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Methodological Issues in Evaluation of Innovative Training Approaches to Stroke Rehabilitation

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Methodological Issues in Evaluation of Innovative Training Approaches to Stroke Rehabilitation

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Structured Abstract

Objectives: The assessment was undertaken to describe key methodological issues in studies designed to evaluate stroke rehabilitation therapies.

Data Sources: MEDLINE®, CINAHL®, PsycINFO®, and the Cochrane Database of Systematic Reviews (CDSR). Search scope varied, but the widest range was from January 2000 through late-January 2008.

Review Methods: Purposive sampling (PS) and a review of reviews (RR) were employed to describe study methodology. Eligibility criteria for PS were English-language, comparative studies with human subjects and a main focus on stroke (or cerebrovascular accident). Also, any type of rehabilitation therapy could be included, provided its effect was evaluated using an outcome in one of six domains of interest: ambulation, cognition, quality of life, daily activities, dysphagia and communication. We only included drug studies if the medications were used to treat cognitive impairment. Eligibility for RR was articles that were systematic reviews of the literature.

Results: For the PS, a total of 1,674 citations were retrieved in the literature search. After screening, data were abstracted for 99 studies in six domains. For the RR, the initial literature search yielded a total of 949 English-language citations. After screening, a final set of 38 systematic reviews were data abstracted.

Conclusions: In the PS, major methodological problems involved sample size and the psychometric properties of outcome measurement instruments. Sample size was sometimes too small to have adequate power to detect meaningful effects. Many authors failed to show sample size calculations or report a minimum clinically important difference (MCID). For many of the instruments used to measure outcomes, the psychometric properties were not tested in the stroke population.

Most systematic reviews were of good quality and presented the evidence for stroke rehabilitation adequately. Many of the reviews evaluated high level study designs (e.g., randomized trials). From a methods perspective, the majority of reviews evaluated randomization, blinding, and withdrawals/dropouts. Fewer reviews evaluated baseline comparability, adverse events, or co-intervention or contamination. Many reviews indicated that blinding of the patient and the provider was not possible in stroke rehabilitation and as such did not evaluate eligible studies for this criterion. These findings concur with those of the purposive sampling.

Regarding outcome measures, the PR and RR found that no single stroke-related measure captures all relevant dimensions of important attributes of interest to patients and clinicians. This implies that multiple measures may need to be included in future studies to capture all relevant attributes.

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Executive Summary

Introduction

The Coverage and Analysis Group at the Centers for Medicare and Medicaid Services (CMS) requested this technology assessment on the methodology of studies in stroke rehabilitation therapy from The Technology Assessment Program (TAP) at the Agency for Healthcare Research and Quality (AHRQ). AHRQ assigned this report to the following Evidence-based Practice Center: McMaster University (MU-EPC) (Contract Number: HHSA 290-2007-10060-I). The assessment served as background information for a CMS Evidence Forum and the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting held on May 21, 2008. The primary goal of the assessment was to describe key methodological issues in studies designed to assess rehabilitation therapies administered to patients with stroke. Researchers in stroke rehabilitation may wish to use this assessment as a guide to help avoid pitfalls in the design and conduct of future studies.

Key Question

The overarching, key research question for this technology assessment was: "What are the key methodological issues (internal validity) in comparative studies designed to assess rehabilitation therapies administered to stroke patients?" A secondary purpose of the assessment was to critically appraise the adequacy of measures used to assess outcomes in six domains of interest: ambulation, quality of life (QoL) (including caregiver burden), activities of daily living (ADLs), cognition, speech and communication, and swallowing and dysphagia. Of special importance was the need to evaluate the psychometric properties of these measures when used in comparative studies. The consultation process with AHRQ and CMS also identified 10 key attributes of studies that would be evaluated to address the overarching research question. These attributes included:

1. Study design (e.g., randomized controlled trial, observational study, etc.);
2. Randomization and blinding;
3. Patient selection criteria and characteristics;
4. Characteristics of personnel performing the intervention (including training needed);
5. Timing of the intervention relative to the stroke;
6. Frequency and duration of the intervention;
7. Length of followup in the trial and durability of benefit;
8. Prior and concurrent treatments in relation to the studied intervention;
9. Comparator used and relationship of the comparator to current best practices in stroke rehabilitation; and
10. Outcome measures used;
    a. Relation to ICF domains;
    b. Reliability, validity, and reproducibility; and
    c. MCID.

Methods

Literature Search Strategy

We adopted two strategies. In the first strategy (purposive sampling) the literature search was designed to identify articles that evaluated therapies in the six domains mentioned above. The objective was to identify a maximum of 20 articles per domain. In cases where fewer than 20 articles were selected into a particular domain, the time scope of the search was not broadened because few comparative studies were likely to exist in that domain. MEDLINE® and CINAHL® were the primary databases used in the purposive sampling strategy, with supplementation by PsycINFO® in the case of the three domains with clear psychological components (i.e., cognition, communication, dysphagia). In the second strategy, a search was undertaken to identify systematic reviews on the general topic of stroke rehabilitation. MEDLINE®, CINAHL®, and the Cochrane Database of Systematic Reviews (CDSR) were the databases searched as part of the second strategy. Search scope varied, but the widest range was from January 2000 through late-January 2008.

Inclusion/exclusion criteria. For purposive sampling, included articles had to be published in English and involve human subjects. The main focus had to be stroke (or cerebrovascular accident). The study design had to contain a distinct comparison group. Included studies had to involve any type of rehabilitation therapy whose effect was evaluated using any type of outcome measure in at least one of the six domains of interest. In the case of drugs used as rehabilitation therapies, included studies had to contain a drug that was employed to treat cognitive impairment. Other types of rehabilitation drug studies were excluded.

These criteria were applied to the review of reviews, although eligible articles had to be systematic reviews of the literature. Also, reviews involving drug treatments had to evaluate medications that were used for rehabilitation, not for prevention or the treatment of post-stroke depression or emotionalism.

Data Screening and Abstraction

Two independent reviewers applied the inclusion and exclusion criteria to the titles and abstracts of all articles retrieved in the literature search. Within each outcome domain, the first 20 matching articles from both reviewers' lists, in order of publication date (most to least recent), advanced to data abstraction. The reviewers entered abstracted data into evidence tables. Disagreements between reviewers were resolved by consensus. Studies or reviews could be excluded at the abstraction stage if they failed to meet the inclusion/exclusion criteria.

Quality assessment. For the primary studies, we evaluated methodological characteristics and summarized them in tabular form. We also summarized two studies per outcome domain in the text: one study that exemplified good methodological quality and one study that exemplified less than high methodological quality. For the review of reviews, we developed a standardized checklist for quality focusing on four main aspects of internal validity, namely randomization allocation concealment, blinding, withdrawals, and control of baseline confounders (for cohort studies).

Results

Purposive Sampling

A total of 1,674 citations were retrieved in the literature search. After screening, the reviewers included and abstracted data for 99 studies. A brief summary of the key characteristics of these 99 studies follows.

Study design. The vast majority of abstracted studies (>88 percent) were Randomized Controlled Trials (RCTs). The highest percentage of RCTs was in the activities of daily living (ADL) (100 percent); the lowest percentage was in the dysphagia group (67 percent). From the viewpoint of evidence-based practice (EBP), good quality RCTs form the highest possible level of evidence for or against a therapeutic intervention.

Patient selection. All except two abstracted studies reported inclusion and exclusion criteria and at least rudimentary sample characteristics such as age and sex.

Randomization and blinding. The authors of virtually all of the abstracted RCTs reported that their subjects were randomized to treatment. Similarly, a majority of authors in all except the cognition domain reported that some type of blinding was pursued in their studies (e.g., blinding of outcome assessors).

Providers. In the abstracted studies, the majority of authors mentioned the type of health professional that was required to administer a therapy. Studies that omitted specific mention of professional status generally reported that rehabilitation interventions were delivered by a rehabilitation team, medical doctor, or one of the study researchers.

Timing of post-stroke initiation of intervention. In the abstracted studies, all of the authors in the ambulation domain reported the timing of initiation. In the other five domains, 65 percent of the authors reported the timing.

Frequency and duration of intervention. In all except the dysphagia domain, most of the studies contained reports of both the frequency and duration of the interventions. In the dysphagia studies, only half contained reports of both items.

Length of followup. In the abstracted studies, lengths of followup varied widely, although they typically fell within a band of 1 to 12 months. The authors of eight studies did not report length of followup.

Prior and concomitant treatments. Slightly more than half of the abstracted studies did not contain reports of prior or concomitant treatment, making this the least often reported key characteristic of the studies.

Standard treatment clearly described. Virtually every study reported details of the standard treatment. For example, they reported what was done to patients as part of standard rehabilitation therapy.

Outcome measurement instruments. At least 20 different outcome measurement instruments were used in each domain. Some of these instruments were well-established scales such as the Barthel Index[1] and others were vaguely described tools such as a "swallowing questionnaire".[2] In the ambulation, quality of life (QoL), ADL, and cognition domains, the most frequently used instruments were reliable and valid in stroke patients. Some of these instruments were also responsive to change in stroke patients. There was very little information on the minimum clinically important difference (MCID) for any of the instruments. In the communication and dysphagia domains, there was no information on any psychometric properties for any of the instruments. It should be noted that our assessment of each instrument's

psychometric properties in stroke was based on whether the authors who used the instrument actually discussed psychometric properties in the methods sections of their study reports. Additional information on the presence or absence of psychometric properties in stroke was gleaned from information presented in the systematic review articles[3-6] and two reviews of outcome measures.[7,8]

With respect to the above summaries, there are several important methodological points to consider when evaluating studies in stroke rehabilitation. The important methodological points are:

1. RCTs or high-quality observational studies (e.g., cohort, case control studies) are the ideal type of study design;
2. The sample characteristics of subjects should be presented in a table (stratified by treatment group);
3. Inclusion and exclusion criteria should be clearly listed in the study methods;
4. Details of randomization and blinding should be reported in the studies;
5. Authors should describe the type of professional needed to provide the therapy;
6. Authors should report the timing, frequency, and duration of the interventions in their study;
7. Authors should report the length of followup;
8. Authors should report any prior or concomitant treatments received by study subjects;
9. The comparator treatment should be clearly described; and
10. Outcome measurement instruments should only be selected if they have strong psychometric properties in stroke patients (reliability, validity, responsiveness to change).

Review of Reviews

The initial literature search yielded a total of 949 English-language citations. After screening, a final set of 38 systematic reviews were eligible for full data extraction. We further categorized these reviews into those published within the Cochrane Database of Systematic Reviews (n = 18) and those that were not (n = 20). Those within the Cochrane systematic reviews were grouped separately, as these reflected a more standardized methodology, and internal peer review process.

Methodologic quality of the systematic reviews. The majority of systematic reviews were well conducted, with only 22 percent (n = 8) of the reviews scoring below 14 out of 18 on the Oxman and Guyatt quality assessment scale[9,10] with adapted scoring.[11]

Methodological quality of studies within the systematic reviews. There were some methodological quality domains that were not sufficiently evaluated or reported in the studies. In particular, the potential for contamination or cointervention was not reported well in all but four Cochrane reviews[12-15] and one non-Cochrane review,[16] indicating poor evaluation of this criterion across all reviews. Similarly, comparing baseline characteristics of the treatment and comparator groups was not evaluated in 10 Cochrane and 11 non-Cochrane reviews, reflecting little differences between the two groups of reviews.

There were some differences between the Cochrane and non-Cochrane reviews. None of the Cochrane reviews failed to report randomization or allocation concealment. Six Cochrane reviews (35 percent) did not evaluate the potential for adverse events compared to 13 (58 percent) of the non-Cochrane reviews. With regards to blinding, many trials evaluated within the systematic reviews indicated that it was impossible to blind the therapist or patient to the

treatment and therefore did not evaluate patient or provider blinding. Both Cochrane and non-Cochrane reviews did not test for the status of the data collector. However, they did assess the blinding status of the outcomes assessor (albeit the non-Cochrane reviews evaluated this less frequently).

Summary of findings. With respect to the review of reviews, there were several trends and methodological points to consider:

1. Most systematic reviews restricted studies to the intervention of interest, and by the type of stroke acuity. Few reviews restricted eligible studies to specific outcomes or to a specific provider of treatment.
2. The Cochrane reviews evaluated predominately randomized trials and the non-Cochrane reviews included all types of designs.
3. Most of the systematic reviews scored relatively high on quality criteria; those that had lower quality scores were non-Cochrane reviews and included multiple design types.
4. Most systematic reviews evaluated methodological aspects of the eligible studies with standardized checklist or criteria. The majority of reviews evaluated randomization, blinding, and withdrawals/dropouts. Fewer reviews evaluated baseline comparability, evaluation of adverse events, and co-intervention or contamination.
5. Many reviews indicated that blinding of the patient and the provider was not possible with the stroke rehabilitation intervention and as such the reviews did not evaluate eligible studies for this criterion.

Systematic Reviews of Outcomes in Stroke Patients

Characteristics of the reviews. Three systematic reviews[3,4,6] evaluating outcomes within stroke populations were identified through the literature search. Two additional systematic reviews[5,17] were identified from searching the reference lists of these reviews. One of these reviews,[5] published in 1998, was added because of its historical value and because this review had a broader scope in the studies it reviewed relative to the other more recent systematic reviews.

Findings. All review authors recommend the selection of outcome measures that have established psychometric properties (reliable, valid, and responsive). In addition, floor and ceiling effects (where scores are extremely high or very low making it difficult to detect changes over time), as well as practical administration issues, should be considered when selecting outcomes.[4] In general, the reviews appear to suggest that no measure is able to capture the breadth of the domains that they are attempting to capture and as such the recommendation is to include other measures that capture other domains (e.g., activity level and not just impairment).[5] Similarly, there is the recommendation to use more than one outcome measure in order to capture all attributes within the domain of interest (for example walking ability); however, there was some acknowledgement that consensus has not yet been achieved to define the concepts that should be captured to most accurately reflect the range of some aspects of function (such as walking).[6]

Only one review[3] evaluated the time-points selected for evaluating final outcomes in stroke patients (e.g., 3 or 6 months post-treatment). In this review, based on 51 studies evaluating the use of drugs in acute stroke, the majority of citations evaluated patients at 3 months and none exceeded 1 year. Two reviews[3,5] described the statistical methods used to evaluate rehabilitation effects; the findings of both reviews would suggest that there is a need to establish the degree of

change that is considered to be clinically significant and that appropriate statistical analyses be undertaken within future studies.

Summary of findings. The systematic reviews of the outcome measures used in studies with stroke patients would indicate the following:

1. A variety of outcomes have been used to measure the same attributes of interest within studies of rehabilitation interventions in persons with stroke.
2. Currently, no single outcome measure captures all relevant dimensions of important attributes of interest to stroke patients and clinicians. This implies that measures that capture these multiple domains be included. Whether a single measure captures more than a one dimension (e.g., body function and activity and participation) or whether several measures are used to capture the dimension is less critical than ensuring that all domains are captured.
3. All dimensions of an outcome of interest should be evaluated. For example, if walking ability is of interest, then walking in all life conditions (including walking within the home, outside the home in uneven ground, and in changing weather conditions) should be evaluated.
4. Future studies evaluating rehabilitation therapies in stroke patients should select outcome measures that have established psychometric properties in stroke (reliable, valid, and responsive).
5. Consideration for selection of measures should also be given to the potential for floor and ceiling effects and practical administration issues.
6. The timing of outcome measurement should be justified, with some consideration of the natural history of stroke recovery.

Discussion

Methodological Issues From the Purposive Sampling

Several consistent themes emerged from the purposive sampling exercise and suggested potential areas of improvement for future studies in stroke rehabilitation. A few RCTs enrolled and randomized less than 10 subjects in total. The ability to draw any meaningful efficacy conclusions from such small studies is severely compromised by the obvious lack of power to detect effects and the high possibility of random sample error. Authors should enrol large enough samples to detect clinically significant effects, not just statistically significant effects. Authors should also be explicit in the methods with respect to their sample size calculations. Specifically, they should provide the MCID and justify their selection of such a difference. Few of the authors of the abstracted studies provided or justified a particular MCID.

Descriptions of blinded assessors and the randomization process suggest that some authors made attempts to minimize bias and confounding. However, many authors reported only rudimentary patient data, which were often limited to a few variables such as age, sex, and education. Comorbidity and concomitant treatments were often not reported. In an RCT with proper randomization, this is less of a concern because the randomization should create comparable treatment groups, thus cancelling the effect of any confounding due to comorbidity and concomitant treatment. In observational studies, though, confounding could occur if the treatment groups differ on these (or other) characteristics. Therefore, it is especially important

for the authors of observational studies to present the details of all possible confounders when they report sample characteristics.

Study authors should provide a complete description of the study sample. This lends itself to establishing generalizability. Strict inclusion and exclusion criteria in many RCTs exclude persons with common comorbidities and concomitant treatments. Full disclosure of sample characteristics is required so that readers of trial reports can assess whether the subjects in an RCT are representative of a particular group of patients. If they are not representative, then the findings of the RCT may not be applicable to that particular group.

Length of followup also requires careful consideration in future studies of stroke rehabilitation therapies. Improvements to cognition and communication may take months, even years, so studies should be long enough to assess these outcomes. For ambulation, short followups are generally adequate due to the relatively rapid recovery periods for motor function and gait. Followups for QoL are less amenable to precise time specification because QoL itself involves a subjective component that may be independent of improvement in any one domain. Ideally, QoL should be measured at the same time points as the primary outcome. ADLs, like cognition, can improve over time. This would suggest medium- to long-term followup. The dysphagia studies tended to focus on interventions that would allow patients to begin adapting to swallowing problems, rather than on interventions that would correct the problems. Therefore, the dysphagia studies typically lasted for periods of weeks, which was long enough to assess whether the interventions would help patients adapt.

The authors of many studies examined a variety of different outcomes. In some studies, one outcome was specified as the primary outcome, while in others there was no named primary outcome. The use of many outcomes reflects the multifaceted nature of both the sequelae of stroke and the impact of the interventions. However, rehabilitation programs and devices are usually designed to make an impact on a narrow band of outcomes, with additional effects on other outcome areas being a 'spin-off' of the main impacts. Consequently, one outcome should be designated as the primary outcome. Sample size calculations should be based on the primary outcome to ensure that important inter-group differences can be detected in the study.[18,19]

Many of the outcome measurement instruments used in the abstracted studies were not assessed for reliability and validity in persons undergoing stroke rehabilitation. Similarly, there were few assessments for responsiveness to change and MCID in stroke. Researchers should make every attempt to employ outcome measurement instruments that have been validated in stroke patients. It is not sufficient to rely on the most popular instrument without consideration of psychometric properties because an often used, invalid instrument will produce invalid results.

Methodological Issues From the Review of Reviews

The individual trials in stroke rehabilitation, regardless of therapy, for the most part did not have blinded patients or healthcare providers, but did have blinded outcome assessors. Adequate randomization and allocation as well as adequate accounting for all subjects continued to be a problem in many trials. Few of the systematic reviews evaluated the comparability of groups at baseline, the potential for adverse events, or problems with contamination and cointervention. In this regard, it is difficult to generalize regarding methodological problems within any of the trials being evaluated in a review. These three factors do affect internal validity and would be important to evaluate in future trials within systematic reviews.

When considering the population characteristics being evaluated in the trials, the variation in the study populations evaluated may reflect that some therapies are logically restricted to specific phases of stroke rehabilitation; however there were a fair number of interventions that were directed to all phases of the recovery continuum and the rationale for this was not always adequately presented. When considering the sample sizes within these trials, there was great variation, but in general they were not large relative to drug trials. As noted previously in the purposive sampling, adequate sample size is related to power and the ability to detect differences amongst groups; this is particularly relevant for studies selecting multiple outcome measures.

The systematic reviews evaluating the use and classification of outcomes used in the treatment of stroke patients were consistent in their recommendations. Although, the evaluation of these outcomes was not restricted to "rehabilitation" studies per se, the conclusions were applicable to this phase of intervention. Most of the reviews on outcomes used in stroke patients, noted that some outcomes frequently used in the studies had not had psychometric properties established for stroke patients. In general, there was some concern with potential difficulties with instruments that are self or interviewer administered questionnaires being applied to stroke patients (due to deficits in cognition and communication). Additionally, at least one review pointed to the timing of outcome assessment; suggesting that the rationale for the interval to measure outcomes during the recovery process was in need of greater refinement (particularly in light of the natural history of stroke recovery).

All the systematic reviews on outcome measures in stroke rehabilitation would support the use of overlap across types of measures (generic versus disease specific) and domains covered within the outcomes selected. In the former case, it was clear that no single measure would capture all the important attributes (considering the ICF framework) to evaluate within stroke patients; as such the recommendation was to include multiple outcomes to cover the breadth of functions or alternatively to develop new and more comprehensive measures. The core set of ICF functions proposed[20] would be an initial, universal frame of reference to assist in selecting a minimum set of functions to be considered when selecting outcome measures for evaluating the efficacy of studies.

Conclusion

The methodological quality of studies in stroke rehabilitation was reviewed in accordance with the components of the key question. Researchers in the field recognize the benefits of investigating interventions using the RCT design, but the reporting of randomization methods and comparability between groups was lacking in some instances. Blinding is difficult to conduct in stroke rehabilitation studies because the nature of the interventions is obvious to patients and healthcare providers alike. Many researchers in stroke recognize these limitations and try to balance the rigor of adequate blinding and the feasibility of applying the interventions.

Major methodological problems involved sample size and the psychometric properties of outcome measurement instruments. Sample size was sometimes too small to have adequate power to detect meaningful effects. Many authors failed to show sample size calculations or report an MCID. For many of the instruments used to measure outcomes, the psychometric properties in the stroke population were not tested. The road forward looks positive regarding the methodological quality of studies in stroke rehabilitation. However, despite some high quality research that conforms to the principles of EBP, there is still room for improvement, especially in the areas outlined above.

The review of reviews showed that most systematic reviews were undertaken with adequate rigour and presented the evidence for stroke rehabilitation adequately. Many of the reviews evaluated high level study designs (e.g., randomized trials); however, not all of these trials were conducted in a sufficiently rigorous manner. Most systematic reviews evaluated methodological aspects of the eligible studies with standardized checklist or criteria. The majority of reviews evaluated randomization, blinding, and withdrawals/dropouts. Fewer reviews evaluated baseline comparability, evaluation of adverse events, and cointervention or contamination. Many reviews indicated that blinding of the patient and the provider was not possible in stroke rehabilitation and as such did not evaluate eligible studies for this criterion. These findings concur with those of the purposive sampling.

Our review of reviews on outcome measures in stroke showed that a variety of outcomes have been used to measure the same attributes of interest within studies of rehabilitation interventions in persons with stroke. Currently, no single outcome measure captures all relevant dimensions of important attributes of interest to patients and clinicians. This implies that multiple measures may need to be included to capture all these important domains. Moreover, there is a need to determine the degree of comprehensiveness required when evaluating some of these outcomes of interest.

All reviews on outcome measures in stroke recommended that future studies evaluating rehabilitation therapies in stroke patients should select outcome measures that have established psychometric properties (reliable, valid, and responsive). Additional consideration should also be given to the potential for floor and ceiling effects and practical administration issues. Moreover, the timing of outcome measurement should be justified, with some consideration of the natural history of stroke recovery. These findings also concur with those of the purposive sampling.

Technical Assessment

Chapter 1. Introduction

The Coverage and Analysis Group at the Centers for Medicare and Medicaid Services (CMS) requested this report from The Technology Assessment Program (TAP) at the Agency for Healthcare Research and Quality (AHRQ). AHRQ assigned this report to the following Evidence-based Practice Center: McMaster University (MU-EPC) (Contract Number: HHSA 290-2007-10060-I). The assessment served as background information for a CMS Evidence Forum and the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting held on May 21, 2008. The primary goal of the assessment was to describe key methodological issues in studies designed to assess rehabilitation therapies administered to patients with stroke. Researchers in stroke rehabilitation may wish to use this assessment as a guide to help avoid pitfalls in the design and conduct of future studies in this area.

Definition and Epidemiology of Stroke

According to the World Health Organization, a stroke or cerebral vascular accident (CVA) is an acute onset of neurological dysfunction due to an abnormality in cerebral circulation. The resultant signs and symptoms of the abnormality must last for more than 24 hours and there must be corresponding involvement in focal areas of the brain.[21] Of all strokes, 87 percent are ischemic, 10 percent are intracerebral hemorrhage, and 3 percent are subarachnoid hemorrhage.[22]

Strokes are the third leading cause of death in the United States, behind heart disease and cancer. Moreover, strokes are the second most common cause of disability.[23] In 2004, 150,074 people died from stroke related problems and stroke accounted for 1 out of every 16 deaths in the United States.[23] Each year, 780,000 people experience a new or recurrent stroke[23] and approximately 600,000 of these are incident cases. Of the people who have had a stroke, two-thirds will survive, but half will be left with permanent disabilities.[24] In 2005, 5.8 million American adults were living with the sequela from stroke.[23]

In the United States, the estimated cost of stroke-related morbidity for 2008 is $65.5 billion.[23] In 2003, $3.7 billion was paid to the facilities and providers of care for Medicare recipients who were discharged from short-stay hospitals with a diagnosis of stroke.[25] The mean lifetime cost of ischemic stroke in the United States is estimated at $140,048 per person (based on estimates in 1999). This number includes the cost of inpatient care, rehabilitation, and followup management.[26]

Risk factors for stroke. There are numerous modifiable and non-modifiable risk factors for strokes. Of these, the single greatest modifiable risk factor is hypertension, which at age 50 results in a 4-fold increase in risk of stroke.[23,27] The presence of atrial fibrillation also increases the risk of stroke by a factor of four. Physical inactivity, cigarette smoking, and obesity are also significant modifiable risk factors for stroke.[27] Non-modifiable risk factors for stroke include a prior stroke, increasing age, race, gender, and family medical history.[23,27]

Clinical Consequences of Stroke

The clinical consequences of stroke are variable and influenced by the location of the stroke in the brain and the extent of cell damage. Following a stroke, patients may have complications that span a wide range of body functions. These can include difficulties related to sensory and

motor control, vision, cognition (perception [i.e., hemispheric neglect] and spatial orientation), balance (i.e., ambulation), basic life function (i.e., respiration), communication (i.e., speech and aphasia), and behavior (i.e., timid behavior and impulsivity).[28] There may also be varying degrees of difficulty with activities of daily living such as bathing, toileting, self care, and cooking. Persons recovering from stroke may also be unable to drive or work.[28] All of these complications can adversely affect a patient's quality of life (QoL). The aim of stroke rehabilitation is to counteract limitations in all areas of patient function, maximize patient ability to be independent and productive, and improve QoL.

The natural history of stroke suggests that functional changes will vary over months and even years, despite the fact that the greatest changes occur within the first 30 days post-stroke.[8] The rate of functional change may be influenced by the initial severity of the stroke and potentially by the timing and intensity of rehabilitation.[14] Additionally, the recovery and selection of treatments will be influenced by the type of stroke, with ischemic requiring subsequent use of blood anti-coagulants such as low molecular weight heparin. There is no consensus as to how to classify the intervals of recovery following stroke. The definitions of acute, subacute, and chronic stroke are arbitrary and variable. The confusion is furthered by assuming that the location of the rehabilitation (e.g., an acute care or inpatient hospital) is synonymous with the acuity or timepoint relative to the initial stroke trauma. For the purposes of this review, we have defined acute stroke as 1 to 90 days, subacute as 91 to 180 days, and chronic stroke as greater than 180 days.

Classifying Functional Changes in Patients Undergoing Rehabilitation

At its best, rehabilitation therapy is an enabling process through which physical, sensory, or mental capacities are restored or enabled.[29] The International Classification of Functioning, Disability, and Health (ICF)[30] is the current framework developed through the World Health Organization to present a consistent terminology for classifying health and health states. It permits comparison of data across countries, health systems, health care disciplines, health services, and time. More importantly, it also provides a common terminology between health professionals, policy makers, and the public (particularly those with disabilities).

The ICF is composed of two main parts: Part 1 describes functioning and disability and Part 2 describes contextual factors (Figure 1). Part 1 is further characterized by two main components, namely physiological functions of the body systems (including psychological) and the anatomical parts of the body (e.g., the limbs, the organs, etc.,). Part 1 also includes activities (the execution of a task or action by an individual) and participation (e.g., involvement in life situations). Part 2 is characterized by two main components that describe external environmental factors (the physical, social, and attitudinal environment in which people are living) and intrinsic personal factors (e.g., genetics or age).

Parts 1 and 2 include positive aspects that describe the health or health related state of an individual. For example, in Part 1 (body functioning and structures), a positive health state is reflected in functional and structural integration, which is classified as functioning. In contrast, a negative aspect reflects impairment (a significant loss or deviation in body function or structure) and a resulting limitation in activity (difficulties in executing a task) or restriction in participation (problems in engaging in life situations). Similarly, for Part 2 (contextual factors), positive environmental factors are classified as facilitators and the corollary are barriers or hindrances;

however, it should be noted that positive or negative aspects cannot be ascribed to the personal factors, which is the second component of Part 2 (Figure 1).

The ICF framework provides a common language to characterize the health of a particular group of patients. As such, it defines the specific body structures and functions that result in impairment, activity limitation, and participation restriction. Once a health state is classified, the ICF constructs can be used to identify the areas that certain therapies, intervention categories, or therapists may address.[31] These constructs may also be used to identify areas that will not be modifiable in the context of care.[32] Similarly, the ICF classification has been used to decompose attributes of outcome measures used to evaluate rehabilitation therapies; as such, the content of these outcomes can be evaluated for deficits or strengths in capturing all aspects of the health state for particular conditions such as stroke.[6,33] Decomposition of the most frequently used outcome measures within stroke rehabilitation studies has been used as a basis for consensus on an important core set of functions affected by stroke.[20]

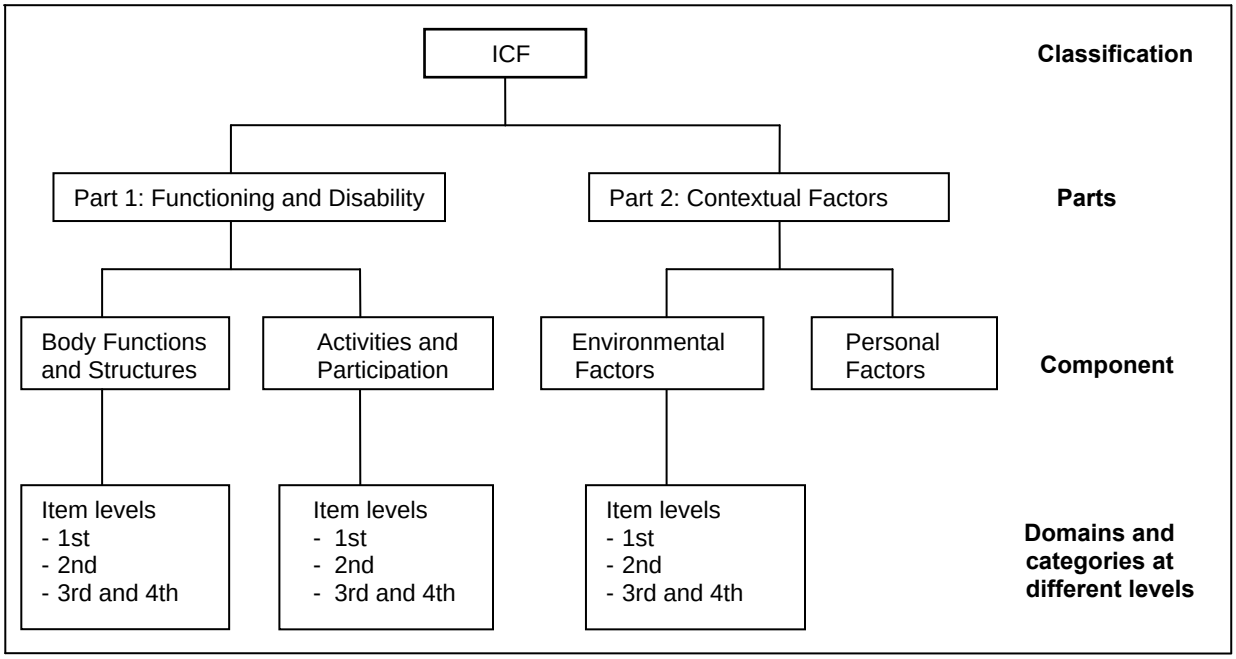

Figure 1. ICF classification[30] (Permission to reprint granted by World Health Organization (WHO))

Modelling the Process of Functioning and Disability

When characterizing a person's health state, there is a relationship between Part 1 and Part 2 components. As a classification system, the ICF (Figure 1) does not necessarily model the process of disablement or functioning because this may vary with the health condition. However, the interrelationship between the ICF components can be used to describe the process of disablement or functioning. For example, Figure 2 shows the relationship between Activities and Body Functions and Structures; in addition it suggests that the environmental factors influence Body Functions and Structures via Activities. Using stroke as a health state, we can hypothesize that the lack of adequate mobility technology (such as wheelchairs) will impact a stroke client's ability to undertake activities, which in turn may affect the Body Function and

Structure of leg strength. Although, a core set of functions within the four domains of the ICF framework have been identified and described for stroke clients,[20] there is a need to model how these components and domains inter-relate to bring about function or disability. Note that there are a number of models within rehabilitation that attempt to provide theoretical explanations for the disablement process (that is for the pathways and directions that lead to disability or restoration of abilities). The scope of this review does not permit detailing these different models. However, the use of the ICF taxonomy is critical for a common understanding of the components within these disability models.

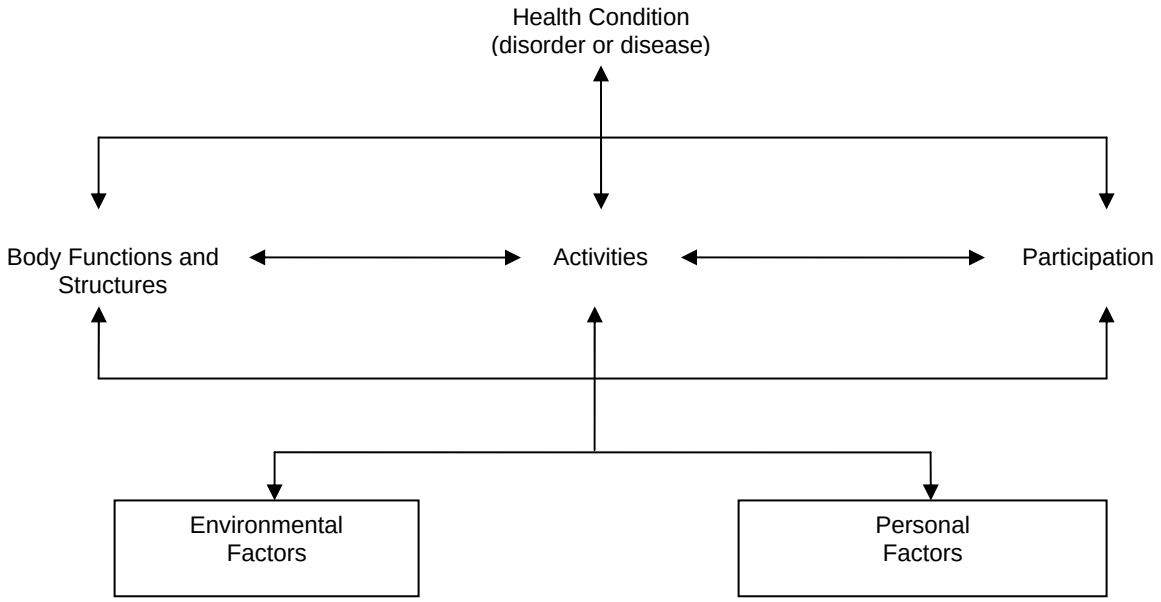

Figure 2. ICF and process of disablement and function[30] (Permission to reprint granted by WHO)

Methodology of Studies of Stroke Rehabilitation Therapies

The evaluation of the methodology of studies in rehabilitation therapies applied to stroke patients should follow the basic tenets of evidence-based practice (EBP). In short, EBP is the use of the best available evidence in healthcare research to make decisions about patient care.[34] The implementation of EBP requires a recognition of the need for evidence, the development of focused and answerable questions about clinical dilemmas, the search for appropriate publications in the medical literature, and the critical appraisal of these publications.[35]

Methodological evaluation falls under the 'critical appraisal' aspect of EBP. The intent is to assess whether studies are designed and executed properly. Poorly designed or executed studies are more likely to produce biased and invalid results. Study design concerns the type of study itself (e.g., randomized controlled trial [RCT], observational study), length of followup (long enough to detect important outcomes), and type of analysis. This forms a portion of what is commonly termed PICOT (Population, Intervention, Comparison, Outcome, Time). PICOT is used to guide the formulation of research questions in EBP. However, all of its components are relevant to study design. The study must include persons sampled from the population in which the therapy will be used. The therapy (intervention) must be clearly described and evaluated in

conjunction with a comparison therapy that is an existing alternative treatment for stroke rehabilitation. Study outcomes must also be clearly defined and linked to the objective of the rehabilitation therapy under consideration. For example, the efficacy of a therapy aimed at improving post-stroke cognition should be evaluated using a valid and reliable measure of cognition in stroke patients. Furthermore, the length of followup should be long enough to show improvement in the outcome domain of interest.

The execution of a study is also important. The people who participate in a study should be representative of the population of interest. This involves taking active efforts during the course of the study to minimize dropout and losses to followup. Prior and concurrent treatments should be described to assess whether study participants received or are receiving atypical treatments that could affect their response to rehabilitation therapy. If study participants do not resemble the population of interest, then selection bias may be introduced into the study. This bias leads to over or underestimates of the true association between a set of therapies and the outcome(s) of interest. Once in the study, participants must be evaluated in an objective and identical manner regardless of the intervention received. Participants must also be correctly categorized on outcome, for example stroke patients who recover half of their pre-stroke mobility should be properly categorized as such. Failure in any of the areas pertaining to patients who are already in the study could result in the introduction of information bias, which like selection bias can lead to an over or underestimate of a true effect size.

In practice, it is difficult to distinguish between design and execution issues in the consideration of bias. Biases may arise at any point in the life of a study. A properly executed study is predicated on good design to minimize bias. However, a well-designed study can still produce biased results such as when an unexpectedly large number of participants dropout after receiving one of the therapies under investigation. Another potential example would occur when it is impossible to blind participants and outcome assessors due to visible differences between therapies. These 'visible differences' may be prevalent in stroke rehabilitation due to different types or appearances of equipment, as well as to multifactorial treatment regimens that may involve several interventions, multiple therapists, and tailoring to meet individual patient needs. There are also some biases and errors that are context specific to the types of interventions employed or to the equipment used to capture data. For example, studies that use force plates to capture ground reaction forces (to assess changes in ambulation and balance) have particular problems with drift (if they get overheated) and they may also constrain the manner in which a person would normally walk or stand.

Bias is not easily quantifiable. There are few statistical tests to examine whether observed results have occurred due to bias. Nor are there effective means to establish the direction and magnitude of any bias that may be present. Persons who use EBP to assess therapies should examine the methodological strength of the pool of studies under consideration and make a judgment as to the presence and magnitude of any bias. Studies thought to contain a great deal of bias may be given little or no weight in subsequent decisions. Please refer to Rothman and Greenland[36] or Silman and Macfarlane[37] for a more complete discussion of general biases in clinical studies.

Types of comparison studies. The most useful evidence for or against a new therapy would come from studies that have a comparison group. Such a group would act as a referent and allow decision makers to evaluate the new therapy against an existing yardstick. This contextualizes the efficacy of a new therapy. For example, the new therapy might improve cognition by 50

percent in stroke patients after six months, but is 50 percent a good figure? If improvement is 70 percent for the comparator therapy, then 50 percent may not be an adequate level of efficacy.

Of course, the validity of the comparison depends on the comparator therapy. The comparator should be clinically relevant and clinically routine. That is, the comparator should be an existing, approved therapy in the same class as the new therapy. The comparator should also be utilized according to standard practice norms. For example, if persons with stroke typically have three treatment sessions per week with the comparison therapy, then this same protocol should be followed in the study. The purpose of having a clinically relevant and routine comparator is to prevent situations where the new therapy might look better because the comparator is being implemented incorrectly. The need to have a comparison group rules out the use of case reports or case series to assess medical evidence.

Figure 3 shows a schematic representation of study designs and their potential for bias. The pyramid suggests that higher-level studies are less prone to bias and reflect stronger evidence for the therapies being evaluated. Studies without comparison groups in general are more prone to biases and as such would indicate lower levels of clinical evidence. Each design type, as noted previously has strengths and limitations and their relative merits are considered in the context of the research purposes that are to be addressed.

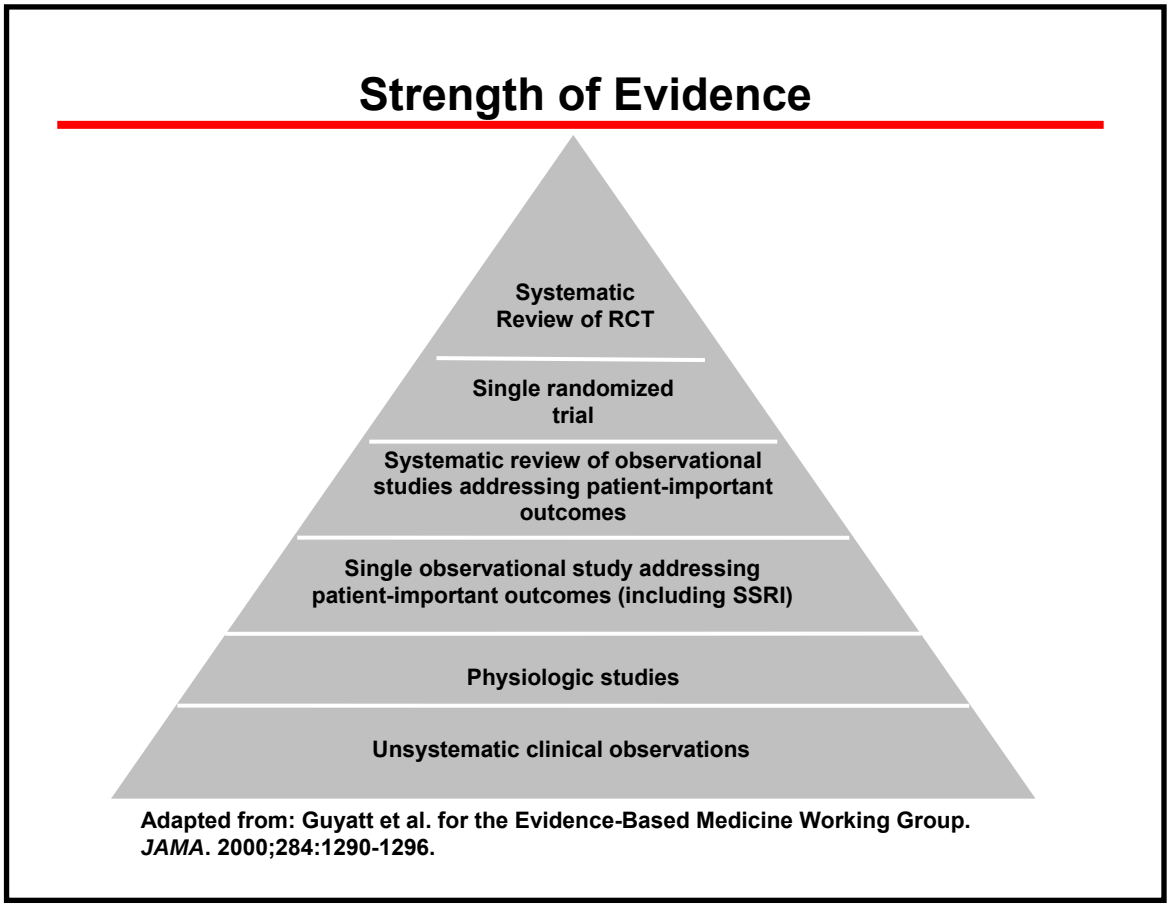

Figure 3. Schematic showing the strength of evidence and the influence of study design

Studies with comparison groups fall into two general categories: intervention or observational studies.[36] An intervention study is one where the investigator controls the exposure (e.g., treatment or risk factor). In healthcare research, intervention studies take the form of RCTs, where participants are randomly allocated to one of two or more treatments. RCTs are considered the gold standard in medical research and EBP because the randomization process (if done properly) will usually ensure that the study subjects assigned to the various treatment groups are similar to one another on all characteristics except the therapy in question.[38] This negates the impact of important biases such as confounding, which occurs when one or more extraneous variables are associated with both the interventions under consideration and the outcomes of interest (provided the extraneous variable is not in the causal pathway between the interventions and outcomes). Confounding can reverse the direction of association between two variables, change the magnitude of the association, create an association where none really exists, or eliminate an association that truly exists. Data on variables that are thought to be confounders should be collected at baseline and at all followup points. Examples of potential confounders in stroke are type of cerebrovascular event, comorbid disorders, concomitant treatments, age, and sex.

In contrast to RCTs, observational studies do not involve randomization to treatment. Study subjects are still divided by intervention, but the division is not controlled by the investigator. For example, investigators may access a medicare database and group persons in the database according to the type of therapy they are shown to be receiving. The investigators do not assign the therapy, but rather accept already existing classifications of subjects. The investigators also do not control how the therapy is provided to patients. They must accept the protocols used to deliver therapy to the patients whose data are contained in the database. The two most prominent observational study designs are cohort and case control studies. In cohort studies, subjects are classified according to the intervention they receive and followed up over time, usually until they have an outcome or the study finishes. In case control studies, subjects are classified according to outcome and the investigators determine whether subjects have been 'exposed' to some agent or treatment in the past. Exposure assessment in case control studies is ascertained via subject or proxy interviews, or by examining records (e.g., databases, death certificates, hospital charts). Observational studies are ranked lower on the evidentiary scale than RCTs because the lack of randomization leads these designs to be more susceptible to confounding than RCTs. However, observational studies are a useful means of harnessing existing data to study associations before undertaking expensive RCTs.

While RCTs are the gold standard, they are subject to selection and information bias, as are observational studies. Furthermore, RCTs are often used to address questions of efficacy (can an intervention work), not effectiveness (does an intervention work in the real clinical world). Therefore, RCTs often include study subjects who are atypical of the wider population that would receive an intervention in standard medical practice situations.[39] This can limit the generalizability of an RCT's results to a very small segment of the wider population (e.g., good compliers). More information on the various types of study designs is available by consulting Silman and Macfarlane[37] or Benson and Hartz.[40]

In stroke rehabilitation, the customized, multifactorial approach to treatment often makes RCTs an impractical means of assessing a specific therapy.[41] RCTs are more suited to situations where a unimodal therapeutic regimen (e.g., one single drug or its comparator) is given to patients. Some stroke researchers have proposed a 'clinical practice improvement' (CPI) research method to overcome the problems of using RCTs to evaluate stroke rehabilitation

therapies.[41] CPI studies are essentially cohort studies designed to address practical questions related to the effectiveness of an intervention, (e.g., does the intervention work in standard clinical settings and for whom does the intervention work best?).

A study design that is sometimes seen in stroke rehabilitation is called a 'single subject research design' (SSRD).[42] SSRDs have recently been used to evaluate things such as body weight support gait training in the enhancement of post-stroke locomotor recovery.[43] In SSRDs, participants serve as their own controls through exposure to both the intervention being evaluated and the comparator. SSRDs do not necessarily involve a sample size of one person. They can include multiple subjects who act as their own controls. Studies wherein subjects are randomized to the order of treatment (intervention followed by comparator or vice versa) are known as 'crossover trials'. SSRDs in stroke typically do not involve randomization. All subjects are given the comparator treatment (often standard therapy) initially, followed by the intervention, and concluding once again with the comparator. When the comparator is standard treatment, the intervention is usually given as a supplement to the standard treatment. The problem with using such SSRDs in stroke rehabilitation is that patients may improve over time on the standard therapy, so it may be difficult to attribute some or all observed improvements during the intervention phase to the intervention itself. This is known as an ordering effect.[44]

Phase I and Phase II trials, which typically involve a single group of subjects who all receive the intervention of interest, may occasionally be used to evaluate a stroke rehabilitation therapy. Caution should be exercised in the use of these studies for evaluative purposes in stroke. Phase I studies involve healthy volunteers and are usually conducted in the realm of drug therapy to establish safety, tolerability, toxicity, and dose range. Efficacy is not the primary motivation for undertaking a Phase I study. Phase II studies, which include subjects with the medical condition of interest, may have efficacy as an outcome. However, Phase II studies still lack a comparison group, so this design cannot be used to directly compare the impact of a new intervention with the impact of an existing intervention.

In short, all aspects of the design and execution of a study are relevant to assessing a new rehabilitation therapy for stroke patients. Poorly designed or executed studies raise the specter of invalid results (e.g., biased results).

Characteristics of comparator treatments. As discussed in the section above, a valid comparator is needed in stroke rehabilitation studies. In many studies, the comparator is some kind of standard therapy that is normally given to all stroke patients. Due to the heterogeneity of case presentation in stroke, the standard therapeutic regimen will differ according to individual patients and their disabilities. Another source of difference is the particular treatment philosophy held by rehabilitation professionals. The generic term 'standard therapy' may therefore be inadequate to describe the comparator treatment in a research study. Researchers should make an effort to carefully describe what they mean by standard therapy in their studies so that the scientific community can assess the validity of the comparator.

Clinical practice guidelines[45-49] for stroke rehabilitation can provide some details of the components of a standard therapy. Authors who employ standard therapies in their research studies should consider using some of these components as descriptors of what they mean by 'standard therapy'. Of course, rehabilitation therapies are tailored to the needs of specific patients, so it is difficult to create a checklist of components that must be described in every study. At a bare minimum, the authors should report the timing, frequency, and duration of the intervention, the type of person conducting the intervention (e.g., physical therapist), and the nature of the intervention itself (e.g., describe devices used in therapy, describe exercise

programs). It would be sufficient to reference well-known, standard devices, tests, etc., without providing lengthy descriptions in the text of a journal article. However, little-known devices or tests (if used as standard treatment) should be explained and referenced. Generic names (e.g., 'gait test') should be avoided unless there is no proper name for the device or test.

The guidelines[45-49] for stroke rehabilitation focus on the general principles of providing standard therapy, rather than on listing specific treatment approaches to particular problems. This reflects the heterogeneity inherent in current stroke rehabilitation approaches. In general, some guidelines recommend that a rehabilitation assessment should take place within 24 to 48 hours post-stroke. These assessments should be made by patients, patients' families, and multidisciplinary care teams consisting of physicians, skilled rehabilitation nurses, physical therapists, occupational therapists, kinesiotherapists, speech and language pathologists, psychologists, recreational therapists, social workers, psychiatrists, and dietitians. Specific team composition would depend on the objective of therapy: speech and language pathologists would be involved in assessing and treating aphasia, dysarthria, and swallowing; a physical therapist is likely to be involved in the assessment and treatment of problems of movement and function; an occupational therapist is likely to be involved in helping to recuperate the ability to perform activities of daily living (ADLs). Assessments should be made using standardized clinical criteria.

A certain degree of caution must be used when incorporating the recommendations of guidelines. In particular, the date of the guideline is important to consider, as the evidence upon which these recommendations are based may no longer be current. Moreover, it is important to consider which subgroup of patients the guideline addresses. For example, some guidelines may focus on recommendations for persons who are older and may not take into account the issues specific to younger stroke patients, with milder manifestations of stroke symptoms and with less comorbidities.

