of moderate to severe stroke patients admitted to either in patient rehabilitation unit (RU) vs. discharged home to the community. 32% of rehab unit patients and 62% of community discharge patients were dead or dependent at 7 months post stroke. This RCT is the only study that compared organized stroke rehabilitation care to ad hoc treatment in the community, the closest thing to a non-treatment control. The benefits of stroke rehabilitation for more severe strokes was quite dramatic with a 48% reduction in death and dependency in the treatment group.***		

Figure 2.5.8 Ronning and Guldvog (1998)



Meta-Analyses of Subacute Stroke Units

Figure 2.5.9 Mortality in Stroke Rehabilitation Units Compared to General Medical Ward

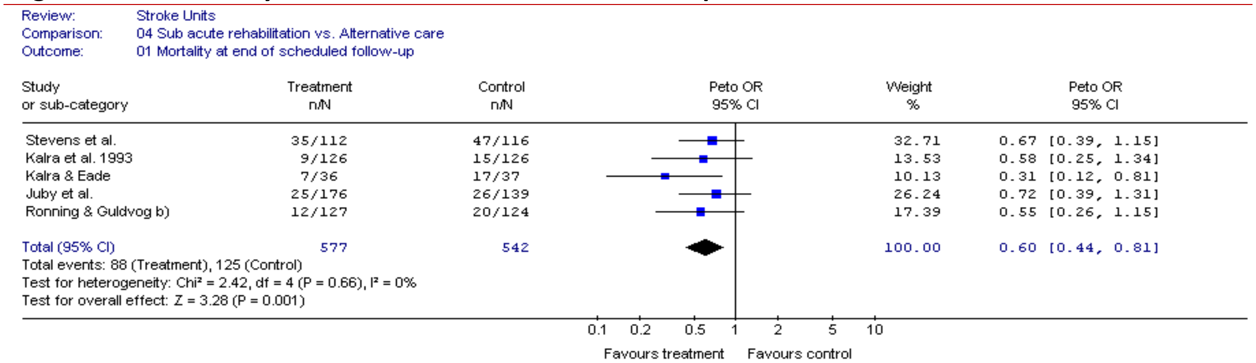


Figure 2.5.10 Combined Death/Dependency in Stroke Rehab Units Compared to General Medical Ward

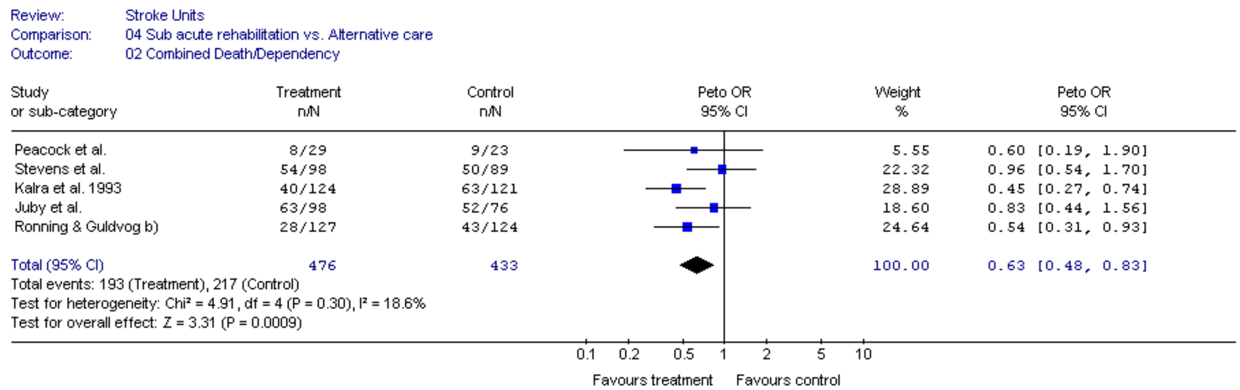


Figure 2.5.11 Need for Institutionalization in Stroke Rehab Units Compared to General Medical Ward

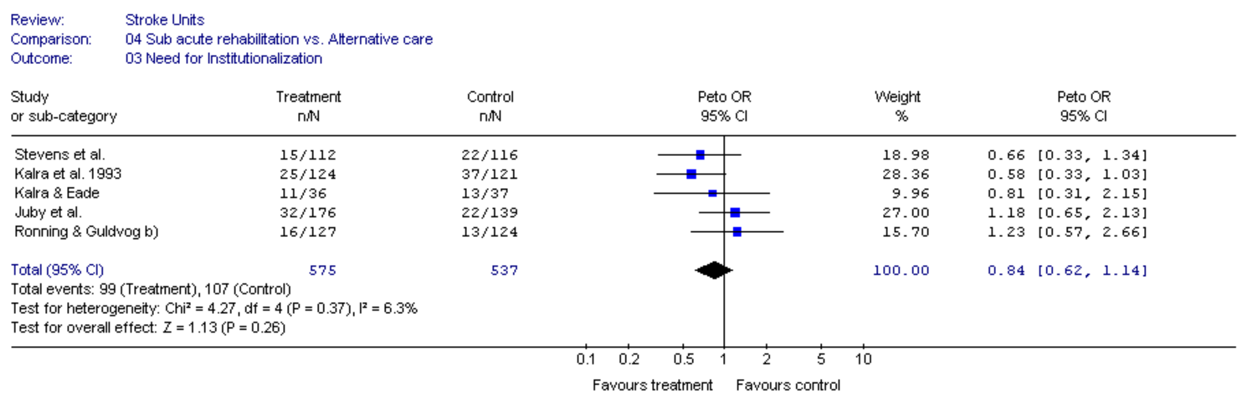
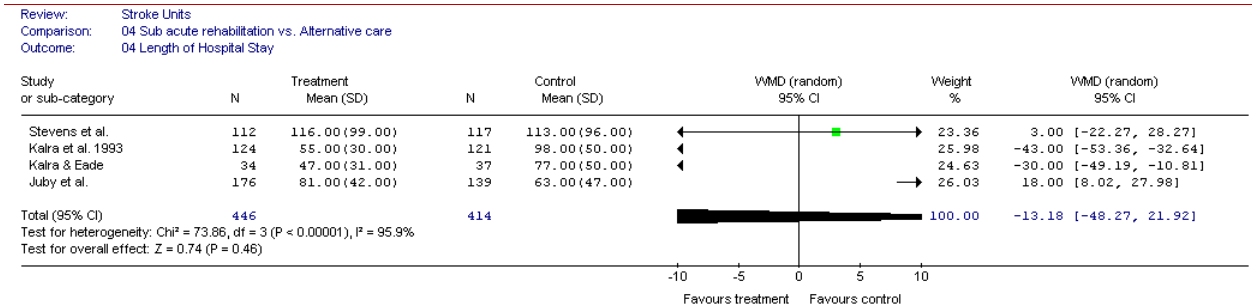


Figure 2.5.12 Length of Hospital Stay in Stroke Rehab Units Compared to General Medical Ward



Conclusions

Interdisciplinary specialized subacute stroke rehabilitation is associated with reduced mortality and combined death/dependency, but not the need for institutionalization or length of hospital stay, when compared to general rehabilitation.

Subgroups of patients will benefit from subacute rehabilitation in different ways: patients with more severe strokes experience reduced mortality; those with moderate strokes experience improved functional outcomes; and those with mild stroke do not improve to a greater extent compared with standard care.

2.5.6 Mobile Stroke Teams

While dedicated stroke units have been associated with improvements in outcome, it is uncertain whether this intervention is transportable. Langhorne et al. (2005) conducted a systematic review of mobile stroke teams evaluating studies that compared care provided by a mobile team of specialized stroke professionals on various wards versus alternative forms of inpatient stroke rehabilitation, most often provided on a general medical ward. While most of the studies evaluating stroke unit care have focused on organized services provided on a discrete ward, the portability of such care has not been extensively investigated. A total of six trials were included in the review, which comprised 1,085 patients.

The proportion of patients who had experienced death, death or institutionalization, and death or dependency at the end of scheduled follow-up were similar between studies comparing mobile stroke teams with general medical ward care (Table 2.5.9). However, patients receiving mobile stroke team care fared significantly poorer compared to patients who had been managed on a comprehensive stroke unit. Although the total number of patients included in the review was relatively small, the authors concluded that mobile stroke team care did not have a major impact on clinically important outcomes.

Table 2.5.9 Results of Meta-Analysis Evaluating Mobile Stroke Teams

Outcome	Comparison	OR (95% CI)
Early Death (median 6 weeks)	Stroke Team vs. General Medical Ward	0.77 (0.52-1.12)
Death		1.03 (0.74-1.42)
Death or Institutionalization		1.10 (0.81-1.49)
Death or Dependency		0.97 (0.71-1.33)
Early Death (median 6 weeks)	Stroke Team vs. Comprehensive Stroke Unit	3.27 (1.26-8.48)
Death		3.08 (1.56-6.11)
Death or Institutionalization		2.62 (1.47-4.67)
Death or Dependency		3.06 (1.73-5.42)

Table 2.5.10 Mobile Stroke Team Compared to Conventional Medical Management

Study (PEDro Score)	Mortality	Dependency	Length of Stay	Institutionalization
Hamrin (1982) (4)	-	-	-	-
Wood Dauphinee et al. (1984b) (6)	+ (Males) - (Females)	+ (Males) - (Females)	NA	NA
Kalra et al. (2000, 2005) (8)	-	-	NA	-
Dey et al. (2005) (8)	-	-	NA	-

Meta-Analyses of Mobile Stroke Teams

Figure 2.5.13 Mortality in Mobile Stroke Team Compared to Conventional Medical Management

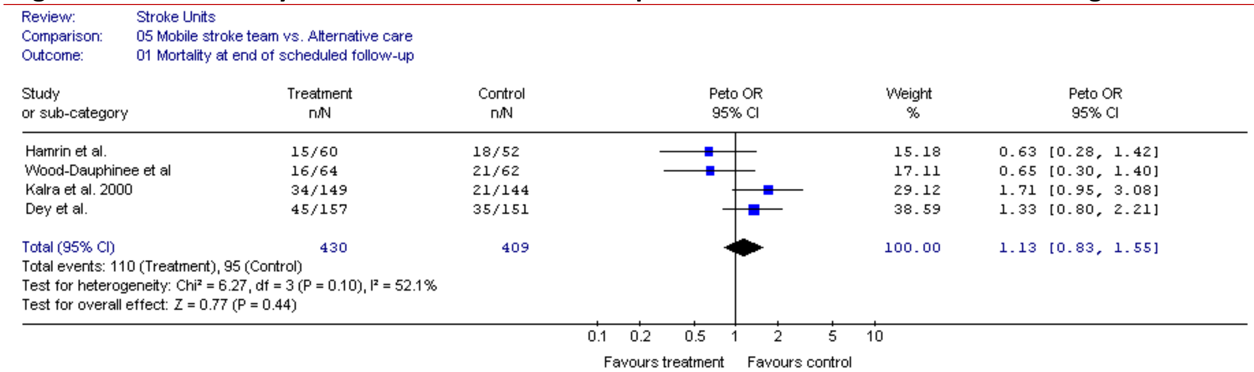


Figure 2.5.14 Combined Death/Dependency in Mobile Stroke Team Compared to Conventional Medical Management

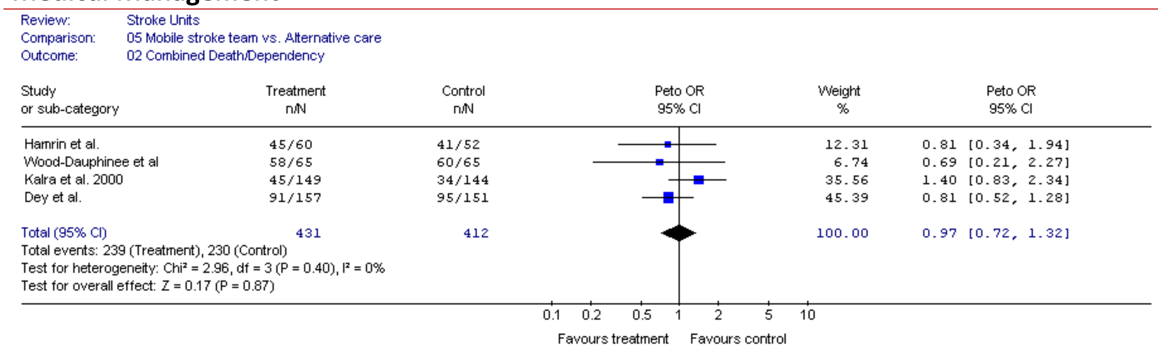


Figure 2.5.15 Need for Institutionalization in Mobile Stroke Team Compared to Conventional Medical Management

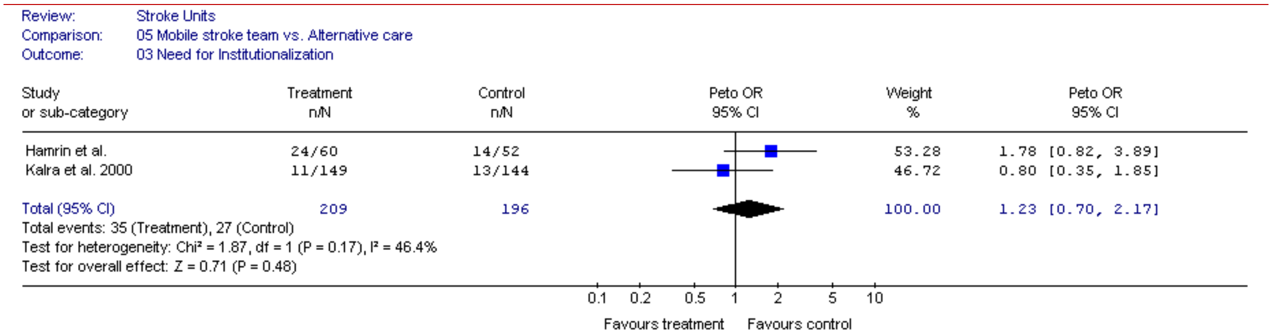


Figure 2.5.16 Length of Hospital Stay in Mobile Stroke Team Compared to Conventional Medical Management

Conclusions

Discrete care elements associated with stroke units do not provide the same benefit when provided by a mobile stroke team.