Rehabilitation therapy should be a goal-driven process, with goals set by patients, families, and care teams. Short- and long-term goals must be tailored to specific patient needs. These goals should involve early mobilization to prevent complications from stroke. Mobilization and activity levels should increase progressively as long as medically tolerated. The aim is to engage persons with stroke in the maximum daily amount of goal-focused activity that can be tolerated in a 7-day period.

The appropriate treatment setting for rehabilitation therapy should be driven by goals and the therapeutic regimen. For example, a regimen involving the use of specialized, fixed equipment would have to take place in a rehabilitation centre, while an exercise-based regimen could be performed in a patient's home. Drug therapy may be a part of this regimen.

When considering what should be in a comparative treatment, recommendations from clinical practice guidelines may be an important source for defining a good comparator treatment (relative to a new therapy). Two sets of guidelines provide more specific recommendations for stroke rehabilitation therapy. Guidelines from the United States Department of Veterans Affairs[50] algorithmically delineate the specific steps that should be taken to assess a patient prior to the commencement of rehabilitation. The guidelines additionally list the steps to follow during in-patient or community rehabilitation. These guidelines may be considered a template for standard therapy, but they are assessment-driven in the sense that they recommend what to assess (e.g., communication, motor function), but do not indicate the specific tool, device, or procedure to use to make the assessment. They would not be informative to judge whether the precise interventions used in standard therapy in a study would be a valid comparator.

The second set of guidelines, produced by the American Heart Association, is for a rehabilitation exercise program designed to help improve functional motor performance.[51] This set of guidelines is an exception to the norm because it lays out specific modes of exercise, provides information on intensity, frequency, and duration of therapy, and lists major goals for patients. Such detailed guidelines, if they were to exist for other areas in the realm of stroke rehabilitation, would serve to define valid comparator treatments.

Another group of guidelines in stroke rehabilitation, published by the National Guideline Clearinghouse (http://www.guideline.gov), summarizes the level of evidence for specific treatment approaches. For example, a set of clinical practice guidelines for balance training[52] reports Grade A evidence for a combination therapy of balance training and visual feedback, versus task-specific training, to improve standing balance over a 2 week followup period. The utility of guidelines such as these is that researchers can assess the level of evidence for certain treatments (e.g., Grade A evidence as defined in these guidelines means that minimum clinically important differences of greater than 15 percent have been observed in at least one RCT). However, there is no prescriptive direction in these guidelines to detail the most appropriate circumstances for using any given treatment.

Clinical practice guidelines in stroke rehabilitation may not, to date, be a comprehensive source for assessing the appropriateness of comparator therapies. Researchers in the field of stroke rehabilitation must establish the adequacy of a comparator on a study by study basis, preferably through the help of an expert such as a trained professional with practical experience who works in rehabilitation, (e.g., a therapist who treats patients in the domain of interest). For researchers who review the literature, it is highly recommended that they include such persons on the research team.

Evaluating Outcome Measures in Stroke Rehabilitation

The assessment of outcomes in stroke is done using outcome measurement instruments. These instruments typically require a patient or proxy, such as a relative of the patient, to answer a series of questions about a specific topic like the ability to perform ADLs. Responses are usually multiple choice (very good/good/poor) or Likert-type scales (1 = poor health; 7 = excellent health). Some instruments are administered by an interviewer and others are completed by the patients themselves. There are also instruments that require patients to perform an activity (e.g., climb a set of stairs while being timed). The answers to the questions, or performance on the activity, are usually assigned a score; the total score after adding together all question- or performance-specific scores represents the level or intensity of an outcome. For example, the Barthel Index[1] contains 10 questions designed to measure a person's daily functioning. The overall score on the index could range from 0 (complete dependence) to 100 (complete independence). A subject's score on the index represents her level of daily functioning. Numerous outcome measures have been developed specifically for stroke (e.g., Scandinavian Stroke Scale[53]), while others are used in stroke even though their original purpose was for a different therapeutic domain (e.g., Mini-Mental State Examination[54]).

Before an outcome measurement instrument is used in stroke rehabilitation, it must be verified to ensure that it is suitable for measuring outcomes in persons with stroke. This verification is an absolute prerequisite for instruments developed specifically for use in stroke rehabilitation. Instruments developed and verified in other areas of health care must be reverified

in stroke patients before they can be used in stroke rehabilitation studies. A measure developed in another area might not be adaptable to the many different and specific nuances of stroke.

The verification of the suitability of an instrument is done through the study of its psychometric properties: reliability, validity, and responsiveness to change.[55] Reliability or reproducibility is the extent to which a measure produces the same result each time it is employed, provided the underlying phenomenon being measured is unchanged. Interrater reliability involves two or more raters who use the outcome measure to independently assess the same subject at the same point in time. Test-retest reliability involves the injection of temporality into the notion of reproducibility: subjects are evaluated twice with the same measure, but at two different points in time. Reliability is high when the results of the separate evaluations are quite similar to one another. A third type of reliability is called 'internal consistency', or the extent to which the subcomponents of a scale all measure the same construct.

Validity is the extent to which the outcome measure adequately captures what it is intended to measure. For example, if the score on an index of ADLs represents actual physical function, then the index would be considered valid. There are three general types of validity: content, construct, and criterion. Content validity concerns the extent to which the outcome measure covers the scope of the construct under study. For example, does the ADL index contain all activities that are necessary to adequately measure physical function?

Construct validity refers to the theoretical linkage between an outcome measure and the construct. If persons with decreased physical function post-stroke have lower scores on the ADL index (assuming lower scores indicate reduced ability to perform ADLs), then the measure can be said to have construct validity. However, if there was an inverse association between physical function and index score, then the outcome measure might be flawed (invalid) or the hypothesized relationship between physical function and ADLs might not bear truth in reality. Criterion validity concerns the extent to which an outcome measure correlates with a 'gold standard'.

Responsiveness is an outcome measure's ability to accurately detect clinically meaningful change. These changes are typically specified using the minimal clinically important difference (MCID), which is the smallest difference in efficacy between treated and untreated groups that could be considered clinically significant.[56] Responsiveness to change may be assessed with the standardized response mean (SRM), which is the mean score change divided by the standard deviation of the change.[55] SRMs between 0.2 and less than 0.5 are small, between 0.5 and less then 0.8 are moderate, and 0.8 or greater are large.[57] The higher the SRM, the greater the likelihood that the outcome measure captures actual changes that occur because of treatment. Note that evaluation of responsiveness may not be applicable to outcomes of events, such as recurrences of a new stroke.

In research to evaluate stroke rehabilitation therapies, outcome measures should only be selected if they have strong psychometric properties established in stroke patients. Before the selection of specific measures, though, researchers must identify a broader series of outcome domains that will be of interest in their studies. These domains are essentially the constructs that individual measures will describe. The ICF[30] may be used as a guide to help link outcome domains with specific outcome measures.[4,6,20]

In general, outcomes measuring impairment (e.g., cognition) should be included in studies of stroke rehabilitation therapies because impairment is most closely linked to volume of brain activity and prognosis (ICF category B1 – mental functions). However, functional outcome measures (e.g., ICF category B114 – orientation functions) should also be included because

persons recovering from stroke are interested in regaining as much normal function as possible.[3] The primary outcome measure should be "modality-specific", rather than generic, and matched to the most important treatment objective of the study. The 'modality-specific' nature of the selected measure is necessary to reflect the fact that the rate and extent of post-stroke recovery differs by outcome domain.[58]

When selecting outcome measures, it is important to consider stroke severity and the natural history of stroke recovery, as well as the mode of administration of the measure (interviewer or self-rated). Outcomes can be measured at three months in efficacy studies and at six months in effectiveness studies.[8] Outcomes should not be dichotomized (e.g., improved by 2 points or improved by less than 2 points) because recovery from stroke is variable across a continuum and often defined individually through goal setting and attainment.[8]

The selection of outcome measures for stroke rehabilitation studies cannot be prescribed with an algorithm. Researchers must be guided by the general principles enumerated in the above discussion. The specific choice of measure will be driven by the outcome under evaluation. The measure should be reliable and valid, and responsive to change, in stroke patients. Other issues related to the study (e.g., design, length of followup) will also play a role in selecting outcomes.

We speculate that space restrictions in journals often prevent authors from fully explaining the rationale behind their selection of outcomes. Therefore, reviewers of stroke rehabilitation studies will need to be familiar with the outcome measures used in the rehabilitation field. Although the most popular outcome measures in stroke rehabilitation have been tabulated,[58,59] reviewers should not judge the appropriateness of these measures based solely on the frequency of use. In the ICF domain of participation (i.e., ability to partake in life situations), the top three outcome measurement instruments by frequency of use (EuroQoL-5D, Medical Outcomes Study Short Form 36, Nottingham Health Profile)[58] are generic health measures that may not capture the nuances of such a widely diverse area. This is especially so if a study is focused on one precise aspect of participation (e.g., ability to engage in paid employment).

Key Methodological Points to Remember

Key methodological points to remember when evaluating stroke rehabilitation studies include:

1. RCTs or high-quality observational studies (e.g., cohort, case control studies) are the ideal study design;
2. Subjects should be sampled from the population in which the new therapy will be used;
3. The sample characteristics of subjects should be presented in a table (stratified by treatment group);
4. Prior and concurrent treatments should be described to assess whether study participants received atypical treatments that could affect their response to rehabilitation therapy;
5. The new therapy must be clearly described and evaluated in conjunction with a comparison therapy, which should also be clearly described;
6. Authors should report the timing, frequency, and duration of the interventions in their study, plus the type of person conducting the intervention (e.g., physical therapist) and the nature of the intervention itself (e.g., describe devices used in therapy, describe exercise programs). This detail should also be provided for the comparison therapy
7. The comparison therapy should be clinically relevant and clinically routine;

8. Study outcomes should be clearly defined and linked to the objective of the rehabilitation therapy under consideration;
9. The primary outcome measure should be "modality-specific", rather than generic, and matched to the most important treatment objective of the study;
10. Participants outcomes must be correctly assessed (e.g., avoid using outcome measures with floor or ceiling effects);
11. Outcome measurement instruments should only be selected if they have strong psychometric properties in stroke patients (reliability, validity, responsiveness to change);
12. ICF categories can be used as a guide to help select outcome measurement instruments;
13. Instruments measuring impairment (e.g., level of cognition) and function, including ability to participate in activities, should be included in studies of stroke rehabilitation therapies;
14. During followup, participants should be evaluated in an objective and identical manner regardless of the intervention received; and
15. Length of followup should be long enough to show improvement in the primary outcome domain of interest.

Key Question

An overarching, key research question for this technology assessment was derived in consultation with the Agency for Healthcare Research and Quality's (AHRQ's) task order officer and representatives of CMS. CMS instructed that the relevant aspects of the research question had to focus on two important issues related to the evaluation of new rehabilitation therapies, i.e., study design and selection of outcome measures. The focus of the technology assessment was not to be on treatment efficacy.

CMS was particularly interested in identifying literature that addressed the selection or characteristics of stroke outcomes in six domains: ambulation, quality of life (including caregiver burden), activities of daily living, cognition, speech and communication, and swallowing and dysphagia. Of special importance was the need to evaluate the psychometric properties (particularly, the MCID) of these outcomes when used in comparative studies in these domains. Another important item to examine was the classification of these outcomes within the ICF taxonomy. As such, a secondary objective of this technology assessment was to undertake a critical appraisal of the adequacy of the outcomes used in stroke rehabilitation studies.

Taking into account the needs of CMS, the overarching research question for this technology assessment was: "What are the key methodological issues (internal validity) in comparative studies designed to assess rehabilitation therapies administered to stroke patients?" A secondary purpose of the assessment was to critically appraise the adequacy of outcome measures used to capture the six domains of interest.

The consultation process with AHRQ and CMS also identified 10 key attributes of studies that would be evaluated to address the overarching research question. These attributes included:

1. Study design (e.g., randomized controlled trial, observational study, etc.);
2. Randomization and blinding;
3. Patient selection criteria and characteristics;
4. Characteristics of personnel performing the intervention (including training needed);
5. Timing of the intervention relative to the stroke;
6. Frequency and duration of the intervention;

7. Length of followup in the trial and durability of benefit;
8. Prior and concurrent treatments in relation to the studied intervention;
9. Comparator used and relationship of the comparator to current best practices in stroke rehabilitation; and
10. Outcome measures used;
    a. Relation to ICF domains;
    b. Reliability, validity, and reproducibility; and
    c. MCID.

Chapter 2. Methods

Literature Search Strategy

There were two different strategies used to identify publications that evaluated rehabilitation therapies for stroke patients. In the first strategy, known as purposive sampling, the literature search was designed to identify articles that evaluated therapies in any one of six possible outcome domains: cognition, ambulation, quality of life (QoL), activities of daily living (ADLs), communication, and dysphagia. The objective was to identify a maximum of 20 articles in each domain. The decision was made to select the 20 most recent publications in each domain to provide the most up-to-date picture of the methodological standards currently employed in stroke rehabilitation research. If fewer than 20 articles were found in a particular domain after conducting the search, then the time scope of the search was not broadened because few comparative studies were likely to exist in that domain.

MEDLINE® and CINAHL® were the primary databases used in the search, although they were supplemented by PsycINFO® in the case of three domains with a clear psychological component (i.e., cognition, communication, dysphagia). For each of the six domains, the literature search was conducted by combining terms for the relevant domain with terms for stroke and rehabilitation. The detailed search strategy is contained in Appendix A.

Tailored search strategies and time scopes for each domain were as follows:

1. Cognition was searched in MEDLINE®, CINAHL®, and PsycINFO® between January 1, 2000 and January 21, 2008;
2. Communication (including speech) was searched in MEDLINE®, CINAHL®, and PsycINFO® between January 1, 2000 and January 22, 2008;
3. Dysphagia was searched in MEDLINE®, CINAHL®, and PsycINFO® between January 1, 2003 and January 18, 2008; and
4. Ambulation, QoL, and ADLs were searched in MEDLINE® and CINAHL® between January 1, 2003 and January 15, 2008.

In the second strategy, a broader search was undertaken to identify systematic reviews on the general topic of stroke rehabilitation. MEDLINE®, CINAHL®, and the Cochrane Database of Systematic Reviews (CDSR) were searched between January 1, 2000 and January 16, 2008. The search terms for the review of reviews were a combination of stroke, rehabilitation, and outcomes, as well as subject terms for systematic review.

Inclusion/exclusion criteria. A purposive sampling approach was taken to select studies for this technology assessment. To be included in the assessment, the main focus of an article had to be stroke (or cerebrovascular accident) in adults. The study design had to contain a distinct comparison group (e.g., randomized controlled trial, controlled clinical trial, cohort or case control study). Studies involving persons who acted as their own controls (e.g., single subject research design (SSRDs)) were excluded because they do not involve distinct comparison groups (see Chapter 1). Included studies could contain any type of rehabilitation therapy whose effect was evaluated using any outcome in the domains of cognition, ambulation, QoL, ADLs, communication, or dysphagia. In the case of drugs used as rehabilitation therapies, included studies had to contain a drug that was employed to treat cognitive impairment. Other types of rehabilitation drug studies were excluded.

Searches were limited to English-language articles involving human subjects. Editorials, letters to the editor, comments, and studies without a comparison group (e.g., case reports, case

series) were excluded from this technology assessment. A further exclusion was applied to studies that focused on primary or secondary stroke prevention.

These same criteria were applied to include systematic reviews in the review of reviews, with some exceptions. First, the focus of a review could be on any rehabilitation therapy administered to a stroke patient, regardless of outcome domain. Second, the article had to be a systematic review of the literature. Narrative reviews or opinion pieces summarizing states of knowledge were excluded from the assessment. Third, there were a large number of reviews that focused on the use of drugs in the immediate acute phase of stroke; there were also a number of reviews that evaluated the use of drugs for prevention of future stroke (primary or secondary) or prevention of thrombosis following stroke. In these reviews, the use of drugs was not considered to be for "rehabilitation", so the reviews were excluded. Reviews in which drugs were used to treat post-stroke depression or emotionalism were also excluded. Similarly, reviews about the treatment of spasticity and pain following stroke were excluded at the request of CMS. Finally due to the large number of systematic reviews, we limited our evaluation to those published from 2005 onward.

Data Screening and Abstraction

Data screening. The search results were imported into Reference Manager® v10 (Thomson ResearchSoft; Carlsbad, CA). At level one of screening (title and abstract screening), two independent reviewers applied the inclusion/exclusion criteria to all articles retrieved in the literature search. This was done for both the purposive sampling and review of reviews. Screening was done separately for each of the six outcome domains. Lists of articles that were selected for inclusion by each reviewer were compiled on a domain-by-domain basis. Within each domain, the first 20 matching articles from both reviewers' lists, in chronological order of publication (most to least recent), were included in the assessment. For the review of reviews, screening yielded a large number of eligible systematic reviews (n = 126); given that such a large number was not feasible, we limited the eligible systematic reviews to the period from 2005 to the present.

Data abstraction. Articles selected for inclusion at level one advanced to level two of screening. This was the data abstraction phase, which was also conducted by two independent reviewers. Disagreements were resolved by consensus. Abstracted data were entered into standardized evidence tables, which were developed iteratively by the McMaster University Evidence-based Practice Center (MU-EPC) team to address the specific information needs of Centers for Medicare and Medicaid Services (CMS). Elements for extraction from the primary studies included characteristics of the study, population, intervention, comparator, outcomes, comparator treatment, and results. Summary information across studies with respect to the frequency of outcomes was also extracted. Elements for extraction in the review of reviews included eligibility criteria for the systematic review (design, outcomes, comparison, population), details of the search strategy, methods of assessing individual study quality, and the main findings. Individual study data for key methodological attributes (randomization, blinding, withdrawals) were also extracted and summarized across systematic reviews.

Studies or reviews could be excluded at each level of screening if they were found to not meet the inclusion/exclusion criteria.

Quality assessment. For the primary studies, we evaluated methodological characteristics, and summarized them in tabular form. We also summarized two studies per outcome domain in

the text: one study that exemplified good methodological quality and one study that exemplified less than high methodological quality. For the review of reviews, we developed a standardized checklist for quality focusing on four main aspects of internal validity, namely randomization (allocation concealment), blinding, withdrawals, and control of baseline confounders (for cohort studies). For the review of reviews, we utilized a standardized quality assessment checklist[9,10] with a modified scoring system[11] whereby the maximum score was 18.

Technical Experts

The MU-EPC enlisted two content advisors to provide advice on data abstraction and the interpretation and significance of results. Communication with these advisors was undertaken on an 'as needed' basis to provide intellectual input and discussion of findings.

The advisors included Drs. Laurie Wishart and Maria Huijbregts. Dr. Wishart is the Assistant Dean of the Physiotherapy program at McMaster University's School of Rehabilitation Science. Her research interests include the development of effective rehabilitation interventions for older adults and individuals post-stroke. Dr. Huijbregts is the Director of Clinical Evaluation at Baycrest, an academic health sciences centre on aging that is affiliated with the University of Toronto. She is also an Associate Scientist at the Kunin Lunenfeld Applied Research Unit, which is part of Baycrest. Dr. Huijbregts conducts research into self-management approaches to programming for stroke survivors in the community.

Chapter 3. Results

Purposive Sampling

Overall, a total of 1,674 citations were retrieved in the literature search. After vetting all citations for applicability of inclusion/exclusion criteria at level one screening (title and abstract), citations encompassing more than one of the six outcome domains were categorized according to primary outcome domain. A total of 126 citations (7.5 percent) passed level one screening, although four did not get forwarded to level two screening (data abstraction phase) because they were outside of the range of the 20 most recently published articles in their respective domains. During data abstraction, 11 citations were excluded because of a failure to meet the inclusion/exclusion criteria, leaving a total of 99 abstracted studies. The flow of studies through the screening and abstraction process is shown in Table 1.

Since the objective was to obtain the 20 most recently published studies in each outcome domain (within the years searched), provided the studies met the inclusion/exclusion criteria, four ambulation studies that were beyond this range were not forwarded to level two screening. In the case of communication and dysphagia, the number of studies that passed level one screening did not reach the initial threshold of 20.

Table 1. Flow of purposive sampling studies through data screening and abstraction

	Ambulation	Quality of Life	Activities of Daily Living	Cognition	Communication	Dysphagia
Total citations screened	165	200	184	522	332	271
Passed level one screening	30	21	23	21	17	14
Not retrievable	0	1	0	0	0	0
Not forwarded to level two screening*	4	0	0	0	0	0
Forwarded to level two screening (data abstraction)	26	20	23	21	17	14
Total duplicates with other domains	6	3	10	2	1	0
Duplicates screened in primary domain at level 2	0	2	7	1	1	0
Duplicates moved to another domain for level 2 screen	6	1	3	1	0	0
Excluded level two	1	2	0	2	4	2
Passed level two screening	20	17	20	18	12	12

*Not within the range of the 20 most recently published studies that met the inclusion/exclusion criteria

The characteristics of all abstracted studies are shown in Appendix Tables B to D. Prior to describing the methodologically superior and methodologically inferior studies in each outcome

domain, a brief summary of the key characteristics of all abstracted studies will be provided below.

Study design. The vast majority of abstracted studies (>88 percent) were Randomized Controlled Trials (RCTs) (Figure 4). The highest percentage of RCTs was in the activities of daily living group (ADL) (100 percent); the lowest percentage was in the dysphagia group (67 percent). From the viewpoint of evidence-base practice (EBP), good quality RCTs form the highest possible level of evidence for or against a therapeutic intervention (Figure 3).

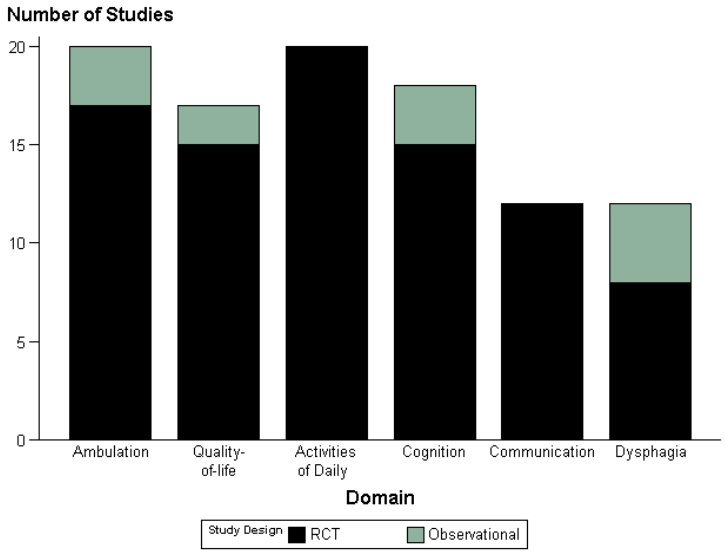

Figure 4. Number of abstracted studies by study design

Patient selection. All except two abstracted studies reported inclusion and exclusion criteria and at least rudimentary sample characteristics such as age and sex (Figure 5). This information is needed to determine the group of people to whom a study's results apply, as well as to help judge whether the results can be generalized to populations beyond the actual group of people in the study. The examination of sample characteristics can also provide an indication of the presence of selection bias. For example, if a certain stroke rehabilitation therapy is known to be most efficacious in persons over 50 years of age, but the study sample is primarily composed of persons 50 years of age and under, then poor therapeutic results could be attributed to sample selection factors, rather than to the therapy itself.

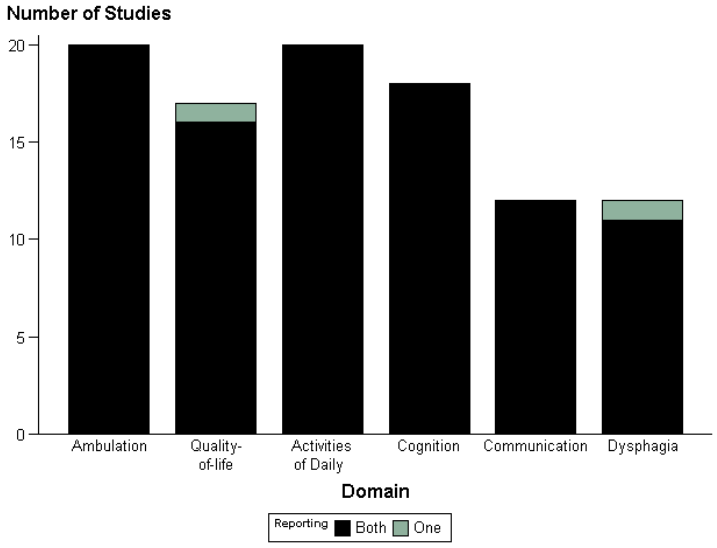

Figure 5. Number of abstracted studies reporting inclusion/exclusion criteria and patient characteristics (both=report both; one=report one only)

Randomization and blinding. Two essential elements of an RCT design are randomization and blinding. Randomization should ensure that the various treatment groups are comparable to one another on all factors except the therapy of interest. Blinding helps to prevent knowledge of the therapy from influencing how subjects are treated and assessed during the course of a trial. The authors of virtually all of the abstracted RCTs reported that their subjects were randomized to treatment (Figure 6a). Similarly, a majority of authors in all except the cognition domain reported that some type of blinding was pursued in their studies (e.g., blinding of outcome assessors [Figure 6b]). The reporting of randomization and blinding is seen as an essential feature to earmark the quality of an RCT.[35]

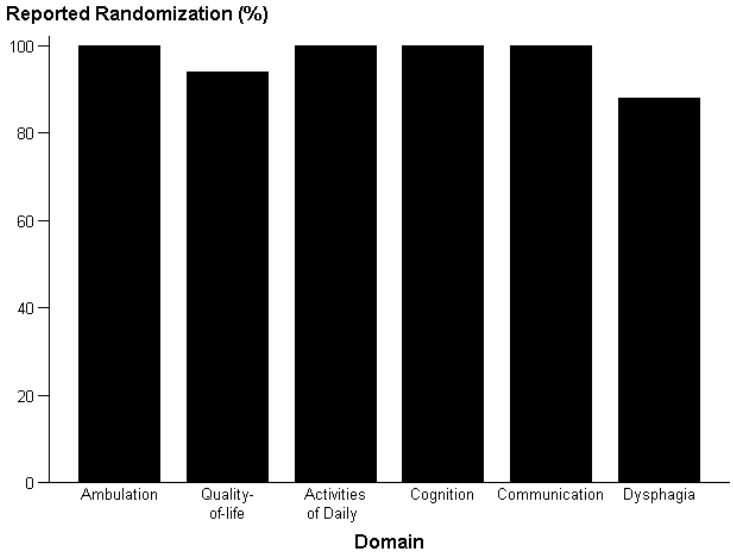

Figure 6a. Percentage of abstracted RCTs reporting patients were randomized

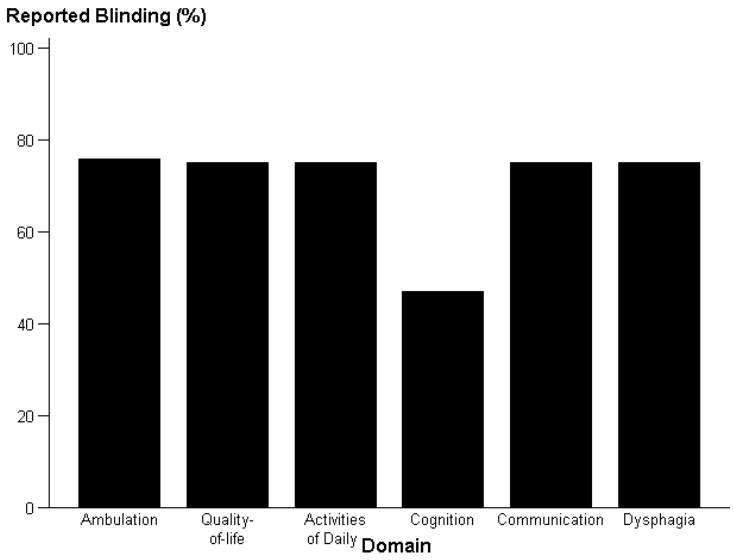

Figure 6b. Percentage of abstracted RCTs reporting patients were blinded

Providers. An important aspect of stroke rehabilitation therapy is the professional background of the person administering the therapy. In many instances, trained occupational, physical, or speech therapists are required to successfully deliver a therapy. The authors of studies in the field of stroke rehabilitation should therefore specify, as part of the description of the therapy under evaluation, the required professional qualifications of the person(s) who administer the intervention(s). In the abstracted studies, the majority of authors mentioned the type of health professional that was required to administer a therapy (Figure 7). Studies that omitted specific mention of professional status generally reported that rehabilitation interventions were delivered by a rehabilitation team, medical doctor, or one of the study researchers.

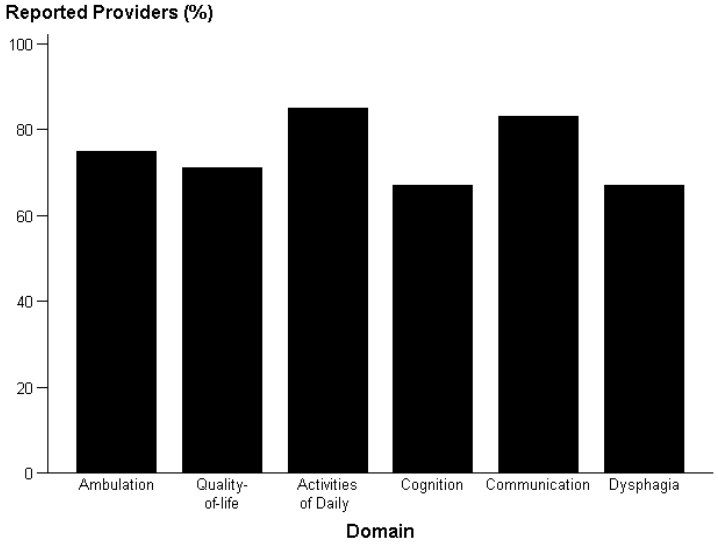

Figure 7. Percentage of abstracted studies reporting the type of provider of therapy

Timing of post-stroke initiation of intervention. An important aspect of any rehabilitation therapy is the timing of its initiation post-stroke. Some therapies may need to be started as soon as possible after the stroke event, while others can be initiated weeks or months later without any deleterious impact on efficacy. To foster a clear understanding of how an intervention is supposed to work, and to judge whether the intervention(s) in a specific study are being applied properly, the authors should report the timing of initiation of therapy. In the abstracted studies, all of the authors in the ambulation domain reported the timing of initiation. In the other five domains, 65 percent of the authors reported the timing (Figure 8).

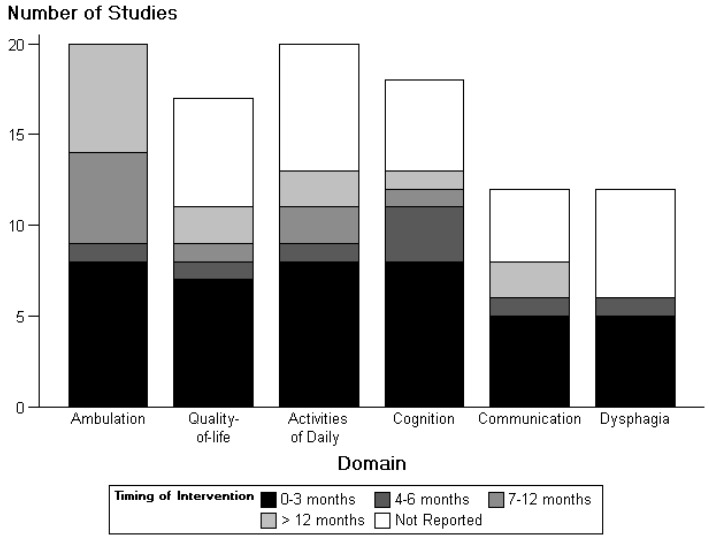

Figure 8. Timing of intervention in abstracted studies

Frequency and duration of intervention. As with the issue of timing, the frequency and duration of an intervention should be reported to foster an understanding of the intervention and judge the appropriateness of its use in a study. In all except the dysphagia domain, most of the studies contained reports of both the frequency and duration of the interventions. In the dysphagia studies, only half contained reports of both items (Figure 9).

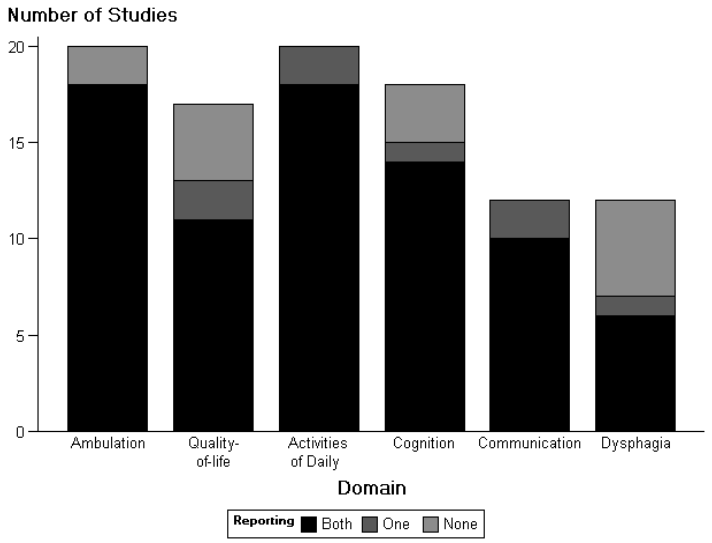

Figure 9. Number of abstracted studies reporting frequency and duration of intervention (both=report both; one=report one only; none=report neither)

Length of followup. The length of followup in any study must be long enough to allow the therapy to work and long enough to allow for the development of outcomes. Given the wide variability in profiles of stroke patients, as well as in prognosis, it is difficult to establish minimum followup times for any specific outcome domain (or outcome measure). However, authors should report lengths of followup so that readers can assess the applicability of a study's results to specific groups of patients. In the abstracted studies, lengths of followup varied widely, although they typically fell within a band of 1 to 12 months. The authors of eight studies did not report length of followup (Figure 10).

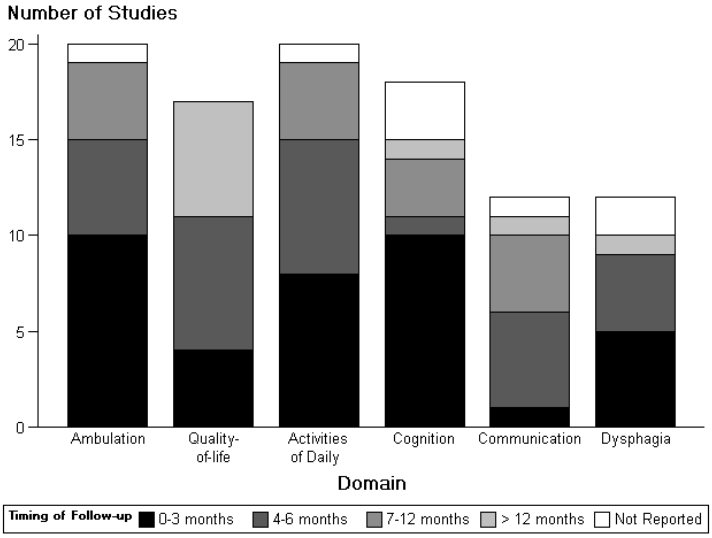

Figure 10. Timing of followup in abstracted studies

Prior and concomitant treatments. As was the case with patient selection, subjects' receipt of prior or concomitant treatment should be reported to determine the applicability and

generalizability of study results to various groups of subjects. Less than half of the abstracted studies contained reports of prior or concomitant treatment (Figure 11), making this the least often reported key characteristic of the studies.

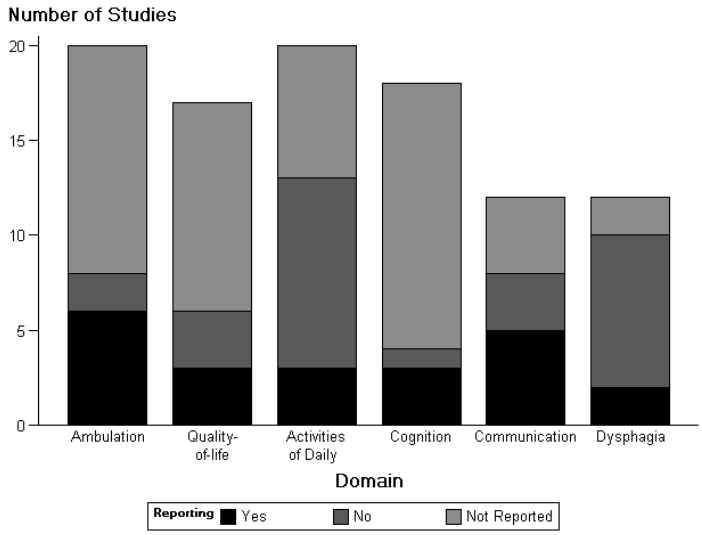

Figure 11. Number of abstracted studies reporting prior/concomitant treatment (no=subjects did not receive prior/concomitant treatment)

Standard treatment clearly described. Virtually every study reported details of the standard treatment. For example, they reported what was done to patients as part of standard rehabilitation therapy. The communication of these details allows readers to evaluate whether the standard treatment was an adequate comparator against the therapy of interest. No figure is provided because almost all studies contained information about the standard treatment.

Outcome measurement instruments. At least 20 different outcome measurement instruments were used in each domain (see Appendix D). Some of these instruments were well-established scales such as the Barthel Index[1] and others were vaguely described tools such as a "swallowing questionnaire".[2] In the ambulation, Quality of Life (QoL), ADL, and cognition domains, the most frequently used instruments were reliable and valid in stroke patients. Some of these instruments were also responsive to change in stroke patients. There was very little information on the minimum clinically important difference (MCID) for any of the instruments. In the communication and dysphagia domains, there was no information on any psychometric properties for any of the instruments. Figure 12 shows the number of instruments in the ambulation, QoL, ADL, and cognition domains for which information was provided on psychometric properties. The communication and dysphagia domains are omitted from the figure due to the aforementioned lack of information.

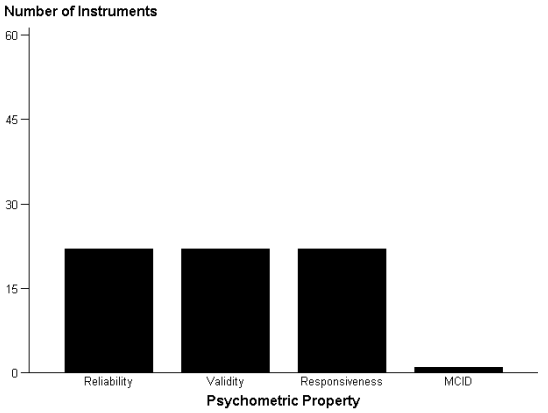

Figure 12a. Ambulation (n = 45 instruments)

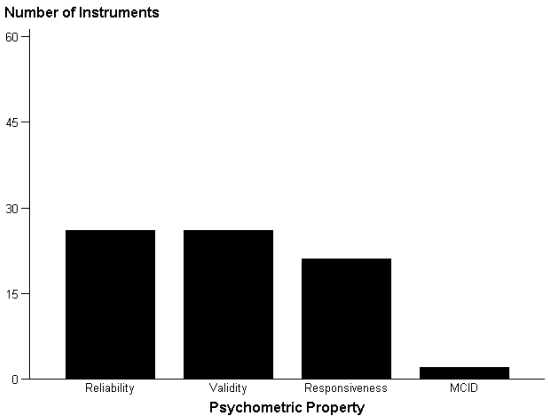

Figure 12b. QoL (n = 54 instruments)

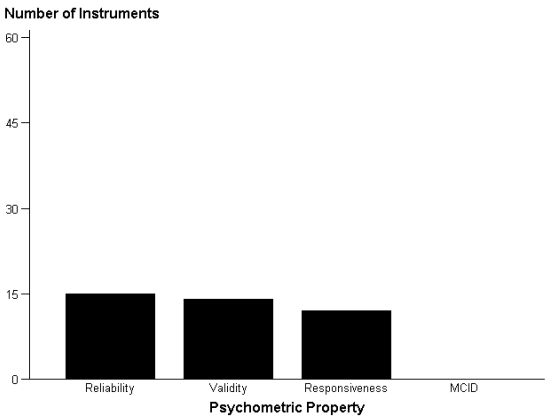

Figure 12c. ADL (n = 25 instruments)

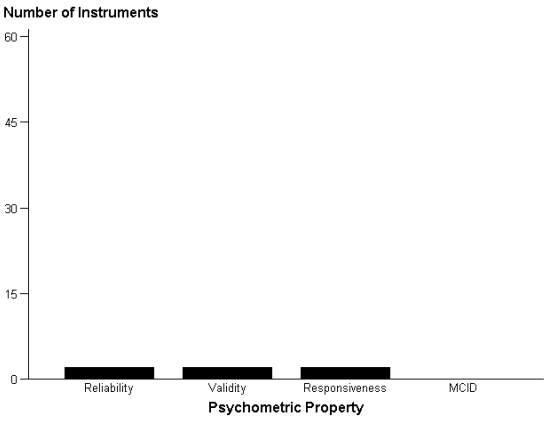

Figure 12d. Cognition (n=36 instruments)

Figure 12. Number of instruments in stroke in four outcome domains with information on psychometric properties (MCID=minimum clinically important difference)

In the four outcome domains for which graphical data are reported, the instruments were found to map onto one of three international classification of functioning (ICF) domains: activity, function, or participation. Figure 13 shows a breakdown of instruments by ICF domain, stratified by outcome domain.

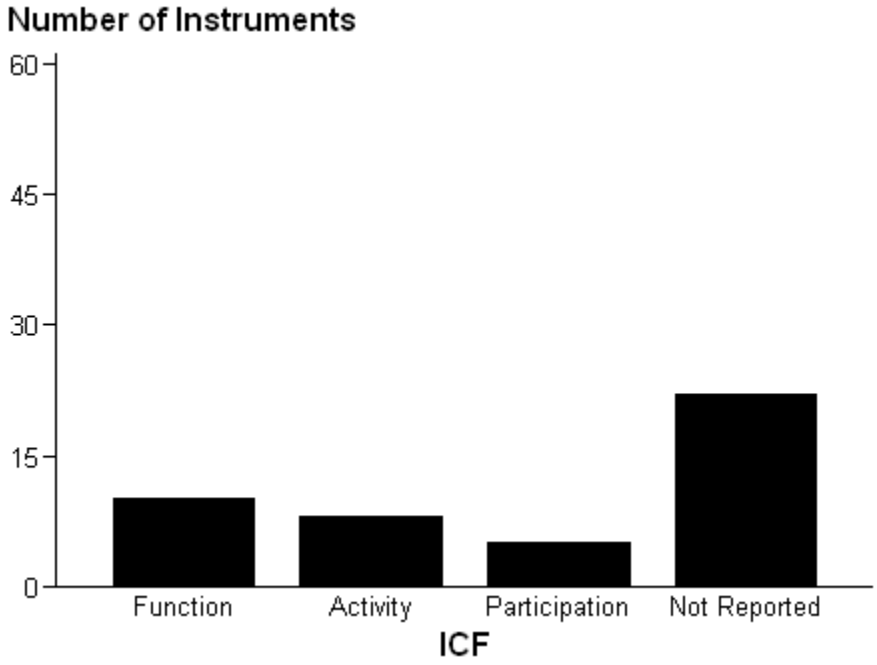

Figure 13a. Ambulation (n = 45 instruments)

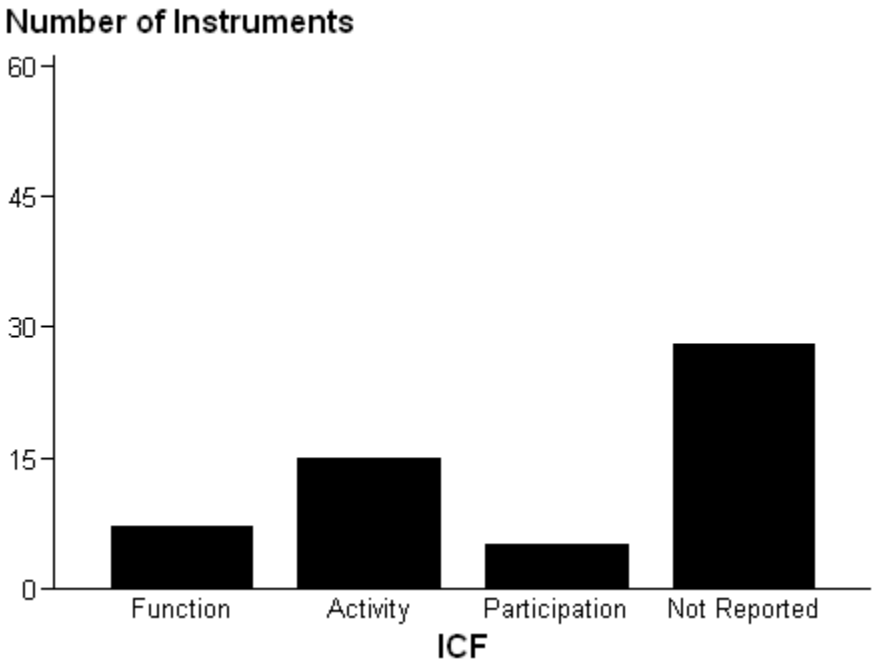

Figure 13b. QoL (n = 54 instruments)

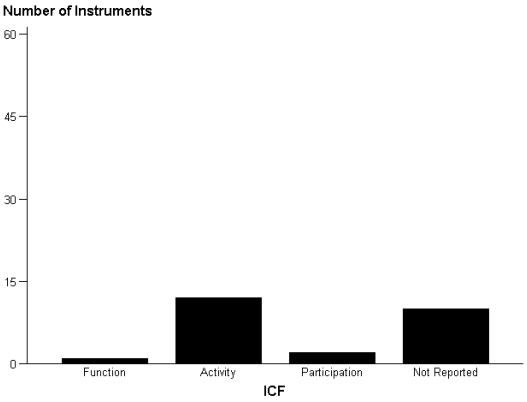

Figure 13c. ADL (n = 25 instruments)

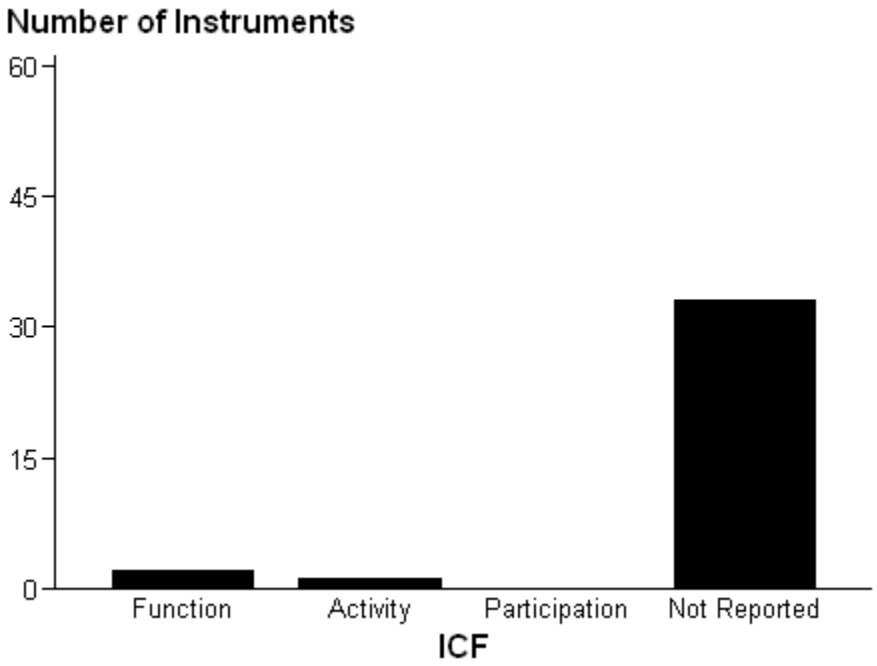

Figure 13d. Cognition (n = 36 instruments)

Figure 13. Breakdown of instruments by ICF domain

It should be noted that the assessment of each instrument's psychometric properties in stroke was based on whether the authors who used the instrument actually discussed psychometric properties in the methods sections of their study reports. Additional information on the presence or absence of psychometric properties in stroke was gleaned from information presented in the systematic review articles[3-6] and two reviews of outcome measures.[7,8] These data formed the source of information for the tables in Appendix D. Primary sources (studies introducing and validating the instruments themselves) were not consulted for this exercise.

With respect to the above summaries, there are several important methodological points to consider when evaluating studies in stroke rehabilitation. These points are listed below to act as a frame of reference for the salient features that will be discussed in the specific study descriptions that follow. The important methodological points are:

1. RCTs or high-quality observational studies (e.g., cohort, case control studies) are the ideal type of study design;
2. The sample characteristics of subjects should be presented in a table (stratified by treatment group);
3. Inclusion and exclusion criteria should be clearly listed in the study methods;
4. Details of randomization and blinding should be reported in the studies;
5. Authors should describe the type of professional needed to provide the therapy;
6. Authors should report the timing, frequency, and duration of the interventions in their study;
7. Authors should report the length of followup;
8. Authors should report any prior or concomitant treatments received by study subjects;
9. The comparator treatment should be clearly described; and

10. Outcome measurement instruments should only be selected if they have strong psychometric properties in stroke patients (reliability, validity, responsiveness to change).

Purposive Sampling – Domain-Specific Study Descriptions

Ambulation. The most methodologically sound study in ambulation was an RCT conducted by Marigold et al.[60] to compare two different community-based exercise programs (i.e., agility versus stretching/weight-shifting) to improve balance, mobility, and standing postural reflex (see Appendix B: Table B1 and Appendix C: Table C1). The sample was clearly described and compared to persons who dropped out of the study. The timing, frequency, and duration of both interventions, as well as the length of followup, were clearly described. Outcome assessors were blinded, the persons responsible for conducting the exercise programs (physical and recreational therapists, kinesiologists) were aware of subjects' group assignments, but not the study outcomes, and subjects themselves were aware that they were in one of two exercise programs, but they were unaware of the differences between programs. The authors described subject comorbidities and concomitant use of assistive devices. The primary outcome measure was the Berg Balance Scale,[61,62] which has demonstrated good reliability and validity in ambulation in stroke rehabilitation.

The study with the least rigorous methodology in ambulation was a cohort study by Roerdink et al.[63] The study was conducted to examine the efficacy of acoustically-paced treadmill walking to improve gait coordination in people after stroke (see Appendix B: Table B1 and Appendix C: Table C1). The 'exposed' group consisted of 10 volunteers who suffered a first-ever ischemic cerebrovascular accident within 3 to 104 months of joining the study. The 'unexposed' group (n = 9) was reported to be similar to the intervention group on age, height, and weight, although the authors do not mention how they were recruited. Although it appears that exposure status was based on prior or no prior stroke, the authors did not report whether the unexposed group had any history of cerebrovascular events. Furthermore, the authors did not report the source population of the study subjects, nor whether these subjects had comorbidities or concomitant treatments. The absence of detail makes it difficult to assess the potential for selection bias. Additionally, it is difficult to ascertain whether the two groups are comparable. In the study, both groups of subjects received the treadmill intervention, which was generally well described in terms of procedure (e.g., belt speed settings). However, the timing, frequency, and duration of the intervention were not reported in the article. The authors took various measurements of stride (frequency, length, time, width) on the treadmill and compared the exposed and unexposed groups. Not surprisingly, the exposed (stroke) group performed worse on these measures than the unexposed (non-stroke) group. The authors then measured the stride parameters on the stroke patients only, stratified by treadmill pace. None of these analyses provide answers as to whether the acoustically-paced treadmill improves gait coordination in stroke patients. This issue would have best been resolved with a comparison treatment. The exposed-unexposed comparison might in some cases be a useful means of establishing a healthy, baseline treatment ceiling with which to evaluate the progress of stroke patients. In this study, though, the utility of comparing exposed and unexposed groups is questionable because there is a lack of reported detail on the degree to which these groups may be similar to one another.

Quality of life. The study by Park et al.[64] is a well-designed research effort to examine QoL in stroke rehabilitation (see Appendix B: Table B2 and Appendix C: Table C2). The study is an RCT to investigate real versus sham acupuncture to improve post-stroke QoL. The

randomization is clearly described (i.e., block randomization), as are the source and basic characteristics of the sample. However, the authors do not mention whether the sample is receiving concurrent treatment, nor is comorbidity clearly described. The real and sham acupuncture interventions are both well-described and the post-stroke timing, frequency, duration of treatment, and length of followup are clearly reported. The authors wrote that all patients received "conventional multidisciplinary stroke rehabilitation" (p.2027) in addition to real or sham acupuncture. While no details of conventional therapy were provided, this is not a serious methodological flaw (in this case) because conventional therapy was not the comparator treatment. If the randomization was conducted properly, then any potential confounding effects of conventional therapy would be evenly distributed across the treatment groups. Even distribution of confounders negates problems with confounding. In this study, patients and physicians were blinded as to treatment, and outcomes were assessed using the EQ-5D, which has been validated for use as a measure of QoL in stroke.[65-67] The two-week followup period might be too short to assess the impact of acupuncture on medium- or long-term QoL.

In contrast to the Park et al. study,[64] the research by Hafsteinsdottir et al.[68] was a cohort design where 'exposed' subjects received neurodevelopmental treatment (NDT) and 'unexposed' subjects did not (see Appendix B: Table B2 and Appendix C: Table C2). The authors clearly describe the sample (source of subjects, sample characteristics, disease history), but they do not explain NDT in clinical terms. The authors also do not explain the comparator treatment, nor do they provide the timing, frequency, or duration of treatment. No mention is made of blinding. QoL is measured using the 30-item, stroke-adapted, Sickness Impact Profile (SA-SIP30)[69] and a self-reported visual analogue scale, which was developed for use in stroke.[70] The lack of detail on NDT and the comparator therapy, as well as the absence of information on the timing of the interventions, means the precise conditions under which NDT may or may not show an effect are not clear. The clinical suitability of NDT can only be judged if more precise information is given.

Activities of daily living. One of the better ADL studies, by Langhammer et al.,[71] examined whether two different strategies of physical exercise would have a differential impact on maintenance or improvement of ADL (see Appendix B: Table B and Appendix C: Table C3). The study was an RCT, but randomization was carried out inappropriately using a die toss rather than a computer-generated sequence. Despite the improper randomization, the treatment groups were similar to one another on basic sample characteristics such as age and sex, but no mention was made of comorbidities or concomitant treatments. The specific exercise regimens for both treatment groups were described, as was the timing, frequency, and duration of treatment. The study was double-blind, with patients and researchers being unaware of treatment assignment. ADL outcome was measured with the Barthel Index, which has good psychometric properties in the field of stroke rehabilitation.[72]

A study by Gilmore and Spaulding[73] was an RCT where 10 subjects were randomized to receive occupational therapy with video feedback or occupational therapy with verbal feedback (see Appendix B: Table B3 and Appendix C: Table C3). The source of subjects was clearly described, but only rudimentary data (i.e., age, sex) was provided about the subjects themselves. The interventions and frequency of interventions were well described, but the post-stroke timing and duration of interventions were not. Each subject received a maximum of 10 sessions, but the interval between sessions and the total elapsed time between first and last session were not reported. The outcome was measured on two portions of the Klein-Bell Activities of Daily Living Scale,[74] which is used often in stroke rehabilitation studies even though its reliability and

validity have never been formally assessed in this area. The portions of the Klein-Bell scale that were used in this study were the socks and shoes subtests, which measure patients' ability to don socks or shoes. The validity of separating these two subtests from the entire scale has never been assessed by researchers. Given the validity issue, it is possible that the observed results were biased due to an inappropriate outcome measure. Also, the very small sample size may have produced random error, thus leading to a further bias of results.

Cognition. Westerberg et al.[75] conducted a pilot RCT to investigate the impact of computerized working memory training on cognition in 18 persons who had a stroke within the previous 12 to 36 months (see Appendix B: Table B4 and Appendix C: Table C4). The source of the study sample was clearly described, although the authors did not specify whether all patients who fell within the 12- to 36-month timeframe were considered for enrollment. The number of dropouts during the trial was given (n = 6), as were the reasons behind the dropouts. The authors did not report subjects' comorbid disorders. The timing, frequency, and duration of the working memory intervention, as well as the tasks composing the intervention, were clearly described in the published study report. Length of followup was also reported. The study was described as randomized, but the text contains no description of the randomization procedure. Outcome assessors were not blinded after the baseline assessment. Eight different neuropsychological tests were used to measure cognition in the study. The authors did not report whether any of these tests had adequate psychometric properties in stroke patients. Persons in the control group did not receive any sort of working memory training. The authors did not report whether the study subjects received any sort of concomitant treatment.

Cherney et al.[76] studied visual scanning versus oral reading in the treatment of unilateral neglect (Appendix B: Table B4 and Appendix C: Table C4). Four subjects were randomized to the scanning or reading groups. Subjects were enrolled at least 7 months post-stroke; the authors report age, sex, and education data, but not data on comorbidity or concomitant treatment. The authors also do not report the source of subjects. The visual scanning and oral reading procedures were well described, although the intervals between the 20 treatment sessions, as well as the interval between the first and last session, was not reported. Unilateral neglect was measured with the Mini-Mental State Examination (MMSE)[54] and the Stroop Neurospychological Screening Test.[77] The MMSE has not been validated in stroke rehabilitation;[78] no sources could be found to indicate whether the Stroop Test has been validated in stroke rehabilitation. The authors found no differences between interventions. This may not have anything to do with the interventions themselves, but may instead be a reflection of the low power due to the small sample size.

Communication. Thorsen et al.[79] compared home versus conventional stroke rehabilitation in 54 patients, 5 years after the study intervention was complete (see Appendix B: Table B5 and Appendix C: Table C5). The authors refer readers to an earlier publication to obtain information on sample characteristics and randomization. Details on the rehabilitation interventions are scarce. The authors report the mean duration and mean number of home visits for the home rehabilitation program, but do not provide details on the conventional rehabilitation program. The length of followup is 5 years, which is helpful in capturing the range of likely changes in subjects' communicative abilities. However, it may have missed interim differences between groups. Outcome assessors were blinded as to the intervention. The specific outcome was aphasia, measured using the Reinvang Aphasia Test.[80] This test measures fluency, naming, comprehension and repetition, as well as writing and reading. There was no literature cited to suggest whether this instrument had been validated in stroke patients.

Rochon et al.[81] conducted a study to investigate the utility of mapping therapy on sentence production and comprehension (see Appendix B: Table B5 and Appendix C: Table C5). They randomized five patients who were at 2 to 9 years post-stroke and assessed outcomes using a battery of instruments (e.g., Caplan and Hanna's Sentence Production Test).[82] The authors clearly described each instrument, but failed to indicate whether the instruments were reliable and valid in stroke patients. The authors describe the mapping therapy in detail, but do not explain the control therapy. Information on the timing, frequency, and duration of the interventions are presented as averages across all five subjects. There is no mention of blinding. The authors report the source of the study subjects, as well as some basic subject data (age, sex, education, years post-stroke, etiology, dominant hand).

Dysphagia. Goulding et al.[83] used a RCT to investigate whether a viscometer or standard practice (i.e., thickening of fluids by nurse) would lead to improved management of dysphagia in stroke patients (see Appendix B: Table B6 and Appendix C: Table C6). The source of subjects and rudimentary sample characteristics were reported. Subjects were randomized by a computer-generated algorithm and the number of withdrawals and dropouts were reported. The interventions and their frequencies were clearly described. Clinical outcomes (i.e., pulmonary aspiration, pulse oximetry) were used to measure the success of the viscometer versus standard practice. A single, blinded assessor conducted the clinical evaluations.

Huang et al.[84] studied the frequency of aspiration pneumonia in patients fed by a family member versus patients fed by a trained nurse (see Appendix B: Table B6 and Appendix C: Table C6). Family members were shown a videotape of general nursing information and the nurses trained patients in various swallowing techniques. The authors mention that patients were recruited into the study within 24 hours of suffering a stroke. Feeding began within this time, but neither the frequency of feedings nor the length of followup are reported. No patient characteristics are provided. The study was non-randomized and patients recruited from January 2000 to July 2003 were fed by family members, while patients recruited from August 2003 to March 2005 were fed by the nurse. Aspiration pneumonia was assessed clinically by the presence of three or more of the following criteria: fever (temperature >38°C); productive cough with purulent sputum; abnormal respiratory examination; abnormal chest radiograph; isolation of a relevant pathogen (positive Gram stain or culture); or arterial hypoxemia (partial pressure of oxygen <9.3 kPa). Outcome assessors were not blinded.

Systematic Reviews of Interventions in Stroke Rehabilitation

The search for systematic reviews yielded at total of 949 English language citations for initial screening. After evaluation at the first level of title and abstract screening, 204 citations were eligible for full text review. From these 78 were excluded because the rehabilitation intervention evaluated drugs used primarily to achieve medical stability for acute stroke rather than rehabilitation. From 126 eligible reviews evaluated at full text, 88 were excluded primarily because they: 1) were not systematic reviews, 2) were review of reviews, or 3) had a year of publication prior to 2005 (see Figure 14). In addition to reasons of feasibility, we focused on reporting from more recent systematic reviews as these would likely include the greatest number of studies, and reflect more current research within stroke rehabilitation. After full text screening, a final set of 38 systematic reviews evaluating the efficacy of various interventions were eligible for full data extraction. We further categorized the systematic reviews into those published within the Cochrane Database of Systematic Reviews (n = 18) and those that were not

(n = 20). Those within the Cochrane systematic reviews were grouped separately, as these reflected a more standardized methodology, and internal peer review process. In addition, Cochrane reviews have detailed protocols for reporting the findings of the reviews and do not have limitations in the length of their publications. Thus, the Cochrane reviews (which are available through the Cochrane database) differ in their detail and format relative to reviews published in traditional journals. Evidence tables detailing the review search strategy, the eligibility criteria, populations evaluated, interventions reviewed, method of quality assessment, outcomes, and study results are found in Appendix E.

Table 2, located at the end of this section, shows the types of interventions, the number of studies and their design, the total sample evaluated and the acuity of the stroke patients evaluated. A large variety of stroke interventions were evaluated. The Cochrane reviews are predominantly based on randomized, quasi-randomized (method of allocation is known but not random), or controlled clinical trials (randomization is not specified but cannot be ruled out). The number of eligible trials included in the reviews ranged from zero to 31 trials. The number of subjects evaluated within the Cochrane systematic reviews varied from 18 subjects to 6,936, not including the review where no trials were eligible. Most studies evaluated subjects with different acuity levels. There were studies that had a more homogeneous population, and these tended to include the population most likely to benefit from the specific intervention. The non-Cochrane reviews had a wider variety of eligible study designs including case series and case reports. The number of studies evaluated varied from three case reports to 29 mixed design studies; similarly the populations varied from three to 125,453 stroke patients (Table 2). Most reviews evaluated patients with mixed acuity levels.

Methodologic quality of the systematic reviews. Appendix F details the criteria used to evaluate the methodological qualities of the systematic reviews; the methodological criteria is based on the Oxman and Guyatt scale[9,10] scored using an adapted method.[11] Table 3 details the scores for the eligible systematic reviews. The majority of systematic reviews published from 2005 forward, were generally well conducted, with only 22 percent (n = 8) of the reviews scoring below 14 out of 18 on our quality assessment checklist. The Cochrane reviews scored highest (range from 16 to 17); Cochrane reviews standardize their reporting and do not have a limit with regards to length of reporting which allows for greater detailing of methods. However, none of the Cochrane reviews met the highest scoring grade (2/2) for question 4 of the Oxman and Guyatt criteria which specified that the reviewers were blinded to identifying features of eligible studies, and assessors were blinded to study outcomes during the selection process. Two Cochrane reviews[14,85] were scored lower with regards to detailing their search strategy sufficiently for duplication.

For the non-Cochrane reviews, 10 systematic reviews scored lower than 14 (out a maximum score of 18). One review[86] combined a systematic review and an economic analysis and had the lowest score of four. The remaining lower composite scores varied from 8[87] to 12,[88,89] reflecting primarily problems with bias during the selection process and reporting of rationale and approaches to synthesizing studies. As was the case with the Cochrane reviews, none of the non-Cochrane reviews scored full marks (2/2) for question 4 regarding blinding.

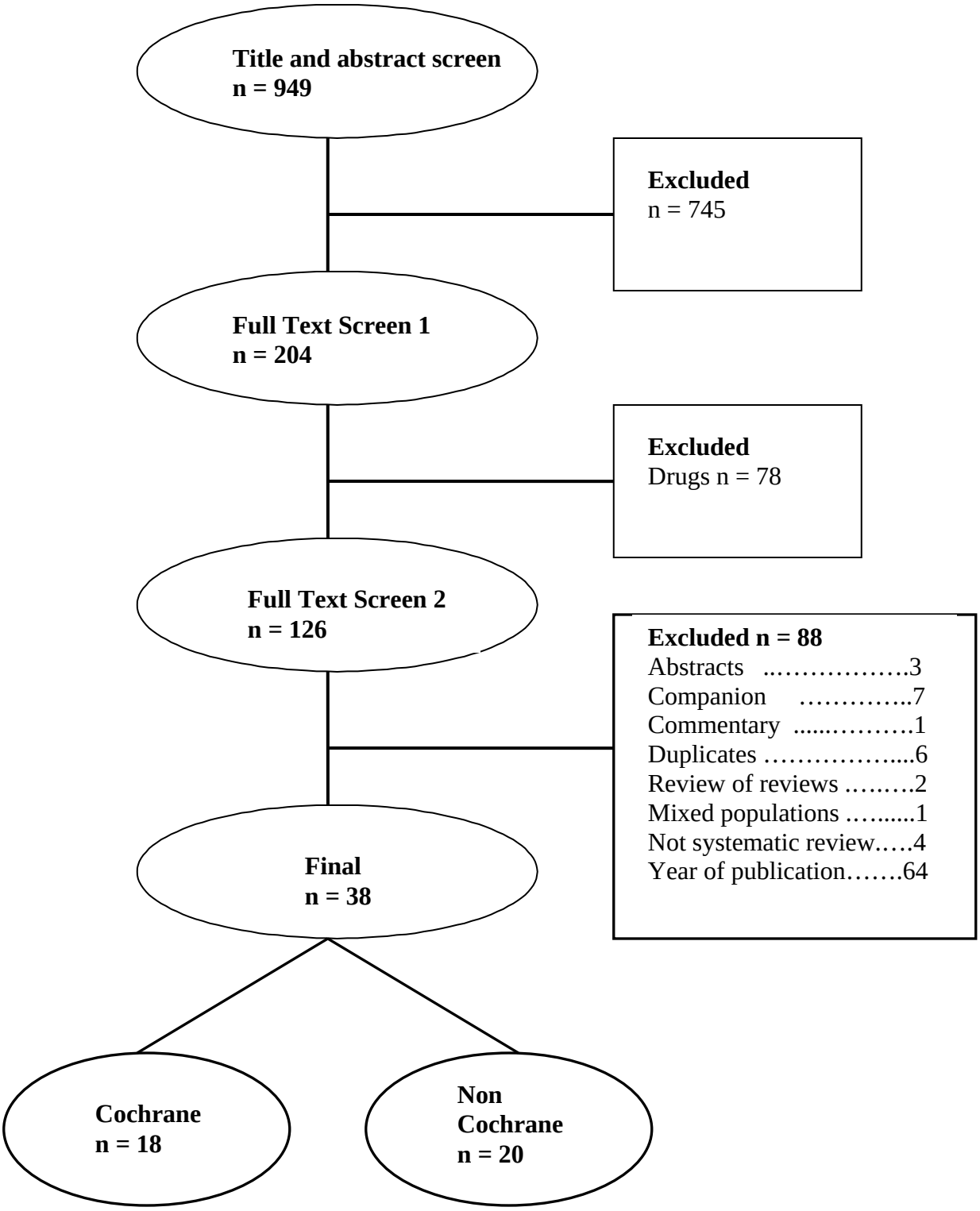

Figure 14. Flow diagram of eligible systematic reviews

Methodological quality of studies within the systematic reviews. There was great variation in the ways that methodological quality of primary trials was evaluated *within* the eligible systematic reviews (Table 4). One Cochrane review[90] had good methodology but found no eligible articles and thus was excluded from further calculations, leaving 17/18 reviews to be reviewed. All the Cochrane reviews explicitly stated the methodological criteria for evaluating quality of included studies; however, only 6 (33 percent) of these reviews used standardized checklists (see Table 3). The majority of non-Cochrane reviews used standardized checklists or evidence grading systems (n = 13, 65 percent). The PEDro quality assessment scale was used in 6 (46 percent) of these reviews[88,91-95] and one review,[96] though it did not label the criteria as PEDro, used the first nine criteria of the PEDro scale. Several reviews[87,97] evaluated non-comparative studies alone and did not employ any form of methodological evaluation.

There were some methodological quality domains that were not sufficiently evaluated or reported. Figure 15 shows the percent of studies that did not evaluate the criteria of interest. In particular, the potential for contamination, or cointervention was only reported well in 4 Cochrane reviews[12,14,15,98] and one non-Cochrane review.[16] Similarly, comparing baseline characteristics of the treatment and comparator groups was not evaluated in 12 Cochrane and 11 non-Cochrane reviews reflecting little differences between the two groups of reviews in this domain.

There were some differences between the Cochrane and non-Cochrane reviews. Figure 15 shows that all of the Cochrane reviews reported randomization or allocation concealment (West[90] was not included in analysis). Six Cochrane reviews (35 percent) did not evaluate the potential for adverse events compared to 13 (58 percent) of the non-Cochrane reviews. With regards to blinding, many trials evaluated within the systematic reviews indicated that it was impossible to blind the therapist or patient to the treatment and therefore did not evaluate patient or provider blinding. However, the Cochrane reviews tended to be less likely to evaluate this specifically. Both Cochrane and non-Cochrane reviews did not report the status of the data collector. However, they did assess the blinding status of the outcomes assessor (albeit the non-Cochrane reviews evaluated this less frequently).

When methodological criteria were evaluated, Table 4 shows the number of studies within each review that achieved the criteria of interest. In general, within each criteria, the proportions of studies achieving the criteria was wide ranging and likely varied as a function of the stroke rehabilitation intervention. For example, there were examples of reviews where a high proportion of the studies were randomized correctly[12] as well as a high proportion of studies that were not.[16] The degree to which the stroke rehabilitation intervention influenced this is not known.

Reporting of Other Study Factors

There are a number of relevant study factors that should have been detailed in the evidence tables within the systematic reviews. Albeit, the degree of information summarized is dependent on the degree it was reported in the original studies. In general, the patient and provider characteristics were better described within the Cochrane reviews than the non-Cochrane reviews (again reflecting the advantage of standardized reporting). The majority of reviews reported sufficient characteristics of the interventions and comparator but less about the "dose" of the therapy to the patients. Similarly, the majority of reviews did not specify the details of the inclusion and exclusion criteria within the studies, or any details of concomitant treatments.

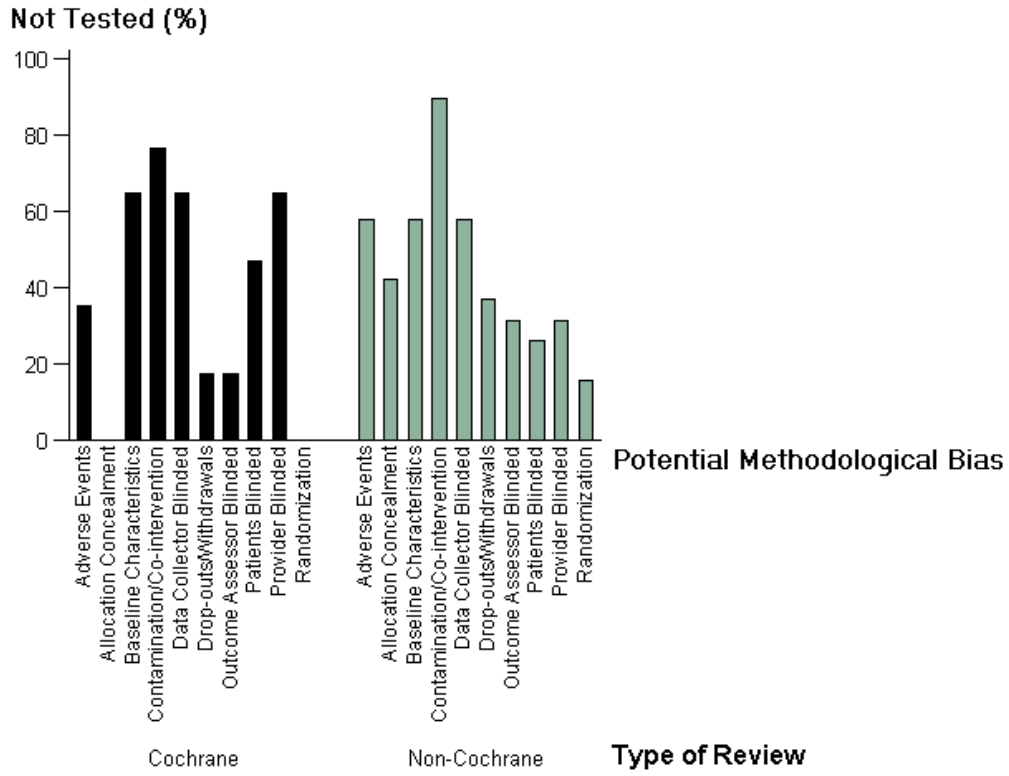

Figure 15. Methodological quality of the systematic reviews

Summary of Findings from Review of Reviews of Stroke Rehabilitation Interventions

With respect to the review of reviews, there were several trends and methodological points to consider and these include:

1. Most systematic reviews restricted studies to the intervention of interest, and by the type of stroke acuity. Few reviews restricted eligible studies to specific outcomes or to a specific provider of treatment.
2. The Cochrane reviews evaluated predominately randomized trials and the non-Cochrane reviews included all types of designs.
3. Most of the systematic reviews scored relatively high on quality criteria; those that had lower quality scores were non-Cochrane reviews and included multiple design types.
4. Most systematic reviews evaluated methodological aspects of the eligible studies with standardized checklist or criteria. The majority of reviews evaluated randomization, blinding, and withdrawals/dropouts. Fewer reviews evaluated baseline comparability, evaluation of adverse events, and cointervention or contamination.
5. Many reviews indicated that blinding of the patient and the provider was not possible with the stroke rehabilitation intervention and as such the reviews did not evaluate eligible studies for this criterion.

Table 2. Summary of systematic review interventions and acuity of stroke populations

	Intervention	Types of Studies	Total Number Subjects	Stroke Acuity Acute (t≤3m), Subacute (3m<t≤6m), Chronic (t>6m)
Cochrane Reviews				
Ada 2005[99]	Devices for shoulder subluxation	4 RCT	142	acute
Bennett 2005[100]	Hyperbaric oxygen therapy	3 RCT	106	acute
Bowen 2007[101]	Cognitive rehabilitation for spatial neglect	12 RCT	306	mixed
Brady 2006[13]	Oral care/hygiene	1 RCT	67	chronic
Discharge Trialists 2005[85]	Services for reducing duration of hospital care	11 RCT	1597	acute
French 2007[12]	Repetitive task training for improving functional ability	14 RCT/ QRCT	680	8 acute 2 subacute 4 chronic
Legg 2006[102]	Occupational therapy	9 RCT	1258	8 acute & subacute 1 chronic
Mehrholz 2007[103]	Electromechanical and robotic-assisted gait training devices	8 RCT/ CO	414	8 subacute, 2nd stroke
Moseley 2005[104]	Treadmill training	15 RCT/ QRCT	622	10 acute 2 subacute 2 chronic
Nair 2007[105]	Cognitive rehabilitation – memory retraining	2 RCT	18	1 subacute 1 mixed
Pollock 2006[15]	Physical therapy treatment approaches	18 RCT 2 QRCT 1 SSRD	1087	mixed
Pomeroy 2006[98]	Electrostimulation delivery to the peripheral neuromuscular system	24 RCT	888	mixed
StrokeTrialists' 2007[14]	Inpatient stroke unit care vs. alternative forms of care	24 RCT 7 CCT	6936	30 acute 1 up to 12m
Thomas 2008[106]	Optimal methods for treating urinary incontinence post stroke	12 RCT/ QRCT	724	mixed
West 2005[90]	Apraxia of speech interventions	None	NA	NA
Woodford 2007[107]	EMG biofeedback for motor function recovery	13 RCT/ QRCT	269	2 acute 3 subacute 7 chronic 1 trial – not specified
Wu 2006[108]	Acupuncture	5 RCT	368	chronic
Zhang 2005[109]	Acupuncture	14 RCT	1208	acute

Abbreviations: BA=Before After study, CaCo=Case control study, CCT=Controlled clinical trial; CO=Crossover trials; CR=Case report; CRS=Cross sectional study; CS=Case series; m=months; EMG=electromyography; MBD=Multiple baseline design; NA=not applicable; NR=not reported; OS=Observational study; PR=Prospective study; PreP=Pre-post study; QRCT=quasi-randomized clinical trial; QE=quasi-experimental study; RCT=randomized controlled trial; SR=Systematic review; t=time

Table 2. Summary of systematic review interventions and acuity of stroke populations (continued)

	Intervention	Types of Studies	Total Number Subjects	Stroke Acuity Acute (t≤ m), Subacute (3m<t≤6m), Chronic (t>6m)
Non-Cochrane Reviews				
Ada 2006[91]	Strengthening interventions (i.e. biofeedback, electrical stimulation, muscle re-education, progressive resistance exercise, and mental practice)	21 RCT/CCT	768	10 acute 1 subacute 10 chronic
Bjorklund 2006[110]	Constraint-induced therapy	11 mixed	179	2 acute 2 subacute 2 subacute/chronic 5 chronic
Bonaiuti 2007[111]	Constraint-induced therapy	9 RCT	243	1 acute 3 subacute 5 chronic
Braun 2006[16]	Mental practice	4 RCT 1 CCT 2 CS 3 CR	121	2 acute 4 subacute 4 chronic
Carson 2005[112]	Hyperbaric oxygen therapy	4 RCT 1 CCT 17 OS	2108	6 acute 2 subacute 3 chronic 3 mixed (2-172m post stroke) 8 not specified
de Kroon 2005[113]	Electrical stimulation	12 RCT 2 CCT 2 MBD 3 CS	578	4 acute 2 subacute 10 chronic 3 mixed acuity
Dumoulin 2005[88]	Behavioural therapies in treating urinary incontinence	4 RCT 1 PR 3 Guidelines	185	chronic
Hakkennes 2005[92]	Constraint-induced movement	14 RCT 4 SR	292	4 acute 3 subacute 1 subacute/chronic 6 chronic
Henderson 2007[93]	Virtual reality for upper limb motor recovery	2 RCT 1 CR 3 PreP	96	3 acute 3 chronic
Larsen 2006[86]	Early home supported discharge	8 RCT	2216	acute
Lynton 2007[87]	Yoga	3 CR	3	chronic
Pang 2006[94]	Aerobic exercise	7 RCT 2 CCT	585	4 acute 1 subacute 3 chronic 1 mixed acuity

Table 2. Summary of systematic review interventions and acuity of stroke populations (continued)

	Intervention	Types of Studies	Total Number Subjects	Stroke Acuity Acute (t≤ m), Subacute (3m<t≤6m), Chronic (t>6m)
Prange 2006[114]	Robot-aided therapy (robotic devices on hemiparetic arm function)	1 RCT 1 CCT 6 BA	178	1 subacute 7 chronic
Riggs 2007[115]	Visual deficit interventions	11 RCT 3 CCT 15 CS	371	10 acute 3 subacute 4 acute/subacute 3 chronic 7 mixed 2 not reported
Robbins 2006[116]	Functional and transcutaneous electric stimulation	4 CCT 4 BA/CO	161	chronic
Seenan 2007[97]	Organized inpatient (stroke unit) care	11 CRS 6 BA 3 PR 1 QRCT 3 CaCo	125,453	mixed
Stewart 2006[117]	Bilateral movement training	11 RCT	171	subacute and chronic
Urton 2007[89]	Treatment interventions (training) for upper extremity hemiparesis	8 RCT 3 QE	269	1 acute 1 subacute 1 acute/subacute 7 chronic 1 mixed
van Dijk 2005[96]	Augmented feedback on motor function	26 RCT 1 NR	937	8 acute 13 chronic 3 subacute 1 mixed 1 not reported
van Peppen 2006[95]	Visual feedback therapy on postural control	6 RCT 2 CCT	214	acute and subacute (< 20 weeks)

Table 3. Summary of quality assessment using the Oxman and Guyatt[9,10] criteria for systematic reviews

Author (Year)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Overall score (max 18)
Cochrane Reviews										
Ada 2005 [99]	2	2	2	1	2	2**p	2	2	2	17
Bennett 2005[100]	2	2	2	1	2	2**	2	2	2	17
Bowen 2007[101]	2	2	2	1	1	2	2	2	2	16
Brady 2006[13]	2	2	2	1	2	2**	2	2	2	17
Discharge Trialists 2005[85]	1	2	2	1	2	2	2	2	2	16
French 2007[12]	2	2	2	1	2	2	2	2	2	17
Legg 2006[102]	2	2	2	1	2	2	2	2	2	17
Mehrholz 2007[103]	2	2	2	1	2	2**p	2	2	2	17
Moseley 2005[104]	2	2	2	1	2	2**p	2	2	2	17
Nair 2007[105]	2	2	2	1	2	2	2	2	2	17
Pollock 2007[15]	2	2	2	1	2	2	2	2	2	17
Pomeroy 2006[98]	2	2	2	1	2	2	2	2	2	17
StrokeTrialists 2007[14]	1	2	2	1	2	2	2	2	2	16
Thomas 2008[106]	2	2	2	1	2	2**	2	2	2	17
West 2005[90]	2	2	2	1	2	2	2	2	2	17
Woodford 2007[107]	2	2	2	1	2	2	2	2	2	17
Wu 2006[108]	2	2	2	1	2	2	2	2	2	17
Zhang 2005[109]	2	2	2	1	2	2	2	2	2	17
Non-Cochrane Reviews										
Ada 2006[91]	2	2	2	1	2	2**p	2	2	2	17
Bjorklund 2006[110]	2	2	2	1	1	0	2	2	2	14
Bonaiuti 2007[111]	2	1	2	0	2	2	1	1	2	13
Braun 2006[16]	2	2	2	1	2	2**	2	2	2	17
Carson 2005[112]	2	2	2	1	2	2**	2	2	2	17
de Kroon 2005[113]	2	2	2	0	0	0	2	2	1	11
Dumoulin 2005[88]	2	2	2	0	2	2**p	0	0	2	12
Hakkennes 2005[92]	2	2	2	1	2	2**p	2	2	2	17
Henderson 2007[93]	1	2	2	0	2	2**p	2	2	2	15
Larsen 2006[86]	1	0	0	0	0	0	1	1	1	4
Lynton 2007[87]	2	2	1	0	0	0	1	0	2	8
Pang 2006[94]	2	2	2	0	2	2**p	2	2	2	16
Prange 2006[114]	2	2	2	1	2	2**	2	2	2	17
Riggs 2007[115]	1	2	2	0	2	1	0	0	2	10
Robbins 2006[116]	2	2	2	1	2	2**	2	2	2	17
Seenan 2007[97]	1	2	2	1	0	0	2	2	2	11
Stewart 2006[117]	2	2	2	1	2	2**	2	2	2	17
Urton 2007[89]	2	1	2	1	2	2**	0	0	2	12
van Dijk 2005[96]	2	2	2	1	2	2**p	2	2	2	17
van Peppen 2006[95]	2	1	2	1	2	2**p	2	2	2	16

** Used a published checklist for quality assessment; ** p used PEDro

Table 4. Comparison of quality elements of individual studies with the systematic reviews

Author (Year)	Mean Score / Number of Items [Range]	Randomization Reported and Described	Allocation Concealment	Baseline Comparability of Groups	Patients Blinded	Healthcare Provider Blinded	Data Collector Blinded	Outcome Assessor Blinded	Dropouts and Withdrawals / ITT	Reporting Adverse Events	Potential for Contamination or Cointervention
Cochrane Reviews											
Ada, L (2005)[99]	PEDro 5.25 /8 [2-8]	2/4	2/4	2/4	NT	NT	3/4	3/4	2/4 ITT	2/4	NT
Bennett, M (2005)[100]	Schulz criteria NR	1/3	1/3	NT	3/3	1/3	2/3	1/3	2/3	2/3	NT
Bowen, A (2007)[101]	NR	8/12	8/12	NT	NT	NT	NT	7/12	NT	NT	NT
Brady, M (2006)[13]	NHSCRD NR	1/1	1/1	1/1	NT	NT	NT	1/1	NT	NT	NT
Discharge Trialists (2005)[85]	NR	9/11	9/11	NT	NT	NT	NT	9/11	9/11	NT	NT
French, B (2007)[12]	NR	13/14	8/14	NT	1/14	NT	NT	11/14	12/14	4/14	4/14
Legg, L (2006)[102]	NR	8/9	8/9	NT	NT	NT	NT	8/9	4/9 ITT	4/9	NT
Mehrholz, J (2007)[103]	PEDro 7/8 [6-8]	7/8	6/8	6/8	0/8	0/8	NA	3/8	5/8 ITT	4/8	NT
Moseley, A (2005)[104]	PEDro 6/8 [4-8]	12/15	9/15	12/15	0/15	0/15	NA	11/15	3/15 ITT	13/15	NT
Nair, R (2007)[105]	NR	0/2	0/2	2/2	NT	NT	0/2	0/2	NT	NT	NT
Pollock, A (2006)[15]	NR	19/21	16/21	NT	3/21	0/21	13/21	NT	18/21	NT	14/21
Pomeroy, VM (2006)[98]	NR	5/24	5/24	24/24	5/24	2/24	NT	11/24	14/24 ITT	8/24	4/24

Abbreviations: AMCL=Amsterdam-Maastricht Consensus List for quality Assessment; ITT=intention to treat; NR=not reported; NT=Not tested; NA=Not applicable; NHSCRD=National Health Service Centre for Review and Dissemination

Table 4. Comparison of quality elements of individual studies with the systematic reviews (continued)

Author (Year)	Mean Score / Number of Items [Range]	Randomization Reported and Described	Allocation Concealment	Baseline Comparability of Groups	Patients Blinded	Healthcare Provider Blinded	Data Collector Blinded	Outcome Assessor Blinded	Dropouts and Withdrawals / ITT	Reporting Adverse Events	Potential for Contamination or Cointervention
StrokeTrialists' (2007)[14]	NR	16/31	17/31	NT	NT	NT	NT	10/31	7/31	22/31	24/31
Thomas, L (2008)[106]	NR	12/12	3/12	NT	1/12	1/12	NT	NT	4/12ITT	NT	NT
West,C (2005)[90]	NR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Woodford, H (2007)[107]	NR	1/13	1/13	NT	NT	NT	NT	13/13	2/13	0/13	NT
Wu, H (2006)[108]	NR	0/5	0/5	NT	1/5	NT	NT	NT	0/5	0/5	NT
Zhang, S (2005)[109]	NR	8/14	5/14	NT	3/14	NT	NT	6/14	4/14 ITT	9/14	NT
Non-Cochrane Reviews											
Ada, L (2006)[91]	PEDro 4.7/8 [2-8]	20/21	8/21	2/5	0/21	0/21	NT	8/21	3/21 ITT	NT	NT
Bjorklund, A (2006)[110]	NR	6/11	NT	NT	NT	NT	NT	NT	NT	NT	NT
Bonaiuti,D (2007)[111]	Van Tulder criteria [5-10]/19	9/9	NR	NT	0/9	0/9	NR	NR	1/9 ITT	NR	NT
Braun, S (2006)[16]	AMCL 5.1/11 [2.5-7]	4/10	3/10	2/10	1/10	1/10	3/10	NT	0/10	NT	4/5
Carson, S (2005)[112]	NR	0/22	1/22	NT	2/22	0/22	NT	1/22	1/22 ITT	12/22	NT
de Kroon, J (2005)[113]	NR	12/19	NT	7/19	NT	NT	NT	NT	NT	NT	NT
Dumoulin, C (2005)[88]	PEDro 5.5/10 [5-6]	4/8	NT	NT	NT	NT	NT	NT	NT	NT	NT

Table 4. Comparison of quality elements of individual studies with the systematic reviews (continued)

Author (Year)	Mean Score / Number of Items [Range]	Randomization Reported and Described	Allocation Concealment	Baseline Comparability of Groups	Patients Blinded	Healthcare Provider Blinded	Data Collector Blinded	Outcome Assessor Blinded	Dropouts and Withdrawals / ITT	Reporting Adverse Events	Potential for Contamination or Cointervention
Hakkennes, S (2005)[92]	PEDro 5/10 [3-7]	13/14	2/14	10/14	0/14	0/14	NT	10/14	4/14 ITT	2/14	NT
Henderson, A (2007)[93]	PEDro 5.5/10 [3-8]	1/6	1/6	2/6	0/6	0/6	NT	1/6	NT	NT	NT
Larsen,T (2006)[86]	NR	NR	NR	7/7	NR	NR	NR	NR	7/7	7/7	NT
Lynton, H (2007)[87]	NR	NA	NA	NT	NA	NA	NA	NA	NA	NA	NA
Pang, M (2006)[94]	PEDro 6.1/10 [4-8]	7/9	3/9	7/9	0/9	0/9	NT	5/9	4/9 ITT	2/9	NT
Prange, M (2006)[114]	Van Tulder Scale 12.75/19 [8-16]	NR	NR	NT	NR	NR	NR	NR	NR	0/8	NR
Riggs, R (2007)[115]	Class evidence NR	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Robbins, S (2006)[116]	Downs and Black checklist 15/32 [13-17]	2/8	NT	0/8	0/8	0/8	0/8	0/8	NT	NT	NT
Seenan, P (2007)[97]	NR	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Stewart, K (2006)[117]	Based on Jadad criteria	9/11	NT	NT	9/11	0/11	0/11	0/11	3/11	NT	NT

Table 4. Comparison of quality elements of individual studies with the systematic reviews (continued)

Author (Year)	Mean Score / Number of Items [Range]	Randomization Reported and Described	Allocation Concealment	Baseline Comparability of Groups	Patients Blinded	Healthcare Provider Blinded	Data Collector Blinded	Outcome Assessor Blinded	Dropouts and Withdrawals / ITT	Reporting Adverse Events	Potential for Contamination or Cointervention
Urton, M (2007)[89]	Sacketts levels [I-V]	8/11	NT	NT	NT	NT	NT	5/11	8/11 ITT	NT	NT
van Dijk, H (2005)[96]	PEDro 4.5/9 [3-7]	NT	3/26	20/26	4/26	0/26	NA	15/26	0/26 ITT	NT	NT
van Peppen, R (2006)[95]	PEDro 4/10 [3-6]	0/8	0/8	NT	0/8	0/8	1/8	1/8	0/8	NT	NT

Systematic Reviews of Outcomes in Stroke Patients

Characteristics of the Reviews

Three systematic reviews[3,4,6] evaluating outcomes within stroke populations were identified through the literature search. Two additional systematic reviews[5,17] were identified from searching the references lists of these reviews. One of these reviews,[5] published in 1998, was added for two reasons, namely the historical value and because this review had a broader scope in the studies it reviewed relative to the other subsequent systematic reviews. Table 5 details the search parameters, search and eligibility criteria, results, and recommendations within these four systematic reviews of outcomes used in stroke patients.

All reviews evaluated English language publications only (one of these reviews[6] had a criterion that all outcomes had to have an English translation). Two reviews[3,5] included studies from 1966 to mid to late 1990s; one review[17] included studies from 1985 to 1998. The remaining two systematic reviews[4,6] included studies from 1990 up to and including 2005.

Types of Outcomes Evaluated and Findings

All reviews attempted to evaluate the range of outcomes used, the frequency of their use, and the breadth of content (classification within theoretical frameworks) (Table 5). One review[3] selected studies that included only acute stroke subjects who were receiving drug therapy. Two reviews[4,17] evaluated studies specific to health related quality of life (HRQoL) outcomes, while another review[6] evaluated only studies with outcomes pertaining to walking ability. Two reviews[3,5] evaluated studies in acute stroke patients, two reviews[4,6] stroke patients in all phases of recovery, and one review[17] did not specify. A distinction between the reviews published earlier and those published in 2007, is the difference in the theoretical frameworks used to classify the content of the instruments evaluated. The later publications use the current ICF classification (1990)[4,6] and the earlier publications an earlier (1980) categorization (including impairment, disability and handicap).[3,5,17]

The difference in frameworks used to classify the attributes of the outcomes, is also reflected in the types of recommendations elicited from these reviews. All the reviews generally conclude that there are a variety of outcomes used to measure the same attributes of interest. All review authors recommend the selection of outcome measures that have established psychometric properties (reliable, valid, and responsive). In addition, floor and ceiling effects (where scores are extremely high or very low making it difficult to detect changes over time), as well as practical administration issues, should be considered when selecting outcomes.[4] In general, the reviews appear to suggest that no measure is able to capture the breadth of the domains that they are attempting to capture and as such the recommendation is to include other measures that capture other domains (e.g., activity level and not just impairment).[5] Similarly, there is the recommendation to use more than one outcome measure in order to capture all attributes within the domain of interest (for example walking ability); however, there was some acknowledgement that consensus has not yet been achieved to define the concepts that should be captured to most accurately reflect the range of some aspects of function (such as walking).[6]

Only one review[3] evaluated the time-points selected for evaluating final outcomes in stroke patients (for example, 3 or 6 months post-treatment). In this review based on 51 studies, evaluating the use of drugs in acute stroke, the majority of studies evaluated patients at 3 months

and none exceeded 1 year. Two reviews[3,5] described the statistical methods used to evaluate rehabilitation effects; the findings of both reviews would suggest that there is a need to establish the degree of change that is considered to be clinical significant and that there appropriate statistical analyses be undertaken within future studies.

Summary of Systematic Reviews of Outcome Measures in Stroke

The systematic reviews of the outcome measures used in studies with stroke patients would indicate the following:

1) A variety of outcomes have been used to measure the same attributes of interest within studies of rehabilitation interventions in persons with stroke.
2) Currently, no single outcome measure captures all relevant dimensions of important attributes of interest to stroke patients and clinicians. This implies that measures that capture these multiple domains be included. Whether a single measure captures more than a one dimension (for example body function and activity and participation) or whether several measures are used to capture the dimension is less critical than ensuring that all domains are captured.
3) All dimensions of an outcome of interest should be evaluated. For example, if walking ability is of interest, then walking in all life conditions (including walking within the home, outside the home in uneven ground, and in changing weather conditions) should be evaluated.
4) Future studies evaluating rehabilitation therapies in stroke patients should select outcome measures that have established psychometric properties in stroke (reliable, valid, and responsive)
5) Floor and ceiling effects, as well as practical administration issues, should be considered when selecting outcomes.
6) The timing of outcome measurement should be justified, with some consideration of the natural history of stroke recovery.

Table 5. Summary of characteristics and findings of reviews evaluating outcomes in stroke patients

Systematic Review	Purpose Search Eligibility Criteria	Outcomes Classification Framework	Results	Recommendations
Roberts 1998[5]	**Purpose:** To assess the appropriateness of outcomes used to measure acute stroke trials in terms of types of outcomes, whether these were assessed blindly, their validity and reliability, and the method of analysis **Search:** Root to 1996 Cochrane Stroke Trial Registry MEDLINE® **Study Eligibility:** English only RCT Acute stroke (rehab commenced within 30 days of stroke)	**Included:** Clinical outcomes **Excluded:** Non-clinical outcomes (for example biochemical outcomes) **Framework:** Based on 1980 ICF classification (impairment, disability, handicap)	174 trials were eligible Most studies did not specify primary and secondary outcomes Most studies used impairment measures (76%) [disability 42% and handicap 2%] The percent of studies using valid and reliable outcomes were as follows: Impairment (35%) Disability (76%) Handicap (25%) For those studies using measures of disability, only 70% used valid and reliable measures; for studies evaluating handicap, only 25% used valid and reliable measures	1) Measure both impairment and disability (the latter being most meaningful to patients) 2) Use measures that are shown to be valid and reliable. 3) Assessment of outcomes should be blinded 4) Appropriate statistics (and methods of categorizing) should be used

Abbreviations: BOSS=Burden of Stroke Scale; EQ-5D=European Quality of Life Instrument; HRQoL=health-related quality of life; HS-Quale=Quality of Life Instrument for Young Hemmorhagic Stroke Patients; ICF=international classification of functioning; LHS=London Handicap Scale; NHP=Nottingham Health Profile; QLI-SV=Quality of Life Index-Stroke Version; RCT=randomized controlled trial; RNL=Reintegration to Normal Living Index; SAQoL=Stroke and Aphasia Quality of Life Scale; SA-SIP30=Stroke Adapted Sickness Impact Profile-30; SF36=Medical Outcomes Study 36-item short form health survey; SIP=Sickness impact profile; SIS=Stroke Impact Scale; SSQoL=Stroke Specific Quality of Life

Table 5. Summary of characteristics and findings of reviews evaluating outcomes in stroke patients (continued)

Systematic Review	Purpose Search Eligibility Criteria	Outcomes Classification Framework	Results	Recommendations
Duncan 2000[3]	**Purpose:** 1) To evaluate the use and timing of outcome measures in drug trials 2) How the use of outcomes is complicated by the natural history of stroke 3) Make recommendations on how to choose measures for drug trials **Search:** 1980 forward (end date not specified) English only Cochrane Stroke Trial Registry MEDLINE® Reference Lists **Study Eligibility:** Phase II and Phase III RCT of pharmacological interventions in the acute phase of stroke	**Included:** No restrictions **Excluded:** Not specified **Framework:** Based on 1980 ICF model used by Roberts 1998[5]	51 studies were eligible 29 of these specifically defined the measure and time frames The majority of instruments selected were reliable and valid Time point for evaluation varied but 3 months was the most frequently selected timepoint The cutpoints indicating “improvement” or favorable response was also variable (usually chosen for arbitrary reasons) often for the same outcomes. This is a reflection of the lack of consistency in defining clinically meaningful changes	1) Primary outcomes should be at the level of activities (to include instrumental ADL and advanced mobility 2) Impairment outcomes should be included to assess whether the drug has affected neurological recovery 3) Assessment of individual emotion should be considered 4) All outcome measures should have established psychometric properties (reliable, valid, sensitive to change) 5) Definition of recovery should not be dichotomized but rather should assess shifts in disability by use of non-parametric statistics 6) Primary outcomes should be assessed at 6 months (especially in severe stroke) to take into account spontaneous recovery (that can occur at 5 or 6 months) 7) Data collection should include baseline characteristics that confound outcomes 8) Stroke specific outcomes that capture domains within the ICF should be used

Table 5. Summary of characteristics and findings of reviews evaluating outcomes in stroke patients (continued)

Systematic Review	Purpose Search Eligibility Criteria	Outcomes Classification Framework	Results	Recommendations
Golomb 2001[17]	**Purpose:** To evaluate HRQoL measures for use with stroke patients with respect to a) coverage of important HRQoL domains that may be related to stroke, b) have administration characteristics suitable for stroke, and c) have undergone reliability and validity assessment in stroke patients **Search:** 1985 to 1998 English only MEDLINE® Excerpta Medica PsychINFO® Mental Health Abstracts **Study Eligibility:** No study design restriction provided individual level data on stroke	**Included:** No restrictions **Excluded:** Not specified **Framework:** Not specified	Identified 32 different outcome measures -physical functioning (n=8) -emotional well-being (n=14) -generic multiple domain (n=10) -stroke specific (n=1) Many measures had not been assessed or validated in stroke specific populations Almost all measures have extremely limited information on responsiveness No existing measure covers all domains of HRQoL that may be relevant for stroke patients	1) Recommend the development of stroke specific measures of HRQoL 2) Future work should validate measures currently used within the stroke population

Table 5. Summary of characteristics and findings of reviews evaluating outcomes in stroke patients (continued)

Systematic Review	Purpose Search Eligibility Criteria	Outcomes Classification Framework	Results	Recommendations
Geyh 2007[4]	**Purpose:** 1) To identify current generic and condition-specific HRQoL measures applied in stroke patients 2) to examine the contents of the measures based on linkages to the ICF 3) To compare contents of the generic and stroke specific HRQoL measures **Search:** 1990 to 2004 English only MEDLINE® EMBASE® PsychINfo® **Study Eligibility:** No study design restriction (except case series and economic evaluations) and psychometric studies of relevant outcomes All phases of stroke recovery	**Included:** No restrictions specified Selected the most frequent generic and five most frequent stroke specific HRQoL measures for content comparison **Framework:** ICF classification	71 studies were eligible and within these 23 different HRQoL measures were used Selected 7 stroke specific instruments (SIS, SSQoL, SAQoL, QLI-SV, SA-SIP30, BOSS, HS-Quale) and six generic instruments (SF36, RNL, SIP, EQ-5D, LHS, NHP) for content analysis 979 ICF concepts were identified within the 13 instruments evaluated Stroke specific outcomes more often address mental functions, while the generic instruments often include environmental factors (i.e. assistive devices, or support) Generic instruments tend to address pain, independence and family relations more often reflecting the burden of the disease; stroke specific measures tend to address walking, speaking, energy, etc, reflecting the direct impact of the stroke on the individual's daily life For 13 outcomes evaluated the content density, content diversity and bandwidth of content coverage has been established	1) The purpose, patients and setting, and resources should be considered when selecting a HRQoL outcome measure in stroke patients 2) Suitability of a HRQoL outcome measure must consider the psychometric properties and feasibility of administration 3) A core ICF set has been established for Stroke (developed with the WHO) and can be used to determine what should be measured in studies on stroke patients. This core set can be compared with the content analysis on any outcome being considered

Table 5. Summary of characteristics and findings of reviews evaluating outcomes in stroke patients (continued)

Systematic Review	Purpose Search Eligibility Criteria	Outcomes Classification Framework	Results	Recommendations
Mudge 2007[b]	**Purpose:** 1) To determine the range of outcomes currently used in stroke that include an assessment of an aspect of walking ability 2) To estimate the researcher acceptance of different measures by calculating the frequency of use in the published literature over the last 15 years 3) To determine the breadth of content of walking assessment with respect to the ICF subclassification **Search:** 1990 to 2005 MEDLINE® CINAHL® EMBASE® PsychINFO® **Study Eligibility:** No study design restriction (including outcome measure development studies) except case series. All phases of stroke recovery	**Included:** To include at least one component of walking ability according to ICF (not focused on measuring mobility) The outcome was to have published psychometric properties **Excluded:** Outcome had to have a version in English **Framework:** ICF classification	357 studies were eligible (65 RCT, 65 prospective cohorts, 6 retrospective, 109 psychometric properties of developmental studies, and 112 experimental studies) identified 61 different outcomes Included acute, sub-acute and unspecified timeframe stroke populations The most frequently used measures of walking ability, self-paced walking speed, spatiotemporal parameters and fast gait speed, only measure one aspect of walking ability Measures that included greater breadth in capturing walking ability are less frequently used Although researchers tended to select more than one walking ability outcome, mobility tasks related to the community were not well represented in the majority of outcome measures and studies	1) Measures of walking ability should represent the breadth of walking ability (include activities that also includes more complex walking, such as around obstacles, and on uneven surfaces or in the community) 2) There is a need for researchers and clinicians to define the most useful concepts that should be captured to more accurately reflect the range of walking ability 3) Further research is required to determine whether the combination of self-report and activity monitor (i.e pedometers, etc.) can minimize some of the limitations of self report questionnaires

Chapter 4. Discussion

The overarching aim of this technology assessment is to provide background material for a Center for Medicare and Medicaid Services (CMS) Evidence Forum and Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting to inform policy on the evaluation of innovative training approaches in stroke rehabilitation. This technology assessment contains descriptions of key methodological issues in studies designed to assess rehabilitation therapies. The focus of the technology assessment is not on the efficacy of specific therapies, but rather on the methodological strengths and weaknesses of the studies undertaken to assess the efficacy of stroke rehabilitation therapies. To this end, we evaluated the methodological quality of both primary studies and systematic reviews.