2.5.7 Meta-Analyses of Combined Results

In addition to conducting pooled analyses for individual models of care, all models of care were combined to provide a point estimate of the effectiveness associated with specialized stroke services for the outcomes of mortality, death or dependency, the need for institutionalization, and length of hospital stay. The results are presented in Tables 2.5.11 to 2.5.13 and Figures 2.5.17 to 2.5.19.

Mortality

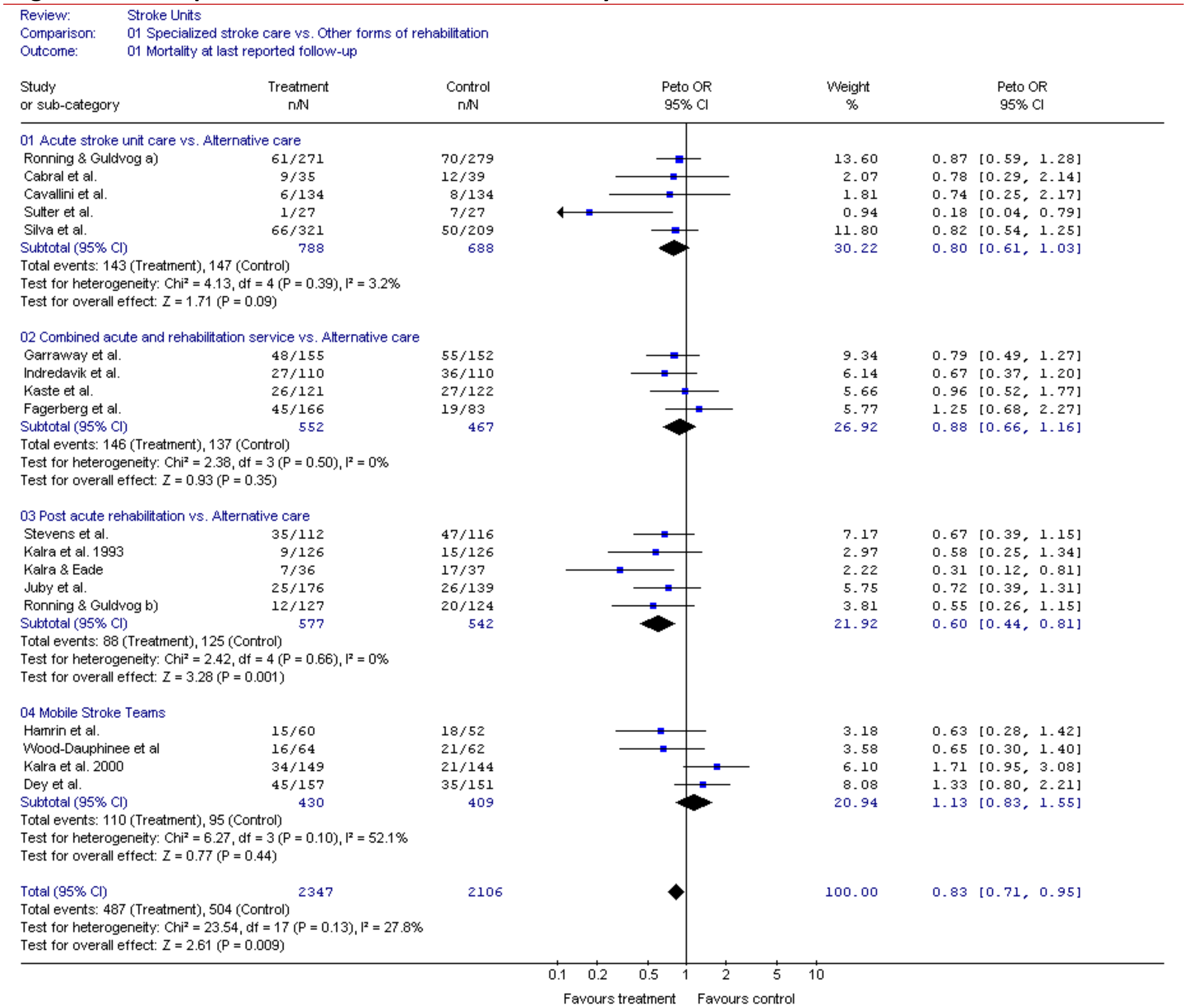
A meta-analysis of 18 RCTs evaluated mortality at the end of scheduled follow-up. There was an overall protective effect associated with specialized stroke care compared to alternative care, although most of the individual RCTs did not report statistically significant results. It could be suspected that the greatest influence on mortality would be realized at the level of acute care, during the very early stages of stroke. Surprisingly, of the six trials evaluating very early care, only one small RCT indicated a protective effect (Sulter et al. 2003). The model of care associated with the greatest reduction in odds of death was subacute rehabilitation. The reasons for this finding are not entirely clear, although it may be due to greater attention to managing medical complications such as pneumonia and venous thromboembolism, which can also occur later in the course of recovery.

Table 2.5.11 Pooled Analysis for Mortality

Model of Care	OR (95% CI)
Acute stroke care	0.80 (0.61, 1.03)

Combined acute and subacute stroke rehabilitation	0.88 (0.66, 1.16)
Subacute rehabilitation	0.60 (0.44, 0.81)
Mobile stroke team	1.13 (0.83, 1.55)
Overall	0.83 (0.71, 0.95)

Figure 2.5.17 Impact of Stroke Unit Care on Mortality



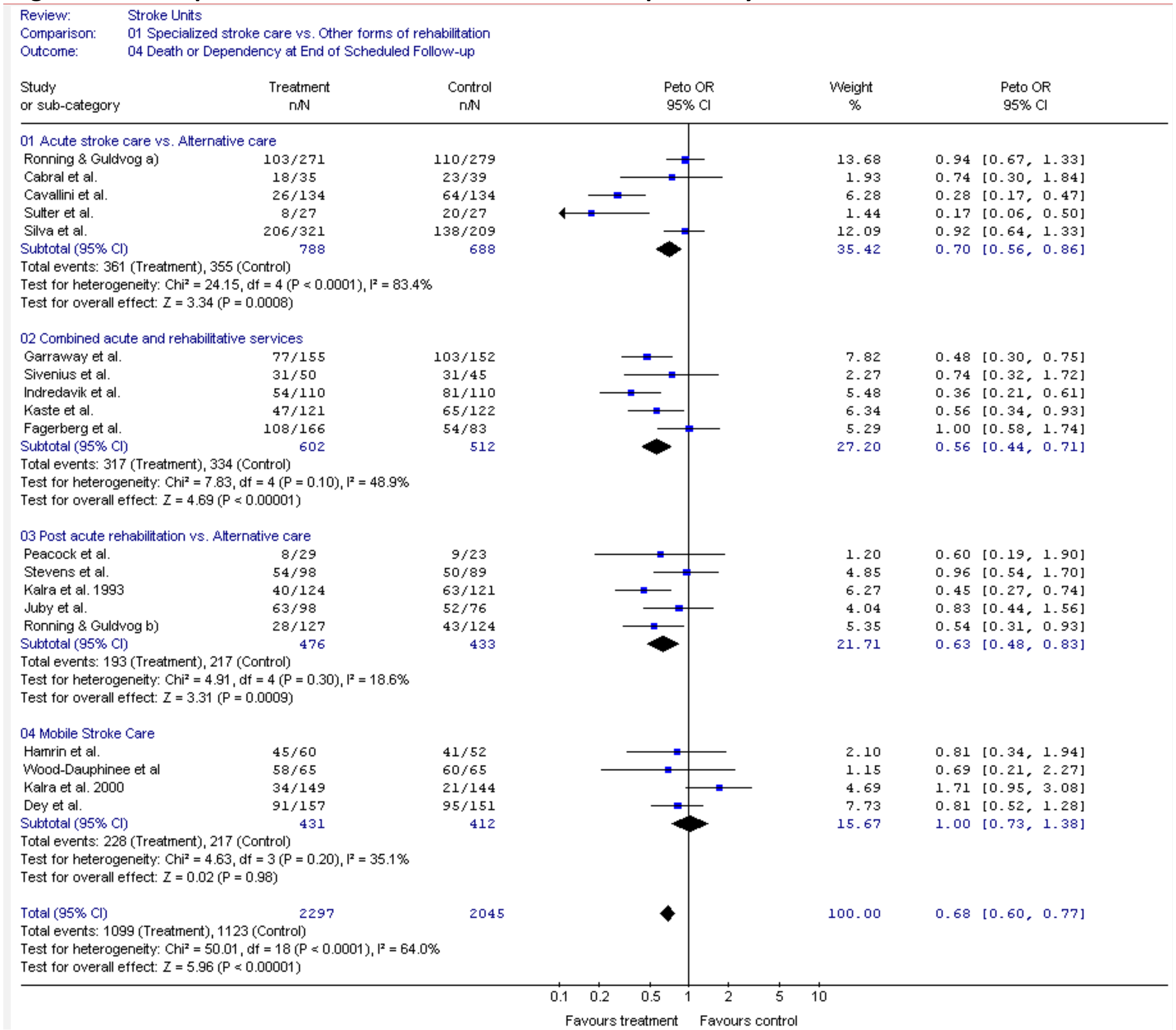
Death or Dependency

All models of care, except for mobile stroke teams, were associated with statistically significant reductions in the odds of death or dependency. The pooled result was similar to that obtained by the Stroke Unit Trialists' Collaboration (2013) for the same outcome (OR 0.79, 95% CI 0.68 to 0.90).

Table 2.5.12 Pooled Analysis for Death or Dependency

Model of Care	OR (95% CI)
Acute stroke care	0.70 (0.56, 0.86)
Combined acute and subacute stroke rehabilitation	0.56 (0.44, 0.71)
Subacute rehabilitation	0.63 (0.48,0.83)
Mobile stroke team	1.00 (0.73, 1.38)
Overall	0.68 (0.60-0.77)

Figure 2.5.18 Impact of Stroke Unit Care on Death or Dependency



Institutionalization

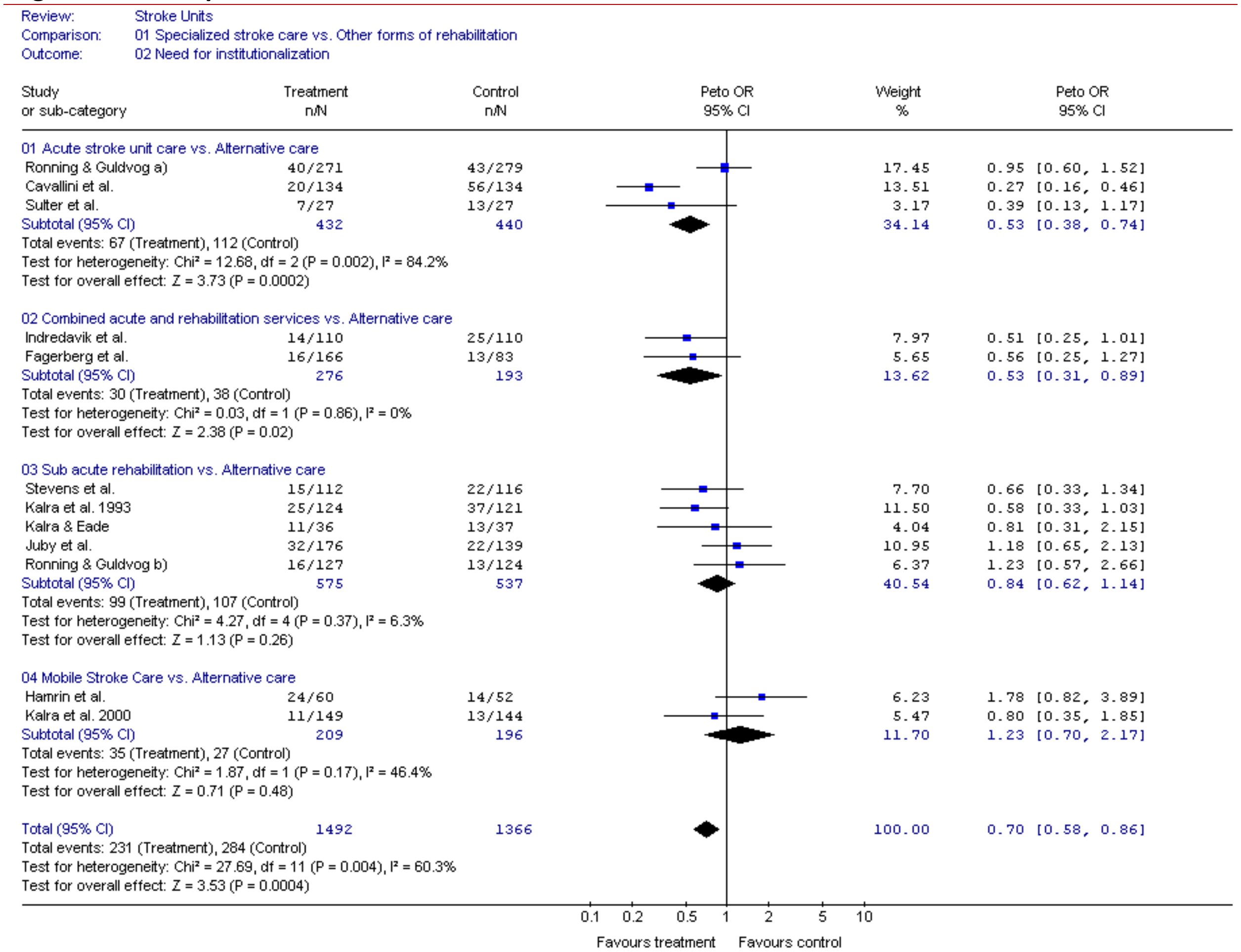
The proportion of patients requiring institutionalization upon discharge was assessed in 12 (57%) studies. Specialized stroke services were associated with reductions in the odds of the need for institutionalization. However, Cavallini et al. (2003) and Brady et al. (2005) assessed the number of patients who were able to live at home or went on to receive intensive rehabilitation at the end of the acute hospitalization period. As well, Sulter et al. (2003) assessed the combined outcome of institutionalization and dependency.

Sensitivity analysis revealed that these studies were influential and the overall protective effect was no longer statistically significant without their inclusion (p=0.06).