For the primary studies, we undertook a purposive sampling of English language, comparative studies that were selected according to the outcome domains used to evaluate the therapy. This approach was conducted under the assumption that the therapy being evaluated would have limited impact on the methodological appraisal of the study in question. From our point of view, good study design should be undertaken in any stroke rehabilitation study, regardless of the type of therapy under evaluation. In choosing to delimit studies within our purposive sampling to comparative studies, we considered only randomized controlled trials (RCTs), quasi-randomized, and observational (cohort, case control, cross sectional) designs. This choice reflects studies with significant potential to reduce biases in their evaluations. The purposive sampling did not reflect the degree to which any specific rehabilitation therapy was evaluated using comparative designs versus other designs that are more prone to bias (e.g., case series).

The systematic reviews, like the primary studies within the purposive sampling, were limited to English-language reviews delimited by publication year. Once again, the assumption was that the rehabilitation therapy being evaluated did not affect the methodological issues of interest for the technology assessment. Evaluating the methodological quality of systematic reviews that included mixed study designs may have been disadvantageous (using conventional quality criteria) because many of these reviews included noncomparative studies.

There are a number of biases that can be evaluated within a primary study or systematic review. Depending on the classification system and study design, these biases can number over 200.[118] We limited the evaluation of biases to ones consistent with internal validity (e.g., randomization rather than funding bias), provided they had a broad level of applicability (i.e., selection bias rather than healthcare access bias) and had attributes that were of specific interest to CMS. We acknowledge that there are many more specific biases that were not reported or evaluated in this technology assessment.

Finally, the extent to which we evaluated methodologic criteria within each primary study or systematic review was a function of the adequacy of reporting within each of these publication types. The dilemma always remains that researchers may have adequately undertaken the means to prevent bias, but they did not adequately report these means in the published study manuscript. No attempt on our part was made to contact authors to resolve this dilemma.

The reporting issue also applies to the assessment of the psychometric properties of outcome measurement instruments. We relied on the authors of individual studies in the purposive sample to report that the instruments used in their research were assessed for reliability, validity, and responsiveness to change in stroke populations. We also relied on the published findings of systematic reviews to assess psychometric properties. Study authors, or the authors of review

articles, may not have reported on the psychometric properties of a particular instrument. Consequently, the assessment of psychometric properties in this report cannot be considered definitive. Also, it was not possible, due to the aforementioned approach, to determine whether a link existed between an instrument's psychometric properties and its mode of administration (e.g., self-report, proxy). Ideally, primary studies on the development of each instrument should be consulted to determine the presence of psychometric properties in stroke applications.

Ideal Reporting Standards for Comparative Studies

Recognizing the problem of poor reporting in studies, there are a number of established guidelines designed to encourage clear and transparent reporting of methods and results. The purpose of these guidelines is to permit a critical appraisal of the methods used in any study. In February 2008, the Consolidated Standards for Reporting Trials (CONSORT) amended their 22-item checklist for reporting RCTs. The amendments take into account new methodologic research and the related reporting requirements. The original reporting criteria (e.g., randomization, blinding, and withdrawals) were adapted or extended if necessary.

In the revised CONSORT guidelines, amendments were undertaken to address specific areas where more detail was required to evaluate the potential for bias in nonpharmacologic interventions such as surgery, rehabilitation, physiotherapy, or behavioral therapy.[119,120] Amendments included improved descriptions of the complexity of the intervention, the training and expertise of the care provider, and difficulties related to blinding.

The CONSORT statement identifies changes in the description of the non-pharmacologic intervention, adding three new criteria and modifying the existing two. The CONSORT statement recommends that there is "precise" description of the experimental and comparator interventions such that:

1. The different components of the intervention are detailed (particularly when interventions are tailored to individuals);
2. The manner in which interventions are standardized;
3. How adherence of the care providers to the protocol was assessed or enhanced;
4. A detailed description of the of the exact manner in which the treatment and comparator interventions were implemented;
5. With regards to the caregivers (and treatment centers), the CONSORT statement recommends adequate reporting such that:
    a. The care providers or centers be described (case volume, qualification, expertise, etc.) in each group;
    b. The number of care providers or centers performing the interventions in each group and the number of patients treated by each care provider, or in each center be shown in the flow diagram; and
    c. Eligibility criteria for those performing the interventions be described.

With regards to blinding, the new recommendations concern the reporting of the masking status of persons administering cointerventions. The reporting of the blind status of the patient, the provider, and the outcomes assessor continues to be recommended. Finally, the amended CONSORT statement requires that the interpretation of study findings take into account the choice of comparator, lack of partial blinding, and unequal expertise of care providers or centers in each intervention group. Moreover, discussions about the generalizability of the study's findings should consider the choice of the comparator and the care providers (and centers) in

addition to the patients. The complete requirements for reporting on clinical trials are described elsewhere.[119,120]

As noted previously, in stroke rehabilitation, the customized, multifactorial approach to treatment often makes RCTs an impractical means of assessing a specific therapy.[41] RCTs are more suited to situations where a unimodal therapeutic regimen (e.g., one single drug or its comparator) is given to patients. As such, we included observational studies with cohort, case control, or cross sectional designs. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement makes reporting recommendations for such study designs.[121,122] The STROBE statement indicates that the outcomes, exposure, predictors, confounders, and effect modifiers should be clearly defined. In the context of rehabilitation therapy, this would include the therapies administered and other concomitant treatments. Detail regarding the care providers is not specified within the STROBE reporting recommendations. However, the nature of professionally delivered stroke rehabilitation therapies suggests that such details should be reported in the case of studies designed to evaluate rehabilitation interventions. The STROBE does recommend an explanation of sample size. Such an explanation would be of benefit in clinical trials as well.

Both the extended CONSORT and STROBE statements provide clear recommendations for reporting in studies that are designed to evaluate new and innovative stroke rehabilitation therapies. Adherence to these reporting recommendations would lead to a clear and transparent understanding of the research undertaken and allow for adequate critical appraisal of methods.

Finally, it should be recognized that the potential for bias in studies continues to exist even if there is adherence to the reporting standards of CONSORT or STROBE. A comparator therapy, for example, can be well described, but the content and dose of the intervention be biased such that the treatment group may appear to have a substantive relative effect. Some justification for the types of comparators, even if well described, would be required.

Study Design Challenges in Stroke Rehabilitation Therapy

There are many challenges inherent in designing studies to evaluate stroke rehabilitation therapies. One such challenge is deciding on a viable comparator. The issue is that the choice of the comparator could influence the observed treatment effect. Choices for a comparator group include a placebo, usual care, another active treatment, or no treatment (e.g., a wait list). If the choice is 'no treatment', the intervention has a greater likelihood to be shown to be effective. In interpreting this type of study, the question is whether 'no treatment' reflects reality in the clinical world. In many rehabilitation situations, clients are receiving some kind of treatment. To evaluate a new intervention, there should be a comparator reflecting usual care or another active treatment. In these trials, the details of both the intervention and comparator are essential to assess the internal and external validity of the study and ultimately decide whether the intervention should be implemented for the targeted client group.

The details about the experimental and control interventions should include information on the intended intervention and the actual intervention that was administered in both groups. The descriptions about the intended experimental and comparator (control) interventions need to include the theoretical basis for choosing the interventions, the characteristics of the care providers, and the timing, intensity, and planned modifications in relation to client characteristics. The theoretical rationale is particularly important for the experimental intervention. Similar to pharmacological research, where the mechanism of action of the drug is

the basis for the research, the theoretical basis in rehabilitation research is essential for designing and understanding the principles of the intervention.[123] In particular, when multimodal therapies are administered, there are many possible explanations within the administered treatment that may account for the changes; a testable hypothesis would assist in disentangling the 'active' ingredient within the administered treatments. Moreover, rehabilitation therapies are often intended to address a wide variety of stroke-related impairment and disability problems, so a number of theories may need to be explicated.[123]

Although there is currently no consensus regarding definitions of acute, subacute, and chronic, with respect to time intervals, consideration should be given to the recovery changes that will occur following the stroke. Phases of recovery have been documented following stroke, and would suggest that the rate of spontaneous recovery of motor function is greater in the earlier time period post stroke and less at later points.[124] Although, spontaneous recovery occurs less as the time interval from onset increases, there is good evidence that the neuroplasticity of the brain, is still responsive to practice-induced plasticity.[124] This has implications for the onset and intensity of rehabilitation and possibly the duration of treatment. Additionally, it suggests that changes in therapy should be measured "serially" rather than being restricted to outcome assessment at baseline and endpoint. Researchers should therefore attempt to provide a rationale in the context of stroke recovery trajectory for the intensity and timing of their interventions, as well as the frequency and timing of the outcome assessments.

The role of the care provider is often pivotal in stroke rehabilitation interventions. The expertise of care providers needs to be described by providing information about professional qualifications, years in practice, and training in preparation for the study. The information about the intervention needs to include how the care provider interacts with the clients, the components of the intervention, the timing and intensity (how much, how often, when), and the expectations of effect on the client (level of participation, homework expectations). Patient engagement and motivation is a key factor that may affect the effectiveness of the rehabilitation therapy. There are a variety of methods that can be employed (e.g., self-efficacy techniques) to produce adequate or at least greater engagement. These methods are context dependent and, as such, some means of describing this may also be warranted in future evaluations of therapies. There is also the potential for 'care provider' effects, where the level of enthusiasm or the unique attributes of the care provider may account for some of the variation in treatment. Awareness and potential monitoring of these care provider effects is therefore warranted.

There needs to be information about how the intervention has been standardized, including care provider training and how the intervention will be monitored to ensure standard administration. This can be challenging in the context of some therapies, where some treatments may be individualized. In essence, the 'treatment' being evaluated is actually an algorithm of possible interventions that a therapist may individualize to a particular patient (e.g., being assigned to one of several possible treatments in the community to prevent falls). In the reporting of results (what actually happened), there needs to be detail about the actual administration of the intervention, including information about the care providers' compliance with the intervention and the content, quality, and quantity received by the clients. In some study designs, where the comparator is usual care, the intervention is not described, but information needs to be documented about all aspects of the "normal" care and reported in the results. Rehabilitation treatments very often involve interaction with the external environment, such as training in a bathroom or kitchen. A description of the environment may also be important in these cases.[123] Similarly, in rehabilitation, a number of services are delivered to

stroke clients (e.g., acute inpatient stroke rehabilitation) and the 'system' or center within which they are delivered may also need to be described and understood. The intensity within each component of the service and the intensity of each service may be complex to describe and monitor.

Finally, heterogeneity within the stroke population should be considered. In addition to the variability of the type of stroke, there are a variety of other factors (such as comorbid conditions, age, social situation, etc.,) that contribute to this heterogeneity. Studies should adequately document these factors and explore their impact on stroke outcome responses to treatment. In other areas of health, there is a move towards identifying subgroups that show the greatest improvement following treatment. Exploring the characteristics of those who demonstrate a strong response to treatment will assist in matching the optimal therapies to maximize subsequent recovery.

Methodological Issues from the Purposive Sampling

The majority of the abstracted studies were RCTs. Almost all of the published RCT manuscripts contained reports of randomization, but the in-depth review of two specific studies in each outcome domain showed that the reporting of randomization was inconsistent. The authors of some studies described the process of randomization (e.g., computer generated), while others reported the type of randomization (e.g., block). Reporting on the details of study samples was more consistent. Most of the authors described the source of their samples, the inclusion/exclusion criteria, and basic sample characteristics such as age and sex. Almost all RCTs contained a table showing comparisons of subjects in different treatment groups.

Approximately 75 percent of the abstracted RCTs contained a mention of blinding. However, the figure was only 50 percent for the cognition domain. The in-depth review of individual studies showed that blinding was difficult because of clearly identifiable differences in the interventions. Many authors were cognizant of the difficulties of blinding in stroke rehabilitation and they designed their studies so that patients and therapists were unaware of the hypotheses being tested; therapists in some studies were restricted to delivering only one of the treatments. Blinding was possible for the persons assessing outcomes, and many authors reported that their assessors were in fact blinded to treatment allocation.

Many of the treatments could only be delivered by a trained professional. Usually these persons were physical, occupational, or speech therapists, although sometimes nurses with training in specific procedures were also used to deliver interventions. About 75 percent of study authors reported the use of trained professionals to deliver interventions. Usually this reporting was a simple mention of the type of professional required (e.g., "speech therapist"); details of background and training were typically not provided in the published manuscripts.

The details of the interventions were clearly described in almost all of the studies. Many interventions were compared against a closely related derivative rather than standard practice. Many authors reported the frequency of the interventions (e.g., number of sessions) and the overall duration of therapy (except in the dysphagia domain, where only half of the authors reported this information). The in-depth review of specific studies suggested that much of the lack of reporting was likely due to space restrictions in journals. These restrictions prevented many authors from describing detailed treatment protocols. Authors tended to report the average number of sessions and the average duration of therapy for subjects in their studies.

Length of followup varied widely in the abstracted studies. Most followup periods fell within a short-term band of 1 to 12 months. In the in-depth review of specific studies, followup periods ranged from a few weeks to one year in studies of quality of life (QoL), activities of daily living (ADL), cognition, and speech. For ambulation and dysphagia, followups ranged from a few weeks to approximately 6 months.

The reporting of comorbidity and concomitant treatment was quite poor across all domains. Less than half of the abstracted studies contained reports of prior or concomitant treatment.

The psychometric properties of a majority of the instruments used in the studies obtained for the purposive sampling portion of the review were not reported, either in the studies themselves or in the review articles. In the case of the more frequently used instruments, reliability and validity had usually been proven to exist in stroke patient populations. Many of these instruments also had responsiveness to change demonstrated in stroke. Problem areas involved the minimal clinically important difference (MCID), study specific measures, and the communication and dysphagia domains. Virtually no information could be found on the MCID for any outcome measure. This can be problematic because differences between groups of study subjects on a scale score might be found to be statistically significant, but not clinically significant. Future research should consider the development of MCIDs for important instruments in stroke rehabilitation. Many outcome measures seemed to be instruments that were developed for a specific study. Some such instruments were questionnaires and others were clinical tests involving timed activities. No matter how intuitively appealing such instruments may appear they should not be assumed to be appropriate for use in stroke patients. Every instrument must first have its psychometric properties tested in stroke patients prior to use in the field of stroke rehabilitation. In the communication and dysphagia domains, there was no information on the psychometric properties of any of the outcome measurement instruments used in the purposive sampling studies. Again, psychometric properties should be assessed prior to the use of any instrument.

In the 12 studies (two per domain) that were subject to in-depth review, outcomes were generally measured using scales. Some dysphagia outcomes were measured clinically. For many of the scales, the psychometric properties were not tested in the stroke rehabilitation population.

Commentary – In-depth review of two studies per domain. The large number of RCTs, and the explicit attempts to describe randomization and blinding in some of the published trial reports, suggests that many researchers in stroke rehabilitation seek to implement the principles of high quality research design and evidence-based practice (EBP). However, several consistent themes emerged from the purposive sampling exercise and suggested potential areas of improvement for future studies in stroke rehabilitation. A few RCTs enrolled and randomized less than 10 subjects in total. The ability to draw any meaningful efficacy conclusions from such small studies is severely compromised by the obvious lack of power to detect effects and the high possibility of random sample error. Power is the probability of detecting a true effect in a study. Studies with larger sample sizes have higher power. Authors should enrol large enough samples to detect clinically significant effects, not just statistically significant effects. Authors should also be explicit in the methods with respect to their sample size calculations. Specifically, they should provide the MCID and justify their selection of such a difference. Few of the authors of the abstracted studies provided or justified a particular MCID. This may not inhibit the possibility of finding statistically significant results, but does not allow for the assessment of clinical significance.

Based on the published trial reports, there were no consistent errors that threatened the internal validity of the abstracted studies. Some studies were methodologically weak in certain areas, while other studies were weak in other areas. Descriptions of blinded assessors and the randomization process suggest that some authors made attempts to minimize bias and confounding. However, many authors reported only rudimentary patient data, which were often limited to a few variables such as age, sex, and education. Comorbidity and concomitant treatments were often not reported. In an RCT with proper randomization, this is less of a concern because the randomization should create comparable treatment groups, thus cancelling the effect of any confounding due to comorbidity and concomitant treatment. In observational studies, though, confounding could occur if the treatment groups differ on these (or other) characteristics. Therefore, it is especially important for the authors of observational studies to present the details of all possible confounders when they report sample characteristics. In this way, the readers of the studies will be able to assess whether the study groups are comparable to one another.

Notwithstanding the issue of confounding in RCTs versus observational studies, the authors of RCTs should also provide a complete description of the study sample. This lends itself to establishing generalizability. Strict inclusion and exclusion criteria in many RCTs exclude persons with common comorbidities and concomitant treatments. Full disclosure of sample characteristics is required so that readers of trial reports can assess whether the subjects in an RCT are representative of a particular group of patients. If they are not representative, then the findings of the RCT may not be applicable to that particular group.

Length of followup also requires careful consideration in future studies of stroke rehabilitation therapies. Improvements to cognition and communication may take months, even years, so studies should be long enough to assess these outcomes. In the abstracted studies under the cognitive domain, followup generally lasted for less than 1 year. Under speech, two studies had 5 year followups and the remainder had followups of 1 year or less. For studies in the other domains, followup lasted for periods of days to months (12 months typically maximum). For ambulation, short followups are generally adequate due to the relatively rapid recovery periods for motor function and gait. Followups for QoL are less amenable to precise time specification because QoL itself involves a subjective component that may be independent of improvement in any one domain. For example, patients with long-term stroke-related disabilities may have accepted and adjusted to their conditions. Consequently, they may rate their QoL higher than patients with less severe disabilities. Ideally, QoL should be measured at the same time points as the primary outcome. ADLs, like cognition, can improve over time. This would suggest medium- to long-term followup. In the abstracted ADL studies, followup times averaged 12 months or less. The dysphagia studies tended to focus on interventions that would allow patients to begin adapting to swallowing problems, rather than on interventions that would correct the problems. Therefore, the dysphagia studies typically lasted for periods of weeks, which was long enough to assess whether the interventions would help patients adapt.

The authors of many studies examined a variety of different outcomes. In some studies, one outcome was specified as the primary outcome, while in others there was no named primary outcome. The use of many outcomes reflects the multifaceted nature of both the sequelae of stroke and the impact of the interventions. However, rehabilitation programs and devices are usually designed to make an impact on a narrow band of outcomes, with additional effects on other outcome areas being a ‘spin-off’ of the main impacts. For example, a novel therapeutic technique may be designed to improve speech following stroke. This technique may

concomitantly improve QoL as a patient's ability to communicate improves. The most immediate and therefore primary outcome, though, would be the improvement in speech. Sample size calculations in stroke rehabilitation studies should be based on the primary outcome to ensure that important inter-group differences can be detected in the study.[18,19]

Many of the outcome measurement instruments used in the abstracted studies were not assessed for reliability and validity in persons undergoing stroke rehabilitation. Similarly, there were few assessments for responsiveness to change and MCID in stroke. Researchers should make every attempt to employ outcome measurement instruments that have been validated in stroke patients. It is not sufficient to rely on the most popular instrument without consideration of psychometric properties because an often used, invalid instrument will produce invalid results.

Recent work on linking ICF domains to stroke rehabilitation[20] has produced a 'brief core set' of 18 ICF categories that reflect the spectrum of problems in persons who have suffered a stroke. Other researchers[8] have slotted popular outcome measurement instruments into the various categories of the core set. The ICF core set and slotted instruments can serve as guides to help researchers focus on the most important outcomes in stroke rehabilitation. However, this agreed-upon focus is not a substitute for judgment. Researchers should still select a primary outcome that reflects the major thrust of the therapy in question; specific outcome measures should have good psychometric properties in stroke rehabilitation. It is not sufficient to select from a 'grab-bag' of outcomes and instruments based solely on their appearance on a list.

Methodological Issues From the Review of Reviews

We undertook a review of reviews as an additional means to evaluate the quality of studies within the broad area of stroke rehabilitation. We found a large number of systematic reviews were available even after limiting the publication date to 2005 forward. Additionally, we found that approximately half of these were Cochrane reviews, which suggested that there were a significant number of randomized trials being undertaken in stroke rehabilitation.

In general, the quality of the majority of the systematic reviews was high, scoring greater than 14 on our quality assessment criteria. It was recognized that some methodological flaws within these systematic reviews may be related to incomplete reporting rather than to a lack of rigour in the methods. The quality of the individual studies was generally judged positively within these systematic reviews, but there was great variation in the criteria used to judge the adequacy of the studies evaluated.

The individual trials in stroke rehabilitation, regardless of therapy, for the most part did not have blinded patients or healthcare providers, but did have blinded outcome assessors. Adequate randomization and allocation as well as adequate accounting for all subjects continued to be a problem in many trials. Few of the systematic reviews evaluated the comparability of groups at baseline, the potential for adverse events, or problems with contamination and co-intervention. In this regard, it is difficult to generalize regarding methodological problems within any of the trials being evaluated in a review. These three factors do affect internal validity and would be important to evaluate in future trials within systematic reviews.

When considering the population characteristics being evaluated in the trials, the variation in the study populations evaluated may reflect that some therapies are logically restricted to specific phases of stroke rehabilitation; however there were a fair number of interventions that were directed to all phases of the recovery continuum and the rationale for this was not always adequately presented. When considering the sample sizes within these trials, there was great

variation, but in general they were not large relative to drug trials. As noted previously in the purposive sampling, adequate sample size is related to power and the ability to detect differences amongst groups; this is particularly relevant for studies selecting multiple outcome measures.

The systematic reviews evaluating the use and classification of outcomes used in the treatment of stroke patients were consistent in their recommendations. Although, the evaluation of these outcomes was not restricted to "rehabilitation" studies per se, the conclusions were applicable to this phase of intervention. Most of the reviews on outcomes used in stroke patients, noted that some outcomes frequently used in the studies had not had psychometric properties established for stroke patients. In general, there was some concern with potential difficulties with instruments that are self or interviewer administered questionnaires being applied to stroke patients (due to deficits in cognition and communication). Additionally, at least one review pointed to the timing of outcome assessment, suggesting that the rationale for the interval to measure outcomes during the recovery process was in need of greater refinement (particularly in light of the natural history of stroke recovery). The interval for measuring outcomes also speaks to issues of responsiveness of the instruments relative to when change is likely to occur. The selection of appropriate intervals to evaluate patients is difficult but important to address and justify in future research.

All the systematic reviews on outcome measures in stroke rehabilitation would support the use of overlap across types of measures (generic versus disease specific) and domains covered within the outcomes selected. In the former case, it was clear that no single measure would capture all the important attributes (considering the ICF framework) to evaluate within stroke patients; as such the recommendation was to include multiple outcomes to cover the breadth of functions or alternatively to develop new and more comprehensive measures. The core set of ICF functions proposed[20] would be an initial, universal frame of reference to assist in selecting a minimum set of functions to be considered when selecting outcome measures for evaluating the efficacy of studies. However, there is still some consensus work to be undertaken to determine the level of detail for the specific activities identified. For example, although walking has been identified as a core function important for persons with stroke, it is not clear if only walking indoors (as opposed to walking outdoors) should be evaluated following stroke rehabilitation.

Conclusion

The methodological quality of studies in stroke rehabilitation was reviewed in accordance with the components of the key question. Researchers in the field recognize the benefits of investigating interventions using the RCT design, but the reporting of randomization methods and comparability between groups was lacking in some instances. Blinding is difficult to conduct in stroke rehabilitation studies because the nature of the interventions is obvious to patients and healthcare providers alike. Many researchers in stroke recognize these limitations and try to balance the rigor of adequate blinding and the feasibility of applying the interventions.

Major methodological problems involved sample size and the psychometric properties of outcome measurement instruments. Sample size was sometimes too small to have adequate power to detect meaningful effects. Many authors failed to show sample size calculations or report an MCID. For many of the instruments used to measure outcomes, the psychometric properties in the stroke population were not tested.

The road forward looks positive regarding the methodological quality of studies in stroke rehabilitation. However, despite some high quality research that conforms to the principles of EBP, there is still room for improvement, especially in the areas outlined above.

The review of reviews showed that most systematic reviews were undertaken with adequate rigour and presented the evidence for stroke rehabilitation adequately. Many of the reviews evaluated high level study designs (e.g., randomized trials); however, not all of these trials were conducted in a sufficiently rigorous manner. Most systematic reviews evaluated methodological aspects of the eligible studies with standardized checklist or criteria. The majority of reviews evaluated randomization, blinding, and withdrawals/dropouts. Fewer reviews evaluated baseline comparability, evaluation of adverse events, and co-intervention or contamination. Many reviews indicated that blinding of the patient and the provider was not possible in stroke rehabilitation and as such did not evaluate eligible studies for this criterion. These findings concur with those of the purposive sampling.

Our review of reviews on outcome measures in stroke showed that a variety of outcomes have been used to measure the same attributes of interest within studies of rehabilitation interventions in persons with stroke. Currently, no single outcome measure captures all relevant dimensions of important attributes of interest to patients and clinicians. This implies that multiple measures may need to be included to capture all these important domains. Moreover, there is a need to determine the degree of comprehensiveness required when evaluating some of these outcomes of interest.

All reviews on outcome measures in stroke recommended that future studies evaluating rehabilitation therapies in stroke patients should select outcome measures that have established psychometric properties (reliable, valid, and responsive). Additional consideration should also be given to the potential for floor and ceiling effects and practical administration issues. Moreover, the timing of outcome measurement should be justified, with some consideration of the natural history of stroke recovery. These findings also concur with those of the purposive sampling.

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Acronyms

2MWT	2 meter walk test
5MWT	5 meter walk test
10MWT	10 meter walk test
6-m TWD	6-minute timed walking distance
10-m TWS	10-minute timed walking speed
ABC	Activities-Specific Balance Confidence Scale
ADL	Activities of Daily Living
AHRQ	Agency for Healthcare Research and Quality
AMAT	Arm Motor Ability Test
AMED	Allied and Complementary Medicine Database
AMT	Abbreviated Mental Test
APS	Aspiration-Penetration Scale
ARA	Action Research Arm Test
AS	Ashworth Scale
AT	Augmented therapy
BA	Before after study
BBS	Berg Balance Scale
BI	Barthel Index
BTX	Botulinum toxin type A
BWSTT	Body Weight Supported Treadmill Training
CaCo	Case control study
CCMFTR	Cochrane Complementary Medicine Field Trials Register
CCRCT	Cochrane Central Register of Controlled Trials (CENTRAL)
CCT	Controlled clinical trial
CDSR	Cochrane Database of Systematic Reviews
CGT	Conventional gait training
CIMT	Constraint-induced movement therapy
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CIRRIE	Center for International Rehabilitation Research Information and Exchange
CMS	Center for Medicare and Medicaid Services
CMSA	Chedoke-McMaster Stroke assessment
Co	Control group
CO	Crossover trials
CONSORT	Consolidated Standards for Reporting Trials
COPM	Canadian Occupational Performance Measure
COVS	Clinical Outcome Variable Score
CPI	Clinical Practice Improvement
CR	Case report
CRS	Cross sectional study
CS	Case series
CSGTR	Cochrane Stroke Group Trials Register
CSS	Composite Spasticity Ccore
CT	Computerized tomography
CVA	Cerebral vascular accident

DEXA	Dual-energy x-ray absorptiometry
DM	Diabetes mellitus
EBP	Evidence-Based Practice
EGT	Electromechanical gait training
EGT-FES	Electromechanical gait training (with) functional electric stimulation
EMS	Elderly Mobility Scale
ES	Electrical stimulation
ESUS	Extended stroke unit service
FAC	Functional Ambulation Categories
FAME	Fitness and mobility exercise
FAP	Functional Ambulation Profile
FIM	Functional Independence Measure
FM	Fugl-Meyer
FOIS	Functional Oral Intake Scale
FP	Fucial pillar
GT	Gait trainer
HR	Health related
HRQoL	Health Related Quality of Life
ICF	International Classification of Functioning, Disability and Health
ILAS	Iowa Level of Assistance Scale
IM	Intramuscular
KB-ADL	Klein Bell Activities of Daily Living Scale
LOF	Length of followup
LOS	Length of stay
MAL	Motor Activity Log
mAS	Modified Ashworth Scale
MAS	Motor Assessment Scale
MBD	Multiple baseline design
MBS	Modified Barium Swallow
MCID	Minimal clinically important difference
MD	Medical doctor
MedCAC	Medicare Evidence Development and Coverage Advisory Committee
MI	Motricity Index
MMAS	Modified Motor Assessment Scale
MMSE	Mini-Mental State Examination
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MU-EPC	McMaster University Evidence-based Practice Center
NA	Not applicable
NEADL	Nottingham Extended Activities of Daily Living
NG	Nasogastric
NHP	Nottingham Health Profile
NIH	National Institutes of Health
NIHSS	National Institute of Health Stroke Scale
NMES	Neuromuscular electric stimulation
NR	Not reported

NT	Not tested
OS	Observational study
OSUS	Ordinary stroke unit service
OT	Occupational Therapist
PASIPD	Physical Activity Scale for Individuals with Physical Disabilities
PED	Physiotherapy Evidence Database
PEG	Percutaneous endoscopic gastronomy
PICOT	Population, Intervention, Comparison, Outcome, Time
PR	Prospective study
PreP	Pre-post study
PT	Physical Therapy
PTA/OTA	Physiotherapy or Occupational Therapy Assistant
QE	Quasi-experimental study
QoL	Quality of Life
QRCT	Quasi-randomized clinical trial
RCT	Randomized controlled trial
RMI	Rivermead Mobility Index
ROM	Range of motion
RT	Recreational Therapist
SD	Standard deviation
sEMG	Surface electromyographic
SLP	Speech Language Pathologist
SPMSQ	Short Portable Mental Status Questionnaire
SR	Systematic review
SRM	Standardized Response Mean
SSRD	Single Subject Research Design
SSS	Scandinavian Stroke Scale
ST	Standard therapy
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TEMPA	Test d'Evaluation des Membres superieurs des Personnes Agees
TS	Thermal-tactile stimulation
TT	Traditional therapy
TUG	Timed Up and Go test
UE	Upper extremity
WHO	World Health Organization
WIQ	Walking Impairment Questionnaire
WMFT	Wolf Motor Function Test
yrs	Years

Appendix A. Detailed Search Strategies

Cognition

Cognition CINAHL

1. (letter or editorial or comment).pt.
2. cerebral vascular accident/
3. Rehabilitation, Cognitive/
4. 2 and 3
5. Cognition/
6. exp Cognition Disorders/
7. Dementia, Multi-Infarct/
8. (cognition or cognitive).ti.
9. or/5-8
10. rehabilitation/
11. (rehabilitation or recovery).ti.
12. or/10-11
13. 2 and 9 and 12
14. 13 or 4
15. 14 not 1
16. limit 15 to english
17. limit 16 to yr="2003 - 2007"
18. limit 16 to yr="2000 - 2007"
19. *Cerebral Vascular Accident/rh [Rehabilitation]
20. *cerebral vascular accident/
21. exp *Rehabilitation/
22. 20 and 21
23. 19 or 22
24. (letter or editorial or comment).pt.
25. Cognition/
26. Rehabilitation, Cognitive/
27. exp Cognition Disorders/
28. (cognition or cognitive).ti.
29. or/25-28
30. 23 and 29
31. 30 not 24
32. limit 31 to english
33. limit 32 to yr="2003 - 2007"
34. limit 33 to yr="2000 - 2007"
35. 18 or 34
36. exp Cognition Disorders/rh, th [Rehabilitation, Therapy]
37. Cognitive Therapy/
38. Rehabilitation, Cognitive/
39. or/36-38
40. exp Cognition Disorders/

41. (cognition or cognitive).ti.
42. mental function.ti.
43. exp Cognition/
44. or/40-43
45. exp Rehabilitation/
46. (rehabilitation or recovery).ti,ab.
47. therapy.ti.
48. or/45-47
49. 44 and 48
50. Cerebral Vascular Accident/rh, th [Rehabilitation, Therapy]
51. 50 and 44
52. stroke.ti.
53. (stroke adj (volume or heat)).ti.
54. 52 not 53
55. Cerebral Vascular Accident/
56. or/54-55
57. 39 or 49
58. 57 and 56
59. 58 or 51
60. (letter or editorial or comment).pt.
61. 59 not 60
62. limit 61 to english
63. limit 62 to yr="2000 - 2007"
64. 63 or 35

Cognition Medline

1. Cognitive Therapy/
2. Cognition Disorders/rh [Rehabilitation]
3. (cognition or cognitive).ti.
4. Dementia, Multi-Infarct/
5. or/1-4
6. exp stroke/
7. "Recovery of Function"/
8. exp rehabilitation/
9. "Recovery of Function"/
10. (rehabilitation or recovery).ti,ab.
11. or/7-10
12. 5 and 6 and 11
13. animals/ not (humans/ and animals/)
14. 12 not 13
15. (letter or editorial or comment).pt.
16. 14 not 15
17. limit 16 to english language
18. limit 17 to yr="2003 - 2008"
19. exp Cognition Disorders/rh, th [Rehabilitation, Therapy]

20. Cognitive Therapy/
21. or/19-20
22. Dementia, Multi-Infarct/
23. (cognition or cognitive).ti.
24. cognition disorders/ or auditory perceptual disorders/
25. 22 or 23 or 24
26. "Recovery of Function"/
27. exp rehabilitation/
28. (rehabilitation or recovery).ti,ab.
29. therapy.ti.
30. or/26-29
31. 25 and 30
32. 21 or 31
33. stroke.ti.
34. (stroke adj (volume or heat)).ti.
35. 33 not 34
36. exp stroke/
37. or/35-36
38. 32 and 37
39. animals/ not (humans/ and animals/)
40. 38 not 39
41. (letter or editorial or comment).pt.
42. 40 not 41
43. limit 42 to english language
44. limit 43 to yr="2000 - 2008"
45. 44 or 18

Cognition PsycINFO

1. cerebrovascular accidents/
2. exp neuropsychological rehabilitation/
3. and/1-2
4. limit 3 to human
5. limit 4 to english language
6. limit 5 to yr="2003 - 2008"
7. limit 5 to yr="2000 - 2008"
8. cognitive rehabilitation/ or exp neuropsychological rehabilitation/
9. cognitive therapy/
10. or/8-9
11. (cognition or cognitive).ti.
12. mental function.ti.
13. cognition/ or cognitive impairment/ or exp cognitive processes/
14. or/11-13
15. (rehabilitation or recovery).ti,ab.
16. therapy.ti.
17. rehabilitation/

18. or/15-17
19. 14 and 18
20. 10 or 19
21. stroke.ti.
22. (stroke adj (volume or heat)).ti.
23. 21 not 22
24. cerebrovascular accidents/
25. or/23-24
26. 20 and 25
27. limit 26 to human
28. limit 27 to english language
29. limit 28 to yr="2000 - 2008"
30. 29 or 7

Ambulation

Ambulation_CINAHL

1. *Cerebral Vascular Accident/rh [Rehabilitation]
2. *cerebral vascular accident/
3. exp *Rehabilitation/
4. 2 and 3
5. 1 or 4
6. (letter or editorial or comment).pt.
7. Walking/
8. ambulation.tw.
9. Physical Mobility/
10. (walking or mobiltiy).ti.
11. or/7-10
12. 5 and 11
13. 12 not 6
14. limit 13 to english
15. limit 14 to yr="2003 - 2007"

Ambulation Medline
Database: Ovid MEDLINE(R) <1950 to January Week 1 2008>
Search Strategy:

1 exp *Stroke/rh [Rehabilitation]
2 exp *Stroke/
3 exp Rehabilitation/
4 2 and 3
5 1 or 4
6 walking/
7 (mobility or ambulation).ti.
8 exp Gait Disorders, Neurologic/

9 or/6-8
10 5 and 9
11 Gait Disorders, Neurologic/rh [Rehabilitation]
12 2 and 11
13 10 or 12
14 animals/ not (humans/ and animals/)
15 13 not 14
16 limit 15 to english language
17 limit 16 to yr="2003 - 2008"

Quality of Life

QOL CINAHL

1. *Cerebral Vascular Accident/rh [Rehabilitation]
2. *cerebral vascular accident/
3. exp *Rehabilitation/
4. 2 and 3
5. 1 or 4
6. (letter or editorial or comment).pt.
7. exp "Quality of Life"/
8. quality of life.tw.
9. QOL.tw.
10. or/7-9
11. 5 and 10
12. 11 not 6
13. limit 12 to english
14. limit 13 to yr="2003 - 2007"

QOL Medline

1. exp *stroke/rh
2. exp *stroke/
3. exp rehabilitation/
4. or/2-3
5. 1 or 4
6. animals/ not (humans/ and animals/)
7. (letter or editorial or comment).pt.
8. "Quality of Life"/
9. quality of life.ti.
10. or/8-9
11. 5 and 10
12. 11 not 6
13. 12 not 7
14. limit 13 to english language
15. limit 14 to yr="2003 - 2008"

Daily Activities

Daily Activities CINAHL

1. *Cerebral Vascular Accident/rh [Rehabilitation]
2. *cerebral vascular accident/
3. exp *Rehabilitation/
4. 2 and 3
5. 1 or 4
6. (letter or editorial or comment).pt.
7. "Activities of Daily Living"/
8. ((daily or routine) adj3 (activities or tasks)).tw.
9. or/7-8
10. 5 and 9
11. 10 not 6
12. limit 11 to english
13. limit 12 to yr="2003 - 2007"

Daily Activities Medline

1. exp *Stroke/rh [Rehabilitation]
2. exp *Stroke/
3. exp Rehabilitation/
4. 2 and 3
5. 1 or 4
6. "Activities of Daily Living"/
7. ((daily or routine) adj3 (activities or tasks)).tw.
8. or/6-7
9. 5 and 8
10. animals/ not (humans/ and animals/)
11. 9 not 10
12. (letter or editorial or comment).pt.
13. 11 not 12
14. limit 13 to english language
15. limit 14 to yr="2003 - 2008"

Communication

Communication CINAHL

1. (letter or editorial or comment).pt.
2. exp "Rehabilitation, Speech and Language"/
3. ((speech or language) adj (therap$ or training)).tw.
4. or/2-3
5. Cerebral Vascular Accident/
6. 5 and 4

7. 6 not 1
8. limit 7 to english
9. limit 8 to yr="2003 - 2007"
10. exp Aphasia/rh, th [Rehabilitation, Therapy]
11. exp "Rehabilitation, Speech and Language"/
12. exp Speech Disorders/rh, th [Rehabilitation, Therapy]
13. ((speech or language) adj2 (therap$ or training or rehabilitation or recovery)).tw.
14. or/10-13
15. exp Cerebral Vascular Accident/
16. stroke.ti.
17. (stroke adj (volume or heat)).ti.
18. 16 not 17
19. 15 or 18
20. 14 and 19
21. (letter or editorial or comment).pt.
22. 20 not 21
23. limit 22 to english
24. limit 23 to yr="2000 - 2007"
25. 24 or 9

Communication Medline

1. exp *stroke/
2. exp Aphasia/rh [Rehabilitation]
3. exp "rehabilitation of speech and language disorders"/
4. ((speech or language) adj2 (therap$ or training or rehabilitation or recovery)).tw.
5. or/2-4
6. 1 and 5
7. animals/ not (humans/ and animals/)
8. 6 not 7
9. (letter or editorial or comment).pt.
10. 8 not 9
11. limit 10 to english language
12. limit 11 to yr="2003 - 2008"
13. exp Aphasia/rh, th [Rehabilitation, Therapy]
14. exp "rehabilitation of speech and language disorders"/
15. exp Speech Disorders/rh, th [Rehabilitation, Therapy]
16. ((speech or language) adj2 (therap$ or training or rehabilitation or recovery)).tw.
17. or/13-16
18. exp stroke/
19. stroke.ti.
20. (stroke adj (volume or heat)).ti.
21. 19 not 20
22. 18 or 21
23. 17 and 22
24. animals/ not (humans/ and animals/)

25. 23 not 24
26. (letter or editorial or comment).pt.
27. 25 not 26
28. limit 27 to english language
29. limit 28 to yr="2000 - 2008"
30. 29 or 12

Communication PsycINFO

1. animals/ not (humans/ and animals/)
2. (letter or editorial or comment).pt.
3. exp Cerebrovascular Accidents/
4. speech therapy/
5. ((speech or language) adj2 (therap$ or training or rehabilitation or recovery)).tw.
6. or/4-5
7. 3 and 6
8. 7 not 1
9. 8 not 2
10. limit 9 to english language
11. limit 10 to yr="2003 - 2008"
12. exp communication disorders/
13. exp treatment/
14. and/12-13
15. speech therapy/
16. ((speech or language) adj2 (therap$ or training or rehabilitation or recovery)).tw.
17. or/14-16
18. stroke.ti.
19. (stroke adj (volume or heat)).ti.
20. 18 not 19
21. exp Cerebrovascular Accidents/
22. or/20-21
23. 17 and 22
24. limit 23 to english language
25. limit 24 to human
26. limit 25 to yr="2000 - 2008"
27. 26 or 11

Dysphagia

Dysphagia CINAHL

1. Cerebral Vascular Accident/
2. stroke.ti.
3. or/1-2
4. Deglutition Disorders/
5. dysphagia.ti.

6. (swallowing adj3 disorder?).ti.
7. or/4-6
8. 3 and 7
9. (letter or comment or editorial).pt.
10. 8 not 9
11. limit 10 to english
12. limit 11 to yr="2003 - 2007"

Dysphagia Medline

1. Deglutition Disorders/
2. dysphagia.ti.
3. (swallowing adj3 disorder?).ti.
4. or/1-3
5. exp Stroke/
6. stroke.ti.
7. or/5-6
8. 4 and 7
9. (letter or comment or editorial).pt.
10. 8 not 9
11. animals/ not (animals/ and humans/)
12. 10 not 11
13. limit 12 to english language
14. limit 13 to yr="2003 - 2008"

Systematic Reviews

Systematic Reviews CINAHL

1. exp Cerebrovascular Disorders/
2. (stroke$ or cerebrovascular$ or cerebral vascular or CVA$).tw.
3. ((cerebral or cerebellar or brainstem or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or apoplexy or emboli$)).tw.
4. ((cerebral or intracerebral or intracranial or parenchymal or brain or intraventricular or brainstem or cerebellar or infratentorial or supratentorial or subarachnoid) adj (haemorrhage or hemorrhage or haematoma or hematoma or bleeding or aneurysm)).tw.
5. poststroke$.tw.
6. post-stroke.tw.
7. or/1-6
8. exp Rehabilitation/
9. exp Physical Therapy Modalities/
10. exp Therapy, Computer-Assisted/
11. exp Therapeutics/
12. (training or re-training or retraining or therap$ or rehabilitat$ or treatment$ or therapeutic$).tw.
13. or/8-12

14. 7 and 13
15. exp Cerebrovascular Disorders/rh [Rehabilitation]
16. or/14-15
17. animals/ not (animals/ and humans/)
18. 16 not 17
19. (letter or editorial or comment).pt.
20. 18 not 19
21. "Systematic Review"/
22. systematic review.pt.
23. systematic.tw.
24. (meta-analysis or metaanalysis).tw.
25. (cochrane adj2 review).tw.
26. or/21-25
27. 20 and 26
28. limit 27 to english
29. limit 28 to yr="1990 - 2007"

Systematic Reviews Medline

1 exp Cerebrovascular Disorders/
2 (stroke$ or cerebrovascular$ or cerebral vascular or CVA$).tw
3 ((cerebral or cerebellar or brainstem or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or apoplexy or emboli$)).tw.
4 ((cerebral or intracerebral or intracranial or parenchymal or brain or intraventricular or brainstem or cerebellar or infratentorial or supratentorial or subarachnoid) adj (haemorrhage or hemorrhage or haematoma or hematoma or bleeding or aneurysm)).tw.
5 poststroke$.tw.
6 post-stroke.tw.
7 or/1-6
8 exp Rehabilitation/
9 exp Physical Therapy Modalities/
10 exp Therapy, Computer-Assisted/
11 exp Therapeutics/
12 (training or re-training or retraining or therap$ or rehabilitat$ or treatment$ or therapeutic$).tw.
13 or/8-12
14 7 and 13
15 exp Cerebrovascular Disorders/rh [Rehabilitation]
16 or/14-15 (92807)
17 exp *child/ or exp *infant/
18 16 not 17
19 animals/ not (animals/ and humans/)
20 18 not 19
21 (addresses or bibliography or biography or comment or congresses or editorial or historical article or in vitro or interview or lectures or letter or news or newspaper article).pt.
22 20 not 21

23 limit 22 to english language
24 limit 23 to yr="2005 - 2008"
25 limit 23 to yr="1990 - 2008"
26 meta-analysis.pt.
27 review.pt.
28 26 or 27
29 25 and 28
30 systematic.tw.
31 meta-analysis.tw.
32 metaanalysis.tw.
33 (cochrane adj2 review).tw.
34 meta-analysis.pt.
35 or/30-34
36 29 and 35

Systematic Reviews CDSR

1. stroke$ or cerebrovascular$ or cerebral vascular or CVA$).ti.
2. ((cerebral or cerebellar or brainstem or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or apoplexy or emboli$)).ti.
3. ((cerebral or intracerebral or intracranial or parenchymal or brain or intraventricular or brainstem or cerebellar or infratentorial or supratentorial or subarachnoid) adj (haemorrhage or hemorrhage or haematoma or hematoma or bleeding or aneurysm)).ti.
4. poststroke$.ti.
5. post-stroke.ti.
6. or/1-5
7. (training or re-training or retraining or therap$ or rehabilitat$ or treatment$ or therapeutic$).tw.
8. and/6-7
9. limit 8 to yr="2000 - 2008"

Appendix B. Demographic Tables

Table B1: Study, population and intervention characteristics for studies with Ambulation outcomes

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Askim[125] 2006 Norway	RCT n=62 Extended stroke unit service (ESUS) n=31 Ordinary stroke unit service (OSUS) n=31	Hospital stroke unit	Ischemic/hemorrhagic NR ESUS: 76.9 yrs 51.6% male OSUS: 76.3 yrs 54.8% male	Inclusion: 1: Diagnosis of an acute stroke according to the WHO definition of stroke; 2: <SSS score <58; 3: living at home before the stroke; 4: inclusion within 72 hours after admission to the stroke unit and within 7 days after the onset of symptoms; 5: able and willing to provide informed consent. Exclusion: 1: SSS score >57; 2: onset of symptoms <7 days before inclusion; 3: already included in the trial; 4: admission from institutional care; 5: lack of informed consent; 6: missed for inclusion because of holiday or other reasons.	Acute phase (≤2 weeks post stroke) ESUS/OSUS: both groups received stroke unit care with focus on early mobilization combined with a standardized medical program. Extended service: Stroke unit treatment combined with a home-based program of followup care (mobile stroke team that offers early supported discharge and works in close cooperation with the primary healthcare system during the first 4 weeks after discharge). Emphasis on early and intensive task-specific exercise therapy in the patients' home. LOF: 52 weeks	NR	5-metre walking speed Berg Balance Scale (BBS) Scandinavian Stroke Scale (SSS)—subscores assess motor function of leg and movement ability.
Bayouk[126] 2006 Canada	RCT n=16 Task-oriented exercise program with altered sensory input (SI) n=8 Task-oriented exercise program without altered sensory input (NoSI) n=8	Clinical exercise physiologist	Hemiparetic secondary to stroke NR SI: 68.4 yrs (7.1) 37.5% male NoSI: 62.0 yrs (4.6) 75% male	Inclusion: 1: be victim of a stroke that resulted in hemiparesis; 2: ≥6 months post-stroke; 3: be fully discharged from any rehabilitation program; 4: obtain written approval from a	≥6 months post-stroke Subjects from both groups participated in 1-hour exercise sessions, bi-weekly for 8 weeks. LOF: 8 weeks	NR	10-metre walking test Displacement of the center of pressure Postural sway

				primary care physician. Exclusion: 1: any severe limitation that would limit the subject's participation in the exercise program or interfere with functional assessments performed in this study.			
Bayram[127] 2006 Turkey	RCT n=12 Low dose botulinum toxin (BTX) injection with electrical stimulation (ES) n=6 High dose BTX injection n=6	Clinical investigator	Ischemic and Hemorrhagic NR Low dose: 55.3 yrs (9.9) 66.7% male High dose: 52.5 yrs (8.5) 66.7% male	Inclusion: 1: hemiparetic patients with spastic drop foot (Modified Ashworth grade of 3-4); 2: ≥6 months post stroke; 3: ability to walk 10 m with or without assistance. Exclusion: 1: Patients with severe plantar flexion contracture (inability to bring the ankle to a neutral position with passive motion); 2: history of BTX treatment.	Rx mean start: 36.6 ± 30.9 months post stroke Low dose: 100 units of BTX into tibialis posterior followed by ES to flexor and extensor muscles 6 x 30 minute sessions/day for 3 days. High dose: 400 Units of BTX to soleus, gastric, tibialis posterior and sham ES at the same frequency and duration as low dose group. LOF: 12 weeks	NR	Ashworth score Brace wear scale Clonus score Global Assessment of Spasticity Scale Range of motion of ankle Time walking 10 meters
Chen[128] 2005 Taiwan	RCT n=24 Electrical Stimulation (ES): n=12 Sham ES: n=12	NR	Right or left hemiplegia NR Total: 57 yrs 58.3% male	Inclusion: 1: neurologically stable stroke patients; 2: spasticity graded 2 or 3 on the mAS. Exclusion: 1: patients with DM and peripheral neuropathy.	12-35 months post stroke 20minutes/day x 6/wk x 1month LOF: 1 month	Yes	10-minute walking time H-reflex latency H-reflex recovery curve Modified Ashworth scale (mAS) Tibial Fmax/Mmax ratio
English[129] 2007 Australia	Non-RCT n=68 Individual therapy session (IT): n=31 Circuit class therapy	PT PTA	Ischemic/hemorrhagic NR IT: 61.6 yrs (11.8)	Inclusion: 1: Subjects who were diagnosed with a cerebrovascular accident resulting	Started within 3 days of admission to rehabilitation (~30days post stroke) Intervention	NR	5-metre walk test (5MWT) 2-metre walk test (2MWT) Berg Balance