Table 2.5.13 Pooled Analysis for Need for Institutionalization

Model of Care	Initial Analysis OR (95% CI)	Modified Analysis OR (95% CI)
Acute stroke care	0.53 (0.38, 0.74)	0.95 (0.60,1.52)
Combined acute and subacute stroke rehabilitation	0.53(0.31, 0.89)	0.53(0.31, 0.89)
Subacute rehabilitation	0.84 (0.62, 1.14)	0.84 (0.62, 1.14)
Mobile stroke team	1.23 (0.70, 2.17)	1.23 (0.70, 2.17)
Overall	0.70 (0.58, 0.85)	0.84 (0.68, 1.04)

Figure 2.5.19 Impact of Stroke Unit Care on Need for Institutionalization



Length of Stay

Twelve studies were included in the meta-analysis that evaluated length of hospital stay. Overall, specialized stroke services were associated with significant reductions in LOS, although only the results from combined stroke units were statistically significant. Specialized care was associated with almost an average 7-day reduction in hospital stay.

Table 2.5.14 Pooled Analysis for Length of Stay

Model of Care	WMD (95% CI) (Days)
Acute stroke care	-2.9 (-10.0, 4.3)
Combined acute and subacute stroke rehabilitation	-17.5 (-30, -4.5)
Subacute rehabilitation	-13.2 (-48.3, 21.9)
Mobile stroke team	13.55 (0.3, 26.8)
Overall	-7.04 (-13.21, -0.9)

Summary

The overall results are summarized in Table 5.8.5.1. Using the results obtained through meta-analyses, specialized stroke care was associated with a significant benefit compared to the alternative intervention for all of the outcomes assessed.

Table 2.5.15 Summary of Results: Effectiveness of Stroke Care

Model of Care	Mortality	Death/Dependency	Institutionalization	Length of Stay
Acute	-	+	+	-
Combined	-	+	+	+
Subacute	+	+	-	-
Mobile	-	-	-	-
Overall	+	+	+	+

Conclusions
Specialized stroke care can improve multiple outcomes including mortality, dependency, need for institutionalization, and length of hospital stay.

Elements of Stroke Rehabilitation

2.6 Earlier Therapy is Better

The brain appears to be "primed" to "recover" early in post-stroke period. Animal studies suggest there is a time window when brain is "primed" for maximal response to rehab therapies, such that delays are detrimental to recovery (Biernaskie et al. 2004). The effects of training after stroke are generally greater when started early after stroke, perhaps because it takes advantage of the "sensitive period" of enhanced neuroplasticity. There has long been a clinical association between early admission to rehab and better outcomes (Bai et al. 2012, Paolucci et al. 2000, Salter et al. 2006).

2.6.1 Benefit of Early Therapy in Animals

Animal studies indicate early rehab is associated with improved recovery; later rehab is not (Biernaskie et al. 2004).

Highlighted Study

Biernaskie J, Chernenko G, Corbett D. Efficacy of rehabilitative experience declines with time after focal ischemic brain injury. J Neurosci 2004; 24(5):1245-1254.

Methods
Rats suffered an induced small motor stroke and were then subjected to rehab for 5 weeks beginning at 5, 14 and 30 days or control group (social housing) post stroke. Rehab consisted of weeks of enriched environment.
Results
The group that got rehab day 5 post admission showed marked improvement, the day 14 group showed moderate improvement and the day 30 group showed no improvement when compared to controls. The animals were subsequently autopsied and there was corresponding cortical reorganization in brain around stroke.

This study demonstrated that in animals early rehabilitation was far superior to later rehabilitation in the eventual functional outcomes, indicating an early window for maximal motor recovery post stroke.

2.6.2 Clinical Evidence for Early Therapy

In clinical studies, earlier rehabilitation is associated with better functional outcomes with reduced formal and informal care needs. There is a strong association between early admission and improved functional outcomes which appears to be causal; however, stroke severity might have confounded the relationship as the above studies are not RCTs. Patients who had suffered more severe strokes (with higher levels of impairment) were also more likely to have suffered medical complications or have been too impaired initially to be able to actively participate in rehabilitation, while patients with mild to moderate strokes, or those considered to be the best rehabilitation candidates were likely admitted to rehabilitation sooner. Clinical Practice Guidelines (Duncan et al. 2005) *"recommend that rehabilitation therapy start as early as possible, once medical stability is achieved".*

Highlighted Study

Paolucci S, Antonucci G, Grasso MG, Morelli D, Troisi E, Coiro P, Bragoni M. Early versus delayed inpatient stroke rehabilitation: A matched comparison conducted in Italy. Archives Phys Med Rehabil 2000; 81:695-700.

Methods
A case-controlled study of 135 stroke patients who received: 1) Rehabilitation within the first 20 days post stroke (short onset); 2) rehabilitation 21 to 40 days post stroke (medium onset); 3) rehabilitation 41 to 60 (long onset) post stroke; all patients received the same physical therapy program.
Results
Higher dropout rate was noted in the short onset group. Barthel Index scores in the short onset group showed significantly greater rate of improvement than the other 2 groups.

This case-controlled study demonstrated that patients who entered into rehabilitation early (<20 days) showed a significantly greater rate of improvement than those who entered rehabilitation later (>20 days).

Highlighted Study

Salter K, Jutai J, Hartley M, Foley N, Bhogal S, Bayona N, Teasell R. Impact of early vs delayed admission to rehabilitation on functional outcomes in persons with stroke. J Rehabil Med 2006; 38(2):113-117.

Methods
435 patients admitted to an inpatient stroke rehab program within 150 days of a first unilateral stroke. Patients admitted early to rehab were compared to those who were admitted later.
Results
FIM scores at admission and discharge as well as FIM change and FIM efficiency were significantly higher for early admission than for delayed admission patients. Length of stay was significantly longer among delayed admission patients.

Highlighted Study

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)

Highlighted Study

Bai et al. (2014)		
RCT (6) N_{Start}=165 N_{End}=156 TPS= Acute	E: Standardized 3-stage rehabilitation (began therapy within 24hr of admission) C: Standard hospital ward/Internal medical intervention Duration: 6mo	• Modified Ashworth Scale – fingers, elbow and ankle (+exp)

Highlighted Study

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)

The AVERT trial is the first RCT to explore the importance of early rehabilitation. This suggests that mobilization in the first few days must be carefully done.

Highlighted Study

Bernhardt et al. (2015)
The AVERT Trial Collaboration Group. Lancet 2015; 386:46-55.
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 (-)
Patients less than 24 hrs post stroke were randomly assigned to Standard Care (SC) or Standard Care and Very Early Mobilization (VEM) until discharge or 14 days post stroke onset. This was a multi-centered 56 site international RCT across 5 countries which took 8 years. 2104 patients were randomized; 1054 in the VEM group and 1050 in the Usual Care group. The VEM group started earlier (18.5 vs. 22.5 hrs post stroke), got more out of bed sessions (6.5 vs. 3.0) and received more therapy (31 minutes/day; total 201 minutes vs. 10 minutes/day; total 70 minutes). More patients in the Usual Care (n=525) than VEM (n=480) (p=0.001) had favourable outcomes (modified Rankin Scale [0-2] at 3 months post stroke). 72 patients (7%) in Usual Care vs. 88 patients (8%) VEM died; 19 vs. 31 died of stroke progression. ***This trial demonstrated that stroke rehabilitation can be conducted too early in that more aggressive mobilization efforts in the first 24 hours can actually be harmful to stroke patients resulting in a greater percentage dying and extending their strokes. The same authors (Bernhardt et al. Neurology 2016; 86:2138-2145) on further analysis did report improved odds of a favourable outcome with increased daily frequency of short out-of-bed sessions. One can conclude that very early on, shorter more frequent early mobilization improves chances of regaining independence whereas higher doses of longer-term mobilization worsened outcomes.***		

The Canadian Stroke Rehabilitation Best Practice Guidelines (Hebert et al. 2016) still recommend that patients should receive rehabilitation therapy as early as possible, once they are determined to be rehabilitation ready and medically able to participate in active rehabilitation. What is not recommended is frequent and extended out-of-bed activity in the very early time frame, with mobilization more reasonable for some medically stable smaller stroke patients.

Conclusions
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.

2.7 Intensity: More is Better

2.7.1 Intensity of Physiotherapy and Occupational Therapy

Post-stroke rehabilitation increases motor brain reorganization, while lack of rehabilitation reduces reorganization. More intensive motor training in animals further increases brain reorganization. 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. 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 hundreds if not thousands of repetitions. Lang et al. (2009) found that in monitoring occupational therapists involved in inpatient stroke rehabilitation, 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 per session, a fraction of the thousands of repetitions seen in animal research. Kwakkel et al. (2004) noted additional therapy time of at least 16-17 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.

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.

It is still not known what the threshold or dosage of rehabilitation intensity is needed. Animals in research studies reached 300 repitititions per session. The EXCITE trial examining the benefit of constraint-induced movement therapy, for instance involved 196 hours of therapy per patient. Pollock eta l. (2014) in a review of upper extremity stroke rehab found that, *“adequately powered high-quality RCTs confirmed the benefit of … a high dose of repetitive task practice.”* Van Peppen et al. (2004) noted additional time of 17 hours over 10 weeks was necessary to see significant positive effects (also see Kwakkel et al. 2004 below); this was affirmed by Verbeek et al. (2014).

Amount of Time Spent in Rehabilitation Therapies

As mentioned above, the Canadian Stroke Guidelines recommend that stroke rehab patients should receive a minimum of 3 hours of direct task-specific therapy, 5 days a week, delivered by the interprofessional team. 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

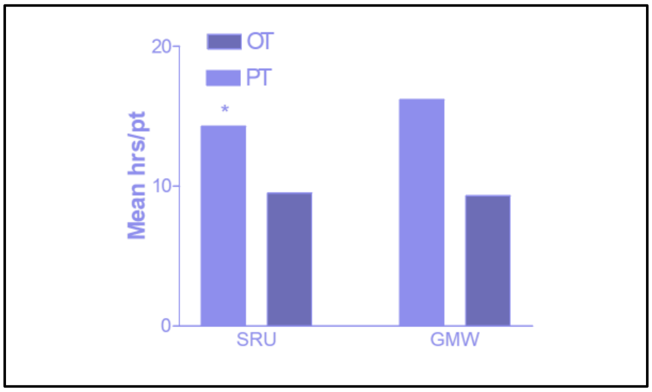
Switzerland. In all of the units, patients spent 72% of their time in non-therapeutic activities. In Ontario/Canada it has been estimated the average rehabilitation patient receives a little under 2 hours of direct patient-therapist time 5 days per week (Foley et al. 2012). In the SIRRACT trial, ankle sensors collecting daily data revealed the average amount of daily walking practice during inpatient rehab for stroke across 16 facilities was only 17 minutes and decreased as patients achieved walking speeds of only 0.8 m/sec (Dorsch et al. 2015).

Even more discouraging are the results from A Very Early Rehabilitation Trial (AVERT) (Bernhardt et al. 2007, Bernhardt et al. 2004a) 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.

Highlighted Study

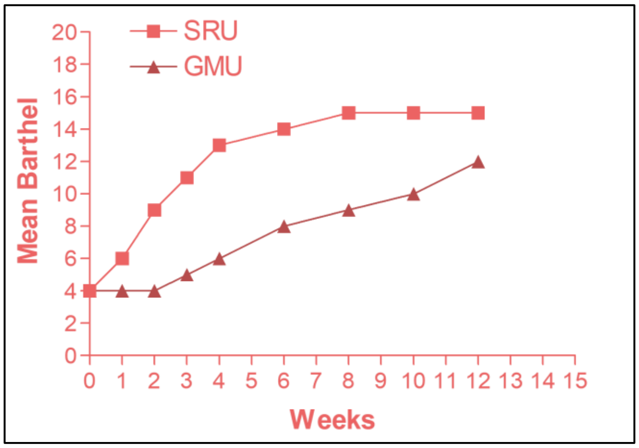
Kalra L. The influence of stroke unit rehabilitation on functional recovery from stroke. Stroke 1994; 25:821-825.		
RCT (5) N_{Start}=146 N_{End}=141 TPS=Acute	E: Stroke rehabilitation unit C: General medical ward Duration: 3mo	1. Barthel Index (+exp) Median Barthel Index scores of patients managed on the stroke unit were significantly higher compared to patients on the medical unit (15 vs. 12). 2. LOS (+exp) Rate of improvement in Barthel Index scores was faster for patients on the stroke unit and these patients had significantly shorter length of stay (6 vs. 20 weeks). 3. Significant gains were achieved at a faster rate without additional physiotherapy or occupational therapy in total.
This study randomized 146 "middle band" strokes to stroke unit (SRU) or general medical unit (GMU) care. The median Barthel Index score was 4/20 in both groups at the beginning of the study. Patients randomized to Stroke Unit care had a Barthel Index score of 15/20 after 6 weeks of treatment and were on average discharged from hospital at 6 weeks. Patients randomized to the General Medical Unit had a Barthel Index score of 12/20 who were discharged at a mean of 20 weeks. The total amount of therapy provided was no different between the stroke rehabilitation unit and the general medical unit. However, the SRU provided the same amount of therapy over a much shorter period of time; intensity of therapy was much higher on the SRU. This frontloading of therapy resulted in a dramatic improvement in outcomes and costs. This study demonstrates that middle-band stroke patients do better in a specialized stroke rehabilitation unit when compared to a general medicine unit in terms of functional outcomes and length of hospital stay. This despite the fact both groups received the same amount of overall therapy. The stroke unit care was more specialized and intensive ("front-loading"). The result was significant improvements in function with shorter lengths of stay; hence, better health outcomes were obtained at a lesser cost.		

Figure 2.5.20 Therapy Intensity Amount of Physiotherapy and Occupational Therapy on Stroke Rehab Unit versus General Medical Unit in Kalra et al. 1994. The amount of therapies are similar. However, stroke rehabilitation patients received it over 6 weeks and General Medical Unit patients over 20 weeks.

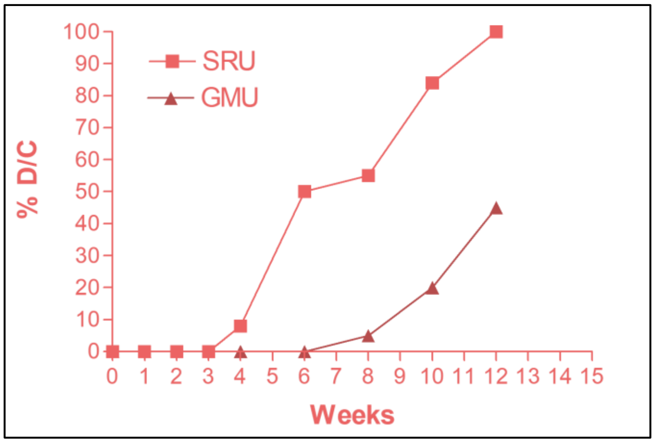


Patients on the SRU who received the same amount of therapy but compressed into a shorter timeframe showed greater and faster improvements in the Barthel Index Score (Figure 2.5.21) and were discharged from hospital much sooner (Figure 2.5.22).