	(CCT): n=37		51.6% male CCT: 68.9 yrs (12.3) 67.6% male	in unilateral motor deficits; 2: had sufficient ability to participate in circuit class therapy (i.e.: ability to follow 3-part commands, sit unsupported and stand with 1 person assisting); 3: were able to give informed consent. Exclusion: 1: Persons who had suffered a cerebellar lesion; 2: had a history of any neurological disorder (excluding previous stroke); 3: regularly used a walking aid (excluding single-point cane); 4: required assistance for activities of daily living prior to their stroke.	continued for the duration of their inpatient stay CCT: 2x 90-minute treatment sessions/day x 5/wk. IT: up to 60 minutes/ day x 5/wk LOF=6 months		Scale (BBS) Iowa Level of Assistance Scale (ILAS) Length of stay (LOS) Motor Assessment Scale (MAS) for stroke Stroke-specific satisfaction questionnaire Upper-limb subscale for LOS
Macko[130] 2005 United States	RCT n=61 Treadmill aerobic training (T-AEX): n=32 Stretching and low-intensity walking (Stretch): n=29	NR	Ischemic NR T-AEX: 63 yrs (10) 68.8% male Stretch: 64 yrs (8) 72.4% male	Inclusion: 1: adequate exercise intensities without signs of myocardial ischemia or other contraindications to training. Exclusion: 1: heart failure, unstable angina, peripheral arterial occlusive disease, aphasia, dementia, untreated major depression, and other medical conditions precluding participation in exercise	Rx start: >6 months post stroke T-AEX: 3x 40 min/wk 60-70% HRR on treadmill Stretch: stretching for 35 min plus 5 min low intensity treadmill walking 3x/wk Both groups, 6 months of treatment LOF=6 months	NR	6-minute walk test 30-feet walk test Rivermead Mobility Index (RMI) Walking Impairment Questionnaire (WIQ)
Marigold[60] 2005 Canada	RCT n=61 Stretching and weight-shifting exercise (WtEx) n=30	PT Kinesiologist Recreation Therapist	Ischemic/hemorrhagic NR WtEx: 67.5 yrs (7.2) 69% male	Inclusion: 1; aged 50+; 2: single stroke; 3: >12 months from onset; 4: ability to walk with or without assistive	Start: at least 12 months post stroke 1 hour sessions 1X week for 10 weeks	NR	Activities-specific Balance Confidence (ABC) Scale Berg Balance

	Agility Exercise (AgEx): n=31		AgEx: 68.1 yrs (9.0) 77% male	device for minimum 10m; 5: activity tolerance of 60 minutes. Exclusion: 1: not medically stable, 2: neurological conditions not related to stroke; 3: severe musculoskeletal conditions; 4: joint replacement; 5: MMSE<22; 6: Berg Balance score of >52.	LOF=1 year		Scale (BBS) Nottingham Health Profile (NHP) Timed Up and Go (TUG) test Step reaction time
Mayr[131] 2007 Austria	RCT n=16 parallel-group (ABA-BAB) Lokomat treatment (LT): n=8 Conventional physical therapy (CPT): n=8	PT	Ischemic/ hemorrhagic NR Total sample: 63.4 yrs 37.5 %male	Inclusion: 1: history of cerebral ischemic or hemorrhagic stroke 2: inability to walk unaided 3: no severe orthopedic or neuropsychological problems 4: all inpatients	0.5-8 months after stroke LT=body weight supported treadmill 30 min x 5 days a week CT=neuro facilitation training 30 min x 5 days a week LT Group=3 wks LT + 3wks CT + 3 wks LT CPT Group=3 wks CT + 3wks LT + 3wks CT Total 9 wks each group LOF=9weeks	Yes	6-minute timed walking distance (6-m TWD) 10-minute timed walking speed (10-m TWS) Ashworth Scale (AS) EU-Walking Scale Medical Research Council (MRC) Scale of strength Motricity Index (MI) Rivermead Mobility Index (RMI)
Pang[94] 2005 Canada	RCT n=63 Fitness and mobility exercise (FAME) program n=32 Upper extremity program (UEP) n=31	PT OT Exercise Instructor	Ischemic NR FAME: 65.8 yrs (9.2) 57% male UEP: 64.7 (8.4) 57% male	Inclusion: 1: single stroke ≥1y; 2: age 50+; 3: able to walk 10m independently with aids; 4: living at home; 5: MMSE >22. Exclusion: 1: cardiac disease; 2: uncontrolled BP; 3: pain while walking;	≥1year post stroke 1 hour sessions tri-weekly for 19 weeks LOF=19 weeks	Yes	6-minute walk test (6MWT) Berg Balance Scale (BBS) Bilateral dual-energy x-ray absorptiometry (DEXA) hip scans Isometric knee extension Physical Activity Scale

				4: any disease that precluded exercise			for Individuals with Physical Disabilities (PASIPD) $V0_2$max
Peurala[134] 2005 Finland	RCT n=45 Gait trainer exercise with functional electric stimulation (GTsim) n=15 Gait trainer exercise without stimulation (GTstim) n=15 Walking over ground (Walk) n=15	PT nurse	Ischemic/hemorrhagic NR GTstim 53.3 yrs (8.9) 86.7% male GT: 51.2 yrs (7.9) 86.7% male Walk: 52.3yrs (6.8) 73.3% male	Inclusion: 1: slow or difficult walking; 2: no unstable cardio disease; 3: no severe malposition of joints; 4: no severe cognitive or communicative disorders.	≥6 months post stroke All patients practiced gait for 15 x 20-minute sessions over 3 weeks, as well as daily 55 minute physiotherapy. LOF=29 weeks (assuming 4.348weeks in each month)	NR	10-metre walk test (10MWT) 6-minute walk test (6MWT) Functional Independence Measure (FIM) scale Lower limb spasticity and muscle force Modified Motor Assessment Scale (MMAS) Postural sway test
Peurala[133] 2005 Finland	Non-RCT n=37 Physiotherapy and electromechanical gait training with body-weight support (PTE) n=23 Conventional physiotherapy (CP) n=14	PT	Ischemic/hemorrhagic NR PTE: 52.5yrs (8.6) 87.0% male CP: 56.0yrs (6.3) 78.6% male	Inclusion: 1: supratentorial, ischemic or hemorrhagic, infarction >6 months; 2: difficulties in walking (aid or supervision); 3: no unstable cardiovascular disease; 4: no severe malposition of joints; 5: no severe cognitive or communicative disorders	Mean Rx start (years ± SD): 2.6±2.3 PTE: 75 min PT plus 20 min electromechanical gait trainer with body weight support 5X week for 3 weeks CP: 45 minutes conventional PT 5 X week for 3 weeks LOF=29 weeks (assuming 4.348weeks in each month)	NR	10-metre walk test (10MWT) Functional Ambulation Profile (FAP) score Functional Independence Measure (FIM) scale Modified Motor Assessment Scale (MMAS) Spatial and temporal gait measurements with GAIT Rite (instrumental walkway)
Roerdink[63] 2007 Netherlands	Non-RCT n=19 Treadmill with acoustic pacing (TAP) n=10 Treadmill (TT) n=9	PT	Ischemic NR TAP: 63 yrs 80.0% male TT: 69 yrs	Inclusion: 1:Ten people with a first-ever ischemic cerebrovascular accident forming the experimental group, and 9 elderly people who were healthy	3-104 months after stroke 3x 3 different pacing frequencies LOF=NR	No	Biomechanical gait analysis: Gait cycle parameters, stride time, interlimb coordination

			44.4% male	forming a control group 2: No hearing deficits in either group 3: All participants able to walk independently			
Sutbeyaz[135] 2007 Turkey	RCT n=40 Mirror Therapy using motor imagery training (MT) n=20 Placebo Therapy (PT) n=20	MD PT OT SLP	unilateral stroke with hemiparesis NR MT: 62.7(9.7) yrs 50% PT: 64.7(7.7) yrs 65%	Inclusion: 1: first episode of unilateral stroke with hemiparesis during the previous 12 months; 2: a score between 1 and 3 on the Brunnstrom stages of motor recovery of the lower extremity; 3: no severe cognitive disorders that would interfere with the study's purpose; 4: ambulatory before stroke.	≤12 months post stroke 5 days/wk, 2-5 hr/day for 4 weeks plus additional 30 min/day of MT or PT LOF=6 months	NR	Brunnstrom stages of motor recovery Functional Ambulation Categories (FAC) Functional Independence Measure (FIM) Modified Ashworth Scales (MAS)
Sze[136] 2002 China	RCT n=106 Group stratification divided by BI scoring, followed by control and treatment division. Group I: BI<11 (Range 3-10) Rx_{GI}:31 Co_{GI}:31 Group II: BI≥11 (Range 11-14) Rx_{GII}:22 Co_{GII}:22 Standard modalities of Rx, including physiotherapy, occupational and speech therapy, and skilled medical and nursing care vs. standard modalities (as listed above) as well as traditional Chinese manual acupuncture.	PT OT SLP Acupuncturist MD	Ischemic/hemorrhagic NR Rx_{GI}: 69.3 yrs (9.6) 45.2% male Co_{GI}: 71.9 yrs (7.5) 51.6% male Rx_{GII}: 69.7 yrs (11.0) 63.6% male Co_{GII}: 72.5 yrs (6.8) 54.5% male	Inclusion: 1: hemorrhagic or ischemic stroke (either CT scan confirmed or CT scan normal, clinically consistent with the WHO definition of stroke); 2: admission within 15 days of stroke; 3: Glasgow Coma Scale of 15; 4: ability to follow simple commands. Exclusion: 1: admission 15≤BI<3, 2: no motor deficit; 3: hemodynamic instability; 4: history of dementia; 5: inability to give consent because of impaired cognition or receptive aphasia.	3 to 15 days post stroke Group I: 5weeks (±1week) of inpatient rehabilitation, followed by 5 weeks (±1week) of day hospital rehabilitation. Group II: 3weeks (±1week) of inpatient rehabilitation, followed by 7 weeks (±1week) of day hospital rehabilitation. Co: 5 60-minute physiotherapy sessions/ week; 5 45-minute occupational therapy sessions/week. Speech therapy and psychological counseling as indicated. Rx: Rx equivalent	Yes	Abbreviated Mental Test (AMT) Barthel Index (BI) Fugl-Meyer Assessment of Physical Performance (FMA) Functional Independence Measure (FIM) National Institute of Health Stroke Scale (NIHSS)

					to control group (above) with a mean intervention of 35 acupuncture sessions on 10 main acupoints for 10 weeks (30 minute sessions occurring 5 times/week (inpatients), 3 times/week, then 2 times/week for the final 2 weeks). LOF=10 weeks		
Thaut[137] 2007 United States	RCT n=78 Rhythmic auditory stimulation (RAS) n=43 Neurodevelopmental therapy/Bobath (NDT) n=35	PT	NR NR RAS 69.2 yrs (11) 51% male NDT 69.7 yrs (11) 54.3% male	Inclusion: 1:ability to complete 5 stride cycles with handheld assistance 2:stroke onset ≤4 weeks	~20 days post stroke 30 minute sessions, 5 times per week x 3 weeks LOF=3 weeks	NR	Barthel Index (BI) Fugl-Meyer Assessment of Physical Performance (FMA) Gait characteristics
Tong[138] 2006 China	RCT n=50 Conventional gait training (CGT) n=20 Electromechanical gait trainer (EGT) n=15 Electromechanical gait trainer plus functional electrical stimulation (EGT-FES) n=15	PT, OT, SLP, Psychologist	Ischemic NR CGT: 71.4(14.0) 60% EGT: 66.1(9.9) 60% EGT-FES: 61.8(10.8) 66.7%	Inclusion: 1:diagnosis of ischemic brain injury or intracerebral hemorrhage on MRI or CT 2: <6 weeks after the onset of stroke 3: sufficient cognition to follow simple instructions and understand the content and purpose of the study (Mini-Mental State Examination score 21) 4: ability to stand upright, supported or unsupported, for 1 minute 5: significant gait deficit (FAC score 3) 6: no skin allergy to electric stimulation. Exclusion: 1: recurrent stroke or other	1-6 weeks post stroke 20 min sessions/day x 5/week x 4 weeks All participants 40 min physical therapy, 5x/week and 1.5 hour of multidisciplinary OT, speech and psychology per day in addition to intervention LOF=4 weeks	NR	5-meter walking speed test Barthel Index (BI) Berg Balance Scale (BBS) Elderly Mobility Scale (EMS) Functional Ambulatory Category (FAC) Functional Independence Measure (FIM) Motricity Index leg subscale

				neurological deficit affecting ambulation 2: additional medical or psychological condition that may affect compliance 3: aphasia with an inability to follow 2 consecutive step commands or a cognitive deficit 4: severe hip, knee, or ankle contracture that would preclude passive range of motion of the leg			
Yan[139] 2005 China	RCT n=46 Functional electrical stimulation plus standard rehabilitation (FES) n=15 Placebo: Standard rehab with sham FES (PSR) n=16 Control: Standard Rehab (SR) n=15	NR	Ischemic or Hemorrhagic NR Mean Age Total Group: 70.9(8.0) % male: FES: 53.8% PSR: 45.7% SR: 46.2%	Inclusion: 1:unilateral stroke within the carotid artery system 2: 45 to 85years 3: independent in daily activities before stroke Exclusion: 1:brain stem or cerebella lesions 2: medical comorbidity 3:receptive dysphagia 4: cognitive impairment scoring <7 on Abbreviated Mental Test	9.2±4.1 days post stroke SR for all patients included 60 minutes each of PT and OT once per day, 5/wk x 3 weeks FES added 30 minutes x treatment day PSR added 60 minutes x treatment day of sham FES LOF=8 weeks	NR	Composite spasticity score (CSS) Maximum isometric voluntary contraction of ankle dorsi flexors and plantar flexors Timed Up and Go (TUG) test
Yang[140] 2007 Taiwan	RCT n=25 Ball exercise training (BE) n=13 Control (C) n=12	PT	NR NR BE: 59.5 (11.83)yrs 53.8% C: 59.2(11.98)yrs 58.3%	Inclusion: 1: Hemiparetic from a single stroke occurring at least a year earlier 2: limited (gait velocity between 58 and 80cm/s) or full community ambulatory ability (minimum gait velocity of 80cm/s) 3: not presently receiving any rehabilitation services 4: ability to walk 10m independently without an assistive device 5: functional use of	≥1year post stroke 30 minutes of a ball exercise program 3/wk x 4 weeks LOF=4 weeks	NR	GAIT Rite (instrumental walkway) analysis of gait performance (preferred walking) gait parameters

				the involved upper extremity 6: stable medical condition to allow participation in the testing protocol and intervention 7: an ability to understand instructions and follow commands. Exclusion: 1: any comorbidity or disability other than stroke that would preclude gait training 2: any uncontrolled health condition for which exercise is contraindicated 3: any neurological or orthopedic diseases that might interfere with the study			
Yavuzer[141] 2006 Turkey	RCT n=25 Conventional rehabilitation plus neuromuscular electric stimulation (NMES) n=12 Conventional rehabilitation (CR) n=13	PT MD	Ischemic/hemorrhagic NR NMES: 56.3(7.5)yrs 58.3% CR: 54.2(8.1)yrs 69.2%	Inclusion: 1: first episode of unilateral stroke with hemiparesis during <6 months; 2: score 1 to 3 on Brunnstrom stages for lower extremity 3: ability to understand and follow simple verbal instructions 4: ambulatory before stroke 5: no medical contraindications to walking or electric stimulation 6: ability to stand with or without assistance and to take 1 or more steps with or without assistance	Average 2.4 months post stroke CR for 2 -5 hours, 5 days/week x 4 weeks NMES group received same CR plus 10 minutes with NMES 5 days/week x 4 weeks LOF=4 weeks	Yes	Brunnstrom stages of motor recovery Kinematics characteristics of Gait
Yavuzer[142] 2006 Turkey	RCT n=50 Usual care plus balance training using Nor-Am Target Balance Training System (NORAM) n=25	PT, OT, SLP	Ischemic/hemorrhagic NR NORAM: 59.8(11.6) 54.5% UC: 62.1(12)	Inclusion: 1: first episode of unilateral stroke with hemiparesis and internal carotid artery 2: ability to follow simple verbal instructions 3: ambulatory	At least 6 months post stroke UC consisted of multidisciplinary care 5x/wk for 2-5 hrs for 8 weeks NORAM received an	NR	Biomechanical Measurements -3 dimensional gait analysis, walking velocity, cadence, step length and single support

	Usual Care (UC) n=25		68.4%	before stroke; 4: ability to stand with or without assistance and to take at least one or more steps 5: no medical contraindication to walking. Exclusion: 1: history of any neurological pathology, conditions affecting balance, neglect, dementia 2: impaired vision or conscious levels 3: concomitant medical illness 4: musculoskeletal conditions of lower limbs.	additional 15 min balance training on the Nor-Am machine, 5x/wk, for 3 wks LOF=8 weeks		time, pelvic excursion, excursion of paretic hip, knee and ankle in sagittal plane

Abbreviations: 6-m TWD=6-minute timed walking distance; 10-m TWS=10-minute timed walking speed; 2,5,10 MWT=meter walk test; 6MWT=6 minute walk test; ABC=Activities-specific Balance Confidence Scale; AMT=Abbreviated Mental Test; AS=Ashworth Scale; BBS=Berg Balance Scale; BI=Barthel Index; BTX=botulinum toxin; CGT=conventional gait training; Co=control group; CSS=composite spasticity score; CT=computed tomography; CVA=cerebrovascular accident; DEXA=dual-energy x-ray absorptiometry; DM=diabetes mellitus; EGT-FES=electromechanical gait training (with) functional electric stimulation; EMS=Elderly Mobility Scale; ES=electrical stimulation; ESUS=extended stroke unit service; FAC=Functional Ambulation Categories; FAME=fitness and mobility exercise; FAP=Functional Ambulation Profile score; FIM=Functional Independence Measure; FMA=Fugl-Meyer Assessment of Physical Performance; GT=gait trainer; GTstim=gait trainer stimulation; HRR=Heart Rate Reserve; ILAS=Iowa Level of Assistance Scale; LOF=length of followup; LOS=Length of stay; mAS=modified Ashworth Scale; MAS=Motor Assessment Scale; MD=Medical Doctor; MI=Motricity Index; MMAS=Modified Motor Assessment Scale; MMSE=mini mental state examination; MRC=Medical Research Council; MRI=magnetic resonance imaging; NHP=Nottingham Health Profile; NIHSS=National Institute of Health Stroke Scale; NMES=neuromuscular electric stimulation; NR=not reported; OSUS=ordinary stroke unit service; OT=Occupational Therapist; PASIPD=Physical Activity Scale for Individuals with Physical Disabilities; PT=Physical Therapist; PTA=Physical Therapy Assistant; RCT=randomized control trial; RFM=RMI=Rivermead Mobility Index; RN=Registered Nurse; SD=standard deviation; SLP=Speech Language Pathologist; SSS=Scandinavian Stroke Scale; Rx=treatment; TUG=Timed Up and Go test; WHO=World Health Organization; WIQ=Walking Impairment Questionnaire.

Table B2: Study, population and Intervention characteristics for studies with Quality of Life outcomes

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Askim[143] 2004 Norway	RCT n=62 Extended care: Mobile team for home support plus ordinary care (EC) n=31 Ordinary care: acute/rehab stoke unit care and rehab clinic or health system followup care (OC) n=31	Nurse PT OT MD Hospital team	Acute stroke according to WHO Scandinavian Stroke Scale (SSS) of >2 and <58 EC: 76.9 yrs (NR) 51.6% male OC: 76.3 yrs (NR) 54.8% male	Inclusion: 1: diagnosis of acute stroke according to WHO 2: Scandinavian Stroke Scale (SSS) of >2 and <58 3: living at home prior to stroke 4: within 72 hours after admission to hospital and within 7 days after onset of symptoms 5: able to give informed consent	0 to 52 weeks post stroke Both arms used services as needed for the entire study time LOF=52 weeks	NR	Barthel Index (BI) Caregiver Strain Index (CSI) Length of initial hospital stay Length of total institutional stay Modified Rankin Scale (mRS) Nottingham Health Profile (NHP)
Barreca[144]2004 Canada	RCT n=48 Extra sit to stand exercise (ESS) n=25 Conventional Practice (CP) n=23	Nurse, PT	Ischemic and Hemorrhagic NR ESS 67 yrs (NR) 68% male CP: 70 yrs (NR) 61% male	Inclusion: 1: 18-90 yrs of age. 2: medically stable. 3: postural control of stage 3 or greater on Chedoke-McMaster Stroke assessment (CMSA) 4: failed the third item of the CMSA stage 4 postural control	NR 45 minute sessions, 6 x a week for 4 weeks LOF=4 weeks	NR	Patient satisfaction Quality of Life
Chae[145] 2005 United States	RCT n=61 Intramuscular electrical stimulation (IES) n=32 Cuff-type sling (CS) n=29	OT, PT, MD	Hemorrhagic or non-hemorrhagic stroke with shoulder pain NR IES: 60(11) yrs 57.6% CS 58(12.9) yrs 57.1 %	Inclusion: 1: >12 weeks post stroke 2: over 18 years of age 3: shoulder pain ≥2 on the BPI 4: palpable inferior glenohumeral separation 5: cognitive ability to fulfill study requirements Exclusion: 1: history of arrhythmia with hemodynamic	>12 weeks post stroke IES 6 hours/day for 6 weeks CS worn for 6 weeks LOF=52 weeks	All drugs were allowed and recorded	Brief Pain Inventory Question 12 (BPI12) Brief Pain Inventory Question 23 (BPI23) Subluxation

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				instability 2: previous stroke with persistent neurologic deficit 3: pre-stroke shoulder pathology 4: complex regional pain syndrome 5: any implantable stimulator 6: uncontrolled seizures			
Childers[146] 2004 United States	RCT n=91 Placebo: n=26 Botox (BTX) 90U: n=21 180U: n=23 360U: n=21 Intramuscular (IM) injection with placebo, 90U, 180U and 360U BTX	NR	Ischemic or hemorrhagic NR Placebo: 60.6 yrs (NR) 50% male BTX 90U: 59.3 yrs (NR) 76% male 180U: 61.1 yrs(NR) 65% male 360U: 59 yrs (NR) 81% male	Inclusion: 1: stroke diagnosed by a neurologist; 2: occurrence of stroke at least 6 weeks prior to study enrolment 3: focal spasticity of an upper limb shown by excessive wrist flexor muscle tone score of ≥3 and elbow flexor tone score of ≥2 on the MAS; 4: informed consent Exclusion: 1: fixed contracture or profound atrophy in affected limb; 2: previous or current treatment with any botulinum toxin serotype, phenol, or surgery; 3: current plaster casting for spasticity of the study limb; 4: current treatment with agents affecting neuromuscular transmission; 5: pulmonary function testing; 6: participation in	≥6 weeks post stroke Up to 2 treatment within 24 weeks Subjects were eligible for a second treatment cycle 12 weeks or more after the first only if they showed MAS scores of 2 or higher at the wrist and/or elbow flexor muscles and pulmonary function measurements did not decrease by more than 15% from baseline LOF=24 weeks	No	Wrist flexor MAS score Elbow MAS scores Finger flexor MAS scores 9-point physician global assessment and patient global assessment of response to treatment a 5-point frequency of pain scale a 5-point severity of pain a 5-point assessment of functional disability Functional Independence Measure (FIM) SF-36.27

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				another clinical trial <30 days prior; 7: diagnosis of myasthenia gravis, Eaton-Lambert syndrome, ALS, or condition that might interfere with the study; 8: sensitivity to any study meds 9: pregnant, breastfeeding, or planning pregnancy			
Fjaertoft[147] 2004 Norway	RCT n=320 Extended Stroke Unit Service (ESUS) n=160 Ordinary Stroke Unit Service (OSUS) n=160	Nurse, OT, PT, MD	NR Age NR % male NR	Inclusion: 1: acute stroke within 72 hours of admission and less than seven days after the onset of symptoms 2: Scandinavian Stroke Scale (SSS) between 2 and 57 points 3: living independently before the onset of stroke 4: not participating in other trials	Within 7 hours and less than 7 days after stroke Details of intervention not reported LOF=52 weeks	No	Primary: Nottingham Health Profile (NHP) Secondary: Frenchay Activity Index Mini-Mental State Examination (MMSE) Montgomery-Asberg Depression Scale
GAPS Group[148] 2004 United Kingdom	RCT n=70 Augmented therapy group (AT) n=35 Standard therapy (ST) n=35	PT	Diagnosis of stroke NR AT: 68 yrs 69% male ST: 67 yrs 49% male	Inclusion: 1: clinical diagnosis of stroke within the previous six weeks 2: able to tolerate and benefit from mobility rehabilitation Exclusion: 1: communication impairment 2: previous history of stroke 3: cognitive impairment 4: no sitting balance 5: pre-stroke Rankin >2	≤25 days after stroke AT: 60-80 min of physiotherapy/day, 5x week ST: 30-40 min of physiotherapy, 5x week LOF=6 months	NR	Barthel Index (BI) EuroQol Motricity Index (MI) Nottingham Extended ADL Rivermead Mobility Index (RMI)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				6: dementia, unconfirmed stroke, carcinoma, arthritis limiting, unstable angina, COPD, major surgery, poorly controlled diabetes, recent MI, PVD limiting exercise			
Hafsteinsdottir[149] 2005 Netherlands	Non randomized parallel group study n=326 Neurodevelopmental treatment (NDT) n=225 Non-Neurodevelopmental treatment (Control) n=101	Nurse, PT	Ischemic/hemorrhagic Moderate (Rankin >3) NDT 68 yrs (13) 55% male Control 72 yrs (11) 50% male	Inclusion : 1: diagnosis of stroke (WHO criteria) 2: Glasgow coma scale score of at least 14. 3: moderate handicap on admission but not before stroke onset. 4: no dementia (MMSE score of over 7) 5: Dutch speaking	3-5 days post stroke NDT: patients treated using NDT approach Control: patients treated using non-NDT care LOF=52 weeks	NR	Barthel Index (BI)
Johnson[150] 2004 United Kingdom	RCT n=18 Botulinum toxin type A (BTX) injection and function electric stimulation plus physiotherapy (BFES) n=10 Physiotherapy (PT) n=8	PT	Stroke with hemiplegia NR BFES: 58.2 yrs (12.7) 80% male PT: 59.3 yrs (12.5) 50% male	Inclusion: 1: first stroke of cerebrovascular origin during previous 12 months. 2: inability to achieve heel strike because of spastic equinus correctable by FES. 3: score between 3 and 6 inclusive on the Hauser Ambulation Index. 4: Modified Ashworth score between 2 and 4. 5: increased calf stretch response Exclusion: 1: medical or psychiatric problems that would interfere with study	1 year after stroke BTX 1 occasion, FES once a day for 16 weeks LOF=16 weeks	Yes	Medical Outcomes Study 36-item Short Form Heath Survey (SF-36) Modified Ashworth Scale Physiological core index Rivermead Motor Assessment Walking speed

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				protocol. 2: changes in prescribed anti-spastic medication. 3: previous treatment with BTX or FES			
Kalra[151] 2005 United Kingdom	Prospective single-blind RCT n=457 Stroke Unit (SU) n=152 Stroke Team (ST) n=152 Domiciliary Stroke Team (DST) n=153	MD, PT, OT, nurse	Ischemic/ Hemorrhagic Moderate Total group 76 yrs 52% Male	Inclusion: 1: within 72 hours of stroke onset. Exclusion: 1: admitted to other hospitals 2: managed at home by GP 3: admitted from residential or nursing home 4: previously severely handicapped (mRS 4 or 5) 5: mild stroke not requiring rehabilitation 6: severe stroke requiring hospitalization 7: patients with transient neurological deficits in whom the deficit resolved within 24 hours	≤72hrs of stroke SU: 24 hour care on stroke unit by multidisciplinary team ST: care on general wards with specialist team support DST: care at home under supervision of MD LOF=12 months	Anti-edema agents were used selectively and limited to patients with rapidly deteriorating consciousness levels and midline shift on CT scan.	Mortality Institutionalization Admission/readmission to hospitals Barthel ADL Index Rankin Scale Frenchay Activities Index (FAI) Hospital Anxiety and Depression Scale (HADS) EuroQol
Kendall[152] 2007 Australia	RCT n=100 Chronic Disease Self-Management (CDSM) course: n=58 Usual/Routine care: n=42	NR	NR NR Total sample: 65.96 yrs (10.7) 67% male	Inclusion: 1: if they had sustained a stroke in the last few months 2: no prior self-reported history of stroke, dementia or psychiatric illness, 3: sufficient expressive/ receptive English language skills to take part in interviews and the intervention, 4: expectation of discharge to their own or a family	First few months The CDSM course involved a small group education process, conducted over a 6-week period, for approx. 2 hours each week. 8 groups were conducted over an 18-month period. LOF=12 months	NR	Self-efficacy Scale Stroke Specific Quality of Life scale (SSQOL)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				member's home, 5: a family member or friend who was willing to participate in the study with them			
Leeds[153] 2004 United Kingdom	Non-RCT n=130 Patients Discharge to their own home: n=65 Discharge to care homes: n=65	MD	Type of stroke was not mentioned. Moderate Own home: 79.9 (7.3) 26% male Care homes: 79.9 (9.5) 26% male	Inclusion: Stroke survivors admitted to a stroke rehabilitation unit whose discharge was planned to a care home (nursing/residential home) Exclusion: 1: serious co-morbidity such as terminal cancer, 2: inability to give informed consent 3: residence in a care home.	~50 days since admission to hospital Outcome measures taken then patients discharged from stroke rehabilitation units Outcomes were measured again at 6 months after discharge LOF=6 months	No	Barthel Index CAMCOG-R, part of the Cambridge Examination for Mental Disorders in the Elderly. EuroQol (EQ-SD) Geriatric Depression Scale GDS
Lincoln[154] 2004 United Kingdom	RCT n=421 Community stroke team (CS) n=189 Routine care (RC) n=232	Community stroke team	Diagnosis of stroke Moderate CS: 72.8 (NR) 50% male RC: 71.2 (NR) 55% male	Inclusion: 1:stroke within the previous two years, 2: over 16 years of age 3: needed intervention from more than one rehabilitation discipline. Exclusion: 1: lived outside the geographical area of the study 2: previous treatment by the community stroke team in the previous two years.	Within two years of previous stroke CS: initial assessment visit at home. All patients were seen in their own homes and were treated for as long as it was considered they were benefiting. Assessment at 6 months after randomization for both study groups LOF=6 months	NR	Barthel Index Carer strain Index EuroQol thermometer form Extended ADL General Health Questionnaire (GHQ) Knowledge of stroke Satisfaction with care
McClellan[155] 2004 Australia	RCT n=26 Home-based mobility program (Home)	PT	Diagnosis of stroke NR Avg. of 5.38 months	Inclusion: 1: stroke within the past 18 months, 2: aged >45 years of age,	≤18 months post stroke Home: mobility exercises Sham: sham	NR	Functional Reach Test (FR) Item 5 of the MAS.

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	n=13 Sham (upper limb) home-based exercise program (Sham) n=13		post stroke Home: 69 yrs (13) 76.9% male Sham: 72 yrs (9) 20 % Male	3: living in the community, 4: scored >0 and <6 on Item 5 of the Motor Assessment Scale (MAS) for stroke and scored <6 on Item 7 or 8 of the MAS Exclusion: 1: unable to give informed consent 2: had uncontrolled cardiac symptoms or other medical conditions that limited exercise 3: had a pacemaker.	mobility exercises Both groups, had intervention, twice daily for 6 weeks LOF=14 weeks		Sickness Impact Profile (SA-SIP30)
Park[64] 2005 United Kingdom	RCT n=116 Acupuncture n=56 Sham n=60	MD	Ischemic or hemorrhagic stroke Moderate or severe Acupuncture: 74.8 yrs (10.0) 51.8 % male Sham: 74.1 yrs (10.2) 51.6% male	Inclusion: 1: Admitted to specialty stroke unit 2: any age 3: able to give conformed consent Exclusion: 1: pre-existing disability leading to modified Rankin score of 3 or more 2: recent history of serious disease, or disease transmissible by blood 3: fear of needling 4: stroke that had occurred under general anesthesia 5: history of previous acupuncture 6: likelihood of full recovery within 2 weeks	≤4 wks of stroke 9-12 sessions over 2 wks (each session at least 20 minutes each), first treatment within 48 hrs of screening LOF=2 weeks	NR	Primary Barthel ADL score Secondary NIH Stroke score, motricity index EuroQol 5 dimensional form (EQ-5D) EuroQol Visual-Analog Scale (EQ-VAS) Nottingham Extended ADL score, Ashworth scale for muscle spasticity timed 10 MW 9 hole peg test swallowing status
Ryan[156] 2006 United Kingdom	Parallel single-blind RCT n=89 Augmented Care: n=45 Routine Care: n=44	PT, OT, SLP	~45.4 days post stroke NR Augmented Care: 76.4 yrs (6.1)	Inclusion: 1: >64yrs 2: recovering from stroke or hip fracture 3: not suffering from a	~1.5months to 4.5months post stroke Augmented Care: Six or more face-to-face	NR	Barthel Index Frechay Activities Index (FAI) Hospital

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
			% male NR Routine Care: 77.3 yrs (6.4) % male NR	concomitant disease (e.g. Parkinson's disease or Dementia)	contacts/week for a maximum of 12 weeks Routine care: 3 or less face to face LOF=3 months from treatment start date		Anxiety and Depression Scale (HADS) Therapy Outcome Measure EuroQol 5D (EQ-5D)
Studenski[157] 2005 United States	RCT n=93 Therapeutic exercise program n=44 Usual care n=49	OT, PT	Ischemic/hemorrhagic mild-mod stroke deficits (FIM score 27-90), Therapeutic: 68.5 (9.0) 52.3% male Usual care: 70.4 (11.3) 55.1% male	Inclusion: 1: 50 yrs or older 2: stroke within 30-150 days 3: residence within 50 miles 4: independent ambulation 25 ft 5: Orpington Prognostic Score 2-2.5 6: palpable wrist extension 7: MMSE 16 or better 8: approval of subject's primary care physician	≤3-28 days post stroke 36 sessions over 12 wks LOF=6 months	NR	Barthel Index FIM Lawton & Brody ADL gait speed thresholds for community ambulation SIS subscales SF-36
Wayne[158] 2005 United States	RCT n=33 Traditional Chinese Medicine (TCM) acupuncture n=16 Sham acupuncture n=17	acupuncturists	Diagnosis of stroke moderate UE dysfunction TCM: 63 yrs (NR) 75% male Sham: 54 yrs (NR) 71% male	Inclusion: 1: UE dysfunction that does not prevent patient from ability to raise the impaired arm from a hanging position to a tabletop while seated, 2: ability to arise independently from a chair, 3: ability to walk independently with or without a cane or walker Exclusion: 1: previous experience with acupuncture 2: contraindications to electro acupuncture, including wearing	≥6 months post stroke TCM=10.5 wks up to 20 treatments, 2x/wk LOF=12 weeks	NR	Barthel Index Centre for Epidemiological Surveys - Depression Scale (CES-D) Grip Strength Nottingham Health Profile (NHP) Modified Ashworth Scale UE function (FMA) UE ROM

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				of pacemakers or embedded neural stimulators, cardiac arrhythmia, epilepsy or women who were pregnant or trying to conceive 3: comorbidities that prohibit participation in study procedures 4: simultaneous participation in other forms of physical or occupational therapy 5: enrollment in other studies that involve active interventions 6: cognitive impairment that would interfere with ability to give informed consent			

Abbreviations: ADL=activities of daily living; ALS=amyotrophic lateral sclerosis; AT=augmented therapy; BPI=brief pain inventory; BTX= botulinum toxin type A; CMSA=Chedoke-McMaster Stroke assessment; COPD=chronic obstructive pulmonary disease; CT=computed tomography; FES=functional electrical stimulation; FIM=functional independence measure; GP=general practitioner; HR=health related; IM=intramuscular; LOF=Length of Followup; MAS=Modified Ashworth Scale; MD=medical doctor; MI=myocardial infarction; MMSE=mini-mental status examination; MW=minute walk; NIH=National Institutes of Health; NR=Not Reported; OT=Occupational Therapist; PT=Physical Therapist; PVD=peripheral vascular disease; QOL=Quality of Life; RCT=Randomized Controlled Trial; ROM=range of motion; Rx=treatment; SF=Short Form Health Survey-36; SIS=Stroke Impact Scale; SLP=Speech Language Pathologist; SSS=Scandinavian Stroke Scale; ST=standard therapy; UE=upper extremity; WHO=World Health Organization.

Table B3: Study, population and intervention characteristics for studies with Daily Activities outcomes

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Boake[159] 2007 USA	RCT n=23 Constraint-induced movement therapy (CIMT) n=10 Traditional Therapy (TT) n=13	PT, OT, PTA, COTA	Ischemic or hemorrhagic stroke moderate CIMT: 63.1yrs (14.3) 70% males TT: 58.9 yrs (14.0) 61.5% males	Inclusion: 1: ischemic or hemorrhagic stroke within 14 days of entering the trial; 2: stroke lesion visualized on computed tomography or MRI scan of the brain performed before enrollment; 3: score of 1-3 on item 5 (arm motor) of the NIHSS; 4: min 10 deg of active movement in thumb and ≥2 fingers of the affected hand; 5: total NIHSS score ≤14 if right, ≤19 if left-sided stroke; 6: ability to provide consent; 7: no previous stroke that interferes with interpretation of the results 8: no neglect or speech comprehension impairment that would prevent participation in the study assessments and treatment 9: no pacemaker or other metallic implant 10: no UE orthopedic limitation that affects results 11: readiness to participate in standard rehabilitation	Within 2 weeks after stroke Therapy began on the day of baseline testing or the following day, at a median of 11 days after stroke (range 5 to 19 days) All patients received either CIMT or traditional UE therapy at an equal frequency and duration of up to 3 h per day, for 14 to 15 days at a frequency of 6 days per week excluding Sundays LOF=3-4 months after stroke	NR	Fugl-Meyer Assessment of Motor Recovery (FM) Grooved Pegboard Test (GPT) Motor Activity Log (MAL) Transcranial magnetic stimulation (TMS)
Daly[160] 2005 USA	RCT n=12 Robotics and motor learning (ROB-ML) n=6 Functional	Researcher	Ischemic and hemorrhagic Moderate to severe (FM) ROB-ML:	Inclusion: 1: Subjects >12 months post stroke 2: required to demonstrate trace (Grade 1) muscle contraction in the wrist extensors	≥12 months post stroke Both groups received treatment 5 hours a day, 5 days a week for 12 weeks. For ROB-ML, during	NR	Primary: Arm Motor Ability Test (AMAT) Secondary: AMAT-shoulder/elbow (AMAT-S/E)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	neuromuscular stimulation and motor learning (FNS-ML) n=6		21-49 yrs: 3 50-62 yrs: 3 100% male FNS-ML: 21-49 yrs: 3 50-62 yrs: 3 50% male	3: a score of >10 in the Fugl-Meyer (FM) upper-limb coordination measure	1.5h of the daily treatment session, subjects used the robot and practiced shoulder/elbow movements with the forearm and hand supported in a cradle and the wrist and hand in fixed positions The remainder of each session (3.5 h) included practice of functional task components and whole task practice without technology assistance. This portion of the treatment protocol was identical for both groups. LOF=6 months		AMAT-wrist/hand (AMAT-W/H) Fugl-Meyer (FM) upper-limb coordination Smoothness of movement (SM) Target Accuracy (TA)
Ertel[161] 2007 USA	RCT n=291 Psychological Intervention (PI): Usual care plus the psychosocial intervention A psychologist or social worker trained in family systems and cognitive behavioral therapy was assigned to each subject in the intervention group. n=146 Usual Care (UC) Patients assigned to usual care were given standard educational material on stroke recovery n=145	Psychologist Social Worker	Ischemic or non-traumatic hemorrhagic stroke Moderate (NIHSS) PI: 69.3 yrs (11.1) 51.4% male UC: 70.2 yrs (10.9) 51.0% male	Exclusion: 1: globally aphasic or had limited comprehension and expressive aphasia (Boston Aphasia Severity Rating Scale=0 or 1) 2: extremely socially isolated 3: residing in a nursing home prior to stroke or discharged to a nursing home 4: cognitively impaired prior to stroke 5: living outside metropolitan Boston 6: only mildly impaired (NIHSS <3) 7: very severely impaired (NIHSS >8)	~38 days post stroke Up to 16 meetings conducted over six months in the patient's home (approximately weekly for 12 weeks, followed by tri-weekly sessions for another 12 weeks). Sessions lasted approximately 1 hour and included the entire support system (stroke survivor, primary caregiver, additional family and friends, and professional caregivers). LOF=6 months	NR	Instrumental activities of daily living (IADL) Global Cognitive Function Score Physical Performance Test
Gilmore[73] 2007	RCT n=10	Researcher	Hemiparesis with no	Inclusion: 1: first stroke as	Average 4.5 weeks after stroke	NR	Canadian Occupational

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Canada	Occupational Therapy Intervention (OT) n=NR Occupation Therapy with Video feedback (OTV) intervention n=NR		functional use of upper extremity NR OT: 72.0 yrs (14.1) OTV: 65.8 yrs (7.8)	confirmed by a computed tomography, magnetic resonance imaging, or by the physician's clinical findings and if the individual required lower extremity dressing intervention 2: hemiparesis with no functional use of the affected upper extremity. Exclusion: 1: did not have adequate sitting balance and endurance to participate 2: serious cognitive deficits existed MMSE score of less than 20/30) 3: serious visual perceptual deficits existed (participants were not able to interpret themselves on videotape completing a beanbag toss) 4: they had received prior training for donning socks and shoes while in hospital as reported on their medical chart	10 sessions of OT or OTV LOF=NR		Performance Measure (COPM) Klein Bell Activities of Daily Living Scale (KB-ADL)
Gladstone[162] 2006 Canada	RCT n=71 Amphetamine and exercise (AE) n=34 Placebo and exercise (PE) n=37	PT	Ischemic and hemorrhagic Mod/severe hemiparesis AE: 67.8 yrs (16.2) 50% male PE: 67.8 yrs (13.9) 55.6% male	Inclusion: 1: medically fit to participate in a rehabilitation program 2: had no significant premorbid disability 3: provided informed consent Exclusions: 1: brain stem, cerebellar stroke; 2: pre-existing deficit that could interfere with assessments [dementia; unstable angina, congestive heart failure, unstable arrhythmia, or	5-10 days post stroke 10 mg of amphetamine or placebo followed by 1 hour of physiotherapy. Drug given every 3-4 days, for a total of 10 drug sessions. All patients also received standard physiotherapy and multidisciplinary care. LOF=3 months	Yes	Primary: Fugl Meyer (FM) motor recovery Secondary: CMSA Arm and Hand Inventory CMSA Disability Inventory for general mobility Clinical Outcome Variable Scale (COVS) Functional Independence Measure (FIM)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				uncontrolled hypertension; psychosis] 3: use of alpha adrenergic antagonists/agonists or monoamine oxidase inhibitors.			
Higgins[163] 2006 Canada	RCT n=91 Arm training n=47 Walking group n=44	PT, OT, exercise therapists	Ischemic and Hemorrhagic NR Arm training: 73 yrs (8) 30% male Mobility training: 71 yrs (12) 26% male	Inclusion: 1: clinical diagnosis of a first or recurrent stroke 2: residual walking deficit 3: a minimum score of 14 out of 22 on the telephone version of the MMSE 4: ability to walk 10 meters independently, with or without supervision or aid 5: sufficient language ability to follow testing procedures 6: living in the community 7: discharged from physical rehabilitation 8: less than 1 year post stroke at the time of recruitment Exclusion: 1: neurological deficit related to metastatic disease 2: recovery of functional walking capacity defined by age- and gender-specific norms on the Six-Minute Walk Test (SMWT) 3: discharge to a long-term care facility 4: comorbid conditions that precluded participation in arm or walking training.	Within one year of first or recurrent stroke Subjects in both groups participated in 18 practice sessions three times a week for six weeks. Each session lasted approximately 90 min. LOF=6 weeks	NR	Primary: Box and Block Test Secondary: Barthel Index Geriatric Depression Scale Grip Strength Nine Hole Peg Test Older Americans Resources and Services Scale-IADL (OARS-IADL) SF-36 Upper Extremity Subscale of the Stroke Rehabilitation Assessment of Movement (STREAM) Test d'Evaluation des Membres supérieurs des Personnes Agées (TEMPA)
Hsieh[164] 2007 Taiwan	RCT n=63 Electro-acupuncture (EA) n=30	Qualified experienced acupuncturist	First Ischemic Stroke moderate EA:	Inclusion: 1: first ever ischemic stroke 2: age over 40 yrs 3: admission within 2 wks of onset	6 months after stroke EA: needle points stimulated with electricity, alternating pulses (3 and 15 Hz).	Yes	Functional Independence Measure (FIM) Fugl-Meyer (FM) Motor Assessment

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	Usual Rehabilitation (UR) n=33		68.8 yrs 40% male UR: 70.7 yrs 70% male	4: stable condition 5: suitable for rehab program after consultation with physicians 6: informed consent from patient or family	Total time 20 min 4 weeks treatment LOF=3 months		
Langhammer[71] 2007 Norway	RCT n=75 Intensive exercise n=35 Regular exercise n=40	PT	First ever stroke with neurological signs NR Intensive: 76 yrs (12.7) NR % male Regular: 72 yrs (13.6) NR % male	Inclusion: 1: computer-tomography confirmed stroke Exclusion: 1: more than one stroke incident 2: subarachnoid bleeding 3: tumor 4: other serious illness 5: brainstem or cerebellar stroke	Acute phase (3 days after admission) all patients put into program. At discharge, randomized to intensive (45 minute sessions twice per week) or regular exercise group. LOF=12 months	NR	Barthel Index Grip Strength Motor Assessment Scale (MSA)
Mead[165] 2007 United Kingdom	RCT n=66 Mixed exercise training (MET) n=32 Relaxation therapy (RT) n=34	Exercise physiologist	Inpatient or had attended stroke clinic NR MET: 72.0 yrs (10.4) 56% male RT: 71.7 yrs (9.6) 53% male	Inclusion: 1: independent ambulation 2: living central or south Edinburgh 3: absence of dysphasia or confusion severe enough to prevent informed consent or impair safety in exercise classes 4: absence of medical contraindications to exercise training	~160 days since stroke Sessions 3 x a week for 12 weeks MET includes aerobic and resistance training RT seated deep-breathing and muscle relaxation LOF=7 months	NR	Comfortable walking speed Elderly Mobility Score Explosive leg extensor power Functional Independence Measure (FIM) Functional Reach Hospital Anxiety & Depression Scale (HADS) Nottingham Extended Activities of Daily Living (NEADL) Rivermead Mobility Index (RMI) SF36 Sit to Stand Timed up and go (TUG) Walking economy
Ng[166] 2007 Hong Kong	RCT n=88 TENS+TRT n=22 TENS n=22 TRT + placebo n=22	PT	Hemorrhagic Moderate and severe TENS+TRT: 58.4 yrs (7.1) 76.2% male TENS: 56.4 yrs (9.1)	Inclusion: 1: single stroke at least one year prior 2: Able to walk 10 m unassisted with or without walking aid 3: composite specificity score of greater than 10 in ankle plantar flexors Exclusion:	≥1 year post stroke 5 days a week for 4 weeks LOF=4 weeks	NR	Composite spasticity scale (CSS) Peak torques generated during maximum isometric voluntary contraction of ankle dorsiflexors and plantar flexors. Gait velocity

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	Control n=22		89.5% male TRT + placebo: 57.1 yrs (7.8) 85.0% male Control: 57.3 yrs (8.6) 85.0%male	1: medical comorbidity 2: receptive dysphasia 3: cognitive impairment			
Olney[167] 2006 Canada	RCT n=72 Supervised exercise n=38 Unsupervised exercise n=36	PT	Ischemic and hemorrhagic NR Supervised: 63.5 yrs (12.0) 62.2% male Unsupervised: 65.8 yrs (11.6) 62.9% male	Inclusion: 1: age 20 years; 2: thromboembolic or hemorrhagic cerebrovascular disorder with many, but not all, confirmed by CT scan 3: able to walk a total of 15 minutes with rests, with or without assistive devices (except a 4-point walker) 4: able to tolerate activity for 45 minutes with rests 5: no coronary artery disease of sufficient severity that would limit involvement in an exercise program as judged by cardiologist and determined by the Dobutamine Stress Echocardiography criteria 6: no contraindications to exercise testing as specified by American College of Sports Medicine (1995) and as reported by the cardiologist.	Supervised 4.1 years post stroke Unsupervised 3.4 years post stroke Both groups: 1.5-hour sessions 3 days per week for 10 weeks Supervised included: (1) walking, mild stretching, and range of motion exercises of lower limbs; (2) aerobic exercise; (3) strength training; a (4) a cool-down period Subjects in the unsupervised group were given written and verbal instructions on advancing in their exercises. LOF=1 year	Yes	Primary: Six minute Walk Test Secondary: Human Activity Profile (HAP) Physiological Cost Index SF-36 activity score SF-36 Mental component Sum of the strength of lower limb muscles
Page[168] 2007 United States	RCT n=32 Mental Practice (MP) n=16 Relaxation + Physical Practice (RPP) n=16	Therapists Psychologist	Chronic stroke NR MP: 58.7 yrs (12.9) % male NR RPP: 60.4 yrs (14.2) % male NR	Inclusion: 1: history of no more than one stroke, 2: ability to actively flex at least 10 degrees from neutral at the affected wrist and the metacarpophalangeal and interphanlangeal joints of two digits, 3: stroke experienced more than 12 months	~42 months post stroke All patients received 30-minute therapy sessions 2 days a week for 6 weeks. The sessions emphasized activities of daily living (ADLs): MP condition concurrently received sessions requiring daily MP of	Subjects and caregivers reported not engaging in any additional mental practice, relaxation or physical practice at their homes	Action Arm Research (ARA) Fugl-Meyer (FM)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
			Total Population 56.3% male	before study enrollment, 4: score equal or greater than 69 on MMSE Exclusion: 1: excessive spasticity (score equal or greater than 3 on Mod Ashworth Scale, 2: excessive pain in the affected upper limb, 3: still enrolled in any form of physical rehab, 4: participating in any experimental rehab or drug studies	the ADLs; control group received an intervention consisting of relaxation techniques LOF=1 wk post treatment		
Pohl[169] 2007 Germany	RCT n=155 Repetitive Locomotor training and physiotherapy (RLT+PT) n=77 Physiotherapy (PT) n=78	Nurse, PT	Ischemic or hemorrhagic NR RLT+PT: 62.3 yrs (12.0) 64.9% male PT: 64.0 yrs (11.6) 69.2% male	Inclusion: 1: first-time supratentorial stroke, either ischemic or hemorrhagic 2: age range 18 to 79 yrs 3: the interval between stroke and study onset was less than 60 days. 4: They were able to sit unsupported, with feet supported, could not walk at all, or required the help of one or two therapists regardless of the use of an ankle-foot orthosis or walking aid. 5: gave their written informed consent of participation in the study Exclusion: An unstable cardiovascular condition, following a 12-lead electrocardiogram and examined by a cardiologist, a restricted passive range of motion in the major lower limb joints, and the existence of other neurological or orthopedic diseases impairing walking ability	<60 days post stroke RLT+PT patients received 20 min of repetitive locomotor therapy on the gait trainer, immediately followed by 25 min of one-on-one physiotherapy every week day for four weeks PT patients received 20 45-min sessions of physiotherapy in the same period. LOF=6 months	NR	Primary: Barthel Index Functional Ambulation Category Secondary: Motor power of the paretic lower limb Rivermead Mobility Index (RMI) Walking velocity Walking endurance