Figures 2.5.21. Improvement in Mean Barthel Score on Stroke Rehab Unit and General Medical Ward



Figures 2.5.22. Percentage of Patients Discharged Over Time for Stroke Rehab Unit and General Medical Ward



Highlighted Study

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 (-)

Highlighted Study

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 (-)

Highlighted Study

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)

Highlighted Review

Kwakkel G, van Peppen R, Wagenaar RC, et al. Effects of augmented exercise therapy time after stroke: a meta-analysis. Stroke 2004; 35:2529-2539.

Methods
A systematic review to study the effects of augmented exercise therapy time (AETT) on various stroke outcomes was conducted of candidate articles published between 1966 and 2003. Using a fixed and random effects model, effect sizes were computed for ADL, walking speed and dexterity.
Results
31 studies met the inclusion criteria, of which 20 were used for analysis, establishing a sample of 2686 stroke patients. At end of intervention, a small heterogeneous summary effect size was established for ADL ($p<.05$). A homogeneous summary effect size ($p<.001$) was established when therapy occurred within the first 6 months after stroke but not thereafter. A significant homogeneous summary effect size was also noted for walking speed ($p=.017$), but not for dexterity.

This study is an extension of a previous meta-analysis, evaluating the benefit of augmented physical therapy, including 20 studies which had assessed many 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 speeds, 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.

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 suggested 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.

Conclusions

Greater intensities of physiotherapy and occupational therapy appeared to result in improved functional outcomes. There are significant problems delivering an optimal dose of therapy intensities in actual clinical practice.

2.7.2 Intensity of Aphasia Therapy Post Stroke

Bhogal et al. (2003) (see Highlighted Study below) observed 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).

Highlighted Study

Bhogal SK, Teasell R, Speechley M. Intensity of aphasia therapy, impact on recovery. Stroke 2003; 34(4):987-993.

Methods

A systematic review to explore how the intensity of aphasia therapy (speech and language therapy) is associated with aphasia recovery in stroke patients. Intensity was determined by length (weeks), hours per week, and total hours of therapy. A database (MEDLINE) search for candidate articles that were published between 1975 and 2002 was conducted. Primary outcome measures were the PICA, FCP, and Token Test, and Pearson's correlation coefficient was used to assess the relationship between intensity and outcome of therapy.

Results

10 studies met the inclusion criteria which established a sample of 864 stroke patients. Hours of therapy per week ($p=.001$, $p=.027$), and total hours of therapy ($p<.001$) were both significantly correlated with improvement on the PICA and Token Test, whereas total length of therapy was found to be inversely correlated ($p=.003$) with change in PICA scores, suggesting that therapy lasting longer (in weeks) was less intense.

Highlighted Study

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 (-)

Bakheit et al. (2007) in a large RCT failed to uncover a benefit of intensive aphasia therapy as assessed using the Western Aphasia Battery. The average time from 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.

Highlighted Study

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)

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).

Conclusion

For patients who can tolerate it, more intensive speech and language therapy appears to result in improved outcomes.

2.7.3 Weekend Therapy and Other Innovative Approaches to Increase Therapy Intensity

Innovative approaches from group therapy to videogames to altering therapist mix:

- Group therapy. 73 inpatient stroke patients referred to group therapy gait task training or individual gait task training did equally well (Renner et al. 2016).
- Videogames (non-immersive virtual reality) improves outcomes but are equal to spending a comparable amount of time playing board games (Saposnik et al. 2016).
- Weekend therapy is becoming increasingly common.
- General rehab assistants are a less expensive alternative to increase intensity and have become very popular; can cross disciplines.

Highlighted Study

Sonoda S, Saitoh E, Nagai S, Kawakita M, Kanada Y. Full-time integrated treatment program, a new system for stroke rehabilitation in Japan: comparison with conventional rehabilitation. Am J Phys Med Rehabil 2004; 83(2):88-93.

Methods

Historical comparison of 48 stroke patients treated admitted to a conventional stroke rehabilitation program in December 1999, compared to 58 patients treated by the Full-time Integrated Treatment (FIT) program.

The key difference between the 2 programs was the intensity and frequency of treatment (80 minutes of OT/PT therapy 5x/week vs. same daily total of therapy time, but provided 7x/week, although patients were encouraged to remain active outside of structured sessions).

Results

Admission FIM scores between the 2 groups were similar (80.9, conventional vs. 81.2, FIT), however at discharge the FIT group had higher average FIM scores (97.1 vs. 105.0, p<0.01) and FIM efficiency, (change/LOS) (0.19 vs. 0.33, p<0.01). Hospital stays were also shorter for patients in the FIT group (72.9 vs. 81.1 days). The time from onset of stroke to admission into rehabilitation was 54 days for patients in the conventional group and 50 days for patients in the FIT group.

Sonoda et al. (2004) conducted a trial in Japan comparing outcomes of stroke patients admitted to a conventional stroke rehabilitation program 5 days per week and patients admitted to a Full-time Integrated Treatment (FIT) program 7 days per week. Additional weekend therapy resulted in significant improvements in FIM efficiency as well as a reduction in length of stay.

Highlighted Study

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 (-)

Conclusion

The evidence on weekend therapy providing better outcomes on 5 day per week therapy is mixed.

2.7.4 Inactive and Alone

Bernhardt et al. (2004b) found that on a stroke unit during a therapeutic day, stroke patients were shown to spend their time largely inactive. More than 50% of patients' time was spent in bed, 28% was spent sitting out of bed and only 13% of time was spent in therapeutic activities. Patients were alone for 60% of the time which is contrary to the evidence that increased activity and environmental stimulation is important to neurological recovery. Lenze et al. (2004) noted that poor participation in therapy during inpatient rehabilitation was common and was associated with less improvement in FIM scores and longer lengths of stay even when controlling for admission FIM scores. Simpson et al. (2018) conducted an observational study of 34 stroke patients. Patients had an activity monitor worn continuously for the final 7 days in hospital for rehabilitation and the first 7 days at home after discharge. At home participants spent more time upright and walking and less time sitting; depression at discharge predicted greater sitting time and less upright time at home (p=0.03). This raises question about how did rehab get to be less active than being home? Safety overconcerns? Paperwork? Motivation? Culture? If nothing else, it argues very strongly for early supported discharge.

2.7.5 Time Accountability: The Collaboration Evaluation of Rehabilitation in Stroke Across Europe (CERISE) Trial

An important but not particularly popular concept is the importance of ensuring therapists provide appropriate intensity of therapy. Studies show that face-to-face patient-therapist time is often less than scheduled time and brings up the whole issue of who is monitoring how much time is actually spent with patients. This is one means of improving clinical care without additional resources.

Highlighted Study

De Wit L, Putman K, Schuback B, Komárek A, Angst F, Baert I, Berman P, Bogaerts K, Brinkmann N, Connell L, Dejaeger E, Feys H, Jenni W, Kaske C, Lesaffre E, Leys M, Lincoln N, Louckx F, Schupp W, Smith B, De Weerdt W. Motor and functional recovery after stroke: a comparison of 4 European rehabilitation centers. Stroke 2007; 38(7):2101-2107.

Methods

This study, the CERISE study, compared motor and functional recovery after stroke between 4 European Rehab Centers.

Results

Gross motor and functional recovery was better in Swiss and German than UK center with Belgian center in middle. Time sampling study showed avg. daily direct therapy time of 60 min in UK, 120 min in Belgian, 140 min in German and 166 min in Swiss centers. Differences in therapy time not attributed to differences in patient/staff ratio (similar staffing). No differences were found in the content of physiotherapy and occupational therapy. In German and Swiss centers, the rehabilitation programs were strictly timed (therapists had less freedom), while in UK and Belgian centers they were organized on an ad hoc basis (therapists had more freedom to decide). The authors reported *"More formal management in the German center may have resulted in the most efficient use of human resources, which may have resulted in more therapy time for the patients".*

In summary, although the exact of amount of therapy needed to optimize outcomes has yet to be determined, given the evidence, it seems prudent to provide therapies on a more intensive schedule. The beneficial effect may be greatest if high-intensity therapies are provided in the early stages of rehabilitation. One study has suggested that the addition of weekend treatment contributed to an almost doubling of FIM efficiency scores.

2.7.6 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.

Highlighted Study

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 (-)

Highlighted Study

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 (-)

Highlighted Study

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)

Conclusions Regarding Caregiver-Mediated Intensity of Therapy
There is strong 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.

2.8 Task-Specific Treatment

2.8.1 Stroke Rehabilitation Must Be Task-Specific

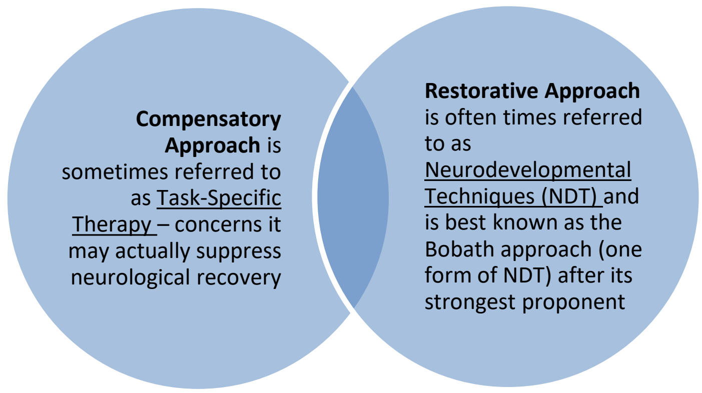
Functional reorganization of cortex is greater for tasks meaningful to the animal; repetitive activity is not enough (Nudo 2003). An element of skilled motor learning is required in addition to repetition for cortical reorganization/plasticity to occur. There is growing evidence that the cortex adjacent to the stroke-damaged region is important to recovery but only if stimulated and trained in the lost function (Hallett 2001). The best way to relearn a given task, if the ability to perform it is lost following a stroke, is to train specifically for that task. Rehabilitation must be task-specific, focusing on tasks important and meaningful to patient. Trends have been moving away from traditional Bobath and other NDT forms of treatment because they slow recovery and increase length of stay. Proponents of task-specific training cite that intense training is not always necessary for positive outcomes in stroke patients, but instead suggest that therapy designed to be more task-specific within normal contact time (30 to 45 minutes per session) could be more efficacious (Page 2003).

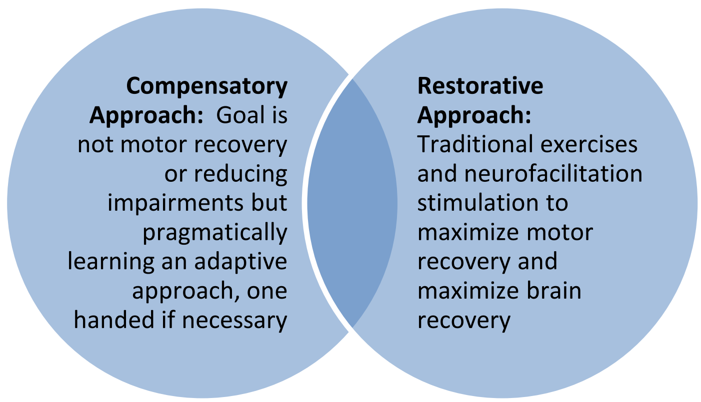
Several trials have evaluated task-specific therapies focusing on gait restoration.

- A pilot study by Richards et al. (1993) demonstrated that focused therapy on specific gait activities leads to positive outcome and not the amount of total therapy time.
- The results from the studies of both Dean et al. (2000) and Salbach et al. (2004) suggest that therapy designed to improve the strength and endurance of the affected lower limb and functional performance demonstrated improvement that was specific to the training.
- Monger et al. (2002) reported that six patients improved their sit-to-stand performance following a home-based, task-specific exercise program. Task-specific interventions associated with neglect have been especially promising.
- Enhanced visual scanning techniques improve visual neglect with subsequent improvement in function (Paolucci et al. 1996, Weinberg et al. 1977, Weinberg et al. 1979).

In summary, task-specific therapy allows for the best recovery. NDT or the Bobath restorative approach results in longer lengths of stay and offers no advantage over other therapy approaches. Task-specific therapeutic approaches allow for the best recovery with improved FIM scores, improved discharge destination and shorter lengths of stay.

2.8.2 Therapy Philosophies





Neurodevelopmental Training (NDT) Approaches

Approach	Description
Bobath	Aims to reduce spasticity and synergies by using inhibitory postures and movements in order to facilitate normal autonomic responses that are involved in voluntary movement (Bobath 1990).
Brunnstrom's Movement Therapy	Emphasis on synergistic patterns of movement that develop during recovery from hemiplegia. Encourages the development of flexor and extensor synergies during early recovery, assuming that synergistic activation of the muscle will result in voluntary movement (Brunnstrom 1970).
Proprioceptive Neuromuscular Facilitation (PNF)	Emphasis on using the patient's stronger movement patterns for strengthening the weaker motions. PNF techniques use manual stimulatin and verbal instructions to induce desired movement patterns and enhance motor function (Myers 1995).

2.8.3 Bobath Approach/Neurodevelopmental Technique (NDT)

The Bobath approach is based upon a theoretical framework in a reflex-hierarchical theory. Synergistic movements are suppressed while normal movements are facilitated and encouraged. It is designed to maximize neurological recovery and limit impairment although there is not sufficient evidence that it actually improves impairment.

The goal of NDT is to normalize tone, to inhibit primitive patterns of movement, and to facilitate automatic, voluntary reactions and subsequent normal movement patterns. It is based on the concept that pathologic movement patterns (limb synergies and primitive reflexes) must not be used for training because continuous use of these pathologic pathways may make it too readily available at the expense of normal pathways. The goal is to suppress abnormal muscle patterns before normal patterns are introduced. Mass synergies are avoided, although they may strengthen weak, unresponsive muscles, because these reinforce abnormally increased tonic reflexes, spasticity.

There is strong evidence that NDT is not superior to other approaches. Based on the highlighted study below (Langhammer & Stanghelle 2000, Langhammer & Stanghelle 2003) there is moderate evidence that Motor Relearning Program (task-specific training) results in short-term improvements in motor functioning and shorter lengths of hospital stay when compared to NDT.