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Rydwik[170] 2006 Sweden	RCT n=18 Treatment with stimulo device (a portable device developed to maintain or increase range of motion in the ankle by passive and active dorsal extension in plantar flexion). n=9 No treatment n=9	Chiropodist	Ischemic or hemorrhagic NR Treatment: 74.9 yrs (8.7) 77.7% male No Treatment: 75.3 yrs (4.9) 66.6% male	Inclusion: 1: Ischemic or hemorrhagic stroke in the right or left hemisphere at least one year prior to the study 2: remaining spasticity and/or decreased active range of motion in the hemiparetic leg/ankle Exclusion: 1: no walking ability	≥1 year post stroke 3x a week for 30 min for six weeks (18 training sessions) LOF=12 weeks	NR	AROM/PROM ankle dorsiflexion and plantar flexion FIM (instrumental Activity Measure) Functional Independence Measure (FIM) (personal ADL) Modified Ashworth Scale One repetition maximum strength test Romberg's test SF-36 Time Up and Go (TUG) 10-meter timed walk test
Sackley[171] 2006 United Kingdom	RCT n=118 OT intervention n=63 Usual care n=55	OT	NR Moderate to severe stroke (score 4-15 Barthel) OT intervention: 88.6 yrs (6.5) 17% male Usual care: 86.3 yrs (8.8) 18% male	Inclusion: 1: moderate to severe stroke related disability (BI score 4-15) Exclusion: 1: acute illness or admitted for end-of life care	NR OT patients received an average of 4.5 hrs/month with the OT over 3 months LOF=6 months	NR	Barthel Index (BI) Rivermead Mobility Index (RMI)
van Nes[172] 2006 Netherlands	RCT n=53 Whole Body Vibration (WBV) n=27 Exercise with Music (ETM) n=26	PT, OT, SLP	Ischemic and hemorrhagic Mod/severe balance impairment (score less 40 BBS) WBV: 59.7 yrs (12.3) 59% male ETM: 62.6 yrs (7.6) 54% male	Inclusion: 1: post stroke interval less than 6 weeks 2: moderate or severe balance impairment, score less 40 Berg balance scale Exclusion: 1: non-stroke related sensory or motor impairment 2: use of medication that could interfere with postural control 3: concomitant medical problems that impaired ability to follow simple verbal instructions 4: contraindications for WBV such as	Within 6 weeks post stroke and within 3 days of admission to rehab centre 5 sessions per week of 4x 45sec with 1 min rest for 6 weeks (both WBV and ETM) Standard care administered to both groups 5 x 30 min PT, 5 x 60 min PT, 3 x 30 min OT over 6 weeks LOF=12 weeks post Rx	NR	Primary: Berg Balance Scale (BBS) Secondary: Barthel Index (BI) Functional Ambulation Categories Motricity Index Rivermead Mobility Index (RMI) Somatosensory Threshold Trunk Control Test

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				pregnancy, recent fractures, gallbladder of kidney stones, malignancies and cardiac pacemaker			
Wittenberg[173] 2003 United States	RCT n=16 Constraint Induced Movement Therapy (CIMT) + task oriented therapy n=9 Less intensive task oriented therapy (Control) n=7	PT, OT, Recreational Therapist	Ischemic stroke "significant functional impairment (score <2.7 on MAL) CIMT: 65.0 yrs 88.8% male Control 63.0 yrs 71.4% male	Inclusion: 1: single subcortical infarction 2: >12 months post stroke 3: significant functional impairment (score <2.7 on MAL) Exclusion: 1: Patients without voluntary extension of at least 10 degrees of the affected fingers or 20 degrees of the wrist	>1 y post stroke CIMT: restraint of unaffected upper extremity on 10 continuous days for 6 hours/day Control: 3 hours/day weekdays, no treatment on weekends LOF=6 months	NR	Assessment of Motor and Process Skills (AMPS) Motor Activity Log (MAL) Wolf Motor Function Test (WMFT)
Wolf[174] 2006 United States	RCT n=222 Constraint Induced Movement Therapy (CIMT) n=106 Usual Care (varied) n=116	Clinician	Ischemic or Hemorrhagic High and low function Wolf Binder Macleod motor criteria CIMT: 61.0 yrs (13.5) 65.1% male Usual Care: 63.3 yrs (12.6) 62.9% male	Inclusion: 1: met higher or lower functioning motor criteria 2: balance requirements 3: adequate range of motion Exclusion: 1: score of <24 on MMSE 2: score of ≥2.5 on MAL 3: previous stroke 4: excessive pain 5: <18 yrs 6: previous participation in pharmacologic or physical intervention studies 7: insufficient stamina 8: medical contraindication	3-9 months post-stroke Required to wear restraining device for 90% of waking hours for 14 days also received shaping and standard task training for up to 6 hours/day LOF=12 months	NR	Motor Activity Log (MAL) Wolf Motor Function Test (WMFT)
Wu[175] 2007 Taiwan	RCT n=26 Modified constraint-induced movement therapy (M-CIMT) n=13	OT, inter-disciplinary care	First-time stroke patients M-CIMT: 71.4 (6.4) 61.5% male Usual care: 71.9 (6.8) 53.8% male	Inclusion: 1: reached Brunnstrom stage III for proximal part of UE or above 2: no serious cognitive deficits, 3: considerable nonuse of affected limb, 4: no balance problems sufficient to	~7.5 months post stroke M-CIMT 2 hour therapy sessions, 5 times/week for 3 weeks Shaping adaptive and repetitive tasks	NR	Functional Independence Measure (FIM) Fugl-Meyer (FM) Motor Activity Log (MAL) Stroke Impact Scale (SIS)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	Usual Care n=13			compromise safety when wearing project's constraint device 5: no excessive spasticity in any of the joints of the affected UE	Usual care 2 hours neurodevelopmental techniques 2 hours/ 5times/week for 3 weeks. LOF=3 weeks		
Yagura[176] 2006 Japan	RCT n=49 Body Weight Supported Treadmill Training with Facilitation Technique (BWSTT-FT) n=23 Body Weight Supported Treadmill Training with mechanical assistance (BWSTT-MA) n=26	PT, OT, SLP	Ischemic and hemorrhagic Severe stroke (failed to reach independent gait within 4 weeks of inpatient rehab) BWSTT-FT: 62.9 (7.4) 72.7% male BWSTT-MA: 59.3 (5.7) 76.0% male	Inclusion: 1: patients within 3 months after the onset 2: failed to reach independent gait within 4 weeks of inpatient rehab Exclusion: 1: more than 80 years of age 2: inability to understand the informed consent form because of impaired cognitive function 3: previous stroke or dependence in ADLs prior to stroke 4: history of myocardial infarction within 1 year 5: uncontrolled hypertension 6: symptomatic orthostatic hypotension 7: atrial fibrillation with uncontrolled rate	1 month after admission BWSTT 3 days/wk for 6 weeks for 20 min for each group. In the FT group, therapists assisted the flexion of the knee for initiation of swing phase. The MA group had mechanical control of the paretic leg Standard care consisting of an additional 2 sessions of BWSTT, OT, SLP LOF=up to 16 weeks post start of intervention	NR	Functional Independence Measure (FIM) Fugl-Meyer (FM) Gait Speed

Abbreviations: ADL=Activity of Daily Living; BI=Barthel Index; BBS=Berg Balance Scale; BWSTT=Body Weight Supported Treadmill Training; CIMT=Constraint-induced movement therapy; COTA=Occupational Therapy Assistant; CT=computed tomography; FIM=Functional Independence Measure; FM=Fugl-Meyer; LOF=Length of Followup; MAL=Motor Activity Log; MMSE=Mini-Mental State Examination; MRI=magnetic resonance imaging; NIHSS=National Institutes of Health Stroke Survey; NR=not reported; OT=Occupational Therapist; OTV=program of videotape feedback and a program of occupational therapy; PT=Physical Therapist; PTA=Physical Therapy Assistant; RCT=Randomized Controlled Trial; RX=treatment; SF=Short Form Health Survey; SLP=Speech Language Pathologist; TENS=transcutaneous electrical nerve stimulator; TRT=task related training; TT=Traditional Therapy; UE=upper extremity

Table B4: Study, population and intervention characteristics for studies with Cognition outcomes

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Cherney[76] 2003 USA	RCT n=4 Visual scanning treatment n=2 Oral reading treatment: n=2	clinician	Right hemisphere stroke Mild stroke All patients: Mean age: 65.75 25% male	Inclusion: 1) documented right hemisphere stroke 2) clinical evidence of neglect 3) 6 months post onset 4) hearing loss did not significantly interfere with communication 5) Corrected visual acuity was sufficient for newspaper-size print	≥6 months post onset Visual scanning patients received 20 sessions of the treatment. Oral reading patients received 20 sessions of the treatment Length of the session and duration of the treatment were not mentioned. LOF=20 sessions	No	Behavioral Inattention Test (BIT) Mental State Examination (MMSE) Stroop Neuropsychological screening Test (SNST)
Cirstea[177] 2006 Canada	RCT n=37 Feedback condition group -knowledge of results (KR) n=14 Feedback condition group - knowledge of performance (KP) n=14 Non-reaching task (control) n=9	PT	Ischemic or hemorrhagic NR Mean age (SD): KR: 55.7 (15.4) KP: 59.1 (17.9) Control: 64.5 (14.1) All Patients: 62% Male	Inclusion: 1) single stroke in the dominant hemisphere 3 to 24 months previously, and 2) able to reach with the impaired arm (at least stage 2 on Chedoke-McMaster Stroke Assessment). Exclusion: 1) occipital, cerebellar, or brain stem lesions 1) multiple strokes, major perceptual deficits, apraxia, shoulder subluxation, pain, or other neurological disorders	11.6 months post stroke onset 1hr/day in 10 sessions delivered over 2 weeks LOF=6 weeks	NR	Kinematic: movement time, precision, segmentation, variability of velocity and precision
Edmans[178] 2000 UK	RCT n=80 Patients Transfer of training approach (PT)	OT	Type not mentioned Moderate to mild PT:	Inclusion: 1) Patients had to be well enough to be assessed on the RPAB. 2) Patients had to have sufficient functional	~ 30 days post stroke Perceptual treatment was given for 2.5	NR	Barthel ADL Index Edmans ADL Index Rivermead Motor Assessment (RMA) -

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	n=40 Functional approach (FA) n=40		69.75 yrs (47-84) 45% male FA: 67.85 yrs (26-86) 55% male	use of one hand to complete the RPAB and to carry out perceptual treatment activities. 3) Consent to participate in the treatment by patient or nearest relative.	hours per week for six weeks, in addition to their general OT treatment. LOF=6 weeks		Gross Function scale Rivermead Perceptual Assessment Battery (RPAB)
Frassinetti[179] 2002 Italy	Non-RCT n=13 Patients Prism adaptation (PPA) n=7 General cognitive and motor treatments (GC) n=6	Researcher	Unilateral lesions confirmed by CT scans NR All patients: Mean age 64 yrs 46% male	Inclusion: 1) right-brain-damaged patients with chronic left hemispatial neglect 2) unilateral lesions due to cerebrovascular accidents, confirmed by CT scans 3) right-handed 4) normal or corrected-to-normal vision	≥3 months post stroke Prism adaptation (PA): two daily sessions (10 sessions a week), which took about 20 min each, over a period of 2 weeks, giving a total of 20 sessions. Frequency and dose of control group were not mentioned LOF=7 weeks	NR	Adaptation effect After effect BIT (behavioral inattention test battery) Cancellation tests Duration of the after-effect Fluff test Motricity index Patient R.D. (results from a special patients) Pointing task Reading test Room description and objects reaching tests
Harvey[180] 2003 UK	Non-RCT n=14 Visuomotor feedback training (VFT) n=7 Non-visuomotor feedback training (NVFT) n=7	Experimenter and Self administered	Ischemic or Hemorrhagic Moderate or mild All patients: Mean age (SD) 69 (9.3) 57% male	Inclusion: 1) cerebrovascular attack within the previous 5-25 months 2) left hemiparesis. 3) right handed 4) free of any other confounding neurological deficits or intellectual impairments.	cerebrovascular attack within the previous 5-25 months. 3 consecutive daily sessions that lasted approximately an hour each, then 10 days of home based intervention LOF=1.5 month	NR	BIT conventional scores BIT behavioral scores Laterality bias from the Balloons test Elevator and lottery sub-tests of the Test of Everyday Attention (TEA) Barthel indexes The patient and caregiver neglect rating scores
Kimura[181] 2000 USA	RCT n=47 Nortriptyline (two groups	nurse	Ischemic or Hemorrhagic NR	Inclusion: 1) diagnosis of mood disorder based on DSM-IV criteria	Acute or subacute Baltimore:	NR	Hamilton Rating Scale for Depression (HAM-D)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	Baltimore and Iowa) n=21 Placebo: n=26		 Nortriptyline: 59.6 yrs (9.1) 47.6% male Placebo: 60.7 yrs (11.8) 65.4%	"depression due to stroke with major depressive like episode" or "minor depression" 2) agree to be treated with Nortriptyline or placebo Exclusion: 1) patients with no depression diagnosis 2) scores below 10 on the HAM-D	20 mg/d for 1 week, 50 mg/d for 2 weeks, 70 mg/d for 1 week, and 100 mg/d for the last 2 weeks of the study. (6 week treatment period) Iowa: 25 mg/d for 1 week, 50 mg/d for 2 weeks, 75 mg/d for 3 weeks, and 100 mg/d for the last 6 weeks of the study. (12-week treatment period) Placebo occurred for both patient groups LOF=12 weeks		Mini-Mental State Examination (MMSE)
Malouin[182] 2004 Canada	Non-RCT n=26 Healthy subjects: n=14 Stroke patients: Normal working memory subgroup (NWM) n=7 Impaired working memory subgroup (IWM) n=5	NR	Hemiparesis from stroke NR Stroke patients group: 56.10 yrs (9.89) 83% male Healthy subjects: 53.7 yrs (11.6) 78.6% male	Inclusion: 1) between the ages of 30 and 75 years, 2) have a unilateral locomotor disability consecutive to a stroke 3) demonstrate motor imagery ability 4) be able to stand up and sit down from a chair without using their hands Exclusion: 1) cerebellar or brainstem lesion 2) receptive aphasia 3) moderate to severe body and visuospatial hemineglect or apraxia.	~13.6 months prior Single training session combining mental and physical practice. LOF=2 days	Yes	Kinesthetic and visual imagery questionnaire (a modified version of the movement imagery questionnaire) Motor imagery screening test Motor performance Working memory
McKinney[183] 2002 UK	RCT n=228 Routine care plus a detailed cognitive assessment (Ax)	Psychologist Rehabilitation staff	Hemiparesis NR All patients: 71 years (12.2)	Inclusion: 1) able to complete assessments for at least 30 minutes at a time, 2) did not have visual or hearing impairments	≤4 weeks post admission to hospital Both groups received	Yes	Barthel Index (BI) Cognitive Failures Questionnaires (CFQ)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	n=112 Control n=116		53% male	to the extent that they could not be assessed 3) were conscious on admission to hospital.	cognitive assessment from psychologist Ax group received further detailed battery of cognitive tests LOF=6 months		General Health Questionnaire 28 item (GHQ-28) London Handicap Score (LHS) Nottingham Extended Activities of Daily Living Scale (NEADL) Satisfaction with Care Scale (SWCS)
Nys[184] 2006 Netherlands	Comparative clinical trial: n=92 intravenous recombinant tissue plasminogen activator (rt-PA) treatment n=25 No rt-PA n=67	NR	First ever Ischemic stroke All levels of severity rt-PA: 59.9 yrs (13.9) 86% male No rt-PA 61.7 yrs (12.7) 57% male	Inclusion: 1) patients with first-ever symptomatic ischemic stroke (based on presence of both an acute focal deficit and an associated lesion on CT or MRI) Exclusion: 1) with a neurological or psychiatric history, 2) a history of preexistent cognitive deterioration (as defined by a score of 3.6 or higher on the short Informant Questionnaire on Cognitive Decline in the Elderly - IQCODE Dutch Version), 3) patients who were admitted to the hospital >24 hours following the first symptoms. d) patients older than 85 years	3 hrs post stroke rt-PA or not LOF=6 to 10 months	NR	Barthel Index cognitively intact Frenchay Activities Index (FAI) severity of cognitive impairment
Ozdemir[185] 2001 Turkey	RCT n=60 Multi-disciplinary rehab team (Rehab) n=30 Family caregivers with limited team supervision (Home) n=30	Multi-disciplinary rehab team Family caregivers with limited team supervision	Stroke diagnosis NR Rehab: 49-79 yrs 70% males Home: 43-84 yrs 63% males	Inclusion: 1) Patients with recurrent strokes Exclusion: 1) age >80 years; 2) being unconscious; 3) medically unstable; 4) significant complications that would inhibit the rehabilitation recovery 5) history of transient	~41 days from diagnosis to admission Rehab 2 hrs/day 5 days a week with neuromuscular facilitation Home 2 hrs/day 7 days a week. No	NR	Ashworth Score Brunnstrom Score FIM Score Mini Mental State Examination (MMSE)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				ischemic attacks	neuromuscular facilitation LOF=60 days		
Purdy[186] 2007 USA	Comparative clinical trial n=63 Cognitive rehabilitation in stroke patients (CR) n=27 No cognitive rehabilitation in non-stroke patients with cognitive defects (NR) n=36	nurse SLP OT PT	Right/left Hemisphere Mild/moderate cognitive deficits CR: 66.7 yrs (8.8) % male NR NR: 63 yrs (9.6) % male NR	Inclusion: 1) willing to participate in the study 2) anticipated length of stay greater than 10 days 3) mild to moderate communication and/or cognitive deficits	NR 30 to 60 minutes per day for 5 days per week for the length of stay LOF=Length of stay in rehab unit varied	NR	Progress through a SMP (self-medication program)
Pyoria[187] 2007 Finland	Comparative clinical trial n=80 Activating therapy n=40 Traditional therapy n=40	PT	Ischemic/hemorrhagic Moderate-severe (Barthel Index) Activating therapy: 72 yrs 70% male Traditional therapy: 72 yrs (47-85) 45% Male	Inclusion: 1: independent living at home pre-stroke Exclusion: 1) mild disability and did not need physiotherapy services 5 days after stroke onset 2) premorbid conditions such as cancer or diagnosed dementia.	~ 30 days post stroke Activating: Motor learning, client centered Traditional Therapy: therapist centered, manual inhibition of abnormal movement Time: 12 months LOF=12 months	NR	Barthel Index Postural Control and Balance for Stroke (PCBS) test 10-m gait speed
Robertson[188] 2002 UK	RCT n=40 Limb activation + perceptual training (LA+PT) n=19 Perceptual training (PT) n=21	Research therapist	Ischemic/hemorrhagic NR Limb activation + perceptual training (LA+PT): 69.3yrs (9.0) 68% male Perceptual training (PT)	Inclusion: 1) Diagnosis of right hemisphere stroke according to WHO criteria 2) No history of major psychiatric problems or organic disorder 3) No other co-existing disease or disability preventing testing. 4) Provide informed consent to participate in	~ 152.4 days post stroke 45min weekly sessions for 12 weeks. LOF=24 months	NR	Behavioral Inattention Test score Barthel Index Depression (Hospital Anxiety and Depression Scale) Frenchay Arm Test Motricity Index (left

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
			67.0yrs (9.4) 76% male	the study. 5) Presence of unilateral left visual neglect score of ≤51 on the Star Cancellation Test of the Behavioral Inattention Test or score ≤7 on the Line Bisection Test of the BIT 6) Sensory, physical and cognitive capacities to carry out all the assessment procedures described later. 7) Age <80. 8) No other disability or disease likely to prevent or contaminate assessment or followup. 9) Right handed. 10) Score ≥7 on the Hodkinson Mental Test for dementia			arm + leg) Stimuli detected in lower left visual field Stimuli detected in upper left visual field Tactile Sensory Detections (left) Test of Everyday Attention - Elevator Counting Verbal Memory - immediate recall
Robinson[189] 2000 USA	RCT n=104 Fluoxetine n=40 Nortriptyline n=31 Placebo n=33	nurse	Hemorrhagic and ischemic NR Mean age: Depressed: Fluoxetine: 65 Nortriptyline: 64 Placebo: 73 Non depressed: Fluoxetine: 66 Nortriptyline: 65 Placebo: 67 Male: Depressed: Fluoxetine: 17/23 Nortriptyline:5/16 Placebo: 9/17 Non depressed: Fluoxetine: 15/17 Nortriptyline: 7/15 Placebo: 12/16	Inclusion: 1: acute stroke within 6 months of the onset of the study 2: age 18-85 Exclusion: 1: any other significant medical illness that would threaten the patient's life or recovery from stroke 2: severe comprehension deficit that precluded a verbal interview (defined as failing part 1 of the Token Test) 3: prior history of head injury 4: prior history of other brain disease with the exception of prior stroke	≤6 months post stroke Nortriptyline doses were 25 mg/day for the first week, 50 mg/day for weeks 2 and 3, 75 mg/day for weeks 3-6, and 100 mg/day for the final 6 weeks. Fluoxetine doses were 10 mg/day for the first 3 weeks, 20 mg/day for weeks 4-6, 30 mg/day for weeks 7-9, and 40 mg/day for the final 3 weeks.	Yes	Hamilton rating scale for Anxiety Hamilton rating scale for depression Functional independence measure Johns Hopkins Inventory and Functional Independence measure Mini Mental State Examination (MMSE) social functioning exam

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
					Doses were decreased if side effects were severe LOF=3 weeks		
Rorsman[190] 2006 Sweden	RCT n=54 Electroacupuncture: n=18 High intensity, low frequency, transcutaneous electrical nerve stimulations (TENS): n=19 Low intensity, high frequency, subliminal TENS: n=17	PT OT SLP MD Psychologist	Non-hemorrhagic Moderate - Severe were according to World Health Organization criteria for acute cerebrovascular disease Mean 75.6y 48.1% Male	Inclusion: 1) acute stroke between 5 and 10 days prior to randomization 2) if the stroke was a recurrent one, the patient was not functionally impaired from the previous events 3) Patients with moderate or severe functional impairment at randomization were included. Exclusion: 1) previous neurological, psychiatric, or other disorder making it difficult to pursue the treatment or evaluations 2) inability to comprehend information about the trial 3) concurrent participation in another trial of interventions supposed to affect long-term neurological and functional outcome 4) failure to obtain informed consent	5-10 days after stroke onset 30min sessions twice weekly for 10 weeks. LOF=12 months	Yes	Cognitive functioning Emotional functioning (HADS scales for anxiety/depression, as well as behavioral and activity oriented measures)
Tang[191] 2005 China	RCT n=47 Problem-oriented willed-movement (POWM): n=25 Neurodevelopmental Treatment (NDT): n=22	PT	Brain lesion NR POWM: 56.8 yrs (11.0) 72 % male NDT 54.9 yrs (13.4) 82 % male	Inclusion: 1) first stroke confirmed by CT or MRI 2) not being treated at a rehabilitation center 3) not having global aphasia and severe apraxia, 4) not being delirious 5) having stable vital signs and neurologic problems	6 to 608 days post stroke All treatments 5 or 6 sessions per week in 50 minute sessions LOF=8 weeks	NR	Mini Mental State Examination (MMSE) STREAM (Stroke Rehabilitation Assessment of Movement)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				6) being alert 7) having cognitive function impairments			
Westerberg[75] 2007 Stockholm	RCT n=18 Computerized training on working memory tasks: n=9 passive control group: n=9 Note: Passive control group participants only performed the neurological test battery and completed the CFQ twice with no training in between at the same time-points as the training group performed their pre- and post training tests	Psychologist	Hemorrhagic and ischemic moderate Mean age: 54 years 66.6% male	Inclusion: 1:suffering stroke between 12 and 36 months ago 2:Stroke documented by PET, MRI or CT, 3:ages 30-65, 4:having daily access to a PC with internet connection at home 5: Self-reported deficits in attention Exclusion: 1:IQ <70 2: Motor or perceptual handicap that would prevent use of the computer program. 3: Changing medication during the study period 4: major, depressive-disorder diagnosis as per the DSM-IV diagnostic code 4: history of abuse of alcohol or illicit drugs	12-36 month post stroke 40 minutes per day, 5 days a week for 5 weeks LOF=5 weeks	NR	Neuropsychological tests: including span board, digit span, stoop time, stoop raw score, Raven, PASAT, Ruff 2&7, word list learning, No. of repetitions, delayed recall Ratings of cognitive failure symptoms
Zeloni[192] 2002 Italy	First phase of the study is RCT second phase of the study is non-RCT total n=11 First phase: One week of Treatment (T+): n=4 Control (T-):n= 4 Second phase: Treatment (T+): n=1 Control (T-):n=2	NR	Right hemisphere stroke moderate T+: Mean age 70.6 yrs 80% male T-: Mean age 73.2 yrs 66.6% male	Inclusion: 1) post-acute patients (1-24 months) 2) with neglect following right hemisphere vascular lesions	≥1 month post stroke 2 weeks T+ hemiblinding goggles x1 week. No goggles second week. T- group, patients no hemiblinding goggles. Both groups of patients undertook the battery tests (Albert, letters, Bells, Drawing Line Bisection) Testing sessions	Yes	Accuracy was calculated as a function of test and session

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
					always performed without goggles. LOF=NR		

Abbreviations: ADL=Activities of Daily Living; BIT=Behavioral Inattention Test; CFQ=cognitive failure questionnaire; CT=Computed Tomography; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th edition; FIM=Functional Independence Measure; HADS=Hospital Anxiety and Depression Scale; HAM-D=Hamilton Rating Scale for Depression; IQ=Intelligence Quotient; LOF=Length of Followup; MD=Medical Doctor; MRI=Magnetic Resonance Imaging; NR=Not Reported; OT=Occupational Therapist; PASAT=paced auditory serial addition test; PET=Positron Emission Tomography; PT=Physical Therapist; RCT=Randomized Controlled Trial; RPAB=Rivermead Perceptual Assessment Battery; Rx=treatment; SD=Standard Deviation; SLP=Speech Language Pathologist; WHO=World Health Organization

Table B5: Study, population and Intervention characteristics for studies with Communication outcomes

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Ashtary[193] 2006 Iran	RCT n=38 Bromocriptine: n=19 Placebo: n=19	SLP	Non-fluent aphasic stroke patients from neurology emergency departments NR Bromocriptine: 54.4 (11.4) % male Placebo: 52.8 (14.4) % male	Inclusion: 1) age 80 years and younger 2) right-handedness 3) Persian speaking 4) availability for followup for 4 months 5) no evidence of cardiac, hepatic, renal, or other chronic or neuropsychiatric disorder	NR Patients in Bromocriptine group receive bromocriptine in a 2.5-mg/day increment over 4 weeks to 10 mg/day for a total of 4 months. The dose of bromocriptine or matching placebo remained constant during the following 16 weeks of the study. 4 months of treatment; LOF=4 months	NR	Language assessment, which includes a standardized Persian language test (composed of 7 subsets to evaluate naming, verbal fluency, gesture to command, single-word responses, repetition, automatic speech, prosody. A global score of aphasia was calculated from a total score of 70)
Bakheit[194] 2007 UK	RCT n=116 Intensive therapy: n=51 Standard therapy: n=46 National Health Service Treatment (NHS): n=19	SLP NHS staff	Thromboembolic or Hemorrhagic stroke NR Intensive therapy: 71.2 yrs (14.9) 51% male Standard therapy 69.7 yrs (15.0) 46% male NHS 72.9 yrs (14.7) 53% male	Inclusion: 1) A diagnosis of first ever stroke. The diagnosis is made on clinical grounds and is based on the World Health Organization criteria and confirmed with a CT head scan 2) A score of less than 93.8 on the Western Aphasia Battery 3) Native English language speaker 4) Medically stable and able to undergo the assessments and treatment	Avg 30 days post stroke Intensive therapy: 5 sessions per week of 1 hour each week for 12 weeks Standard therapy and NHS: 2 sessions per week of 1 hour for 12 weeks LOF=24 weeks	NR	Western Aphasia Battery

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				Exclusion: 1) A diagnosis of depressive illness or Parkinson's disease 2) If the patient is moribund and is unlikely to survive the acute stroke 3) Severe dysarthria 4) Residence in an area 15 miles or more from the hospital			
Berthier[195] 2006 Spain	RCT n=26 Donepezil n=13 Placebo n=13	Clinician SLP	Unilateral stroke lesion and chronic aphasia NR Mean age (SD) 48.1 yrs (9.7) 69.2% male	Inclusion: 1) younger than 70 years 2) with a chronic aphasia (≥1 year since onset) and a unilateral stroke lesion.	≥1y post-stroke Donepezil (5 mg/day) or placebo during a 4 week titration phase, followed by a 12-week maintenance phase (10 mg/day of donepezil or placebo) with the possibility of dose adjustment to improve tolerability and a 4 week washout phase. LOF=20 weeks	Yes	Primary: Aphasia Quotient of the Western Aphasia Battery (WAB) Communicative Activity Log (CAL) Secondary: Stroke Aphasic Depression Questionnaire (SADQ) Psycholinguistic Assessment of Language Processing in Aphasia (PALPA)
Doesborgh[196] 2003 Netherlands	RCT n=58 Phonological treatment (FIKS) n=29 Semantic treatment (BOX) n=29 Note: BOX, the semantic treatment, is focused on the interpretation of written words, sentences, and texts.	SLP	Ischemic or hemorrhagic Moderate/Severe NR FIKS: Mean age (SD) 58 (14) 52% male Semantic treatment (BOX) Mean age (SD) 66 (10) 62% Male	Inclusion: 1) Stroke patients with aphasia (age, 20 to 85). 2) Therapists are asked to refer patients whom they consider candidates for an intensive treatment program, taking into account practical, psychological, physical, and cognitive factors. Exclusion: 1) Therapists are	Treatment starts at 3 to 5 months after onset Total treatment is comprised of 40-60 hours of individual treatment which is 1.5 to 3 hours a week in 2 or 3 sessions. LOF=7 month	NR	Primary outcome: Amsterdam Nijmegen Everyday Language Test (ANLET) scores: verbal communicative ability Secondary outcomes: Phonological measures: Repetition non-words (PALPA) and auditory lexical decision (PALPA)

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	FIKS, the phonological treatment, is focused on sound structure.			asked not to refer illiterates, nonnative speakers, or patients with dysarthria, developmental dyslexia, severe acquired dyslexia, or a visual perceptual deficit. 2) patients with "global aphasia" or "recovered or no aphasia" (Aachen Aphasia Test [AAT12] classification) are excluded.			Semantic measures: Semantic Association Test (patient chooses from 4 written words the word semantically closest to a given word), Synonym Judgment (PALPA) (patients judges whether 2 written words are synonyms) Note: PALPA= Psycholinguistic Assessment of Language Processing in Aphasia
Kessler[197] 2000 Germany	RCT n=24 Pirecetam n=12 Placebo n=12	SLP	Ischemic stroke of the left hemisphere and acute aphasia NR Pirecetam : Mean age (SD) 57.41 (13.53) %male: NR Placebo Mean age (SD) 56.33(9.95) %male: NR	Inclusion: 1) right handed 2)suffer from acute aphasia after ischemic stroke of the left hemisphere 3) native speakers 4) between 18 and 75 years 5) without cognitive or mnestic deficits before stroke. 6) Mild to moderate aphasia measured with the Token test. Patients have to reach a score on PET image measurement >50 of 150. 7) Within 14 days after stroke. Exclusion: 1) previous ischemic events 2) hearing/sight disturbances, neurodegenerative disorders, psychiatric disease, drug-induced	within 14 days after stroke Patients receive either pirecetam 2 x 2400 mg/d or placebo for 6 weeks. Plus standard multidisciplinary care LOF=6 weeks	Yes	Neuropsychological Test Battery: include verbal fluency task (Aachen Aphasia), Corsi's block span test, modified laterally score after Oldfield, tests for apraxia, progressive matrices of Raven, and the Benton test. PET/MRI image data

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				dementia, epilepsy, renal insufficiency, treat with other nootropics or with blood-flow supporting medication before baseline			
Laska[198] 2005 Sweden	RCT n=89 Moclobemide n=45 Placebo n=44	MD, Nurses, Pharmacist, SLP	Ischemic or hemorrhagic NR Moclobemide 75 yrs (NR) 57% male Placebo 74 yrs (NR) 56% Male	Inclusion: 1) 18 years or older, 2) acute stroke according to WHO criteria 3) first week after the onset of stroke 4) degree of aphasia is 1.0-4.0 according to the ANELT Exclusion: 1) terminal stage of disease 2) drug abuse 3) ongoing antidepressant treatment during the last month or other ongoing treatment for psychiatric diseases 4) history of dementia or current neuropsychological testing suggesting dementia 5) previous stroke with sequels, acute myocardial infarction 6) risk of suicide 7) pregnancy	≤3 weeks post stroke onset Patients given moclobemide or placebo: 1st Week: 2x150mg/day 2nd week to 1 month: 3x150mg/day 1 month to 6 months: 4x150mg/day LOF=12 months	Yes	ANELT: aphasia assessment Reinvang's aphasia tests: aphasia assessment Note: ANELT=Amsterdam-Nijmegen-Everyday-Language-Test
Pulvermuller[199] 2001 UK	RCT n=17 Constraint induced (CI) Aphasia therapy n=10 Conventional language therapy (CLT) n=7	SLP, MD	Single ischemic stroke NR CI: 55.4 yrs (10.9) CLT: 53.9 yrs (7.4)	Inclusion: 1) fully competent monolingual native speakers of German before stroke. Exclusion: 1) severe perceptual or cognitive deficits	2 to 233 months after stroke onset Conventional language therapy: syndrome-specific standard approach. Therapy is administered for 3 to 5 weeks, resulting in a total	NR	Standard Aphasia tests

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
			70% male	2) left-handed patients 3) those with additional neurological diagnosis	of 20 to 54 hours Constraint induced (CI) Aphasia therapy: 3-4 hours a day for 10 days, total 22 to 33 hours LOF=4 weeks		
Rochon[81] 2005 Canada	RCT n=5 Mapping therapy n=3 Unstructured conversation and narrative telling task n=2	SLP	left hemisphere cerebral accident Severity level 1 or 2; on BDAE Total population: 51 yrs (24.9) 0% male	Inclusion: 1) Chronic aphasia, to demonstrate a profile in symptoms consistent with Broca's aphasia on BDAE, and to produce enough speech to be analyzed.	Start: 2 to 9 years post onset Both groups: one hour sessions, twice a week, 47 sessions (approx. 6 months) in total LOF=7 month	NR	Caplan and Hanna sentence production test Narrative Production Task Picture Comprehension Test Picture Description with Structure Modeling Test (PDSM) Sentence comprehension subtest from the PCB (Philadelphia Comprehension Battery)
Smania[200] 2006 Italy	RCT n=33 Rehabilitative treatment for limb apraxia (LA) n=18 Conventional treatment for aphasia (Conv) n=15 Rehabilitative treatment for limb apraxia (LA) Conventional treatment for aphasia (Conv)	NR	Ischemic or hemorrhagic NR LA: 65.67 yrs (9.83) 67% male Conv: 65.73 yrs (8.78) 73% male	Inclusion: 1: presence of limb apraxia (IA or IMA) lasting at least 2 months. Exclusion: 1: history of previous cerebrovascular attacks or other neurologic disorders 2: age over 80 years 3: uncooperativeness 4: presence of orthopedic or other disabling disorders	10-17 months post stroke All patients receive 30 treatment sessions, three per week, each lasting 50 minutes. LOF=18 weeks	NR	Before and after treatment: ADL questionnaire by patient's caregiver constructional apraxia gesture comprehension tests ideational apraxia (IA) ideomotor apraxia (IMA) intelligence oral apraxia

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
							verbal comprehension Followup evaluation: ADL questionnaire gesture comprehension tests
Thorsen[79] 2005 Sweden	RCT n=83 Home rehabilitation group (HRG) n=42 Conventional rehabilitation group (CRG) n=41	OT, PT, SLP	Diagnosis of stroke NR Total: Mean age 72 HRG: 50% male CRG: 14/10	Inclusion: 1: Acute stroke 2: Independence in feeding and continence 3: Mini-Mental State Examination score of >23 4: Impaired motor capacity 5: and/or Dysphasia Exclusion: 1: Discharged before 5 days of hospitalization 2: Progressive stroke 3: Subdural hematoma 4: Subarachnoid hemorrhage 5: Clinical sign of massive perceptual deficit 6: Renal, heart, or respiratory failure 7: Non-stroke epilepsy 8: Alcoholism 9: Psychiatric disease 10: Other comorbidity likely to shorten length of life dramatically.	After discharge from stroke unit HRG: mean duration is 14 weeks, mean number of home visits=12. CRG: received additional rehabilitation in the Geriatrics or Rehabilitation Department. LOF=5 years	Yes	activities of daily living (ADL) dysphasia motor capacity self-reported falls social activities subjective dysfunction Survival
Walker-Batson[201] 2001 USA	RCT n=21 DEXamphetamine 10 mg n=12 Placebo n=9	SLP	Aphasic patients with an acute non hemorrhagic infarction NR 10 mg	Inclusion: 1) single, left, non-hemorrhagic middle cerebral artery distribution infarction, 2) native English speakers	16 to 45 days after stroke onset Patients receive an oral dose of 10mg dextroamphetamine or placebo paired	Yes	PICA: the Porch Index of Communicative Abilities, which was used as the dependent language measure.

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
			DEXamphetamine 61.3 yrs (7:2) 78% male Placebo: 51.8 yrs (6:6) 50% male	3) aged 41 to 71 years 4) diagnosis based on neurological and radiological examination, confirmed the presence of a single infarction at entry Exclusion: a) terminal medical condition (AIDS, cancer, other coincident neurological disease b) history of psychiatric illness or extensive alcohol or drug abuse, unstable cardiac dysarrhythmia or uncontrolled hypertension or untreated hyperthyroidism 3) receiving alpha-adrenergic antagonists or agonists 4) aged >80 years	with speech/language therapy on 3-day/4-day cycle for 10 sessions over 5 weeks. LOF=6months		PICA score at 1 week off drug PICA score at 6 month followup Speech/language therapy hours at 1 week off drug
Wolfe[202] 2000 UK	RCT n=43 Home treatment by a Rehabilitation team n=23 Usual community care n=20	Rehabilitation team	Diagnosed with stroke NR Rehabilitation team: 72 yrs (12) 43% male Usual community care: 76 yrs (7.04) 40% male	Inclusion: 1) all patients who remained at home after their stroke were eligible	NR The mean number of physiotherapy sessions is 3 (range 1-14) for the rehabilitation team group and 2 for the usual care group LOF=1 year	NR	Primary outcome: Barthel score Secondary outcomes: 5-meter timed walk Albert Test Caregiver strain FAST:Frechany Aphasia Screening Test Hospital Anxiety and Depression scale Mini-mental state examination Motricity Index Nottingham Health

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
							Profile Rivermead activities of daily living score Speech disturbance

Abbreviations: ADL=activities of daily living; ANELT=Amsterdam-Nijmegen-Everyday-Language-Test; BDAE=Boston Diagnostic Aphasia Examination; IA=ideational apraxia; IMA=ideomotor apraxia; LOF=length of followup; MD=Medical Doctor; NHS=National Health Service; NR=not reported; OT=Occupational Therapist; PICA=Porch Index of Communicative Abilities; PT=Physical Therapist; RCT=Randomized Controlled Trial; SD=standard deviation; SLP=Speech Language Pathologist; yrs=years; WHO=World Health Organization

Table B6: Study, population and Intervention characteristics for studies with Dysphagia outcomes

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Carnaby[203] 2006 United States	RCT n=306 High-intensity intervention n=102 Low-intensity intervention n=102 Usual care n=102	SLP	Ischemic or hemorrhagic Severity varies High-intensity intervention: 71.4 yrs (12.7) 58% male Low-intensity intervention: 72 yrs (12.4) 58% male Usual care: 69.8 yrs (12.5) 59% male	Inclusion: 1: WHO definition of stroke; 2: onset of stroke within the previous 7 days; 3: clinical diagnosis of swallowing difficulty as measured by a score of less than 85 on the Paramatta Hospital's assessment of dysphagia; 4: no history of swallowing treatment or surgery of the head or neck; 5: written informed consent to participate in the trial and to be followed up for the next 6 months.	Within 7 days of stroke onset low intensity: 3x wk for a month, or for the duration of the hospital stay (if less than a month). Standard high intensity every working day for a month or daily for the duration of the hospital stay. Usual care: consists mainly of supervision for feeding and precautions for safe swallowing. LOF=6 months	No	Primary: normal diet - the proportion of patients who returns to their normal pre-stroke diet with 6 months after randomization. Secondary: Any complication: dysphagia related complications (chest infection, death, dependency, institutionalization) Functional swallowing: the time to return to a normal diet
Crary[204] 2004 United States	Retrospective outcomes analysis n=45 patients with dysphagia secondary to stroke n=25 patients with dysphagia secondary to head/neck cancer n=20	SLP	Mix of single hemisphere, multiple hemisphere lesions and brain stem stroke NR Stroke patients: 69 yrs 67.8% male Head/neck cancer patients: 67 yrs 65% male	Inclusion: 1: individuals demonstrates sufficient cognitive abilities to interact verbally with the speech-language pathologist and to understand the instructions and cooperate with a biofeedback approach. 2: demonstrated pharyngeal dysphagia on videofluorographic examination characterized by reduced hyolaryngeal elevation during swallowing, reduced pharyngoesophageal segment opening, and postswallow residue	NR Intervention timing: daily, excluding weekends, for 50-min. clinical sessions. Plus two home therapy sessions per day in which they practice the activities completed during the clinical therapy session LOF=NR	No	Functional Oral Intake Scale (FOIS), a 7-point ordinal scale reflecting patient report of food/liquid safely ingested by mouth on a consistent basis. This scale is used to estimate the change in functional oral intake
Dennis[205] 2005 United Kingdom	RCT n=859 Early tube n=429	Clinician Clinical team	Diagnosis of stroke NR	Inclusion: 1: within 7 days of stroke (first-ever or recurrent) 2: responsible clinician	Intervention timing: within 7 days Patients are allocated to start enteral tube feeding	No	Poor outcome is defined as Modified Rankin Scale score 4-5

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
Study A: early tube vs avoid tube	Avoid tube n=430		Early tube: 76 (11) 45% male Avoid tube: 76 (11) 46% male	is uncertain of the best feeding policy 3: patient or a relative consents Exclusion: 1: subarachnoid hemorrhage	(via the clinician's preferred tube) as soon as possible or to avoid any enteral tube feeding for at least 7 days. Patients who are not tube fed are given parenteral fluids either intravenously or subcutaneously, but not nutrition LOF=6 months		
Dennis[205] 2005 United Kingdom Study B: PEG vs nasogastric	RCT n=321 Percutaneous endoscopic gastronomy (PEG) n=162 Nasogastric n=159	Clinician Clinical team	Diagnosis of stroke NR PEG: 76 (10) 45% male Nasogastric 76 (10) 45% male	Inclusion: 1: within 7 days of stroke (first-ever or recurrent) 2: responsible clinician is uncertain of the best feeding policy and 3: patient or a relative consented Exclusion: 1: subarachnoid hemorrhage	Intervention timing: recent (within 7 days before admission) stroke (first-ever or recurrent) Patients are allocated to enteral tube feeding via PEG or nasogastric tube within 3 days of enrolment. The allocation method is continued as long as it remains practical, or as the patient's condition dictates LOF=6 months	No	Poor outcome is defined as Modified Rankin Scale score 4-5
Ebihara[206] 2006 Japan	RCT n=105 Nasal inhalation of black pepper oil n=35 Nasal inhalation of lavender oil n=35 Nasal inhalation of distilled water n=35	NR	Chronic cerebrovascular disease NR Total Population: 85.8 (2.2) 23% Male	Inclusion: 1: physical symptoms and cognitive impairment of the patients must have been stable for the preceding 3 months. Exclusion: 1: unstable health conditions such as pyrexia or heart and respiratory disease, 2: obvious sinus problems such as sinus infection or nasal congestion on the day of the examination	≥3 months post stroke 1minute treatment prior to each meal (~3/day) for 30 days LOF=30 days	Yes	Latency of swallowing reflex (seconds) Log concentration of citric acid for cough Number of swallows for 1 minute Olfactory identification test Serum substance P Levels
Freed[207] 2001 United States	RCT n=99 Transcutaneous electrical stimulation (ES) n=63	SLP, MD, PT	Primary diagnosis of stroke NR TS:	Inclusion: 1: Primary diagnosis of stroke. 2: Confirmation of swallowing disorder by modified barium swallow (MBS).	Within 24 hours TS was given in three 20-min intervals daily ES is delivered at the therapy current for a	NR	Swallow function score: based on substances the patients can swallow during a MBS

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	Thermal-tactile stimulation (TS) n=36		78.1 (NR) 56% male ES: 75.7 (NR) 52% Male	Exclusion: 1: inability to complete at least 2 consecutive days of therapy 2: any behavioral disorder that interferes with administration of therapy 3: substantial reflux from feeding tube 4: dysphagia from drug toxicity	total of 60 min sessions, with 1 second pauses between each minute Both groups received standard treatment LOF: 3 years		
Goulding[83] 2000 United Kingdom	RCT n=46 Manual preparation of fluid viscosity (Manual): n=23 Viscometer preparation (Viscometer): n=23	Nurses SLP	Ischemic or hemorrhagic stroke NR Manual: 78.5 (50-91) 52% male Viscometer: 77.2 (58-91) 48% Male	Inclusion: 1: dysphagia as a result of an acute ischemic or hemorrhagic stroke. 2: Stroke is diagnosed according to the WHO criteria and confirmed with CT brain scans. 3: dysphagia is confirmed by an experienced SALT Exclusion: 1: premorbid swallowing difficulties	7 day period at an unreported time post stroke 75 ml of thickened orange juice solution, daily at meal times for 7 days LOF=7days	NR	Pulmonary aspiration: patients are observed for signs of aspiration while swallowing 75ml of the thickened orange juice solution.
Hamidon[208] 2006 Malaysia	RCT n=22 Nasogastric (NG) feeding tube n=12 Percutaneous endoscopic gastronomy (PEG) n=10	MD, Dietician	Acute ischemic stroke with persistent dysphagia for 7 or more days NR NG: 72 (54-77) 50% male PEG: 65 (48-79) 50% male	Inclusion: 1: admitted with acute ischemic stroke (acute cerebral infarct) 2: persistent dysphagia for seven or more days	≥7 days post stroke with dysphagia 1 to 2 days: Intervention consists of the insertion of the feeding tube, hence the duration of the surgical procedure. Dietary regime for all daily meals post surgery LOF=4 weeks	Yes	Nutritional markers (blood serum albumin levels)
Huang[84] 2006 China	Cohort Study n=96 Fed by family member: n=48 Fed by trained nurse: n=48	Family member nurse	Diagnosis of stroke NR NR	Inclusion: 1: consecutive patients presenting with dysphagia due to acute stroke 2: within 24 hours of the stroke 3: receiving oral feeding from day 0. Exclusion:	within 24 hours of the stroke Patients are examined daily LOF=NR	No	Incidence of aspiration pneumonia

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
				1: admission more than 24 hours after stroke onset 2: tube feeding from day 0 3: coma on admission and during hospital stay 4: endotracheal intubation in hospital.			
Iizuka[209] 2005 United States	Retrospective case-matched controlled study n=386 Percutaneous endoscopic gastronomy (PEG): n=193 Non-PEG: n=193	PT, OT, SLP	Primary ischemic or hemorrhagic stroke NR PEG: 71.2 yrs (10.7) 60.6% male Non- PEG: 71.0 yrs (10.8) 60.6% male	Inclusion: 1: primary diagnosis of ischemic or hemorrhagic stroke; 2: duration from stroke onset to rehabilitation admission 90 days or less	≤90 days of stroke onset 3 therapy sessions/day with a treatment period lasting an average of 78.7 days LOF=approximately 175 days	No	Change in functional independence measure (FIM) score from rehabilitation hospital admission to discharge FIM efficiency score
Lin[2] 2003 Taiwan	Quasi-experimental parallel cluster design n=49 Swallowing training n=35 No therapy n=14	MD, nurse, SLP	Diagnosis of stroke NR Swallowing: 70.6 yrs (11.5) 74.3% Male No therapy: 71.2 yrs (11.1) 78.6% male	Inclusion: 1: diagnosis of stroke 2: video-fluoroscopic evidence of dysphagia characterized by the sum of oral transit time, pharyngeal transit time and a swallowing trigger time of over 2.5 seconds 3: receiving nutrition and hydration via oral intake 4 : SPMSQ score of 4 or higher 5: able to communicate in Mandarin or Taiwanese dialect	5 to 312 months post stroke Each treatment session lasts 30 minutes, and treatments are performed for 6 days per week for 8 weeks LOF=8 weeks	NR	Blood examination for Hemoglobin and albumin Body Mass Index (BMI) Body weight Coughing/choking frequency during meal Efficacy of swallowing (volume per second, volume per swallow) Mid-arm circumference Neurological examination Signs and/or symptoms on a swallowing questionnaire
Power[210] 2006 United Kingdom	RCT n=16 Active faucial pillar (FP) stimulation n=8 Sham FP stimulation	MD	Ischemic or hemorrhagic NR FP: 74 yrs (2) 75% male Sham FP:	Inclusion: 1: hemispheric stroke patients 2: diagnosis of dysphagia 3: admitted to an acute hospital 4: consent to participate in the study	≤2 weeks of stroke FP: electrical stimulation to FP at 75% of max tolerated intensity for 5 min on each side. Sham: electrodes used but not current passed	No	Aspiration-penetration scale Cricopharyngeal Opening Duration Laryngeal Closure Duration Oral Transit Time Pharyngeal Transit Time Sensory and Pain

Author Year Country	Study Design Comparator vs. Interventions Sample Size	Care providers	Population Severity Mean age (SD) % Male	Inclusion/ Exclusion	Intervention Timing Frequency/ duration Length of Followup	Prior or concomitant Rx present	Outcomes Measured
	(sham) n=8		72 yrs (4) 75% male	Exclusion: 1: a history of swallowing difficulty 2: neurologic disease other than stroke 3: intercurrent illness or upper gastrointestinal disease 4: inability to give informed consent	LOF=none		Threshold Stimulus Intensity Swallow Response Time
Seki[211] 2005 Japan	RCT n=32 Acupuncture with usual care n=18 Usual care: n=14	Staff at an elderly care facility	Chronic stroke trouble swallowing NR Acupuncture: 77 yrs (9.0) 44.5% Male Usual care: 79 yrs (5.0) 28.6% Male	Inclusion: Post-stroke patients with episodes of choking while eating or drinking	NR Acupuncture sessions: 3 times/week for 4 weeks LOF=4 weeks	No	Pharyngeal retention Swallowing time of water and fluid measured by videofluoroscopic study Total number of days of fever above 37.8C Tracheobronchial post-deglutitive aspiration

Abbreviations: APS=Aspiration-penetration scale; CT=Computerized tomography; ES=Transcutaneous electrical stimulation; FIM=functional independence measure; FOIS=Functional Oral Intake Scale; FP=faucial pillar; LOF=Length of Followup; MBS=Modified Barium Swallow; MD=medical doctor; NG=Nasogastric; NR=Not Reported; OT=Occupational Therapist; PT=Physical Therapist; PEG=percutaneous endoscopic gastronomy; RCT=Randomized Controlled Trial; Rx=treatment; SLP=Speech Language Pathologist; SD=Standard Deviation; sEMG=surface electromyographic; SPMSQ=Short Portable Mental Status Questionnaire; TS=Thermal-tactile stimulation; WHO=World Health Organization; yrs=years