Highlighted Study

Langhammer B, Stanghelle JK. Bobath or motor relearning programme? A comparison of two different approach of physiotherapy in stroke rehabilitation: a randomized controlled study. Clinical Rehabilitation 2000; 14:361-369.
Langhammer B, Stanghelle JK. Bobath or Motor Relearning Programme? A follow-up one and four years post stroke. Clinical *Rehabilitation 2003; 17:731-734*

Methods
Double-blind trial 61 stroke patients randomized to receive Bobath or Motor Relearning Program.
Results
All patients received physiotherapy minimum of 40 mins x 5 days/wk while in hospital. Length of stay was 21 days in Motor Relearning Program vs. 34 days in Bobath (significant difference).

One of the great debates in physiotherapy is whether the neuro-developmental (or restorative) approach, is preferred or whether the compensatory, task-focused, adaptive approach is superior. The most common restorative technique is the Bobath approach that is based upon a theoretical framework in a reflex-hierarchical therapy. Synergistic movements are supported while normal movements are facilitated and encouraged. Langhammer and Stronghelle (2000, 2003), in a RCT, compared the Bobath approach to the Motor Relearning Programme and found the latter resulted in shorter hospital stays and improved motor function.

Highlighted Study

Van Vliet PM, Lincoln NB, Foxall A. Comparison of Bobath based and movement science-based treatment for stroke: a randomized controlled trial. J Neurol Neurosurg Psychiatry (2005); 76:503-508.

Methods

120 patients admitted to stroke rehab ward were randomized to Bobath based or movement science-based rehab approach. Rivermead Motor Assessment (RMA) and Motor Assessment Scale (MAS) scores were assessed at 1, 3 and 6 months.

Results

No significant differences between the two groups. Scores on the subsections of both RAM and MAS associated with lower extremity function were similar.

Highlighted Study

Hafsteindottir TB, Algra A, Kappelle LJ, Grypdonck MH. Neurodevelopmental treatment after stroke: a comparative study. J Neurology Neurosurg Psychiatry (2005); 76(6):788-792.

Methods

Controlled, multi-site cluster trial. 225 patients in 6 hospitals received rehabilitation on units using NDT approach and 101 patients on 6 wards received rehab on units using a conventional (non-NDT) approach.

Results

Primary outcome was a poor outcome (BI <12 or death) at one year. Quality of life also assessed. No differences in the proportion of patients experiencing a poor outcome. Adjusted odds ratio associated with NDT approach was 1.7. No differences in median Quality of Life at 12 months.

2.9 Outpatient Therapy

Rehabilitation is not a place but rather it is a process. Recently there has been a shift, encouraged by funding agencies, from inpatient rehabilitation to outpatient rehabilitation.

2.9.1 Importance of Outpatient Therapy

1. Outpatient therapy allows for earlier discharge of stroke rehabilitation patients into the community. Outpatient stroke rehabilitation is relatively inexpensive.
2. The resources devoted to fund one inpatient stroke rehabilitation bed could fund a full stroke rehabilitation outpatient team (full-time physiotherapist and occupational therapist and half-time speech-language pathologist and social worker) for one year.
3. Patients are often kept in expensive inpatient stroke rehabilitation beds longer than is necessary because of a lack of outpatient therapy.
4. Skills developed in stroke rehabilitation are reinforced and maintained in outpatient therapy.

One of the challenges with outpatient therapy is a ceiling effect of most of our functional measures. We have noted that patients are typically admitted to an outpatient program with a mean FIM score of over 100 which mean on average they are capable of living at home with no or minimal help. Outpatient therapy is typically an adjunct to inpatient rehabilitation and should not be seen as a replacement except for milder strokes who are already at or nearing the ability to live independently.

Outpatient therapy allows for maintenance of gains following stroke rehabilitation and improved community reintegration. Stroke rehabilitation outpatient therapy has been shown to improve outcomes and in particular help to maintain gains made in inpatient stroke rehabilitation. The benefits of outpatient therapy include the fact that the patient is more likely to remain at home through maintenance of gains and are more likely to be discharged home in a timely manner. An outpatient stroke rehabilitation program for severe strokes could significantly improve outcomes with many more patients able to return home and improve FIM scores over time. Outpatient therapy is an essential element of stroke care, yet it is often one of the first casualties of hospital cuts. In Canada, there are inadequate outpatient and community-based rehabilitation services for stroke patients. Unfortunately, this is a shortsighted strategy, which ultimately increases costly inpatient length of stay.

2.9.2 Outpatient Stroke Rehab Therapy

A Cochrane review of 14 RCTs involving 1,617 patients (Trialists & Legg 2003) who were in home-based, day hospital and outpatient clinics. Therapy reduced the odds of a poor outcome (death, deterioration or dependency) (OR 0.72; 95% CI 0.57-0.92; p=0.009). The number needed to treat to spare one person from experiencing a poor outcome was 14. Outpatient therapy reduced rehospitalization and allowed earlier discharge home. Estimated savings was $2 for ever $1 spent on outpatient therapies.

Highlighted Study

Chaiyawat & Kulkantrakorn (2012)		
RCT (7) N_{Start}=60 N_{End}=58 TPS=Acute	E: Home based physiotherapy (6mo) C: Standard care Duration: 2yrs	• Barthel Index (+exp) • Thai Mini-mental State Exam (-) • Hospital Anxiety & Depression Scale (+exp)

Highlighted Study

Welin et al. (2010)		
RCT (6) N_{Start}=163 N_{End}=152 TPS=Subacute	E: Stroke outpatient clinic C: Routine care Duration: 12mo	• Barthel Index (-) • Mortality (-) • Scandinavian Stroke Scale (-) • Percieved Health Status (-) • Montgomery-Asberg Depression Scale (-) • Blood pressure (-) • Modified Rankin Scale (-)

Highlighted Study

Walker et al. (1999) **Walker et al. (2001)**		
RCT (7) N_{Start}=185 N_{End}=163 TPS=Acute	E: Home based occupational therapy C: Conventional care Duration: 6mo	• Extended ADL (+exp) • Barthel Index (+exp) • London Handicap Scale (+exp) • General Health Questionnaire – patient (-) • General Health Questionnaire – carer (-) • Carer Strain Index (+exp)

Highlighted Study

Goldberg et al. (1997)		
RCT (5) N_{Start}=55 N_{End}=41 TPS=Subacute	E: Home-based outpatient care with active case management C: Conventional care Duration: 6mo	• Frenchay Activities Index (+exp)

Conclusions

The evidence is mixed as to whether home- nor clinic-based therapy appeared to improve outcomes during outpatient rehabilitation.

2.9.3 Hospital vs. Home-Based Therapy

The increased focus on patient-driven care versus provider-driven care has sparked a debate as to whether stroke patients should be rehabilitated in hospital-based (inpatient and outpatient) programs or by community rehabilitation programs, which are usually home-based.

Highlighted Study

Gladman JR, Lincoln NB, Barer DH. A randomised controlled trial of domiciliary and hospital-based rehabilitation for stroke patients after discharge from hospital. J Neurol Neurosurg Psychiatry (1993); 56:960-966. Gladman JR, Lincoln NB. Follow-up of a controlled trial of domiciliary stroke rehabilitation (DOMINO Study). Age Ageing (1994); 23:9-13.		
RCT (6) N_{Start}=327 N_{End}=NR TPS=Subacute	E: Domiciliary rehabilitation service C: Hospital-based rehabilitation service Duration: 3mo	• Extended ADL – all subscales (-) • Barthel Index (-) • Nottingham health Profile – all subscales (-) Caregivers • Brief Assessment of Social Engagement (-) • Life Satisfaction Index (-)
327 stroke patients were randomized to receive domiciliary service for up to 6 months or hospital-based rehabilitation services. Domiciliary group showed significantly greater performance on Extended ADL household and leisure sub-scores at 6 months. Relative risk of death or institutionalization in the domiciliary group was 1.6 after one year.		

Highlighted Study

Lincoln et al. (2004)		
RCT (4) N_{Start}=428 N_{End}=188 TPS=Chronic	E: Rehabilitation from a community stroke team C: Rehabilitation to routine care (day hospitals or outpatient departments) Duration: 6mo	• Barthel Index (-) • Extended Activities of Daily Living (-) • General Health Questionnaire (-) • EuroQOL (-) Caregiver • General Health Questionnaire (-) • Caregiver Strain Index (+exp) • EuroQOL (-)

Highlighted Study

Roderick et al. (2001)		
RCT (7) N_{Start}=140 N_{End}=112 TPS=Subacute	E: Rehabilitation at home C: Rehabilitation in clinic Duration: 6mo	• Barthel Index (-) • Rivermead Mobility Index (-) • Frenchay Activities Index (-) • Short Form 36 – Physical (-) • Short Form 36 – Mental (-)

Highlighted Study

Young and Forster (1992)		
RCT (6) N_{Start}=124 N_{End}=108 TPS=Subacute	E: Rehabilitation at home C: Rehabilitation in hospital Duration: 6mo	• Barthel Index (+exp) • Motor Club Assessment (+exp) • Functional ambulation category (+exp) • Frenchay Activities Index (-) • Nottingham Health Profile (-) • General Health Questionnaire – carers (-)

Conclusions

There appears to be no difference in efficacy between home or hospital-based therapy during outpatient rehabilitation.

2.9.4 Early Supported Discharge (ESD)

In a hospital, stroke patients will typically receive acute care and a variable period of rehabilitation with rehabilitation services often reduced after discharge home from hospital (Langhorne 2003). ESD services aim to alter this conventional pathway of care in one of two ways: 1) Expediting earlier discharge from hospital; 2) Providing a more continuous process of rehabilitation spanning the transition period in hospital and at home (Langhorne 2003). Many trials have been conducted to investigate on the effectiveness on ESD, with convincing evidence. The implementation of ESD has now been recommended in Canada, UK and Australia stroke guidelines.

A **Cochrane Review** assessing the efficacy of ESD for acute stroke patients, conducted by the Early Supported Discharge Trialists, was first published in 2001 and most recently updated in 2017 (Fearon & Langhorne 2012). The purpose of this review was to determine whether ESD, with appropriate community support, could be as effective as conventional inpatient rehabilitation and reduce the length of hospital stay. ESD interventions in these studies were designed to accelerate the transition from hospital to home. The review included the results from 17 trials (2,422 patients).

A variety of outcomes were assessed comparing early supported discharge with conventional care at the end of scheduled follow up, which ranged from 3 to 5 years. The results are presented in the Table 2.5.16.

Table 2.5.16. Results of a Cochrane review on ESD

Outcome	Significant Result (Y/N)	OR and 95% CI or * Weighted Mean Difference and 95% CI

Death	No	1.04 (0.77 to 1.40)
Death or need for institutionalization	Yes	0.75 (0.59 to 0.96)
Death or dependency	Yes	0.80 (0.67 to 0.95)
ADL Barthel Index scores	No	0.03 (-0.07 to 0.13) *
Length of initial hospital stay (days)	Yes	-5.54 (-8.81 to –2.91)*
Subjective Health status	No	-0.01 (-0.12 to 0.10) *
Mood Status	No	-0.06 (-0.19 to 0.07)*
Satisfaction with services	Yes	1.60 (1.08 to 2.38) *
Number of readmissions to hospital	No	1.09 (0.79 to 1.51)

The review found there was a **significant reduction in the number of patients requiring institutional care** following discharge as well **as reduced levels of combined death and dependency at 6 months**. **The ESD group also showed significant reductions (P < 0.0001) in the length of hospital stay.** Patients who receive ESD services were **more likely to report satisfaction** with the services. There were no statistically significant differences seen in carers' subjective health status, mood or number of hospital readmissions.

In a further breakdown of the meta-analysis, there were three types of ESD service organization identified in the review:

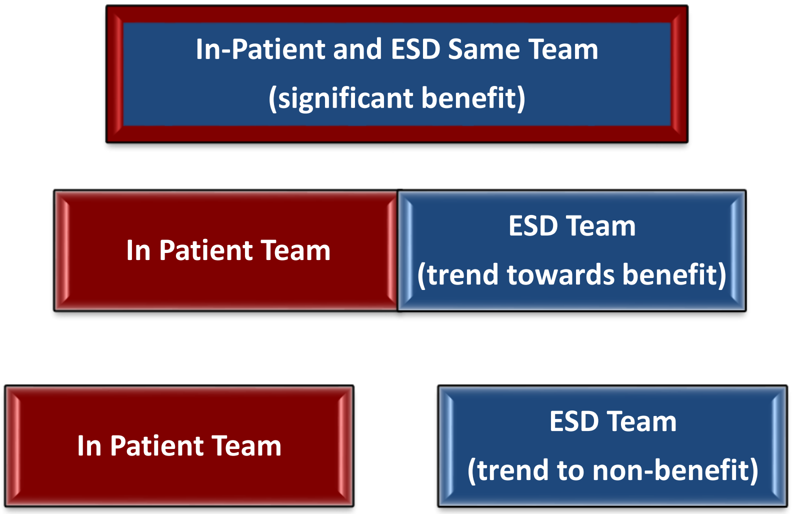
1. ESD team with coordination and delivery: a multidisciplinary team, which coordinated discharge from hospital and post discharge care, and provided rehabilitation therapies in the home.
2. ESD team coordination: discharge and immediate post discharge plans were coordinated by a multidisciplinary care team, but rehabilitation therapies were provided by community-based agencies.
3. No ESD team coordination: therapies were provided by uncoordinated community services or by health-care volunteers.

As hypothesized by the authors, the increasing coordination of services was associated with an improved outcome (see Table 2.5.17 and Figure 2.5.23).

Table 2.5.17 Outcome at End Of Scheduled Follow-Up (ESD Vs. Conventional Care) Stratified By Level Of Service Provision (More Coordinated To Less Coordinated) (Langhorne et al. 2017)

Death or dependency	Significant Result	Odds Ratio (OR) and 95% CI
Overall result	Yes	0.80 (0.67 to 0.95)
ESD team with coordination and delivery	Yes	0.67 (0.52 to 0.87)
ESD team coordination	Yes	0.82 (0.61 to 1.10)
no ESD team coordination	No	1.11 (0.75 to 1.62)

Figure 2.5.23 Visual picture of above Table 2.5.17 showing the three types of ESD formats and benefits.