Appendix C: Quality Tables

Table C1a: Quality measures of randomized controlled trials with Ambulation outcomes

Study	Study reported as Random-ized	Random-ized Process Described	Conceal-ment of random-ization	"Blinding" as described by author	Patients blinded	Health-care provider Blinded	Data Collector Blinded	Out-come assessor blinded	Reasons and No. of Dropouts and With-drawals Reported	Report-ing adverse events	Authors report co-morbidity	Authors report co-inter-vention	Con-sistency of the therapy in the groups (was it applied to all patients)
Askim[125] 2006 Norway	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	No	Yes	No	Yes
Bayouk[126] 2006 Canada	Yes	No	NR	NR	NR	NR	NR	NR	Yes	No	No	No	Yes
Bayram[127] 2006 Turkey	Yes	No	NR	Yes	NR	NR	NR	Yes	Yes	No	Yes	No	Yes
Chen[128] 2005 Taiwan	Yes	No	NR	Yes	NR	NR	NR	NR	No	No	No	Yes	Yes
Macko[130] 2005 United States	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes
Marigold[60] 2005 Canada	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Mayr[131] 2007 United States	Yes	Yes	NR	Yes	No	No	NR	Yes	Yes	No	Yes	Yes	Yes
Pang[132] 2005 Canada	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes
Peurala[133] 2005 Finland	Yes	No	Yes	NR	NR	NR	NR	NR	Yes	No	Yes	No	Yes
Sutbeyaz[135] 2007 Turkey	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	No	Yes
Sze[136] 2002 Hong Kong	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Thaut[137] 2007 United States	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	No	No	No	Yes
Tong[138] 2006 China	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	No	No	Yes
Yan[139] 2005 China	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	Yes	Yes	No	Yes
Yang[140] 2007 Taiwan	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	No	Yes	No	Yes

Yavuzer[141] 2006 Turkey	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	No	Yes
Yavuzer[142] 2006 Turkey	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	No	No	No	Yes

Abbreviations: NR—not reported

Table C1b: Quality measures of other comparative clinical trials with Ambulation outcomes

Study	Study groups com-parable at baseline for important con-founders	Were all study subjects drawn from the same source population? (answer 'no' for historical controls)	"Blinding" as described by author	Patients blinded	Health-care provider Blinded	Data Collector Blinded	Out-come assessor blinded	Reasons and No. of Dropouts and Withdrawals Reported [# enrolled/ number completing]	Report-ing adverse events	Authors report co-morbidity	Authors report co-inter-vention	Con-sistency of the therapy in the groups (was it applied to all patients)
English[129] 2007 Australia	No	Yes	Yes	No	No	NR	Yes	Yes	Yes	Yes	No	Yes
Peurala[134] 2005 Finland	Yes	Yes	No	No	No	No	No	No	No	No	No	Yes
Roerdink[63] 2007 Netherlands	No	No	No	No	No	No	No	No	No	Yes	No	Yes

Abbreviations: NR = not reported

Table C2a: Quality measures of randomized controlled trials with Quality of Life outcomes

Study	Study reported as Rando-mized	Rando-mized Process Described	Conceal-ment of random-ization	"Blinding" as described by author	Patients blinded	Health-care provider Blinded	Data Collector Blinded	Out-come assessor blinded	Reasons and No. of Dropouts and With-drawals Reported	Report-ing adverse events	Authors report co-morbidity	Authors report co-inter-vention	Con-sistency of the therapy in the groups (was it applied to all patients)
Askim[125] 2006 Norway	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	No	Yes	No	Yes
Barreca[144] 2004 Canada	Yes	Yes	No	Yes	No	No	NR	Yes	No	No	No	No	Yes
Chae[145] 2005 USA	Yes	Yes	NR	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes
Childers[146] 2004 USA	Yes	No	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes
Fjaertoft[147] 2004 Norway	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
GAPS Group[148] 2004 Glasgow	Yes	Yes	Yes	Yes	NR	NR	NR	Yes	Yes	Yes	Yes	No	Yes
Johnson[150] 2004 United Kingdom	Yes	Yes	NR	Yes	No	No	No	No	Yes	No	No	Yes	Yes
Kalra[151] 2005 UK	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kendall[152] 2007 Australia	Yes	Yes	NR	No	NR	NR	NR	NR	Yes	No	Yes	No	Yes
Lincoln[154] 2004 United Kingdom	Yes	Yes	NR	Yes	No	No	NR	Yes	Yes	No	No	No	Yes
McClellan[155] 2004 Australia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes
Park[64] 2005 UK	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Ryan[156] 2006 UK	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes
Studenski[157] 2005 USA	Yes	No	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	No	Yes
Wayne[158] 2005 USA	Yes	Yes	Yes	Yes	Yes	No	Yes	NR	Yes	No	Yes	No	Yes

Abbreviations: NR = not reported

Table C2b: Quality measures of other comparative clinical trials with Quality of Life outcomes

Study	Study groups comparable at baseline for important confounders	Were all study subjects drawn from the same source population? (answer 'no' for historical controls)	"Blinding" as described by author	Patients blinded	Health-care provider Blinded	Data Collector Blinded	Out-come assessor blinded	Reasons and No. of Dropouts and With-drawals Reported	Reporting adverse events	Authors report co-morbidity	Authors report co-inter-vention	Con-sistency of the therapy in the groups (was it applied to all patients)
Leeds[153] 2004 UK	Yes	Yes	Yes	No	No	No	No	Yes	No	Yes	No	Yes
Hafstein-dottir[149] 2005 The Netherlands	Yes	Yes	No	NR	NR	NR	NR	Yes	No	Yes	No	Yes

Abbreviations: NR = not reported

Table C3: Quality measures of randomized controlled trials with Daily Activities outcomes

Study	Study reported as Randomized	Randomized Process Described	Concealment of randomization	"Blinding" as described by author	Patients blinded	Healthcare provider Blinded	Data Collector Blinded	Outcome assessor blinded	Reasons and No. of Dropouts and Withdrawals Reported	Reporting adverse events	Authors report comorbidity	Authors report cointervention	Consistency of the therapy in the groups (was it applied to all patients)
Boake[159] 2007 United States	Yes	No	NR	Yes	NR	NR	NR	Yes	Yes	Yes	No	No	Yes
Daly[160] 2005 United States	Yes	No	NR	Yes	No	No	Yes	Yes	Yes	Yes	No	No	Yes
Ertel[161] 2007 United States	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	Yes	No	Yes
Gilmore[73] 2007 Canada	Yes	Yes	NR	No	NR	NR	NR	NR	No	No	No	No	Yes
Gladstone[162] 2006 Canada	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Higgins[163] 2006 Canada	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Hsieh[164] 2007 Taiwan	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes
Langhammer[73] 2007 Norway	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes
Mead[165] 2007 United Kingdom	Yes	Yes	Yes	Yes	Yes	NR	NR	Yes	Yes	Yes	Yes	No	Yes
Ng[166] 2007 Hong Kong	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	No	Yes
Olney[167] 2006 Canada	Yes	Yes	Yes	Yes	NR	NR	NR	No	Yes	No	No	No	Yes
Page[168] 2007 United States	Yes	Yes	Yes	Yes	NR	NR	NR	Yes	Yes	No	Yes	No	Yes
Pohl[169] 2007 Germany	Yes	Yes	Yes	Yes	No	Yes	NR	Yes	Yes	Yes	Yes	No	Yes
Rydwik[170] 2006 Sweden	Yes	Yes	NR	Yes	No	No	NR	Yes	Yes	No	No	No	Yes
Sackley[171] 2006 United Kingdom	Yes	Yes	Yes	Yes	NR	No	NR	Yes	Yes	Yes	No	No	Yes
van Nes[172]	Yes	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	No	Yes

2006 Netherlands													
Wittenberg[173] 2003 United States	Yes	Yes	NR	Yes	NR	NR	NR	Yes	Yes	No	No	No	No
Wolf[174] 2006 United States	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	No
Wu[175] 2007 Taiwan	Yes	Yes	NR	Yes	Yes	NR	Yes	NR	Yes	No	No	No	Yes
Yagura[176] 2006 Japan	Yes	Yes	Yes	Yes	No	NR	NR	No	Yes.	Yes	Yes	No	Yes

Abbreviations: NR = not reported

Table C4a: Quality measures of randomized controlled trials with Cognition outcomes

Study	Study reported as Random-ized	Random-ized Process Described	Conceal-ment of random-ization	Author described blinding	Patients blinded	Health-care provider Blinded	Data Collector Blinded	Out-come assessor blinded	Reasons and No. of Dropouts and With-drawals Reported	Report-ing adverse events	Authors report co-morbidity	Authors report co-inter-vention	Con-sistency of the therapy in the groups (was it applied to all patients)
Cherney[76] 2003 USA	Yes	No	NR	No	NR	NR	NR	NR	Yes	No	No	No	Yes
Cirstea[177] 2006 Canada	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes
Edmans[178] 2000 UK	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	No	Yes	No	Yes
Frassinetti[179] 2002 Italy	Yes	Yes	NR	No	No	No	No	No	Yes	No	Yes	No	Yes
Harvey[180] 2003 UK	Yes	Yes	NR	NR	NR	NR	NR	NR	Yes	No	Yes	No	Yes
Kimura[181] 2000 USA	Yes	No	NR	Yes	Yes	Yes	NR	Yes	Yes	No	Yes	No	Yes
Malouin[182] 2004 Canada	Yes	No	NR	No	No	No	NR	NR	Yes	No	Yes	Yes	Yes
McKinney[183] 2002 UK	Yes	Yes	Yes	Yes	No	NR	Yes	Yes	Yes	No	Yes	Yes	Yes
Ozdemir[185] 2001 Turkey	Yes	Yes	NR	NR	No	No	NR	NR	No	Yes	Yes	Yes	No
Robertson[188] 2002 UK	Yes	No	NR	Yes	Yes	No	Yes	NR	Yes	No	Yes	No	Yes
Robinson[189] 2000 USA	Yes	No	NR	Yes	Yes	NR	NR	Yes	Yes	Yes	Yes	Yes	Yes
Rorsman[190] 2006 Sweden	Yes	No	Yes	NR	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Tang[191] 2005 China	Yes	Yes	NR	Yes	No	No	No	Yes	No	No	Yes	No	NR
Westerberg[75] 2007 Stockholm	Yes	No	No	No	NR	NR	NR	NR	No	No	Yes	No	No
Zeloni[192] 2002 Italy	Phase 1: Yes Phase 2: No	No	No	No	No	No	NR	NR	Yes	No	No	No	Yes

Abbreviations: NR = not reported

Table C4b: Quality measures of other comparative clinical trials with Cognition outcomes

Study	Study groups com-parable at baseline for important con-founders	Were all study subjects drawn from the same source popul-ation?	Author described blinding	Patients blinded	Health-care provider Blinded	Data Collector Blinded	Outcome assessor blinded	Reasons and No. of Dropouts and With-drawals Reported	Reporting adverse events	Authors report co-morbidity	Authors report co-inter-vention	Consistency of the therapy in the groups (was it applied to all patients)
Nys[184] 2006 Netherlands	Yes	Yes	NR	NR	NR	NR	NR	No	Yes	Yes	No	No
Purdy[186] 2007 USA	No	Yes	No	No	No	No	No	No	No	Yes	No	Yes
Pyoria[187] 2007 Finland	No	Yes	No	No	No	No	No	Yes	No	Yes	No	No

Abbreviations: NR = not reported

Table C5: Quality measures of randomized controlled trials with Communication outcomes

Study	Study reported as Randomized	Randomized Process Described	Concealment of randomization	Author described blinding	Patients blinded	Healthcare provider Blinded	Data Collector Blinded	Outcome assessor blinded	Reasons and No. of Dropouts and Withdrawals Reported	Reporting adverse events	Authors report co-morbidity	Authors report co-intervention	Consistency of the therapy in the groups (was it applied to all patients)
Ashtary[193] 2006 Iran	Yes	Yes	NR	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	No	Yes
Bakheit[194] 2007 UK	Yes	Yes	Yes	Yes	NR	NR	NR	Yes	Yes	No	Yes	No	Yes
Berthier[195] 2006 Spain	Yes	Yes	Yes	Yes	Yes	Yes	NR	NR	Yes	Yes	No	Yes	Yes
Doesborgh[196] 2004 Netherlands	Yes	Yes	Yes	Yes	NR	NR	Yes	Yes	Yes	No	Yes	No	Yes
Kessler[197] 2000 Germany	Yes	Yes	NR	Yes	NR	NR	NR	NR	No	No	Yes	Yes	Yes
Laska[198] 2005 Sweden	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Pulvermuller[199] 2001 UK	Yes	Yes	NR	Yes	NR	NR	NR	Yes	No	No	No	No	No
Rochon[81] 2005 Canada	Yes	No	NR	No	NR	NR	NR	NR	No	No	No	No	Yes
Smania[200] 2006 Italy	Yes	No	NR	Yes	NR	NR	NR	Yes	Yes	No	Yes	No	Yes
Thorsen[79] 2005 Sweden	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Walker-Batson[201] 2001 USA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wolfe[202] 2000 UK	Yes	Yes	Yes	Yes	No	NR	NR	Yes	Yes	No	No	No	Yes

Abbreviations: NR = not reported

Table C6a: Quality measures of randomized controlled trials with Dysphagia outcomes

Study	Study reported as Randomized	Randomized Process Described	Concealment of randomization	Author described blinding	Patients blinded	Healthcare provider Blinded	Data Collector Blinded	Outcome assessor blinded	Reasons and No. of Dropouts and Withdrawals Reported	Reporting adverse events	Authors report comorbidity	Authors report cointervention	Consistency of the therapy in the groups (was it applied to all patients)
Carnaby[203] 2006 United States	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	Yes	Yes	No	No
Dennis[205] 2005 United Kingdom	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	Yes	No	No	Yes
Study A													
Dennis[205] 2005 United Kingdom	Yes	Yes	Yes	Yes	No	No	NR	Yes	Yes	Yes	No	No	Yes
Study B													
Ebihara[206] 2006 Japan	Yes	Yes	NR	Yes	NR	NR	NR	Yes	Yes	No	Yes	No	Yes
Goulding[83] 2000 United Kingdom	Yes	Yes	NR	Yes	NR	NR	NR	Yes	Yes	Yes	Yes	No	No
Hamidon[208] 2006 Malaysia	Yes	Yes	NR	No	NR	NR	NR	NR	Yes	Yes	No	No	Yes
Power[210] 2006 United Kingdom	Yes	No	NR	Yes	NR	NR	NR	NR	Yes	No	No	No	Yes
Seki[211] 2005 Japan	Yes	No	NR	Yes	NR	NR	NR	Yes	Yes	Yes	No	No	Yes

Abbreviations: NR = not reported

Table C6b: Quality measures of other comparative clinical trials with Dysphagia outcomes

Study	Study groups comparable at baseline for important confounders	Were all study subjects drawn from the same source population? (answer 'no' for historical controls)	"Blinding" as described by author	Patients blinded	Health-care provider Blinded	Data Collector Blinded	Outcome assessor blinded	Reasons and No. of Drop-outs and Withdrawals Reported	Reporting adverse events	Authors report co-morbidity	Authors report co-intervention	Consistency of the therapy in the groups (was it applied to all patients)
Crary[204] 2004 United States	No	No	No	NR	NR	NR	NR	Yes	No	No	No	Yes
Freed[207] 2001 United States	Yes	Yes	No	NR	NR	NR	NR	Yes	Yes	Yes	No	Yes
Huang[84] 2006 China	Yes	Yes	No	NR	NR	NR	NR	No	Yes	No	No	Yes
Iizuka[209] 2005 United States	Yes	Yes	No	NR	NR	NR	NR	No	Yes	No	No	Yes
Lin[2] 2003 Taiwan	Yes	Yes	No	NR	NR	NR	NR	Yes	No	No	No	Yes

Abbreviations: NR = not reported

Appendix D. Outcome Tables

Table D1: Outcome measurement instruments used in Ambulation studies*

Outcome	Mode of Adminis-tration**	Fre-quency in studies	ICF domain	Reliability in Stroke	Validity in Stroke	Tested for Responsive-ness	MCID in stroke	Range of follow up time for studies	Study Author
Fugl-Meyer	Observation performance	3	Function[44,51]	Yes	Yes	Yes	NR	4 weeks to 6 month	Sutbeyaz[135] Yavuzer[141] Thaut[137]
Modified Ashworth Scale (MAS)	Performance	2	Function[51]	Yes	Yes	Yes	NR	0-6 months	Sutbeyaz[135] Chen[128]
Scandinavian Stroke Scale	NR	1	Function[44,52]	Yes	Yes	Yes	NR	1-52 weeks	Askim[125]
Motricity Index	NR	2	Function[52]	Yes	Yes	Yes	NR	4-9 weeks	Mayr[131] Tong[138]
10-metre walking test	NR	6	Activity[44]	Yes	Yes	Yes	NR	2 weeks-6 month	Peurala[133] Chen[128] Bayram[127] Peurala[134] Mayr[131] Bayouk[126]
Barthel Index	Self report, observation/ performance, proxy	2	Activity[44,51,52]	Yes	Yes	Yes	NR	3-4 weeks	Tong[138] Thaut[137]
Berg Balance Scale (BBS)	Performance	5	Activity[51]	Yes	Yes	Yes	NR	1-52 weeks	Askim[125] Marigold[60] Tong[138] English[129] Pang[132]
Functional Independence Measure (FIM)	Interview, proxy	4	Activity[51]	Yes	Yes	Yes	NR	4 weeks-6 month	Sutbeyaz[135] Peurala[133] Peurala[134] Tong[138]
Functional Ambulation Categories (FAC)	Interview/ Observation	2	Activity[51]	Yes	Yes	Yes	NR	4 weeks to 6 months	Sutbeyaz[135] Tong[138]
Time up and go (TUG)	Observation/ performance	2	Activity[51]	Yes	Yes	Yes	NR	8 weeks to 1 year	Marigold[60] Yan[139]
Rivermead Motor Assessment Scale	NR	1	Activity[9]	Yes	Yes	Yes	Yes	9 weeks	Mayr[131]
6-minute walk test (6MWT)	NR	4	Activity[9]	Yes	Yes	Yes	NR	0-6 months	Mayr[131] Peurala[133] Macko[130] Pang[132]
5-minute walk test (5MWT)	NR	2	Activity[16]	Yes	Yes	Yes	NR	6 months to 52 weeks	Askim[125] English[129]

2-minute walk test (2MWT)	NR	1	Activity[16]	Yes	Yes	Yes	NR	6 months	English[129]
Activities Balance confidence (ABC)	NR	1	Activity[16]	Yes	Yes	Yes	NR	1 year	Marigold[60]
Kinematic characteristics of gait	NR	1	Function[16]	Yes	Yes	Yes	NR	8 weeks	Yavuzer[141]
Rivermead Mobility Index (RMI)	NR	1	Activity[16]	Yes	Yes	Yes	NR	6 months	Macko[130]
Gait velocity	NR	1	Activity[16]	Yes	Yes	Yes	NR	3 weeks	Thaut[137]
Biomechanical measurements- 3 dimensional gait analysis, walking velocity, cadence, step length and single support time, pelvic excursion, excursion of paretic hip, knee and ankle in saggital plane	NR	1	Function[16]	Yes	Yes	Yes	NR	8 weeks	Yavuzer[141]
Gait Assessment	NR	1	Function[16]	Yes	Yes	Yes	NR	29 weeks	Peurala[134]
Preferred walking (walking speed, cadence, stride time, stride length, and temporal symmetry index)	NR	1	Function[16]	Yes	Yes	Yes	NR	4 weeks	Yang[140]
Walking carrying a tray with glasses (walking speed, cadence, stride time, stride length, and temporal symmetry index)	NR	1	Function[16]	Yes	Yes	Yes	NR	4 weeks	Yang[140]
Composite Spasticity Score	NR	1	NR	NR	NR	NR	NR	4 weeks	Yan[139]
Displacement of the Center of Pressure	NR	1	NR	NR	NR	NR	NR	8 weeks	Bayouk[126]
Postural Sway	NR	2	NR	NR	NR	NR	NR	0-6 months	Bayouk[126] Peurala[133]
5 meter walk speed	NR	1	NR	NR	NR	NR	NR	4 weeks	Tong[138]
Asymmetry in step length	NR	1	NR	NR	NR	NR	NR	NR	Roerdink[63]
Cadence	NR	1	NR	NR	NR	NR	NR	3 weeks	Thaut[137]
Clonus Score	NR	1	NR	NR	NR	NR	NR	12 weeks	Bayram[127]
Elderly mobility scale (EMS)	NR	1	NR	NR	NR	NR	NR	4 weeks	Tong[138]
EU-Walking Scale	NR	1	NR	NR	NR	NR	NR	9 weeks	Mayr[131]

Global Assessment of Spasticity Scale	NR	1	NR	NR	NR	NR	NR	12 weeks	Bayram[127]
Interlimb Coordination and Auditory Motor Coordination	NR	1	NR	NR	NR	NR	NR	NR	Roerdink[63]
Iowa Level of Assistance Scale	NR	1	NR	NR	NR	NR	NR	6 month	English[129]
Lower limb spasticity and muscle force	NR	1	NR	NR	NR	NR	NR	29 weeks	Peurala[133]
Maximum Isometric Voluntary Contraction of ankle	NR	1	NR	NR	NR	NR	NR	4 weeks	Yan[139]
Medical Research Council Scale	NR	1	NR	NR	NR	NR	NR	9 weeks	Mayr[131]
Range of motion of ankle	NR	1	NR	NR	NR	NR	NR	12 weeks	Bayram[134]
Step reaction time	NR	1	NR	NR	NR	NR	NR	1 year	Marigold[60]
Step time	NR	1	NR	NR	NR	NR	NR	NR	Roerdink[63]
Stride length	NR	1	NR	NR	NR	NR	NR	3 weeks	Thaut[137]
Swing symmetry	NR	1	NR	NR	NR	NR	NR	3 weeks	Thaut[137]
Modified Motor Assessment Scale (mMAS)	NR	2	NR	NR	NR	NR	NR	29 weeks	Peurala[133] Peurala[134]
Functional Ambulation Profile (FAP)	NR	1	NR	NR	NR	NR	NR	29 weeks	Peurala[134]
Ashworth Scale	NR	2	Function[52]	No	No	No	NR	9 to 12 weeks	Mayr[131] Bayram[127]

Abbreviations: ICF=International classification of functioning, disability and health; NR=Not reported

*Psychometric properties of outcomes measures established for use in stroke patients not specific domains of functions (e.g ambulation) (Refers to all tables in this Appendix).

**This report did not examine if a link existed between an instrument's psychometric properties and mode administration (e.g self-report, proxy) (Refers to all tables in this Appendix).

Table D2: Outcome measurement instruments used in Quality of Life studies*

Outcome	Mode of Adminis-tration**	Fre-quency in studies	ICF domain	Reliab-ility in Stroke	Validity in Stroke	Tested for Responsive-ness	MCID in stroke	Range of follow up time for studies	Study Author
Nottingham Health Profile (NHP)	Self, interviewer	3	Participation[43,51]	Yes	Yes	NR	NR	12-52 weeks	Askim[143] Fjaertof[147] Wayne[158]
Stroke Adapted Sickness Impact Profile (SA-SIP30)	Self, interviewer	2	Participation[43,51]	Yes	Yes	Yes	NR	14-52 weeks	Hafsteins-dottir[149] McClellan[155]
Stroke Specific Quality of Life scale (SSQOL):	Interviewer proxy	1	Participation[43,51]	Yes	Yes	Yes	NR	12 months	Kendall[152]
Subscales of the stroke impact scale (SIS)	Self, interviewer, proxy	1	Participation[43,51]	Yes	Yes	Yes	Yes	6 months	Studenski[157]
Medical Outcomes Study 36-item short form heath survey (SF-36)	Self, interviewer, proxy, telephone	3	Participation[51]	Yes	Yes	Yes	NR	6-24 months	Johnson[150] Childers[146] Studenski[157]
Center for Epidemiological Surveys Depression (CES-D)	NR	1	Function[9]	Yes	Yes	Yes	NR	12 weeks	Wayne[158]
Geriatric Depression Scale (GDS)	Interview, proxy	1	Function[9,51]	Yes	Yes	Yes	NR	6 months	Leeds[153]
National Institutes of Health Stroke Scale (NIHSS)	Observation/ performance	1	Function[44,51,52]	Yes	Yes	No	NR	2 weeks	Park[64]
Mini-Mental State Examination (MMSE):	Observation/ performance	1	Function[51]	Yes	Yes	Yes	NR	52 weeks	Fjaertof[147]
Modified Ashworth Scale	Performance	3	Function[51]	Yes	Yes	NR	NR	12-24 weeks	Wayne[158] Johnson[150] Childers[146]
Motricity Index (MI)	NR	2	Function[9,52]	Yes	Yes	NR	NR	2 weeks-6months	GAPS Group[148] Park[64]
Ashworth scale	NR	1	Function[52]	No	No	No	NR	2 weeks	Park[64]
Rankin Scale	NR	1	Activity[44,52]	Yes	Yes	Yes	NR	12 months	Kalra[151]
10-meter walk	NR	1	Activity[44]	Yes	Yes	Yes	NR	2 weeks	Park[64]
Rivermead Motor Assessment (RMA):	NR	1	Activity[9]	Yes	Yes	Yes	Yes	16 weeks	Johnson[150]
Rivermead Mobility Index (RMI):	NR	1	Activity[16]	Yes	Yes	Yes	NR	6 months	GAPS Group[148]

Walking speed	NR	2	Activity[16]	Yes	Yes	Yes	NR	16 weeks-6 months	GAPS Group[148] Johnson[150]
Mobility milestones:	NR	1	Activity[16]	Yes	Yes	Yes	NR	6 months	GAPS Group[148]
Frenchay Activity Index	Interview, proxy	3	Activity[51]	Yes	Yes	Yes	NR	3-12 months	Fjaertof[147] Kalra[151] Ryan[156]
Nine-Hole Peg Test (NHPT)	Performance	1	Activity[51]	Yes	Yes	Yes	NR	2 weeks	Park[64]
Barthel Index (BI)	Self report, observation/ performance proxy	10	Activity[51]	Yes	Yes	Yes	NR	2-52 weeks	Askim[143] Wayne[158] GAPS Group[148] Hafsteins-dottir[149] Park[64] Wayne[158] Ryan[156] Kalra[151] Leeds[153] Lincoln[154]
Functional Independence Measure (FIM)	Interview, proxy	2	Activity[51]	Yes	Yes	Yes	NR	24 weeks-6 months	Studenski[157] Childers[146]
Fugl-Meyer Assessment	Observation/ performance	1	Activity[51]	Yes	Yes	Yes	NR	12 weeks	Wayne[158]
Modified Rankin Scale (mRS)	Interview	1	Activity[51]	Yes	Yes	Yes	NR	52 weeks	Askim[143]
Motor Assessment Scale (MAS)	Performance	1	Activity[51]	Yes	Yes	Yes	NR	14 weeks	McClellan[155]
Nottingham Extended ADL	NR	2	Activity[52]	Yes	Yes	NR	NR	2 weeks-6 months	GAPS group[153] Park[64]
EuroQoL: Quality of life for patient and carer	Self, interviewer, proxy	5	Activity[16]	Yes	Yes	Yes	NR	2 weeks-12 months	Kalra[151] Ryan[156] Lincoln[154] GAPs Group[153] Park[64]
5-point frequency of pain scale	NR	1	NR	NR	NR	NR	NR	24 weeks	Childers[146]
5-point severity of pain scale	NR	1	NR	NR	NR	NR	NR	24 weeks	Childers[146]
Admission/re-admission to hospitals	NR	1	NR	NR	NR	NR	NR	12 months	Kalra[151]
Brief Pain Inventory Question 12 (BPI12)	NR	1	NR	NR	NR	NR	NR	52 weeks	Chae[145]
Brief Pain Inventory Question 23 (BPI23)	NR	1	NR	NR	NR	NR	NR	52 weeks	Chae[145]

CAMCOG-R, part of the Cambridge Examination for Mental Disorders in the Elderly	NR	1	NR	NR	NR	NR	NR	6 months	Leeds[153]
Caregiver Strain Index (CSI)	NR	3	NR	NR	NR	NR	NR	6 months-52 weeks	Askim[143] Fjaertof[147] Lincoln[154]
COOP score	NR	1	NR	NR	NR	NR	NR	4 weeks	Barreca[144]
EQ-VAS: (EuroQoL—Visual Analog Scale)	NR	2	NR	NR	NR	NR	NR	2 weeks-3 months	Park[64] Ryan[156]
Extended activities of daily living ADL	NR	1	NR	NR	NR	NR	NR	6 months	Lincoln[154]
Functional Reach Test (FR)	NR	1	NR	NR	NR	NR	NR	14 weeks	McClellan[155]
Gait speed thresholds for community ambulation	NR	1	NR	NR	NR	NR	NR	6 months	Studenski[157]
General Health Questionnaire (GHQ) 12	NR	1	NR	NR	NR	NR	NR	6 months	Lincoln[154]
General Health Questionnaire (GHQ-12)	NR	1	NR	NR	NR	NR	NR	6 months	Lincoln[154]
Global rating scale:	NR	1	NR	NR	NR	NR	NR	4 weeks	Barreca[144]
HADS (Hospital Anxiety and Depression Scale)	NR	2	NR	NR	NR	NR	NR	3-12 months	Kalra[151] Ryan[156]
Health-related quality of life (HRQoL):	NR	1	NR	NR	NR	NR	NR	6 months	Leeds[153]
Knowledge of stroke	NR	1	NR	NR	NR	NR	NR	6 months	Lincoln[154]
Lawton & Brody instrumental ADL	NR	1	NR	NR	NR	NR	NR	6 months	Studenski[157]
Length of initial hospital stay:	NR	1	NR	NR	NR	NR	NR	52 weeks	Askim[143]
Length of total institutional stay:	NR	1	NR	NR	NR	NR	NR	52 weeks	Askim[143]
Montgomery-Asberg Depression Scale	NR	1	NR	NR	NR	NR	NR	52 weeks	Fjaertof[147]
Mortality or Institutionalizatio n	NR	1	NR	NR	NR	NR	NR	12 months	Kalra[151]
Patient-practitioner interactions	NR	1	NR	NR	NR	NR	NR	12 weeks	Wayne[158]

Physiological core index (PCI)	NR	1	NR	NR	NR	NR	NR	16 weeks	Johnson[150]
Satisfaction with care	NR	1	NR	NR	NR	NR	NR	6 months	Lincoln[154]
Self-administered Treatment Credibility Scale	NR	1	NR	NR	NR	NR	NR	12 weeks	Wayne[158]
Self-efficacy Scale	NR	1	NR	NR	NR	NR	NR	12 months	Kendall[152]
Swallowing status	NR	1	NR	NR	NR	NR	NR	2 weeks	Park[64]
UE range of motion (ROM)	NR	1	NR	NR	NR	NR	NR	12 weeks	Wayne[158]
Visual analogue scale (VAS)	NR	1	NR	NR	NR	NR	NR	52 weeks	Hafsteins-dottir[149]

Abbreviations: NR=Not reported

*Psychometric properties of outcomes measures established for use in stroke patients not specific domains of functions (e.g ambulation) (Refers to all tables in this Appendix).

**This report did not examine if a link existed between an instrument's psychometric properties and mode administration (e.g self-report, proxy) (Refers to all tables in this Appendix).

Table D3: Outcome measurement instruments used Daily Activity studies*

Outcome	Mode of Adminis-tration**	Frequency in studies	ICF domain	Reliability in Stroke	Validity in Stroke	Tested for Responsive-ness	MCID in stroke	Range of follow up time for studies	Study Author
Canadian Occupational Performance Measure (COPM)	Interview	1	Participation[51]	Yes	Yes	Yes	NR	NR	Gilmore[73]
Nottingham Extended Activities of Daily Living (NEADL)	NR	1	Participation[52]	Yes	Yes	Yes	NR	7 months	Mead[165]
Fugl-Meyer Assessment of Motor Recovery (FM)	Observation/ performance	7	Function[44,51]	Yes	Yes	NR	NR	1 week-6 months	Boake[159] Daly[160] Hsieh[164] Page[168] Wu[175] Gladstone[162] Yagura[176]
Wolf Motor Function Test (WMFT)	NR	2	Activity[9]	Yes	Yes	Yes	NR	6-12 months	Wittenberg[173] Wolf[174]
Older Americans Resources and Services Scale	NR	1	Activity[9]	Yes	NR	NR	NR	6 weeks	Higgins[163]
CMSA Disability Inventory	NR	1	Activity[9,16]	Yes	Yes	Yes	NR	3 months	Gladstone[162]
Rivermead Mobility Index (RMI)	NR	3	Activity[16]	Yes	Yes	Yes	NR	12 weeks-6 months	Pohl[169] Sackley[171] Van Nes[172]
Barthel Index	Self report, observation/ performance proxy	4	Activity[44,51,52]	Yes	Yes	Yes	NR	6 weeks-12 months	Pohl[169] (primary) Sackley[171] Langhammer[71] Van Nes[172] Higgins[163]
Functional Independence Measure (FIM)	Interview, proxy	6	Activity[51]	Yes	Yes	NR	NR	3 weeks-7 months	Rydwik[170] Hsieh[164] Mead[165] Wu[175] Gladstone[162] Yagura[176]
Berg Balance Scale	Performance	1	Activity[51]	Yes	Yes	Yes	NR	12 weeks	Van Nes[172]
Clinical Outcome	Observation/ performance	1	Activity[51]	Yes	Yes	Yes	NR	3 months	Gladstone[162]

Variable Score (COVS)									
Nine-Hole Peg Test	Performance	1	Activity[51]	Yes	Yes	Yes	NR	6 weeks	Higgins[163]
Timed up and go (TUG)	Performance	1	Activity[51]	Yes	Yes	Yes	NR	7 months	Mead[165]
Action Research Arm Test (ARA)	Observation/ performance	1	Activity[51]	Yes	Yes	Yes	NR	1 week	Page[168]
CMSA arm and hand for Upper Limb Function	NR	1	Activity[9]	Yes	Yes	Yes	NR	3 months	Gladstone[162]
Motor Activity Log (MAL)	NR	3	NR	NR	NR	NR	NR	3 weeks-12 months	Wu[175] Wolf[174] Wittenberg[173] Boake[159]
Arm Motor Ability Test (AMAT)	NR	1	NR	NR	NR	NR	NR	6 months	Daly[160]
Box and Block Test	NR	1	NR	NR	NR	NR	NR	6 weeks	Higgins[163]
Elderly Mobility Scale (EMS)	NR	1	NR	NR	NR	NR	NR	7 months	Mead[165]
Functional Reach	NR	1	NR	NR	NR	NR	NR	7 months	Mead[165]
Instrumental ADL	NR	1	NR	NR	NR	NR	NR	6 months	Ertel[161]
Klein Bell Activities of Daily Living Scale (KB-ADL)	NR	1	NR	NR	NR	NR	NR	NR	Gilmore[73]
Physical Performance Test	NR	1	NR	NR	NR	NR	NR	6 months	Ertel[161]
Sit to Stand	NR	1	NR	NR	NR	NR	NR	7 months	Mead[165]
Test d'Evaluation des Membres superieurs des Personnes Agees (TEMPA)	NR	1	NR	NR	NR	NR	NR	6 weeks	Higgins[163]

Abbreviations: ADL=Activities of Daily Living; AMAT=Arm Motor Ability Test; ARA=Action Research Arm Test; CMSA=Chedoke McMaster Stroke Assessment; COPM=Canadian Occupational Performance Measure; COVS=Clinical Outcome Variable Score; EMS=Elderly Mobility Scale; FIM=Functional Independence Measure; FM=Fugl-Meyer Assessment of Motor Recovery; KB-ADL; Klein Bell Activities of Daily Living Scale; MAL=Motor Activity Log; NEADL=Nottingham Extended Activities of Daily Living; RMI=Rivermead Mobility Index; TEMPA=Test d'Evaluation des Membres superieurs des Personnes Agees; TUG=Timed up and go; WMFT=Wolf Motor Function Test.

*Psychometric properties of outcomes measures established for use in stroke patients not specific domains of functions (e.g ambulation) (Refers to all tables in this Appendix).

**This report did not examine if a link existed between an instrument's psychometric properties and mode administration (e.g self-report, proxy) (Refers to all tables in this Appendix).

Table D4: Outcome measurement instruments used in Cognition studies*

Outcome	Mode of Administration**	Frequency in studies	ICF domain	Reliability in Stroke	Validity in Stroke	Tested for Responsiveness	MCID in stroke	Range of follow up time for studies	Study Author
Barthel Index (BI)	Self report, observation/ performance, proxy	5	Activity[44,51,52]	Yes	Yes	Yes	NR	1.5-24 months	Harvey[180] McKinney[183] Nys[184] Pyoria[187] Robertson[188]
Motricity Index	NR	2	Function[52]	Yes	Yes	Yes	NR	7 weeks-24 months	Frassinetti[179] Robertson[188]
Behavioral Inattention Test (BIT)	NR	4	NR	NR	NR	NR	NR	7 weeks-24 months/ 20 sessions	Cherney[76] Frassinetti[179] Harvey[180] Robertson[188]
Accuracy was calculated as a function of test and session	NR	1	NR	NR	NR	NR	NR	NR	Zeloni[192]
Adaptation effect	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
After effect	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
Cancellation tests	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
Cognitive Failures Questionnaires (CFQ)	NR	1	NR	NR	NR	NR	NR	6 months	McKinney[183]
Cognitive functioning	NR	1	NR	NR	NR	NR	NR	12 months	Rorsman[190]
Cognitively intact	NR	1	NR	NR	NR	NR	NR	6-10 months	Nys[184]
Duration of the after-effect	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
Elevator and lottery sub-tests of the TEA (test of everyday attention)	NR	1	NR	NR	NR	NR	NR	1.5 months	Harvey[180]
Fluff test	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
Frenchay Arm Test	NR	1	NR	NR	NR	NR	NR	24 months	Robertson[188]
Kinematic	NR	1	NR	NR	NR	NR	NR	6 weeks	Cirstea[177]
Kinesthetic and visual imagery questionnaire (a modified version of the movement imagery questionnaire)	NR	1	NR	NR	NR	NR	NR	2 days	Malouin[182]
Laterality bias from the Balloons test	NR	1	NR	NR	NR	NR	NR	1.5 months	Harvey[180]
Motor imagery screening test	NR	1	NR	NR	NR	NR	NR	2 days	Malouin[182]

Motor performance	NR	1	NR	NR	NR	NR	NR	2 days	Malouin[182]
Neuropsychological tests	NR	1	NR	NR	NR	NR	NR	5 weeks	Westerberg[75]
Pointing task	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
Progress through a self-medication program)	NR	1	NR	NR	NR	NR	NR	Varied	Purdy[186]
Reading test	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
Rivermead Perceptual Assessment Battery (RPAB)	NR	1	NR	NR	NR	NR	NR	6 weeks	Edmans[178]
Room description and objects reaching tests:	NR	1	NR	NR	NR	NR	NR	7 weeks	Frassinetti[179]
Self-rating on cognitive functioning in daily life (CFQ)	NR	1	NR	NR	NR	NR	NR	5 weeks	Westerberg[75]
Severity of cognitive impairment	NR	1	NR	NR	NR	NR	NR	6-10 months	Nys[184]
Stimuli detected in lower left visual field	NR	1	NR	NR	NR	NR	NR	24 months	Robertson[188]
Stimuli detected in upper left visual field	NR	1	NR	NR	NR	NR	NR	24 months	Robertson[188]
Stroop Neuropsychological screening Test (SNST)	NR	1	NR	NR	NR	NR	NR	20 sessions	Cherney[76]
Tactile Sensory Detections	NR	1	NR	NR	NR	NR	NR	24 months	Robertson[188]
Test of everyday attention-elevator counting	NR	1	NR	NR	NR	NR	NR	24 months	Robertson[188]
Patient and carer neglect rating scores	NR	1	NR	NR	NR	NR	NR	1.5 months	Harvey[180]
Verbal memory-immediate recall	NR	1	NR	NR	NR	NR	NR	24 months	Robertson[188]
Working memory	NR	1	NR	NR	NR	NR	NR	2 days	Malouin[182]
Behavioral Inattention Tests (BIT) behavioral scores	NR	1	NR	NR	NR	NR	NR	1.5 months	Harvey[180]
Behavioral Inattention Tests (BIT) conventional scores	NR	1	NR	NR	NR	NR	NR	1.5 months	Harvey[180]
Mini-Mental State Examination	Observation/ performance	5	Function[71]	No	No	No	NR	3-12 weeks /20 sessions	Cherney[76] Kimura[181]

(MMSE)									Tang[191] Ozdemir[185] Robinson[190]

Abbreviations: NR=Not reported

*Psychometric properties of outcomes measures established for use in stroke patients not specific domains of functions (e.g ambulation) (Refers to all tables in this Appendix).

**This report did not examine if a link existed between an instrument's psychometric properties and mode administration (e.g self-report, proxy) (Refers to all tables in this Appendix).

Table D5: Outcome measurement instruments used in Communication studies*

Outcome	Mode of Administration**	Frequency in studies	ICF domain	Reliability in Stroke	Validity in Stroke	Tested for Responsiveness	MCID in stroke	Range of follow up time for studies	Study Author
Amsterdam Nijmegen Everyday Language Test (ANLET)	NR	2	NR	NR	NR	NR	NR	7-12 months	Doesborgh[196] Laska[198]
Aphasia Quotient of Western Aphasia Battery (WAB)	NR	1	NR	NR	NR	NR	NR	20 weeks	Berthier[195]
Caplans and Hanna Sentence Production Test	NR	1	NR	NR	NR	NR	NR	7 months	Rochon[81]
Communicative Activity Log (CAL)	NR	1	NR	NR	NR	NR	NR	20 weeks	Berthier[195]
Constructional Apraxia	NR	1	NR	NR	NR	NR	NR	18 weeks	Smania[200]
Dysarthria	NR	1	NR	NR	NR	NR	NR	1 years	Wolfe[202]
Dysphagia	NR	1	NR	NR	NR	NR	NR	1 year	Wolfe[202]
Frenchay Aphasia Screening Test (FAST)	NR	1	NR	NR	NR	NR	NR	1 year	Wolfe[202]
Gesture Comprehension Tests	NR	1	NR	NR	NR	NR	NR	18 weeks	Smania[200]
Language assessment: (standardized Persian language test)	NR	1	NR	NR	NR	NR	NR	4 months	Ashtary[193]
Narrative Production Task	NR	1	NR	NR	NR	NR	NR	7 months	Rochon[81]
Neuropsychological Test Battery	NR	1	NR	NR	NR	NR	NR	6 weeks	Kessler[197]
Oral apraxia	NR	1	NR	NR	NR	NR	NR	18 weeks	Smania[200]
Picture Description with Structure Modeling (PDSM)	NR	1	NR	NR	NR	NR	NR	7 months	Rochon[81]
Phonological measures	NR	1	NR	NR	NR	NR	NR	7 months	Doesborgh[196]
Porch Index of Communicative Ability (PICA)	NR	1	NR	NR	NR	NR	NR	6 months	Walker-Batson[201]
Picture comprehension test	NR	1	NR	NR	NR	NR	NR	7 months	Rochon[81]
Reinvang's aphasia tests	NR	1	NR	NR	NR	NR	NR	12 months	Laska[198]

Semantic Association Test	NR	1	NR	NR	NR	NR	NR	7 months	Doesborgh[196]
Philadelphia Comprehension Battery (PCB)	NR	1	NR	NR	NR	NR	NR	7 months	Rochon[81]
Speech disturbance	NR	1	NR	NR	NR	NR	NR	1 year	Wolfe[202]
Standard Aphasia tests	NR	1	NR	NR	NR	NR	NR	4 weeks	Pulvermuller[199]
Psycholinguistic Assessment of Language Processing in Aphasia (PALPA)	NR	1	NR	NR	NR	NR	NR	20 weeks	Berthier[195]
Verbal comprehension	NR	1	NR	NR	NR	NR	NR	18 weeks	Smania[200]
Western Aphasia Battery (WAB)	NR	1	NR	NR	NR	NR	NR	24 weeks	Bakheit[194]

Abbreviations: NR=Not reported

*Psychometric properties of outcomes measures established for use in stroke patients not specific domains of functions (e.g ambulation) (Refers to all tables in this Appendix).

**This report did not examine if a link existed between an instrument's psychometric properties and mode administration (e.g self-report, proxy) (Refers to all tables in this Appendix).