In summary, the greatest benefits were seen in the trials evaluating a co-ordinated ESD team, which coordinated the hospital discharge, post-discharge care and delivery of home rehabilitation and support.

The usual key argument for ESD is that home provides an optimal rehabilitation environment, since the goal of rehabilitation is to establish skills which are appropriate to the home setting. Nevertheless, it is difficult to fully delineate the specific reasons for the success of ESD services as the reasons for success may be multi-factorial. Langhorne & Widen-Holmqvist (2007) noted it was not possible to specifically determine how ESD services improve patient outcomes as the different components of ESD services cannot be adequately separated within the trials used in the review. Nevertheless, the authors have listed the potential reasons for better results with ESD services, which are explained along the ESD pathway.

Table 2.5.24 ESD Advantages at Each Stage in Pathway

Stage in ESD Pathway	Potential Advantages of ESD
In hospital	Avoiding some complication of hospital admission
Discharge planning	Improving patient and carer morale Focusing on more realistic rehabilitation goals
Home rehabilitation	Providing rehabilitation in a more relevant environment Encouraging more focus on self-directed recovery ESD services able to provide higher levels of therapy input over the whole patient journey
Discharge from ESD service	More realistic understanding of future recovery

(Langhorne & Widen-Holmqvist, 2007)

Early Supported Discharge Trialists (2012) have demonstrated that the greatest benefit is seen in mild to moderate stroke patients, specifically reduction in death or dependence. However, the greatest reduction in hospital length-of-stay were seen in the severe subgroup (Barthel score <10/20).

Tabel 2.5.25 Outcome for ESD based on Stroke Severity; Severe (Barthel <10) vs. Mild to Moderate (Barthel 10-20).

Outcome	Initial Barthel <10	Initial Barthel 10-20
Death or dependence	OR 1.40, 95% CI 0.83 to 2.36	OR 0.77, 95% CI 0.61 to 0.98

Length of stay	MD 28.32, 95% CI 17 to 40	MD 3.11, 95% CI 1 to 7

Highlighted Study

Mayo NE, Wood-Dauphinee S, Cote R, Gayton D, Carlton J, Buttery J, Tamblyn R. There's no place like home: an evaluation of early supported discharge for stroke. Stroke 2000; 31:1016-1023. **Teng J, Mayo NE, Latimer E, Hanley J, Wood-Dauphinee S, Cote R, Scott S. Costs and caregiver consequences of early supported discharge for stroke patients. Stroke. (2000); 34(2):528-36.**		
RCT (7) N_{Start}=114 N_{End}=96 TPS=Acute	E: Receive home intervention after early supported discharge C: Receive usual post stroke care Duration: 4wks	• Barthel Index (-) • Timed Up &Go (-) • Reintegration to Normal Living (-) • Stroke Rehabilitation Assessment of Movement (-) • Older Americans Resource Scale - IADL (-) • Short Form 36 – all subscales (-) • Except: Physical health (+exp)
114 of 1542 admitted stroke patients were randomized after discharge to receive either home intervention or usual post stroke care. Eligibility criteria included patients with persistent motor deficits post stroke with caregivers willing and able to provide live-in care over a 4-week period. At 28 days those stroke patients who still needed >1 assist to walk, or those with cognitive impairment or with disabling coexisting conditions were excluded. Barthel scores were approximately 84 on average. Duration of hospital stay reduced by 2.6 days (9.8 vs. 12.4) in the home treatment group. Barthel score did not change significantly between the two groups. Home therapy group did better on SF-36 physical health component and a community reintegration score vs. usual care. The total costs after 3 mos. associated with the home care group were significantly less compared to the usual care group ($7,784 vs. $11,065 Canadian, p<0.0001). Lower caregiver burden scores were associated with home intervention group.		

<u>Conclusions</u>
Early supported discharge may not be efficacious compared to conventional care for outpatient stroke rehabilitation.
Early supported discharge with home therapy may not be more beneficial than early supported discharge with day clinic therapy for ambulation or balance.

2.9.5 Canadian Best Practice Guideline Update 2015

Recommendations 4.1: Outpatient & Community-Based Rehabilitation
Hebert D … Teasell R. Canadian Stroke Best Practice Recommendations: … Update 2015. *International Journal of Stroke* July (2016).

1. Stroke survivors with ongoing rehabilitation goals **should continue to have access to specialized stroke services after leaving hospital** [Evidence Level A]. **This should include in-home community-based rehabilitation services … or facility-based outpatient services** [Evidence Level A].
2. Outpatient and/or community based rehabilitation services should be available and **provided by a specialized inter-professional team, when needed by patients, within 48 hours of discharge from an acute hospital or within 72 hours of discharge from inpatient rehabilitation** [Evidence Level C].

3. Outpatient and/or community-based services **should be delivered in the most suitable setting based on patient functional rehabilitation needs, participation-related goals, availability of family/social support, patient and family preferences which may include in the home or other community settings** [Evidence Level C].
4. Outpatient and/or community-based rehabilitation services **should include the same elements as coordinated rehabilitation services:**
   i) An interprofessional stroke rehabilitation team [Evidence Level A].
   ii) A case coordination approach including regular team communication to discuss assessment of new clients, review client management, goals and plans for discharge or transition [Evidence Level B].
   iii) **Therapy should be provided for a minimum of 45 minutes per da**y [Evidence Level B] per discipline, 2 to 5 days per week, based on individual patient needs and goals [Evidence Level A] for at least 8 weeks [Evidence Level C].

References

Alexander MP. Stroke rehabilitation outcome. A potential use of predictive variables to establish levels of care. *Stroke 1994;25:128-134.*

Andersen KK, Olsen TS, Dehlendorff C, Kammersgaard LP. Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk factors. *Stroke 2009;40:2068-2072.*

Astrup J, Siesjö BK, Symon L. Thresholds in cerebral ischemia-the ischemic penumbra. *Stroke 1981;12:723-725.*

Bai Y, Hu Y, Wu Y, Zhu Y, He Q, Jiang C, . . . Fan W. A prospective, randomized, single-blinded trial on the effect of early rehabilitation on daily activities and motor function of patients with hemorrhagic stroke. *J Clin Neurosci 2012;19:1376-9.*

Bai YL, Hu YS, Wu Y, Zhu YL, Zhang B, Jiang CY, . . . Fan WK. Long-term three-stage rehabilitation intervention alleviates spasticity of the elbows, fingers, and plantar flexors and improves activities of daily living in ischemic stroke patients: a randomized, controlled trial. *Neuroreport 2014;25:998-1005.*

Bakheit AM, Shaw S, Barrett L, Wood J, Carrington S, Griffiths S, . . . Koutsi F. A prospective, randomized, parallel group, controlled study of the effect of intensity of speech and language therapy on early recovery from poststroke aphasia. *Clin Rehabil 2007;21:885-94.*

Barzel A, Ketels G, Stark A, Tetzlaff B, Daubmann A, Wegscheider K, . . . Scherer M. Home-based constraint-induced movement therapy for patients with upper limb dysfunction after stroke (HOMECIMT): a cluster-randomised, controlled trial. *Lancet Neurol 2015;14:893-902.*

Beninato M, Gill-Body KM, Salles S, Stark PC, Black-Schaffer RM, Stein J. Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. *Archives of physical medicine and rehabilitation 2006;87:32-39.*

Bernhardt J. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): A randomised controlled trial. *The Lancet 2015;386:46-55.*

Bernhardt J, Chan J, Nicola I, Collier JM. Little therapy, little physical activity: rehabilitation within the first 14 days of organized stroke unit care. *J Rehabil Med 2007;39:43-8.*

Bernhardt J, Churilov L, Ellery F, Collier J, Chamberlain J, Langhorne P, . . . Donnan G. Prespecified dose-response analysis for A Very Early Rehabilitation Trial (AVERT). *Neurology 2016;86:2138-2145.*

Bernhardt J, Dewey H, Thrift A, Donnan G. Inactive and alone: physical activity within the first 14 days of acute stroke unit care. *Stroke 2004a;35:1005-9.*

Bernhardt J, Dewey H, Thrift A, Donnan G. Inactive and alone: physical activity within the first 14 days of acute stroke unit care. *Stroke 2004b;35:1005-1009.*

Bhogal SK, Teasell R, Speechley M. Intensity of aphasia therapy, impact on recovery. *Stroke 2003;34:987-93.*

Biernaskie J, Chernenko G, Corbett D. Efficacy of rehabilitative experience declines with time after focal ischemic brain injury. *Journal of Neuroscience 2004;24:1245-1254.*

Bleiberg J. Psychological and neuropsychological factors in stroke management. *Stroke Rehabilitation 1986;197-232.*

Blum L, Korner-Bitensky N. Usefulness of the Berg Balance Scale in stroke rehabilitation: a systematic review. *Physical therapy 2008;88:559-566.*

Bobath B. Adult hemiplegia: evaluation and treatment. *1990;*

Bonita R, Beaglehole R. Recovery of motor function after stroke. *Stroke 1988;19:1497-1500.*

Bour A, Rasquin S, Boreas A, Limburg M, Verhey F. How predictive is the MMSE for cognitive performance after stroke? *Journal of neurology 2010;257:630-637.*

Brady BK, McGahan L, Skidmore B. Systematic review of economic evidence on stroke rehabilitation services. *Int J Technol Assess Health Care 2005;21:15-21.*

Brady MC, Kelly H, Godwin J, Enderby P, Campbell P. Speech and language therapy for aphasia following stroke. *Cochrane Database Syst Rev 2016;CD000425.*

Brandstater ME, Basmajian JV. Stroke Rehabilitation. *1987;*

Brown AW, Marlowe KJ, Bjelke B. Age effect on motor recovery in a post-acute animal stroke model. *Neurobiology of aging 2003;24:607-614.*

Brunnstrom S. Movement therapy in hemiplegia. *A neurophysiological approach 1970;113-122.*

Bugge C, Hagen S, Alexander H. Measuring stroke patients' health status in the early post-stroke phase using the SF36. *International journal of nursing studies 2001;38:319-327.*

Bushnell CD, Johnston DC, Goldstein LB. Retrospective assessment of initial stroke severity: comparison of the NIH Stroke Scale and the Canadian Neurological Scale. *Stroke 2001;32:656-660.*

Byblow WD, Stinear CM, Barber PA, Petoe MA, Ackerley SJ. Proportional recovery after stroke depends on corticomotor integrity. *Annals of neurology 2015;78:848-859.*

Cabral NL, Moro C, Silva GR, Scola RH, Werneck LC. Study comparing the stroke unit outcome and conventional ward treatment: a randomized study in Joinville, Brazil. *Arq Neuropsiquiatr 2003;61:188-93.*

Cavallini A, Micieli G, Marcheselli S, Quaglini S. Role of monitoring in management of acute ischemic stroke patients. *Stroke 2003;34:2599-603.*

Cavanagh SJ, Hogan K, Gordon V, Fairfax J. Stroke-specific FIM models in an urban population. *Journal of Neuroscience Nursing 2000;32:17-17.*

Chaiyawat P, Kulkantrakorn K. Randomized controlled trial of home rehabilitation for patients with ischemic. *Psychogeriatrics 2012;12:193-9.*

Chan DK, Levi C, Cordato D, O'Rourke F, Chen J, Redmond H, . . . Hankey GJ. Health service management study for stroke: a randomized controlled trial to evaluate two models of stroke care. *Int J Stroke 2014;9:400-5.*

Chippala P, Sharma R. Effect of very early mobilisation on functional status in patients with acute stroke: a single-blind, randomized controlled trail. *Clinical Rehabilitation 2016;30:669-75.*

Ciccone A, Celani MG, Chiaramonte R, Rossi C, Righetti E. Continuous versus intermittent physiological monitoring for acute stroke. *Cochrane Database Syst Rev 2013;Cd008444.*

Claesson L, Gosman-Hedstrom G, Fagerberg B, Blomstrand C. Hospital re-admissions in relation to acute stroke unit care versus conventional care in elderly patients the first year after stroke: the Goteborg 70+ Stroke study. *Age Ageing 2003;32:109-13.*

Claesson L, Gosman-Hedstrom G, Johannesson M, Fagerberg B, Blomstrand C. Resource utilization and costs of stroke unit care integrated in a care continuum: A 1-year controlled, prospective, randomized study in elderly patients: the Goteborg 70+ Stroke Study. *Stroke 2000;31:2569-77.*

Clark MS, Smith DS. Changes in family functioning for stroke rehabilitation patients and their families. *Int J Rehabil Res 1999;22:171-9.*

Cotman CW, Anderson KJ. Synaptic plasticity and functional stabilization in the hippocampal formation: possible role in Alzheimer's disease. *Advances in neurology 1988;47:313-335.*

Cramer SC. Functional magnetic resonance imaging in stroke recovery. *Phys Med Rehabil Clin N Am 2003;14:S47-55.*

de Haan R, Limburg M, Bossuyt P, van der Meulen J, Aaronson N. The clinical meaning of Rankin 'handicap' grades after stroke. *Stroke 1995;26:2027-30.*

De Weerdt W, Selz B, Nuyens G, Staes F, Swinnen D, van de Winckel A, . . . Feys H. Time use of stroke patients in an intensive rehabilitation unit: a comparison between a Belgian and a Swiss setting. *Disabil Rehabil 2000;22:181-6.*

De Wit L, Putman K, Dejaeger E, Baert I, Berman P, Bogaerts K, . . . De Weerdt W. Use of time by stroke patients: a comparison of four European rehabilitation centers. *Stroke 2005;36:1977-83.*

Dean CM, Richards CL, Malouin F. Task-related circuit training improves performance of locomotor tasks in chronic stroke: a randomized, controlled pilot trial. *Arch Phys Med Rehabil 2000;81:409-17.*

Dey P, Woodman M, Gibbs A, Steele R, Stocks SJ, Wagstaff S, . . . Chaudhuri MD. Early assessment by a mobile stroke team: a randomised controlled trial. *Age Ageing 2005;34:331-8.*

Di Lauro A, Pellegrino L, Savastano G, Ferraro C, Fusco M, Balzarano F, . . . Grasso A. A randomized trial on the efficacy of intensive rehabilitation in the acute phase of ischemic stroke. *J Neurol 2003;250:1206-8.*

Dick J, Guiloff R, Stewart A, Blackstock J, Bielawska C, Paul E, Marsden C. Mini-mental state examination in neurological patients. *Journal of Neurology, Neurosurgery & Psychiatry 1984;47:496-499.*

Dorsch AK, Thomas S, Xu X, Kaiser W, Dobkin BH. SIRRACT: an international randomized clinical trial of activity feedback during inpatient stroke rehabilitation enabled by wireless sensing. *Neurorehabilitation and neural repair 2015;29:407-415.*

Drummond AE, Pearson B, Lincoln NB, Berman P. Ten year follow-up of a randomised controlled trial of care in a stroke rehabilitation unit. *Bmj 2005;331:491-2.*

Duncan PW, Goldstein LB, Matchar D, Divine GW, Feussner J. Measurement of motor recovery after stroke. Outcome assessment and sample size requirements. *Stroke 1992;23:1084-1089.*

Duncan PW, Min Lai S. Stroke Recovery. *Topics in Stroke Rehabilitation 1997;4:51-58.*

Duncan PW, Zorowitz R, Bates B, Choi JY, Glasberg JJ, Graham GD, . . . Reker D. Management of Adult Stroke Rehabilitation Care: a clinical practice guideline. *Stroke 2005;36:e100-43.*

English C, Bernhardt J, Crotty M, Esterman A, Segal L, Hillier S. Circuit class therapy or seven-day week therapy for increasing rehabilitation intensity of therapy after stroke (CIRCIT): a randomized controlled trial. *International Journal of Stroke 2015;10:594-602.*

Fagerberg B, Claesson L, Gosman-Hedstrom G, Blomstrand C. Effect of acute stroke unit care integrated with care continuum versus conventional treatment: A randomized 1-year study of elderly patients: the Goteborg 70+ Stroke Study. *Stroke 2000;31:2578-84.*

Fearon P, Langhorne P. Services for reducing duration of hospital care for acute stroke patients. *Cochrane Database Syst Rev 2012;9:Cd000443.*

Ferrucci L, Bandinelli S, Guralnik J, Lamponi M, Bertini C, Falchini M, Baroni A. Recovery of functional status after stroke. A postrehabilitation follow-up study. *Stroke 1993;24:200-205.*

Foley N, Salter K, Teasell R. Specialized stroke services: a meta-analysis comparing three models of care. *Cerebrovascular Diseases 2007;23:194-202.*

French B, Thomas LH, Coupe J, McMahon NE, Connell L, Harrison J, . . . Watkins CL. Repetitive task training for improving functional ability after stroke. *Cochrane Database of Systematic Reviews 2016;11:CD006073.*

Galvin R, Cusack T, O'Grady E, Murphy TB, Stokes E. Family-mediated exercise intervention (FAME): evaluation of a novel form of exercise delivery after stroke. *Stroke 2011;42:681-6.*

Garraway M. Stroke rehabilitation units: concepts, evaluation, and unresolved issues. *Stroke 1985;16:178-181.*

Garraway WM, Akhtar AJ, Prescott RJ, Hockey L. Management of acute stroke in the elderly: Preliminary results of a controlled trial. *British Medical Journal 1980;280:1040-1043.*

Garraway WM, Akhtar AJ, Smith DL, Smith ME. The triage of stroke rehabilitation. *J Epidemiol Community Health 1981;35:39-44.*

Gladman J, Whynes D, Lincoln N. Cost comparison of domiciliary and hospital-based stroke rehabilitation. DOMINO Study Group. *Age Ageing 1994;23:241-5.*

Gladman JR, Lincoln NB, Barer DH. A randomised controlled trial of domiciliary and hospital-based rehabilitation for stroke patients after discharge from hospital. *J Neurol Neurosurg Psychiatry 1993;56:960-6.*

Glasgow Augmented Physiotherapy Study (GAPS) group. Can augmented physiotherapy input enhance recovery of mobility after stroke? A randomized controlled trial. *Clin Rehabil 2004;18:529-37.*

Godecke E, Hird K, Lalor EE, Rai T, Phillips MR. Very early poststroke aphasia therapy: a pilot randomized controlled efficacy trial. *Int J Stroke 2012;7:635-44.*

Golicki D, Niewada M, Buczek J, Karlińska A, Kobayashi A, Janssen M, Pickard AS. Validity of EQ-5D-5L in stroke. *Quality of Life Research 2015;24:845-850.*

Guilfoyle MR, Seeley HM, Corteen E, Harkin C, Richards H, Menon DK, Hutchinson PJ. Assessing quality of life after traumatic brain injury: examination of the short form 36 health survey. *Journal of neurotrauma 2010;27:2173-2181.*

Hafsteinsdóttir T, Algra A, Kappelle L, Grypdonck M. Neurodevelopmental treatment after stroke: a comparative study. *Journal of Neurology, Neurosurgery & Psychiatry 2005;76:788-792.*

Hallett M. Plasticity of the human motor cortex and recovery from stroke. *Brain research reviews 2001;36:169-174.*

Hamrin E. Early activation in stroke: Does it make a difference? *Scandinavian Journal of Rehabilitation Medicine 1982;14:101-109.*

Hebert D, Lindsay MP, McIntyre A, Kirton A, Rumney PG, Bagg S, . . . Garnhum M. Canadian stroke best practice recommendations: stroke rehabilitation practice guidelines, update 2015. *International Journal of Stroke 2016;11:459-484.*

Heldner MR, Zubler C, Mattle HP, Schroth G, Weck A, Mono M-L, . . . Lüdi R. National Institutes of Health stroke scale score and vessel occlusion in 2152 patients with acute ischemic stroke. *Stroke 2013;44:1153-1157.*

Himann JE, Cunningham DA, Rechnitzer PA, Paterson DH. Age-related changes in speed of walking. *Medicine and science in sports and exercise 1988;20:161-166.*

Indredavik B, Bakke F, Slordahl SA, Rokseth R, Haheim LL. Stroke unit treatment. 10-year follow-up. *Stroke 1999a;30:1524-7.*

Indredavik B, Bakke F, Slordahl SA, Rokseth R, Haheim LL. Treatment in a combined acute and rehabilitation stroke unit: which aspects are most important? *Stroke 1999b;30:917-23.*

Indredavik B, Bakke F, Solberg R, Rokseth R, Haaheim LL, Holme I. Benefit of a stroke unit: a randomized controlled trial. *Stroke 1991;22:1026-31.*

Indredavik B, Slordahl SA, Bakke F, Rokseth R, Haheim LL. Stroke unit treatment. Long-term effects. *Stroke 1997;28:1861-6.*

Inoue Y, Takemoto K, Miyamoto T, Yoshikawa N, Taniguchi S, Saiwai S, . . . Komatsu T. Sequential computed tomography scans in acute cerebral infarction. *Radiology 1980;135:655-662.*

Janssen M, Pickard AS, Golicki D, Gudex C, Niewada M, Scalone L, . . . Busschbach J. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. *Quality of Life Research 2013;22:1717-1727.*

Jordan K, Challis JH, Newell KM. Walking speed influences on gait cycle variability. *Gait & posture 2007;26:128-134.*

Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Intracerebral hemorrhage versus infarction: stroke severity, risk factors, and prognosis. *Ann Neurol 1995a;38:45-50.*

Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Recovery of walking function in stroke patients: the Copenhagen Stroke Study. *Arch Phys Med Rehabil 1995b;76:27-32.*

Jørgensen HS, Nakayama H, Raaschou HO, Vive-Larsen J, Støier M, Olsen TS. Outcome and time course of recovery in stroke. Part I: Outcome. The Copenhagen Stroke Study. *Arch Phys Med Rehabil 1995c;76:399-405.*

Jørgensen HS, Nakayama H, Raaschou HO, Vive-Larsen J, Støier M, Olsen TS. Outcome and time course of recovery in stroke. Part II: Time course of recovery. The Copenhagen Stroke Study. *Arch Phys Med Rehabil 1995d;76:406-12.*

Juby LC, Lincoln NB, Berman P. The effect of a stroke rehabilitation unit on functional and psychological outcome: A randomised controlled trial. *Cerebrovascular Diseases 1996;6:106-110.*

Kalra L. Does age affect benefits of stroke unit rehabilitation? *Stroke 1994a;25:346-51.*

Kalra L. The influence of stroke unit rehabilitation on functional recovery from stroke. *Stroke 1994b;25:821-5.*

Kalra L, Dale P, Crome P. Improving stroke rehabilitation. A controlled study. *Stroke 1993;24:1462-7.*

Kalra L, Eade J. Role of stroke rehabilitation units in managing severe disability after stroke. *Stroke 1995;26:2031-4.*

Kalra L, Evans A, Perez I, Knapp M, Donaldson N, Swift CG. Alternative strategies for stroke care: a prospective randomised controlled trial. *Lancet 2000;356:894-9.*

Kalra L, Evans A, Perez I, Knapp M, Swift C, Donaldson N. A randomised controlled comparison of alternative strategies in stroke care. *Health Technol Assess 2005;9:iii-iv, 1-79.*

Kaste M, Palomaki H, Sarna S. Where and how should elderly stroke patients be treated? A randomized trial. *Stroke 1995a;26:249-53.*

Kaste M, Palomäki H, Sarna S. Where and how should elderly stroke patients be treated? A randomized trial. *Stroke 1995b;26:249-53.*

Kelly-Hayes M, Wolf PA, Kase CS, Gresham GE, Kannel WB, D'Agostino RB. Time Course of Functional Recovery After Stroke: The Framingham Study. *Journal of Neurologic Rehabilitation 1989;3:65-70.*

Kelly PJ, Furie KL, Shafqat S, Rallis N, Chang Y, Stein J. Functional recovery following rehabilitation after hemorrhagic and ischemic stroke. *Arch Phys Med Rehabil 2003;84:968-72.*

Kendall BJ, Gothe NP. Effect of Aerobic Exercise Interventions on Mobility among Stroke Patients: A Systematic Review. *Am J Phys Med Rehabil 2016;95:214-24.*

Kim S-G, Ashe J, Hendrich K, Ellermann JM, Merkle H, Ugurbil K, Georgopoulos AP. Functional magnetic resonance imaging of motor cortex: hemispheric asymmetry and handedness. *Science 1993;261:615-617.*

Kugler C, Altenhöner T, Lochner P, Ferbert A, ASH HSDBSG. Does age influence early recovery from ischemic stroke? *Journal of neurology 2003;250:676-681.*

Kwakkel G. Impact of intensity of practice after stroke: issues for consideration. *Disabil Rehabil 2006;28:823-30.*

Kwakkel G, Kollen B, Twisk J. Impact of time on improvement of outcome after stroke. *Stroke 2006;37:2348-53.*

Kwakkel G, Kollen BJ, Wagenaar RC. Long term effects of intensity of upper and lower limb training after stroke: a randomised trial. *J Neurol Neurosurg Psychiatry 2002;72:473-9.*

Kwakkel G, van Peppen R, Wagenaar RC, Wood Dauphinee S, Richards C, Ashburn A, . . . Langhorne P. Effects of augmented exercise therapy time after stroke: a meta-analysis. *Stroke 2004;35:2529-39.*

Kwakkel G, Wagenaar RC, Twisk JW, Lankhorst GJ, Koetsier JC. Intensity of leg and arm training after primary middle-cerebral-artery stroke: a randomised trial. *Lancet 1999;354:191-6.*

Lang CE, Macdonald JR, Reisman DS, Boyd L, Jacobson Kimberley T, Schindler-Ivens SM, . . . Scheets PL. Observation of amounts of movement practice provided during stroke rehabilitation. *Arch Phys Med Rehabil 2009;90:1692-8.*

Langhammer B, Stanghelle JK. Bobath or motor relearning programme? A comparison of two different approaches of physiotherapy in stroke rehabilitation: a randomized controlled study. *Clin Rehabil 2000;14:361-9.*

Langhammer B, Stanghelle JK. Bobath or motor relearning programme? A follow-up one and four years post stroke. *Clinical Rehabilitation 2003;17:731-734.*

Langhorne P. Editorial Comment—Early Supported Discharge: An Idea Whose Time Has Come? *Stroke 2003;34:2691-2692.*

Langhorne P, Baylan S, Trialists ESD, Group CS. Early supported discharge services for people with acute stroke. *The Cochrane Database of Systematic Reviews 2017;2017:*

Langhorne P, Dey P, Woodman M, Kalra L, Wood-Dauphinee S, Patel N, Hamrin E. Is stroke unit care portable? A systematic review of the clinical trials. *Age Ageing 2005;34:324-30.*

Langhorne P, Holmqvist LW. Early supported discharge after stroke. *J Rehabil Med 2007;39:103-8.*

Langhorne P, Lewsey JD, Jhund PS, Gillies M, Chalmers JW, Redpath A, . . . MacIntyre K. Estimating the impact of stroke unit care in a whole population: an epidemiological study using routine data. *J Neurol Neurosurg Psychiatry 2010a;81:1301-5.*

Langhorne P, Stott D, Knight A, Bernhardt J, Barer D, Watkins C. Very early rehabilitation or intensive telemetry after stroke: a pilot randomised trial. *Cerebrovasc Dis 2010b;29:352-60.*

Lenze EJ, Munin MC, Quear T, Dew MA, Rogers JC, Begley AE, Reynolds CF. Significance of poor patient participation in physical and occupational therapy for functional outcome and length of stay. *Arch Phys Med Rehabil 2004;85:1599-601.*

Linacre JM, Heinemann AW, Wright BD, Granger CV, Hamilton BB. The structure and stability of the Functional Independence Measure. *Arch Phys Med Rehabil 1994;75:127-32.*

Lincoln NB, Walker MF, Dixon A, Knights P. - Evaluation of a multiprofessional community stroke team: a randomized controlled. *Clin Rehabil 2004;18:40-7.*

Lincoln NB, Willis D, Philips SA, Juby LC, Berman P. Comparison of rehabilitation practice on hospital wards for stroke patients. *Stroke 1996;27:18-23.*

Lipson DM, Sangha H, Foley NC, Bhogal S, Pohani G, Teasell RW. Recovery from stroke: differences between subtypes. *Int J Rehabil Res 2005;28:303-8.*

Lo RC. Recovery and rehabilitation after stroke. *Can Fam Physician 1986;32:1851-3.*

Lohse KR, Lang CE, Boyd LA. Is more better? Using metadata to explore dose-response relationships in stroke rehabilitation. *Stroke 2014;45:2053-2058.*

Lyden P, Zivin J. Cytoprotective therapies in ischemic stroke. *Cohen SN, editor. Management of ischemic stroke. New York: McGraw-Hill, Health Professions Division 2000;225-240.*

Ma R-H, Wang Y-J, Qu H, Yang Z-H. Assessment of the early effectiveness of a stroke unit in comparison to the general ward. *Chinese medical journal 2004a;117:852-855.*

Ma RH, Wang YJ, Qu H, Yang ZH. Assessment of the early effectiveness of a stroke unit in comparison to the general ward. *Chin Med J (Engl) 2004b;117:852-5.*

Mayo NE, Wood-Dauphinee S, Côté R, Gayton D, Carlton J, Buttery J, Tamblyn R. There's no place like home : an evaluation of early supported discharge for stroke. *Stroke 2000;31:1016-23.*

McDowell I, Newell C. A guide to rating scales and questionnaires. *A guide to rating scales and questionnaires 1996;*

McKellar J, Cheung D, Huijbregts M, Cameron J. The impact of a community re-engagement cue to action trigger tool on re-engaging in activities post-stroke: a mixed-methods study. *Topics in stroke rehabilitation 2015;22:134-143.*

Monger C, Carr JH, Fowler V. Evaluation of a home-based exercise and training programme to improve sit-to-stand in patients with chronic stroke. *Clin Rehabil 2002;16:361-7.*

Mulder M, Nijland R. Stroke Impact Scale. *Journal of physiotherapy 2016;62:117.*
Myers B. Proprioceptive neuromuscular facilitation approach. *Occupational Therapy for Physical Dysfunction 1995;*
Nakayama H, Jørgensen HS, Raaschou HO, Olsen TS. Compensation in recovery of upper extremity function after stroke: the Copenhagen Stroke Study. *Arch Phys Med Rehabil 1994;75:852-7.*
Nilsson L, Carlsson J, Danielsson A. Fugl-Meyer 20. A, Hellström K, Kristensen L, et al. Walking training of patients with hemiparesis at an early stage after stroke: a comparison of walking training on a treadmill with body weight support and walking training on the ground. *Clin Rehabil 2001;15:515-27.*
Nudo R. Adaptive plasticity in motor cortex: implications for rehabilitation after brain injury. *Journal of Rehabilitation Medicine-Supplements 2003;41:7-10.*
Nudo RJ, Plautz EJ, Frost SB. Role of adaptive plasticity in recovery of function after damage to motor cortex. *Muscle Nerve 2001;24:1000-19.*
Page SJ. Intensity versus task-specificity after stroke: how important is intensity? *Am J Phys Med Rehabil 2003;82:730-2.*
Palmer S, Glass TA. Family Function and Stroke Recovery: A Review. *Rehabilitation Psychology 2003;48:255-265.*
Paolucci S, Antonucci G, Grasso MG, Bragoni M, Coiro P, De Angelis D, . . . Pratesi L. Functional outcome of ischemic and hemorrhagic stroke patients after inpatient rehabilitation: a matched comparison. *Stroke 2003;34:2861-5.*
Paolucci S, Antonucci G, Grasso MG, Morelli D, Troisi E, Coiro P, Bragoni M. Early versus delayed inpatient stroke rehabilitation: a matched comparison conducted in Italy. *Arch Phys Med Rehabil 2000;81:695-700.*
Paolucci S, Antonucci G, Guariglia C, Magnotti L, Pizzamiglio L, Zoccolotti P. Facilitatory effect of neglect rehabilitation on the recovery of left hemiplegic stroke patients: a cross-over study. *J Neurol 1996;243:308-14.*
Park C-S. The test-retest reliability and minimal detectable change of the short-form Barthel Index (5 items) and its associations with chronic stroke-specific impairments. *Journal of physical therapy science 2018;30:835-839.*
Peacock PB, Riley CP, Lampton TD, Raffel SS, Walker JS. The Birmingham Stroke, Epidemiology and Rehabilitation Study. *Trends in Epidemiology 1972;*
Popa-Wagner A, Schröder E, Schmoll H, Walker LC, Kessler C. Upregulation of MAP1B and MAP2 in the rat brain after middle cerebral artery occlusion: effect of age. *J Cereb Blood Flow Metab 1999;19:425-34.*
Post MW, Festen H, van de Port IG, Visser-Meily JM. Reproducibility of the Caregiver Strain Index and the Caregiver Reaction Assessment in partners of stroke patients living in the Dutch community. *Clinical Rehabilitation 2007;21:1050-1055.*
Prabhakaran S, Zarahn E, Riley C, Speizer A, Chong JY, Lazar RM, . . . Krakauer JW. Inter-individual variability in the capacity for motor recovery after ischemic stroke. *Neurorehabil Neural Repair 2008;22:64-71.*
Quinn TJ, Dawson J, Walters M, Lees KR. Reliability of the modified Rankin Scale: a systematic review. *Stroke 2009;40:3393-3395.*
Rankin J. Cerebral vascular accidents in patients over the age of 60. II. Prognosis. *Scott Med J 1957;2:200-15.*
Renner C, Outermans J, Ludwig R, Brendel C, Kwakkel G, Hummelsheim H. Group therapy task training versus individual task training during inpatient stroke rehabilitation: a randomised controlled trial. *Clin Rehabil 2016;30:637-48.*
Richards CL, Malouin F, Wood-Dauphinee S, Williams JI, Bouchard JP, Brunet D. Task-specific physical therapy for optimization of gait recovery in acute stroke patients. *Arch Phys Med Rehabil 1993;74:612-20.*
Richardson M, Campbell N, Allen L, Meyer M, Teasell R. The stroke impact scale: performance as a quality of life measure in a community-based stroke rehabilitation setting. *Disability and rehabilitation 2016;38:1425-1430.*
Roberts L, Counsell C. Assessment of Clinical Outcomes in Acute Stroke Trials. *Stroke 1998;29:986-991.*
Roderick P, Low J, Day R, Peasgood T, Mullee MA, Turnbull JC, . . . Raftery J. Stroke rehabilitation after hospital discharge: a randomized trial comparing. *Age Ageing 2001;30:303-10.*
Ronning OM, Guldvog B. Outcome of subacute stroke rehabilitation: a randomized controlled trial. *Stroke 1998a;29:779-84.*
Ronning OM, Guldvog B. Stroke unit versus general medical wards, II: neurological deficits and activities of daily living: a quasi-randomized controlled trial. *Stroke 1998b;29:586-90.*

Salbach NM, Mayo NE, Wood-Dauphinee S, Hanley JA, Richards CL, Côté R. A task-orientated intervention enhances walking distance and speed in the first year post stroke: a randomized controlled trial. *Clin Rehabil 2004;18:509-19.*

Salter K, Jutai J, Hartley M, Foley N, Bhogal S, Bayona N, Teasell R. Impact of early vs delayed admission to rehabilitation on functional outcomes in persons with stroke. *J Rehabil Med 2006;38:113-7.*

Sanford J, Moreland J, Swanson LR, Stratford PW, Gowland C. Reliability of the Fugl-Meyer assessment for testing motor performance in patients following stroke. *Physical therapy 1993;73:447-454.*

Saposnik G, Cohen LG, Mamdani M, Pooyania S, Ploughman M, Cheung D, . . . Dukelow S. Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (EVREST): a randomised, multicentre, single-blind, controlled trial. *The Lancet Neurology 2016;15:1019-1027.*

Schauwecker PE, Cheng HW, Serquinia RM, Mori N, McNeill TH. Lesion-induced sprouting of commissural/associational axons and induction of GAP-43 mRNA in hilar and CA3 pyramidal neurons in the hippocampus are diminished in aged rats. *J Neurosci 1995;15:2462-70.*

Scheff SW, Bernardo LS, Cotman CW. Decrease in adrenergic axon sprouting in the senescent rat. *Science 1978;202:775.*

Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Physical therapy 2000;80:896-903.*

Silva Y, Puigdemont M, Castellanos M, Serena J, Suner RM, Garcia MM, Davalos A. Semi-intensive monitoring in acute stroke and long-term outcome. *Cerebrovasc Dis 2005;19:23-30.*

Simpson DB, Breslin M, Cumming T, de Zoete S, Gall SL, Schmidt M, . . . Callisaya ML. Go home, sit less: the impact of home versus hospital rehabilitation environment on activity levels of stroke survivors. *Archives of physical medicine and rehabilitation 2018;99:2216-2221. e1.*

Sivenius J, Pyorala K, Heinonen OP, Salonen JT, Riekkinen P. The significance of intensity of rehabilitation of stroke--a controlled trial. *Stroke 1985;16:928-31.*

Skilbeck CE, Wade DT, Hewer RL, Wood VA. Recovery after stroke. *J Neurol Neurosurg Psychiatry 1983;46:5-8.*

Slade A, Tennant A, Chamberlain MA. A randomised controlled trial to determine the effect of intensity of therapy upon length of stay in a neurological rehabilitation setting. *J Rehabil Med 2002;34:260-6.*

Steffen TM, Hacker TA, Mollinger L. Age-and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. *Physical therapy 2002;82:128-137.*

Stevens RS, Ambler NR, Warren MD. A randomized controlled trial of a stroke rehabilitation ward. *Age Ageing 1984;13:65-75.*

Stinear C. Prediction of recovery of motor function after stroke. *Lancet Neurol 2010;9:1228-1232.*

Stinear CM, Barber PA, Smale PR, Coxon JP, Fleming MK, Byblow WD. Functional potential in chronic stroke patients depends on corticospinal tract integrity. *Brain 2007;130:170-80.*

Stineman MG, Fiedler RC, Granger CV, Maislin G. Functional task benchmarks for stroke rehabilitation. *Arch Phys Med Rehabil 1998;79:497-504.*

Stineman MG, Granger CV. Outcome, efficiency, and time-trend pattern analyses for stroke rehabilitation. *Am J Phys Med Rehabil 1998;77:193-201.*

Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev 2013;9:Cd000197.*

Sulter G, Elting JW, Langedijk M, Maurits NM, De Keyser J. Admitting acute ischemic stroke patients to a stroke care monitoring unit versus a conventional stroke unit: a randomized pilot study. *Stroke 2003;34:101-4.*

Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. *Journal of the American Geriatrics Society 1992;40:922-935.*

Trialists OS, Legg LA. Therapy-based rehabilitation services for stroke patients at home. *The Cochrane database of systematic reviews 2003;2003:*

Van Peppen RP, Kwakkel G, Wood-Dauphinee S, Hendriks HJ, Van der Wees PJ, Dekker J. The impact of physical therapy on functional outcomes after stroke: what's the evidence? *Clinical rehabilitation 2004;18:833-862.*

Van Swieten J, Koudstaal P, Visser M, Schouten H, Van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke 1988;19:604-607.*

Van Vliet P, Lincoln N, Foxall A. Comparison of Bobath based and movement science based treatment for stroke: a randomised controlled trial. *Journal of Neurology, Neurosurgery & Psychiatry 2005;76:503-508.*

Veerbeek JM, van Wegen E, van Peppen R, van der Wees PJ, Hendriks E, Rietberg M, Kwakkel G. What is the evidence for physical therapy poststroke? A systematic review and meta-analysis. *PLoS ONE [Electronic Resource] 2014;9:e87987.*

Wade D, Langton-Hewer R, Wood V, Skilbeck C, Ismail H. The hemiplegic arm after stroke: measurement and recovery. *Journal of Neurology, Neurosurgery & Psychiatry 1983;46:521-524.*

Wade D, Wood V, Heller A, Maggs J, Langton RH. Walking after stroke. Measurement and recovery over the first 3 months. *Scandinavian journal of rehabilitation medicine 1987;19:25-30.*

Wade DT, Collen FM, Robb GF, Warlow CP. Physiotherapy intervention late after stroke and mobility. *Bmj 1992;304:609-613.*

Walker MF, Gladman JR, Lincoln NB, Siemonsma P, Whiteley T. Occupational therapy for stroke patients not admitted to hospital: a randomised. *Lancet 1999;354:278-80.*

Walker MF, Hawkins K, Gladman JR, Lincoln NB. Randomised controlled trial of occupational therapy at home: results at 1 year. *J Neurol Neurosurg Psychiatry 2001;70:MID-11237160.*

Wang TC, Tsai AC, Wang JY, Lin YT, Lin KL, Chen JJ, . . . Lin TC. Caregiver-mediated intervention can improve physical functional recovery of patients with chronic stroke: A randomized controlled trial. *Neurorehabilitation and Neural Repair 2015;29:3-12.*

Weimar C, Konig I, Kraywinkel K, Ziegler A, Diener H. Age and National Institutes of Health Stroke Scale Score within 6 hours after onset are accurate predictors of outcome after cerebral ischemia: development and external validation of prognostic models. *Stroke 2004;35:158-162.*

Weinberg J, Diller L, Gordon W, Gerstman L, Lieberman A, Lakin P, . . . Ezrachi O. Visual scanning training effect on reading-related tasks in acquired right brain damage. *Archives of physical medicine and rehabilitation 1977;58:479-486.*

Weinberg J, Diller L, Gordon W, Gerstman L, Lieberman A, Lakin P, . . . Ezrachi O. Training sensory awareness and spatial organization in people with right brain damage. *Archives of Physical Medicine and Rehabilitation 1979;60:491-496.*

Welin L, Bjalkefur K, Roland I. Open, randomized pilot study after first stroke: a 3.5-year follow-up. *Stroke 2010;41:1555-7.*

Whittemore SR, Nieto-Sampedro M, Needels DL, Cotman CW. Neuronotrophic factors for mammalian brain neurons: Injury induction in neonatal, adult and aged rat brain. *Developmental Brain Research 1985;20:169-178.*

Wilson JT, Hareendran A, Grant M, Baird T, Schulz UG, Muir KW, Bone I. Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. *Stroke 2002;33:2243-6.*

Wood-Dauphinee S, Shapiro S, Bass E, Fletcher C, Georges P, Hensby V, Mendelsohn B. A randomized trial of team care following stroke. *Stroke 1984a;15:864-872.*

Wood-Dauphinee S, Shapiro S, Bass E, Fletcher C, Georges P, Hensby V, Mendelsohn B. A randomized trial of team care following stroke. *Stroke 1984b;15:864-72.*

Yagura H, Miyai I, Suzuki T, Yanagihara T. Patients with severe stroke benefit most by interdisciplinary rehabilitation team approach. *Cerebrovasc Dis 2005;20:258-63.*

Young JB, Forster A. The Bradford community stroke trial: results at six months. *Bmj 1992;304:1085-9.*