Table D6: Outcome measurement instruments used in Dysphagia studies*

Outcome	Mode of Administration**	Frequency in studies	ICF domain	Reliability in Stroke	Validity in Stroke	Tested for Responsiveness	MCID in stroke	Range of follow up time for studies	Study Author
Aspiration Penetration Scale	NR	1	NR	NR	NR	NR	NR	None	Power[210]
Coughing/ choking frequency during meal	NR	1	NR	NR	NR	NR	NR	8 weeks	Lin[2]
Cricopharyngeal Opening Duration	NR	1	NR	NR	NR	NR	NR	None	Power[210]
Efficacy of swallowing (volume per second, volume per swallow)	NR	1	NR	NR	NR	NR	NR	8 weeks	Lin[2]
Functional Oral Intake Scale (FO1S)	NR	1	NR	NR	NR	NR	NR	NR	Crary[204]
Functional swallowing	NR	1	NR	NR	NR	NR	NR	6 months	Carnaby[203]
Incidence of aspiration pneumonia	NR	1	NR	NR	NR	NR	NR	NR	Huang[84]
Laryngeal Closure Duration	NR	1	NR	NR	NR	NR	NR	None	Power[210]
Latency of swallowing reflex (seconds)	NR	1	NR	NR	NR	NR	NR	30 days	Ebihara[206]
Neurological examination	NR	1	NR	NR	NR	NR	NR	8 weeks	Lin[2]
Normal diet	NR	1	NR	NR	NR	NR	NR	6 months	Carnaby[203]
Number of swallows for 1 minute	NR	1	NR	NR	NR	NR	NR	30 days	Ebihara[206]
Oral Transit Time	NR	1	NR	NR	NR	NR	NR	None	Power[210]
Pharyngeal retention	NR	1	NR	NR	NR	NR	NR	4 weeks	Seki[211]
Pharyngeal Transit Time	NR	1	NR	NR	NR	NR	NR	NR	Power[210]
Pulmonary aspiration	NR	1	NR	NR	NR	NR	NR	7 days	Goulding[83]
Signs and/or symptoms on a swallowing questionnaire	NR	1	NR	NR	NR	NR	NR	8 weeks	Lin[2]
Swallow Response Time	NR	1	NR	NR	NR	NR	NR	None	Power[210]
Swallowing time of water and fluid	NR	1	NR	NR	NR	NR	NR	4 weeks	Seki[211]
Tracheobronchial post deglutitive aspiration	NR	1	NR	NR	NR	NR	NR	4 weeks	Seki[211]

Abbreviations: NR=Not reported

*Psychometric properties of outcomes measures established for use in stroke patients not specific domains of functions (e.g ambulation) (Refers to all tables in this Appendix)

**This report did not examine if a link existed between an instrument's psychometric properties and mode administration (e.g self-report, proxy) (Refers to all tables in this Appendix)

Appendix E. Review of Reviews' Tables

Table E1: Cochrane Reviews

Author, Year Country, Ref ID #	Designs Reviewed, Total Sample Size	Search Years, Databases, Other	Aim of Therapy, Types of inter-ventions, Comparator treatment	Quality Assessment, Mean score, Individual item rating	Outcomes, Primary Types/ domain, Analysis	Population, Acuity	Authors conclusions
Ada[99] 2007 Australia	Designs: 4 RCT Total Sample: n=142	Years: 1966 to 2004 Sources: -CSGTR -MEDLINE® -EMBASE -CINAHL -CCRCT -AMED Other: Handsearching of relevant conference proceedings	Aim: To investigate the effect of supportive devices in preventing subluxation, re-positioning the head of humerus in the glenoid fossa, decreasing pain, increasing function and adversely increasing contracture in the shoulder after stroke. Therapy: Supportive devices for shoulder subluxation Comparators: Use of supportive devices vs. no supportive devices	Checklist: PEDro scale Mean Score: NR Individual Item Rating: Binary scoring for each item yielding overall scores of (range 2-8)/10	Primary: Subluxation: continuous variables (mm of subluxation); dichotomous variables (presence or absence of subluxation). Outcomes: -Pain -Function -Contracture Analysis: Qualitative summary	Population: Participants of any age with clinical diagnosis of stroke Acuity: Acute (≤2 weeks post stroke)	Insufficient evidence to conclude whether slings and wheelchair attachments prevent subluxation, decrease pain, increase function or adversely increase contracture in the shoulder after stroke. Some evidence that strapping the shoulder delays the onset of pain but does not decrease it, nor does it increase function or adversely increase contracture.
Bennett[100] 2005 Australia	Designs: 3 RCT Total Sample: n=106	Years: 1966 to 2004 Sources: -CSGTR -MEDLINE® -EMBASE -CINAHL -CCRCT -DORCTHIM Other: -Hand searching of journals and conference proceedings -Hyperbaric textbooks	Aim: To assess the effectiveness and safety of adjunctive hyperbaric oxygen therapy (HBOT) in the treatment of acute ischemic stroke. Therapy: HBOT Comparators: All trials compared the effects of HBOT	Checklist: Schulz criteria Mean Score: NR Individual Item Rating: Quality assessment (fair-high range) for each item in the QA criteria	Primary: -Mortality -Severe functional disability Outcomes: -Functional status scale; -Good functional outcome assessed as binary outcome(s) of functional status scales; -Activities of daily living; -CT or MRI estimate of infarct	Population: Participants of any age with acute ischemic stroke. Acuity: Acute (≤2 weeks post stroke)	This systematic review has not found evidence to show that HBOT improves clinical outcomes when applied during the acute presentation of ischemic stroke. While evidence from the three randomized

		-Reference lists -Author contact	with no HBOT		size/volume; -Adverse events post HBOT. Analysis: Qualitative summary		controlled trials is insufficient to provide clear guidelines for practice, clinical benefit does not seem likely. Further research is required to better define the role of HBOT in this condition.
Brady[13] 2006 UK	Designs: 1 RCT Total Sample: n=67	Years: 1966 to 2006 Sources: -MEDLINE® -CINAHL -CCRCT -Cochrane Stroke Group and Oral Health Group -Research Findings Electronic Register -National Research Register Other: ISI Science and Technology proceedings, Dissertation Abstracts and Conference Papers Index -Reference lists -Author contact	Aim: To compare the effectiveness of staff led oral health intervention after stroke Therapy: Oral care training for carers in nursing home setting or ensuring oral hygiene for individuals after a stroke. Comparators: Staff-led oral care interventions vs. standard care	Checklist: Adaptation of NHS CRD Report Mean Score: NR Individual Item Rating: Individual scores for some items	Primary: -Dental plaque (plaque scale) -Denture plaque (denture cleanliness scale) Outcomes: -Patient satisfaction; -Presence of oral disease: gingivitis, denture-induced stomatitis, periodontal disease; -Staff oral health knowledge and attitudes. Analysis: None	Population: Patients with a diagnosis of stroke receiving assisted oral care within a healthcare facility. Acuity: Chronic	Based on one study with a small number of stroke survivors, providing oral care training for carers in a nursing home setting improves their knowledge of and attitudes towards the provision of oral care. In turn, residents' dentures were cleaner, though other oral hygiene measures did not change. Further evidence relating to oral care interventions is severely lacking, in particular with reference to care in hospital for those following stroke.
Early Supported Discharge Trialists[78] 2005 UK	Designs: 11 RCT Total Sample: n=1597	Years: August 2004 (last searched) Sources: -CSGTR	Aim: To establish the effects and costs of early supported discharge (ESD) services compared with conventional	Checklist: Author criteria Mean Score: NR Individual Item Rating:	Primary: -Death -Physical dependency -Place of residence	Population: Adults with a clinical diagnosis of stroke in the acute phase. (Average age range in the	Appropriately resourced ESD services provided for a selected group of stroke patients can reduce long

		Other: -Individual trialist contact	services. Therapy: -ESD team co-ordination and delivery; -ESD team co-ordination; -No ESD team Comparators: ESD services (policy of early discharge with home-cased support and rehabilitation) vs. conventional services (policy of hospital rehabilitation and conventional discharge arrangements)	Assessment of 3 methodological quality criteria, with scoring reported for only one item (allocation concealment)	Outcomes: -Activities of daily living score (+extended score) -Subjective health status -Mood or depression score -Carer outcomes -Patient and carer satisfaction Analysis: Qualitative summary	included trials 66-78 years) Acuity: Acute	term dependency and admission to institutional care as well as reducing the length of hospital stay. No adverse impact was observed on the mood of subjective status of patients or carers.
French[12] 2007 UK	Designs: 13 RCT 1 QRCT (n=14) Total Sample: n=680	Years: 1966 to 2006 Sources: -CSGTR -CCRCT -MEDLINE® -EMBASE -CINAHL -AMED -SportDiscus -Science Citation Index -Index to Theses -ZETOC -PEDro -OT Seeker Other: -Reference lists -Bulletin board information requests - Author contact	Aim: To determine if repetitive task training after stroke improves global, upper or lower limb function, and if treatment effects are dependent on the amount, type or timing of practice. Therapy: Repetitive task training for improving functional ability Comparators: Whole therapy approaches such as motor relearning or movement science approaches, limb-specific mixed task training or single task training vs. an attention or usual care control group.	Checklist: Author criteria Mean Score: NR Individual Item Rating: Assessment of 4 methodological quality criteria, with scoring reported for only one item (allocation concealment).	Primary: -Upper limb function (sitting balance and reach); -Lower limb function (walking distance, walking speed, functional ambulation, sit-to-stand, standing balance and reach); -Global motor function. Outcomes: -Activities of daily living; -Impairment; -Quality of life/health status; -Adverse events. Analysis: Qualitative summary	Population: ≥18 yrs, male or female, suffering a stroke as defined by the WHO Acuity: -8 acute -2 subacute -4 chronic (study populations)	Repetitive Task training resulted in modest improvement in lower limb function, but not upper limb function. Training may be sufficient to impact on daily living function. However, there is no evidence that improvements are sustained once training has ended. The review potentially investigates task specificity rather more than repetition. Further research should focus on the type and amount of training and how to

							maintain functional gain.
Legg[102] 2006 UK	Designs: 9 RCT Total Sample: 1258	Years: 1945-2006 Sources: -CSGTR -CCRCT -MEDLINE® -EMBASE -CINAHL -PsycLIT -AMED -Wilson Social Sciences Abstracts -Web of Science databases Other: - Occupational Therapy Research Index and Dissertation Abstracts register -Reference lists -Author contact	Aim: To determine whether occupational therapy focused specifically on personal activities of daily living improves recovery for patients following stroke. Therapy: Occupational therapy focusing on personal activities of daily living and subsequent performance Comparators: Occupational therapy intervention compared to usual care or no care.	Checklist: Author criteria Mean Score: NR Individual Item Rating: Individual item assessments available for 3 of the 5 methodological quality criteria (randomization/allocation concealment, blinding, intention-to-treat analysis), grading reported for concealment of allocation item.	Primary: Proportion of patients who had deteriorated or were dependent in personal activities of daily living and subsequent performance in personal activities of daily living. Outcomes: -Death or dependency; -Quality of life (patients and carers); -Mood (patients and carers) Analysis: Qualitative summary	Population: Patients recently suffering a stroke, with a mean age range lying between 55 to 87.5 years. Acuity: Predominantly acute/subacute trials, with one chronic trial included.	Patients who receive occupational therapy interventions are less likely to deteriorate and are more likely to be independent in their ability to perform personal activities of daily living. However, the exact nature of the occupational therapy intervention to achieve maximum benefit needs to be defined.
Mehrholz[103] 2007 Germany	Designs: 8 RCT/CO Total Sample: n=414	Years: 1949-2006 Sources: -CSGTR -CCRCT -MEDLINE® -EMBASE -CINAHL -AMED -SPORTDiscus -PEDro -COMPENDEX -INSPEC Other: -Hand searching relevant conference proceedings, trials and research registers -Author contact	Aim: To investigate the effect of automated electromechanical and robotic-assisted gait training devices for improving walking after stroke. Therapy: Automated electromechanical and robotic-assisted gait training devices Comparators: Electromechanical and robot-assisted gait training plus physiotherapy vs. physiotherapy (or usual care)	Checklist: PEDro scale Mean Score: Median total score: 7/10 (range 6-8) Individual Item Rating: Binary scoring for each item in all included studies	Primary: Proportion of patients walking independently at follow up Outcomes: -Measures of impairments in body structures; -Death from all causes; -Adverse events. Analysis: Qualitative summary	Population: Predominantly ischemic (72%), male (65%) with left-sided hemiparesis (55%) and mean age range of 52-68 years. Acuity: -4 acute -1 subacute -1 chronic -2 NR (study populations)	Patients who receive electromechanical-assisted gait training in combination with physiotherapy after stroke are more likely to achieve independent walking than patients receiving gait training without these devices. Further research should address specific questions (i.e. which frequency or duration of electromechanical-assisted

							gait training might be most effective and at what time after stroke) Follow-up studies are needed to find out how long the benefit lasts. Future research should include estimates of the costs (or savings) due to electromechanical gait training.
Moseley[104] 2005 Australia	Designs: 15 RCT/QRCT Total Sample: n=622	Years: 1966-2005 Sources: -CSGTR -CCRCT -MEDLINE® -EMBASE -CINAHL -PEDro Other: -Hand searching of relevant conference proceedings -Reference lists -Trialists contact	Aim: To assess the effectiveness of treadmill training and body weight support, individually or in combination, in the treatment of walking after stroke, and to determine the safety and acceptance of the method of gait training. Therapy: Treadmill training and body weight support Comparators: Treadmill training and body weight support, compared to other physiotherapy gait training interventions after stroke.	Checklist: PEDro scale Mean Score: Median total score: 6/10 (range 4-8) Individual Item Rating: Ratings for each PEDro item plus the total PEDro score for each study.	Primary: -Walking speed -Endurance -Dependency Outcomes: -Patient quality of life; -Activities of daily living; -Combined outcomes of death/dependency; - Death or institutional care; -Adverse events. Analysis: Qualitative summary	Population: Adults who suffered a stroke and exhibited abnormal gait patterns (including an inability to walk) Acuity: -10 acute -2 subacute -2 chronic (Study populations)	No statistically significant differences between treadmill training, with or without body weight support, and other interventions for walking speed or dependence. Secondary analysis indicated that among people with stroke who could walk independently at the start of treatment, treadmill training may improve walking speed. Individual trial data suggest that stroke patients who are dependent on help for walking at the start of treatment may

							benefit from treadmill training with body weight support but there are very limited data to support this conclusion.
Nair[105] 2007 UK	Designs: 2 RCT Total Sample: n=18	Years: 1966-2005 Sources: -CSGTR -CCRCT -MEDLINE® -EMBASE -CINAHL -PsycINFO -AMED -British Nursing Index -CAB Abstracts -National Research Register Other: -Hand searching -Reference lists	Aim: To determine the effectiveness of cognitive rehabilitation for memory problems following stroke. Therapy: Memory retraining strategies aimed at cognitive rehabilitation. Comparators: -Mnemonic strategy vs. "drill and practice" control; -Imagery mnemonics vs. "pragmatic" memory rehabilitation	Checklist: Author criteria Mean Score: NR Individual Item Rating: Assessment of 3 methodological quality criteria, with scoring reported for only one item (allocation concealment).	Primary: Functional outcome measures (including quality of life)—neither of the included trials reported any functional outcome measures. Outcomes: Objective, subjective and observer-rated measures of memory Analysis: Qualitative summary	Population: Patients with memory deficits following stroke. Acuity: Subacute and mixed etiology	There was no evidence to support or refute the effectiveness of memory rehabilitation on functional outcomes, and objective, subjective, and observer-rated memory measures. There is a need for more robust, well-designed and better-reported trials of memory rehabilitation using common standardized outcome measures.
Pomery[98] 2006 UK	Designs: 24 RCT Total Sample: n=888	Years: 1966-2004 Sources: -CSGTR -CCRCT -MEDLINE® -EMBASE -CINAHL -AMED -PEDro -REHABDATA -ISI Science Citation Index Other: -Request placed on the PHYSIO E-mail discussion list -Author contact -Reference lists	Aim: To find if electrostimulation improved functional motor ability, and the ability to undertake activities of daily living Therapy: Electrostimulation (including various types—transcutaneous and /or functional electrical stimulation) Comparators: - Electrostimulation vs. no treatment	Checklist: Author criteria Mean Score: NR Individual Item Rating: 9 criterions of quality assessment are graded (not possible—adequate) for each item of each included study	Primary: Functional motor ability and the ability to undertake activities of daily living Outcomes: Motor impairment and the normality of movement (voluntary movement control) Analysis: Qualitative summary	Population: Adults with a clinical diagnosis of stroke (WHO definition) with a diagnosis of either ischemic stroke or hemorrhagic stroke at any time after stroke. Acuity: Mixed—17/24 trials provided a mean time after stroke which ranged from 9.4 days to 4.29 years	At present, there are insufficient robust data to inform clinical use of electrostimulation for neuromuscular re-training. Research is needed to address specific questions about the type of electrostimulation that might be most effective, in what dose and at what time after stroke.

			- Electrostimulation vs. placebo - Electrostimulation vs. conventional therapy interventions - Acceptability of electrostimulation				
Stroke Unit Trialists' Collaboration[14] 2007 UK	Designs: 7 CCT 24 RCT (n=31) Total Sample: n=6936	Years: April 2006+ Sources: -CSGTR Other: -Reference lists -Colleague and researcher contact -Publication of preliminary findings at stroke conferences in the UK	Aim: To assess the effect of stroke unit care compared with alternative forms of care for patients following stroke Therapy: -Stroke ward -Mixed rehabilitation ward -Mobile stroke team -General medical ward Comparators: Organized inpatient stroke unit care vs. an alternative service	Checklist: Author criteria Mean Score: NR Individual Item Rating: Assessment of 4 methodological quality criteria, with scoring reported for only one item (allocation concealment).	Primary: -Death -Dependency -Requirement for institutional care Outcomes: - Quality of life; - Patient and carer satisfaction; - Duration of stay in hospital or institution or both. Analysis: -Sensitivity analyzes by trial characteristics -Subgroup analyzes by patient characteristics	Population: Any patients admitted to hospital who had suffered a stroke Acuity: Predominantly acute (30/31 trials), with 1 trial including patients ≤12 months post stroke.	Acute stroke patients are more likely to survive, regain independence, and be living at home one year after stroke if they receive organized inpatient (stroke unit) care. The benefits were most apparent in units based in a discrete ward. No systematic increase was observed in the length of inpatient stay.
Thomas[106] 2008 UK	Designs: 12 RCT/QRCT Total Sample: n=724	Years: 1982-2007 Sources: -Cochrane Incontinence and Stroke Groups specialized registers -CINAHL Other: -Search of national and international trial databases for unpublished data; -Reference lists	Aim: To determine the optimal methods for treatment of urinary incontinence after stroke in adults. Therapy: Interventions classified as: -Behavioral -Specialized professional input -Complementary therapy -Pharmacotherapy -PT Comparators: -Intervention vs. no intervention usual care -Intervention vs.	Checklist: Author criteria Mean Score: NR Individual Item Rating: Assessment of 3 methodological quality criteria, with scoring reported for only one item (allocation concealment).	Primary: In/continence measured by participant symptoms and physical measures. Outcomes: -Symptom scores or participant/carer report of other urinary symptoms; -Physical measures; -Health status or measure of psychological health; -Economic outcomes.	Population: Adults with a diagnosis of stroke, from a mixture of settings, age groups and phases of stroke recovery Acuity: Mixed	Data from the available trials are insufficient to guide continence care of adults after stroke. However, there was suggestive evidence that professional input through structured assessment and management of care and specialist continence nursing may reduce urinary incontinence and related

			placebo -Specific intervention vs. another intervention -Combined intervention vs. single intervention		Analysis: Qualitative summary		symptoms after stroke. Better quality evidence is required of the range of interventions that have been suggested for continence care after stroke.
West[90] 2007 UK	Designs: NR Total Sample: NR	Years: 1966 to 2004 Sources: -CSGTR -MEDLINE® -EMBASE -CINAHL -CCRCT -PsycINFO -National Research Register -Current Controlled Trials Register Other: -Author contact -Reference Lists -Written communication with key international publications read by those treating and researching apraxia of speech	Aim: To assess whether therapeutic interventions improve functional speech in stroke patients with apraxia of speech and which individual therapeutic interventions are effective. Therapy: Therapeutic interventions such as PROMPT, phonetic derivation, phonetic placement, key word, minimal pairs, VCIU, MIPT and prosodic therapy. Comparators: NR	Checklist: Author Criteria Mean Score: NR Individual Item Rating: NR	Primary: Functional speech Outcomes: -Functional speech at the scheduled end of intervention; -Measures of connected speech; -Quality of speech; -Non-verbal communication; -Mood; -Quality of life measures; -Adverse events. Analysis: NR	Population: Adults with apraxia of speech following stroke Acuity: NR	There is no evidence from randomized trials to support or refute the effectiveness of therapeutic interventions for apraxia of speech. There is a need for high quality randomized trials to be undertaken in this area.
Woodford[107] 2007 UK	Designs: 13 RCT/QRCT Total Sample: n=269	Years: 1966-2006 Sources: -CSGTR -CCRCT -MEDLINE® -EMBASE -CINAHL -PsycINFO -First Search Other: -Reference lists -Contact with equipment manufacturers and distributors	Aim: To assess the effects of electromyographic biofeedback (EMG-BFB) for motor function recovery following stroke. Therapy: EMG-BFB Comparators: EMG-BFB vs. no EMG-BFB or sham EMG-BFB	Checklist: Author criteria Mean Score: NR Individual Item Rating: Assessment of 5 methodological quality criteria, with scoring reported for only one item (allocation concealment).	Primary: Change in muscle power relative to baseline Outcomes: Changes relative to baseline: -Range of motion through a specified joint; -Gait measures and need for ambulation aids; -Function ability -EMG activity -Proportion of subjects with	Population: Patients of any age or gender with a clinical diagnosis of stroke Acuity: -2 acute -3 subacute -7 chronic -1 NR (Study populations)	Despite evidence from a small number of individual studies to suggest that EMG-BFB plus standard physiotherapy produces improvements in motor power, functional recovery and gait quality when compared to

					muscle weakness Analysis: Qualitative summary		standard physiotherapy alone, combination of all the identified studies did not find a treatment benefit. Overall the results are limited because the trials were small, generally poorly designed and utilized varying outcome measures.
Wu[108] 2006 China	Designs: 5 RCT Total Sample: n=368	Years: 1966-2005 Sources: -CSGTR -CCMFTR -CCRCT -MEDLINE® -EMBASE -CINAHL -AMED -Chinese Stroke /Acupuncture Trials Register -Chinese Biological Medicine Database -National Center for Complementary and Alternative Medicine Register -National Institute of Health Clinical Trials Database Other: -Hand searching journals -Reference lists	Aim: To assess the efficacy and safety of acupuncture for patients with stroke in the subacute or chronic stage. Therapy: Acupuncture Comparators: - Acupuncture only vs. placebo or sham treatment; - Acupuncture in addition to baseline medication or treatment compared with placebo or sham treatment in addition to baseline medication or treatment; -Acupuncture in addition to baseline medication or treatment compared with baseline medication or	Checklist: Author criteria Mean Score: NR Individual Item Rating: Assessment of 4 methodological quality criteria, with scoring reported for only one item (allocation concealment).	Primary: Death or dependency, where dependency is defined as relying on other in activities of daily living. Outcomes: -Proportion of those requiring institutional care or extensive family support; -Changes in neurological deficit; -Death from any causes; -Quality of life; -Adverse events. Analysis: Qualitative summary	Population: Patients of any age or sex with ischemic or hemorrhagic stoke in the subacute or chronic phases Acuity: Predominantly chronic (some subacute)	Currently there is no clear evidence on the effects of acupuncture on subacute or chronic stoke. Large, methodologically-sound trials are required.

			treatment alone.				
Zhang[109] 2005 China	Designs: 14 RCT Total Sample:	Years: 1966-2003 Sources: -CSGTR -Chinese Stroke/Acupuncture Trials Register -CCRCT -MEDLINE® -EMBASE -Alternative Medicine Database -CINAHL -Chinese Biological Medicine Database Other: -Reference lists -Hand searching	Aim: To assess the effectiveness and safety of acupuncture in patients with acute stroke. Therapy: Acupuncture (traditional or contemporary) Comparators: Acupuncture vs. placebo acupuncture, sham treatment, or no treatment	Checklist: Author criteria Mean Score: NR Individual Item Rating: Assessment of 5 methodological quality criteria, with scoring reported for only one item (allocation concealment).	Primary: -Death or dependency, where dependency is defined by reliability on others in activities of daily living; -Death or requiring institutional care -Adverse events Outcomes: -Changes in neurological deficit; -Death from all causes; -Quality of life Analysis: Qualitative summary	Population: Patients of any age or sex with any type of acute stroke (within 30 days) Acuity: Acute (≤30 days post stroke)	Acupuncture appears to be safe but without clear evidence of benefit. The number of patients is too small to be certain whether acupuncture is effective for treatment of acute ischemic or hemorrhagic stroke. Larger, methodologically-sound trials are required.

Abbreviations: AMED=Allied and Complementary Medicine Database; BA=Before After study; BWSTT=Body Weight Supported Treadmill Training; CaCo=Case-control study; CCMFTR=Cochrane Complementary Medicine Field Trials Register; CCRCT=Cochrane Central Register of Controlled Trials (CENTRAL); CCT=Controlled clinical trial; CDSR=Cochrane Database of Systematic Reviews; CIMT=Constraint-induced movement therapy; CINAHL=Cumulative Index to Nursing and Allied Health Literature; CIRRIE=Center for International Rehabilitation Research Information and Exchange; CO=Cross-over trials; CS=Case series; CR=Case report; CRD=Center for Review and Dissemination; CRS=Cross-sectional study; CSGTR=Cochrane Stroke Group Trials Register; CT=computed tomography; EMG=electromyography; EMG-BFB=electromyographic biofeedback; FM=Fugl-Meyer; LOF=Length of Follow-up; MBD=Multiple baseline design; MRI=magnetic resonance imaging; NHS=National Health Service; NIHSS=National Institutes of Health Stroke Survey; NR=not reported; NT=Not tested; OS=Observational study; OT=Occupational therapy intervention; OTV=program of videotape feedback and a program of occupational therapy; PED=Physiotherapy Evidence Database; PR=Prospective study; PreP=Pre-post study; PT=Physical Therapy; PTA/OTA=Physiotherapy or Occupational Therapy Assistant; QRCT=quasi-randomized clinical trial; QE=quasi-experimental study; RCT=randomized controlled trial; SR=Systematic review; SLP=Speech Language Pathologist; TT=Traditional Therapy; UE=upper extremity; vs=versus; WHO=World Health Organization

Table E2: Non-Cochrane Reviews

Author Year Country, Ref ID #	Designs Reviewed, Total Sample Size	Search Years, Databases, Other	Aim of Therapy, Types of inter-ventions, Comparator treatment	Quality Assessment, Mean score, Individual item rating	Outcomes, Primary Types/ domain, Analysis	Population, Acuity	Authors conclusions
Ada[91] 2006 Australia	Design: -21 RCT/ CCT Total Sample: n=476	Years: 1966 to 2005 Sources: MEDLINE® CINAHL EMBASE PEDro Other: Reference list screening Hand searching of recent conference proceedings World Congress of Physical Therapists and Australian PT Association National Neurology Group	Aim: To strengthen muscles and improve function with a variety of approaches Types of Therapy: -progressive resistance exercise -biofeedback -electrical stimulation -muscle re-education -mental practice Comparator: Sham/placebo such as no treatment, or a therapy that was not a strengthening intervention	Checklist: PEDro Mean Score: 4.7/ 8 Individual item rating: NR	Primary: not specified Outcomes: -Measures had to include strength and the strength measurement had to be of force generation such as manual muscle test or torque -Strength (manual muscle testing -Spasticity (Ashford scale, pendulum test) -Activity (walk test and Box and block test) Analysis: Meta-analyzes	Population Participants had to have had a stroke Acuity: All stages stroke recovery (grouped into 5 categories)	Strengthening interventions increase strength, improve activity, and do not increase spasticity. Suggest including strengthening in stroke rehabilitation programs
Bjorklund[110] 2006 United States	Design: -5 RCT -6 mixed (includes self as control) (n=11) Total sample size: n=179	Years: 1950 to 2004 Sources: CINAHL CCRCT Pub Med Science Direct Other: Reference lists	Aim: To address the decreased motor function in the involved upper extremity after stroke through restraining the unaffected limb while, initiating an intensive rehabilitation program forcing the use of the affected upper extremity Intervention: constraint-induced therapy consisted restraining the unaffected limb while performing intensive therapy with the affected	Checklist type: Author's criteria Mean score: NR Individual item rating: NR	Primary: Not specified Outcomes: Action Research Arm Test (ARA), Fugl-Meyer Assessment of Motor Recovery (FMA) ,Motor Assessment Log (MAL), Wolf Motor Function Test (WMFT), Functional Independence Measure (FIM), Barthel Index , Actual Amount of Use Test (AAUT), Arm Motor Ability Test (AMAT), and Functional Test of the Hemiparetic	Population: Ischemic or hemorrhagic stroke resulting in hemiparesis was stated within the participant description Acuity: All phases of recovery	This review shows that constraint-induced therapy to be an effective treatment method for stroke hemiparesis

			limb Comparators: Most studies were before/after design. In comparative studies, the control group got usual care, no intervention, same PT but no limb constraint therapy		Upper Extremity Analysis: -Qualitative summary -Individual effect size estimates		
Bonaiuti[111] 2007 Italy	Designs: 9 RCT Total Sample: n=243	Years: 1966 to 2005 Sources: -MEDLINE® -EMBASE -CINAHL -Cochrane Library Other: NR	Aim: To analyze the evidence of effectiveness on adult stroke patients of the Constraint Induced Movement Therapy. Therapy: Constraint Induced Movement Therapy (CIMT) Comparators: CIMT or modified CIMT vs. conventional treatment. Discrepancies in the duration and intensity of comparators.	Checklist: van Tulder methodological criteria Mean Score: NR Individual Item Rating: Individual scores (range 5-10)/19 provided.	Primary: -Action Research Arm Test -Motor Activity Log -Fugl Meyer assessment -Wolf Motor Function test Outcomes: - Effectiveness -Minimal clinically important difference (pre/post Rx scoring changes) Analysis: Qualitative summary	Population: Adult stroke patients with an ability to extend at least 10° at the metacarpo-phalangeal and interphalangeal joints and 20° at the wrist; disability in activities of daily living when using the affected upper extremity; no excessive spasticity, balance problems cognitive deficits or uncontrolled medical disorders. Acuity: Mixed (5 chronic, 3 subacute, 1 acute trial)	Although all studies achieved positive results, it is impossible to draw any clear-cut conclusion on the effectiveness of the CIMT. The main limitations are the lack of homogeneity in the outcome measures used, the inadequacy of data provided and the small samples' size. Multicentre studies, using robust outcomes measures and considering both motor- and sensory-disabled patients are needed.
Braun[16] 2006 Netherlands	Design: -4 RCT -1 CCT -2 CS -3 CR (n=10) Total Sample: n=121	Years: 1966 to Aug 2005 Sources: PUBMED MEDLINE® PsycINFO Pedro Rehadat Rehab Trials Other: Reference lists	Aim of Therapy: Mental practice to improve physical recovery during rehab Types of Interventions: Mental practice by tape, daily imagery, by observation then visualization with or without PT or	Checklist Type: Amsterdam-Maastrict Consensus List for Quality Assessment (AMCL) Mean score: 5.1 / 11 [for trials only] (range 2.5 to 7) Individual Item	Primary: Not specified Outcome Domains: -Physical Function, -Somato-sensory function -Attention control -Activity and participation Analysis: Qualitative summary	Population: Stroke patients, otherwise not specified. Acuity: All phases of recovery	No definite conclusions could be drawn except that further research, using clear definitions and the content of mental practice and standardized measurements of outcome, are needed. -Blinding of patients is impossible in

			OT Comparator: No imagery or rehearsal, rehearsal of pictures (not mental tasks), relaxation techniques, and no PT or OT	Rating: Scores for all 11 items provided for each study			cognitive therapy -little is known about the long-term effects of mental practice. - A training period to teach the mental practice should occur prior to evaluation.
Carson[112] 2005 United States	Designs: 4 RCT 1 CCT 17 OS (n=22) Total Sample: NR	Years: 1966 to 2003 Sources: -MEDLINE® -EMBASE -CINAHL -CCRCT -Health STAR -DARE AltHealthWatch - MANTIS Other: -Specialized Undersea and Hyperbaric society and libraries -Reference Lists	Aim: To identify the benefits and harms of using hyperbaric oxygen therapy (HBOT) to treat acute or subacute stroke or the chronic effects of a stroke, and to identify gaps in the evidence to guide future research. Therapy: HBOT Comparators: Only 5 studies had comparators; control groups used air instead of 100% oxygen or sham hyperbaric oxygen AND PT or OT therapy or no treatment.	Checklist type: Author specific criteria Mean Score: NR Individual Item Rating: Grade (poor to good) for each study	Primary: Not specified Outcomes: -Mortality, -Functional health outcomes -Adverse events Analysis: Qualitative summary	Population: Ischemic stroke patients in any inpatient or outpatient setting. Acuity: All phases of stroke recovery	The overall evidence is insufficient to determine the effectiveness of HBOT in any subgroup of stroke patients. There is still a need for good quality studies to determine if HBOT for stroke provides any benefit and that these outweigh potential harms.
de Kroon[113] 2005 Netherlands	Designs: -12 RCT -2 non-RCT -2 MBD -3 CS (n=19) Total Sample: 578	Years: 1966-2003 Sources: -MEDLINE® -EMBASE -database of the Cochrane Field "Rehabilitation and Related Therapies" Other: -Reference lists	Aim: To explore the relationship between characteristics of stimulation and the effect of electrical stimulation (ES) on the recovery of upper limb motor control following stroke. Therapy: -ES applied to the affected upper extremity; -ES provoking muscle contraction;	Checklist: NR Mean Score: NR Individual Item Rating: NR	Primary: -Motor control in upper extremity -Measures assessing movement broadly: Fugl Meyer Motor Assessment, Rivermead Mobility Assessment and Motricity Index Outcomes: -Grip strength -Isometric wrist extensor strength Analysis: Descriptive literature review	Population: Post stroke patients (highly heterogeneous mix in regards to age range, acuity, severity, etiology, etc.) Acuity: -4 acute -2 subacute -10 chronic -3 mixed (Study populations)	Triggered electrical stimulation may be more effective than non-triggered electrical stimulation in facilitating upper extremity motor recovery following stroke. It appears that the specific stimulus parameters may not be crucial in determining the effect of electrical

			-Application of ES with surface electrodes. Comparators: -ES stimulation techniques (triggered/non-triggered) vs. usual care, no therapy, PT, placebo stimulation, or sham stimulation				stimulation. In this review, no relationship between stimulus parameters, duration of treatment, subject characteristics, and clinical outcome could be detected. Future clinical trials should determine the most appropriate method of stimulation, optimal prescriptive parameters, clinical indications and effect of ES at the level of activities of daily living.
Dumoulin[88] 2005 Canada	Design: 4 RCT 1 PC Total Sample: n=185	Years: 1966 to 2004 Sources: MEDLINE® CIANHL EMBASE Web of Science CCRCT PEDro Other: National research registries	Aim: To assess the scientific evidence for the effectiveness of various behavioral therapies for the treatment of urinary incontinence (UI) post stroke. Interventions: Timed voiding, prompted voiding, bladder retraining with urge suppression, and pelvic floor muscle exercises Comparators: No intervention (social visit) or remedial rehabilitation	Checklist: PEDro QA for RCT's only Mean score: NR Individual item ratings: NR	Primary: Outcomes: -Continence -Katz ADL index -Functional independence measure (FIM-G7) -Psychological general well-being index (PGWB) -Mobility score -% reduction in UI episode -% reduction daytime UI episode - SF-36 -Incontinence Impact (IIQ) Analysis: Qualitative summary	Population: Stroke patients with continence problems Acuity: Not specified, but most studies were based on patients within the home or community	The effectiveness of various behavioral approaches in the management of UI in individuals post stroke is not well studied. Preliminary research suggests that important improvements in UI can be achieved using a number of behavioral strategies for UI that are employed for non-stroke patients. Further research is urgently needed, because UI is a strong predictor of functional

							recovery and discharge destination.
Hakkennes[92] 2005 Australia	Designs: 14 RCT 4 SR (n=18) Total Sample: n=292	Years: 1966-2005 Sources: -CCRCT -CDSR -Cochrane Database of Reviews of Effects -MEDLINE® -EMBASE -CINAHL -PEDro -OTseeker Other: -Reference lists	Aim: To assess the effectiveness of constraint-induced movement therapy (CIMT) for improving upper limb function following stroke. Therapy: CIMT Comparators: -Traditional CIMT vs. alternative therapy or control; -Modified CIMT (mCIMT) vs. alternative therapy or control -Traditional CIMT vs. mCIMT	Checklist: PEDro scale Mean Score: 5/10 (range 3-7) Individual Item Rating: Yes—binary scoring and resulting PEDro score given for all included trials (14 RCT's)	Primary: Not specified Outcomes: -Motor activity/ quality of arm movement -Strength -Quality of life; -Activities of daily living -Health care costs -Patient/carer satisfaction Analysis: Meta-analysis	Population: ≥18 years exhibiting reduced functional use of an upper extremity as a result of a stroke (predominantly participants with preserved cognitive function, 10 degrees of active finger, and 20 degrees of active wrist extension) Acuity: -4 acute -3 subacute -1 subacute /chronic -6 chronic (trial populations)	CIMT may improve upper limb function following stroke compared to alternative and/or no treatment. Little can be concluded about the effects of CIMT on quality of life, independence with activities of daily living, and costs associated with the intervention. It is unclear is there is an optimal CIMT protocol. Despite the popularity that CIMT currently enjoys amongst treatments providers, high quality trials involving larger sample sizes are required before definitive conclusions can be drawn about the benefit of CIMT over alternative therapy or no treatment.
Henderson[93] 2007 Canada	Designs: -2 RCT -1 Case study -3 PreP (n=6) Total Sample: n=96	Years: 1982-2006 Sources: -MEDLINE® -CINAHL -CDSR -CCRCT -PsycINFO -PEDro -OT seeker -ISI Web of Science -Evidence-Based Review of Stroke Rehabilitation-	Aim: To evaluate the scientific evidence for the effectiveness of virtual reality (VR) in rehabilitation of the affected upper limb (UL). Therapy: Immersive and non-immersive VR	Checklist: PEDro Scale assessment for 2/6 studies (RCT's) Mean Score: NR (Individual scores of 3/10 and 8/10 given) Individual Item Rating: NR	Primary: Not specified Outcomes: -Fugl-Meyer Arm Scale -Box and Block test -Manual Function Test -manual dexterity/ grip force/ control of arm Analysis: Qualitative summary	Population: Adult patients with any acuity of hemiparesis following ischemic or hemorrhagic stroke. Acuity: -3 acute -3 chronic (study populations)	The current evidence on the effectiveness of VR in the rehabilitation of the UL in patients with stroke is limited but sufficiently encouraging to justify further research efforts in this area.

		Upper Limb Interventions Other: -Reference lists	Comparators: Immersive VR or non-immersive VR vs. conventional therapy or no therapy				
Larsen[86] 2006 Denmark	Designs: 7 RCT Total Sample: n=1108	Years: Jan.1 2000 to April 2005 Sources: Pub Med Other: NR	Aim: To undergo a comprehensive and systematic assessment of early home-supported discharge (EHSD) care to that of conventional rehabilitation in stroke units. Therapy: Early home-supported discharge care (EHSD) by a multidisciplinary team that plans, coordinates, and delivers care at home Comparators: Organized home-supported stroke care vs. conventional rehabilitation care in stroke units	Checklist: NR Mean Score: NR Individual Item Rating: NR	Primary: -Death or institution at follow-up; -Length of hospital stay; Outcomes: -Changes in functional status as measured by the Barthel Index; -Intensity of home rehabilitation; -Economic evaluation Analysis: Meta-analysis	Population: Adult stroke patients, 3-12 months after discharge Acuity: Subacute-Chronic	EHSD is evidenced as a dominant health intervention. However, financial barriers between municipalities and health authorities have to be overcome. For qualitative reasons, a learning path of implementation is recommended where one stroke unit in a region initiated EHSD for dissemination of new experiences to the other stroke units.
Lynton[87] 2007 USA	Design: 3 CS 3 CR Total Sample: NR	Years: 1806-2005 Sources: -MEDLINE® -CINAHL -CDSR -DARE -ACP Journal club -CCRCT -PsycINFO -EMBASE -MANTIS -AMED SPORT Discus Other: -Google Scholar -Reference lists	Aim: To evaluate the use of yoga (all types) in stroke rehabilitation. Interventions: Yoga in Stroke Rehabilitation Comparator: None	Checklist: None specified Mean Score: NR Individual item rating: NR	Primary: Not specified Outcomes: -Berg Balance scale -adverse events Analysis: Qualitative summary	Population: Stroke patients Acuity: Not specified	The use of Yoga in stroke rehabilitation has not been well studied The small sample sizes within studies evaluated make it impossible to draw conclusions Further research is required
Pang[94] 2006	Designs: -7 RCT	Years:	Aim: To determine	Checklist:	Primary: Aerobic capacity	Population: Post stroke patients	There is good evidence that

Canada	-2 CCT (n=9) Total Sample: n=585	1966-2005 Sources: -MEDLINE® -CINAHL -EMBASE -CDSR -PED Other: -Hand searching of reference lists	whether aerobic exercise improves aerobic capacity in individuals with stroke. Therapy: Aerobic training (cycle ergometer, treadmill walking, exercises) Comparators: Aerobic training vs. usual care/therapy without aerobic component	PEDro scale Mean Score: NR Individual Item Rating: Scores for each 11 items provided	(peak oxygen consumption (VO2), peak workload) Outcomes: -Walking velocity -Walking endurance Analysis: Meta-analysis	with predominantly single ischemic or hemorrhagic stroke, mild/moderate impairment, and stable cardiovascular conditions. Acuity: -4 acute -1 subacute -3 chronic -1 mixed (Study populations)	aerobic exercise is beneficial for improving aerobic capacity in people with mild and moderate stroke. Aerobic exercise should be an important component of stroke rehabilitation.
Prange[114] 2006 Netherlands	Design: Clinical Trials n=17 Total sample: n=178	Years: 1975 to 2005 Sources: Pub Med CCTR CIRRIE REHABDATA Other: Reference lists	Aim: To examine the effect of robotic aided therapy on upper limb motor control and functional abilities post-stroke. Interventions: -MIT-Manus system -MIME -ARM Guide Comparator: Conventional therapy with non-contact or non-operational exposure to the robotic device. The nature of the conventional therapy was not specified in most studies.	Checklist: Kottink list (based on Maastricht-Amsterdam criteria) Mean: (Range 8 to 16 out of 19) Individual item rating: NR	Primary: Not specified Outcomes: -10 motor control measures -2 functional ability measures (FIM and FM) Analysis: Qualitative summary	Population: Stroke patients Acuity: Subacute and chronic	Robotic aided therapy of the proximal upper limb can improve short and long term motor control of the paretic shoulder and elbow. No consistent effect on the improvement of functional abilities was observed. The aspects of robotic aided therapy that were most responsible for improvement could not be established
Riggs[115] 2007 USA	Design: 11 RCT 3 PS 15 CR Total Sample Size: n=397	Years: 1980-2004 Sources: MEDLINE® Other: None	Aim: To determine the range and effectiveness of various rehabilitation for vision dysfunction in stroke patients Interventions: Visuoperceptual, visuomotor, or prism therapy or eye patching.	Checklist: None Mean: Individual item rating:	Primary: Not specified Outcomes: -Cognition tests (neuropsychological type included) - Function (FIM, Barthel, Rivermead, etc) -Evaluation of hemispatial neglect -Vision tests (including eye	Population: Patients with the following diagnoses or conditions after brain injury or stroke: unilateral spatial neglect, hemispatial neglect, visuospatial neglect, visual neglect, hemianopsia,	The analysis of this review revealed some success with visual neglect disorders, but not enough evidence to comment definitively on interventions for hemianopsia, quadrantanopsia, diplopia, or

			Corrective vision intervention usually involves the use of prisms, patching, lenses, and therapeutic interventions. Also included were compensatory visual training, computer based visual training, scanning and cuing, hemi-spatial sunglasses, limb activation. Comparator: Standard feedback, oral reading therapy, no eye patch, control use of computer games		movements) - Reading tests -Visual evoked potential (VEP), measurements Analysis: Qualitative summary	quadrantanopsia, convergence insufficiency, or diplopia. Acuity: All phases of recovery	convergence insufficiency. A lack of follow-up limited efforts to assess the durability of documented gains. Additional research is necessary to clarify, quantify, and measure treatment outcomes for acquired visual dysfunction as well as to link laboratory testing to improvement in actual functioning for individuals in their environment.
Robbins[116] 2006 Canada	Design: 4 CCT 4 CO/ BA Total Sample: n=161	Years: 1966 to 2005 Sources: MEDLINE® EMBASE CINAHL Pub Med Other: Reference lists Reviews	Aim: To determine effect of previous treatments of functional electrical stimulation (FES) and transcutaneous electrical stimulation (TENS) on improving gait speed in subjects post stroke. Interventions: FES or TENS with surface electrodes only Comparators: None	Checklist: Downs and Black Mean 15/27 (Range 13-17) Individual item rating: Scores for 4 subscales within the Downs and Black reported for each study	Primary: Gait speed assessed without electrical stimulation Outcomes: -Gait speed -cadence - Fugl-Meyer -Physiological cost index sensation change -spasticity change gait parameters Analysis: Meta-analysis	Population: Stroke (any category) Acuity: All phases of recovery	FES is effective at improving gait speed post stroke Future research should examine the effectiveness of practical and readily available FES units for subjects in sub-acute phase of recovery Studies should attempt to use RCT designs.
Seenan[97] 2007 UK	Design: 18 OS usable data 7 OS not usable data	Years: 2000 to 2005 Sources: -MEDLINE® -EMBASE -CINAHL -CCSTG	Aim: comparison of care in a stroke unit (or units) with non-stroke unit Interventions: Organized inpatient care that	Checklist: NT Mean: NT Individual item rating:	Primary: Death within 1 year Outcomes: -mortality 1year -poor outcome (failure to be discharged home or	Population: Clinical diagnosis of stroke Acuity: All phases of stroke recovery	Although the observational studies did have the potential for bias and heterogeneity, the observed benefit of stroke

	Total Sample: 42236 (usable data studies)	-Cochrane Library -British Nursing Index Other: -Reference lists -Conference abstracts	was provided by a multidisciplinary team of stroke specialists Comparators: Absence of stroke unit care or conventional care	NT	failure to regain independence in daily activities). Analysis: Meta-analysis		unit care was comparable to that seen in clinical trials. Comparing outcomes of stroke patients managed in the stroke unit as opposed to a non-stroke unit setting, stroke unit care was associated with reduced odds of death and reduced odds of poor outcome (death, institutional care, or dependency).
Stewart[117] 2006 United States Australia	Designs: -11 RCT Total Sample: n=171	Years: 1966-2005 Sources: -Pub Med -Cochrane databases Other: -References from stroke and bilateral movement studies, review articles, and book chapters.	Aim: To determine the overall effectiveness of rehabilitating with bilateral movements. Therapy: Bilateral training involving either functional tasks or repetitive arm movements. Comparators: Bilateral movement training alone as a rehabilitation technique or combined bilateral movements with another treatment protocol, such as auditory cuing or active neuromuscular stimulation on the impaired arm while testing subjects.	Checklist: Jadad and Moher criteria Mean Score: NR Individual Item Rating: Binary scoring for individual items of quality assessment criteria	Primary: -Fugl-Meyer upper extremity motor test; -Box and Block test; -Kinematic performance rating Outcome: Not specified Analysis: Meta-analysis	Population: Patients with upper extremity stroke hemiparesis, with enough residual motor control in the impaired arm to perform the motor capabilities test. Acuity: Subacute and chronic	These meta-analysis findings indicate that bilateral movements alone or in combinations with auxiliary sensory feedback are effective stroke rehabilitation protocols during the subacute and chronic phases of recovery.
Urton[89] 2007 USA	Design: 8 RCT 3 mixed	Years: 1999-2005 Sources:	Aim: To evaluate the literature for rehabilitation for upper extremity	Checklist: Sackett's level of evidence and authors	Primary: Not specified Outcomes:	Population: Stroke patients with arm	Electrical stimulation can be used to improve upper limb outcomes

	design Total Sample: n=269	Pub Med Elite, Academic Search Premier, CINAHL Health Source: Nursing/Academic Edition Others:	hemiparesis following stroke Interventions: -Mixed of electrical stimulation, -exercise, -drugs, -constraint induced therapy, -arm training program. Comparators: Mixed of exercise, usual care, standard practice, placebo etc.	own criteria Mean Score: NR Individual item rating: Level of evidence for each study	-Functional outcome measures (i.e. Wolf Motor Arm Test, Functional Independence Measure, upper extremity motor subset of Fugl-Meyer, Box and Block test, stroke impact scale, perception of joint position sense test. - Active/passive range of motion -temporal characteristics of arm trajectory -Caregiver strain index -Quality of life -Ashworth scale for spasticity Analysis: Qualitative	hemiparesis Acuity: All phases of stroke recovery	in patients with moderate to severe upper limb dysfunction and is a feasible home-based intervention. Therapy that utilizes goal-directed reaching behaviors promotes more typical reaching patterns than non-goal-directed interventions. Reach-to-grasp movements show greater improvement when compensatory trunk movements are reduced. As an addition to regular exercise therapy time, Arm BASIS training may enhance selective movements of the upper extremity (i.e. reaching). When performed in conjunction with active neuromuscular stimulation, random and blocked practice may improve pre-motor, motor and total reaction times of the upper extremity.
van Dijk[96] 2005 Netherlands	Designs: 26 RCT 1 NR	Years: 1956-2004 Sources:	To assess the effect of augmented feedback on motor function of the	Checklist: Delphi list Mean Score:	Primary: Not specified Outcomes:	Population: Predominantly post-stroke patients, however	No firm evidence was found of effectiveness regarding the

	(n=27) Total Sample: n=937	-MEDLINE® -EMBASE -Cochrane Controlled Trials Register -CIRRIE -REHABDATA Other: Hand searching reference lists	affected upper extremity in rehabilitation patients. Therapy: -Electromyographic biofeedback (EMG-BF) -Kinetic feedback -Kinematic feedback -Knowledge of results Comparators: Different therapeutic interventions using augmented feedback vs. conventional therapy, no therapy, or placebo EMG-BF and conventional therapy	5.2/9—positive effect trials 4.2/9—negative effect trials Individual Item Rating: Yes—all nine criteria are scored and overall quality scores range from (3-7)/9	-Active and/or passive range of motion; -EMG activity. Analysis: Qualitative summary	populations including TBI, SCI, Parkinson's disease and cerebral palsy were also included. Acuity: -8 acute -3 subacute -13 chronic -1 mixed -1 NR (Study populations)	use of augmented feedback to improve motor function of the upper extremity in rehabilitation patients. Future studies should focus more on the content, form and timing of augmented feedback concerning the therapeutic intervention. It should be emphasized that motor learning effects can only be determined by re-examining the population after a follow-up period.
van Peppen[95] 2006 Netherlands	Designs: -6 RCT -2 CCT (n=8) Total Sample: n=214	Years: 1966- April 2005 Sources: -Pub Med (MEDLINE®) -CCRCT -CINAHL -PEDro -DOC-online Other: Reference lists	Aim: To establish whether bilateral standing with visual feedback therapy (VFT) after stroke improves postural control compared with conventional therapy and to evaluate the generalization of the effects of visual feedback therapy on gait and gait-related activities. Therapy: VFT Comparators: Predominantly VFT vs. conventional balance therapy (CT)	Checklist: PEDro scale Mean Score: 4/10 (range 3-6) Individual Item Rating: Binary scoring on individual items reported	Primary: -Weight distribution and postural sway while bilateral standing; -BERG balance scale. Outcomes: -Timed Up & Go test; -Gait and gait-related activities including activities of daily living. Analysis: Meta-analysis	Population: Adult subjects suffering from stroke as defined by WHO Acuity: Acute and subacute (<20 weeks	The additional value of VFT in bilateral standing compared with CT shows no statistically significant effects on symmetry of weight distribution between paretic and non-paretic leg, postural sway in bilateral standing, gait and gait-related activities. VFT should not be favored over CT. The question remains as to exactly how asymmetry in weight distribution while standing is related to balance control in patients with stroke.

Abbreviations: ADL=activities of daily living; AMED=Allied and Complementary Medicine Database; ARM=assisted rehabilitation measurement; BA=Before After study; BWSTT=Body Weight Supported Treadmill Training; CaCo=Case-control study; CCMFTR=Cochrane Complementary Medicine Field Trials Register; CCRCT=Cochrane Central Register of Controlled Trials (CENTRAL); CCT=Controlled clinical trial; CDSR=Cochrane Database of Systematic Reviews; CIMT=Constraint-induced movement therapy; CINAHL=Cumulative Index to Nursing and Allied Health Literature; CIRRIE=Center for International Rehabilitation Research Information and Exchange; CO=Cross-over trials; CS=Case series; CR=Case report; CRS=Cross-sectional study; CSGTR=Cochrane Stroke Group Trials Register; FM=Fugl-Meyer; LOF=Length of Follow-up; MBD=Multiple baseline design; MIME=mirror image motion enabler; MIT=Massachusetts Institute of Technology; NA=Not applicable; NIHSS=National Institutes of Health Stroke Survey; NR=not reported; NT=Not tested; OS=Observational study; OT=Occupational therapy intervention; OTV=program of videotape feedback and a program of occupational therapy; PED=Physiotherapy Evidence Database; PR=Prospective study; PreP=Pre-post study; PS=prospective study; PT=Physical Therapy; PTA/OTA=Physiotherapy or Occupational Therapy Assistant; QRCT=quasi-randomized clinical trial; QE=quasi-experimental study; RCT=randomized controlled trial; SCI=spinal cord injury; SR=Systematic review; SLP=Speech Language Pathologist; TBI=traumatic brain injury; TT=Traditional Therapy; UE=upper extremity; vs=versus; WHO=World Health Organization

Appendix F. Extraction Criteria for Systematic Reviews

Search Methods (Maximum score _ 4)

1. Were the search methods used to find evidence (primary studies) on the primary question(s) stated?
2 points: Yes—includes description of databases searched, search strategy, and years reviewed; described well enough to duplicate.
1 point: Partially—partial description of methods, but not sufficiently to duplicate search.
0 points: No—no description of search methods.

2. Was the search for evidence reasonably comprehensive?
2 points: Yes—must include at least one computerized database search as well as search of unpublished or nonindexed literature (e.g., manual searches or letters to primary authors).
1 point: Can't tell—search strategy partially comprehensive (e.g., one of the strategies above was performed)
0 points: No—search not comprehensive or not described well enough to make a judgment.

Selection Methods (Maximum score _ 4)

3. Were the criteria used for deciding which studies to include in the review reported?
2 points: Yes—inclusion/exclusion criteria clearly defined.
1 point: Partially—reference to inclusion/exclusion criteria can be found in article but are not defined clearly enough to duplicate.
0 points: No—no criteria defined.

4. Was bias in the selection of articles avoided?
2 points: Yes—key issues influencing selection bias were dealt with; two of three of the following bias avoidance strategies were used:
(i) two or more assessors independently judged study relevance and selection using predetermined criteria; (ii) reviewers were blinded to identifying features of study [i.e., journal title, author(s), funding source]; (iii) assessors were blinded to treatment outcome.
1 point: Can't tell—if only one of the three strategies above were used.
0 points: No—selection bias not avoided or not discussed.

Validity Assessment (Maximum score _ 4)

5. Were the criteria used for assessing the validity of the studies that were reviewed reported?
2 points: Yes—criteria defined explicitly.
1 point: Partially—some discussion or reference to criteria but not sufficiently described to duplicate.
0 points: No—validity or methodologic quality criteria not used or not described.

6. Was the validity for each study cited assessed using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)?

2 points: Yes—the criteria used address the major factors influencing bias (e.g., population, intervention, outcomes, follow-up).
1 point: Partially—some discussion of methodologic review strategy but not clearly described with predetermined criteria.
0 points: No—criteria not used or not described.

Synthesis (Maximum score _ 6)

7. Were the methods used to combine the findings for the relevant studies (to reach a conclusion) reported?
2 points: Yes—qualitative or quantitative methods are acceptable. 1 point: Partially—partial description of methods to combine/tabulate; not sufficient to duplicate. 0 points: Methods of combining studies not stated or described.

8. Were findings of relevant studies combined appropriately relative to the primary question the review addresses?
2 points: Yes—combining of studies appears acceptable.
1 point: Can't tell—if in doubt, mark "can't tell."
0 points: No—no attempt was made to combine findings, and no statement was made regarding the inappropriateness ofcombining findings; if a summary (general) estimate was given anywhere in the abstract, the discussion, or the summary section of the article, and it was not reported how that estimate was derived, mark "no" even if there is a statement regarding the limitations of combining the findings of the studies reviewed.

9. Were the conclusions made by the author(s) supported by the data or analysis reported in the review?
2 points: Yes—data, not just citations, were reported that support the main conclusions regarding the primary question(s) that the
overview addresses
1 point: Partially
0 points: No—conclusions not supported or unclear.
How would you rate the methodologic quality for this review?
Add up the scores from questions 1-9. Maximum quality score is 18 points.

Criteria used to assess methodologic quality of selected review articles. Adapted with permission from Hoving, J. L., Gross, A. R., Gasner, D., et al. A critical appraisal of review articles on the effectiveness of conservative treatment for neck pain. *Spine* 26: 196, 2001.

Appendix G: Excluded Studies

Hyndman D, Ashburn A, Yardley L, Stack E. Interference between balance, gait and cognitive task performance among people with stroke living in the community. *Disability & Rehabilitation* 2006; 28(13-14):849-856.

Lennon O, Carey A, Stephenson J, Gaffney N, Blake C. A single-blinded, randomised, controlled trial to evaluate the effects of a cardiac rehabilitation programme for the non-acute ischaemic stroke population. *Physical Therapy Reviews* 2006; 11(3):211-212. Ref ID: 30

Muro MJ, Pedro-Cuesta J, Almazan J, von Koch L, Holmqvist LW. Outcome and use of health care in patients with moderate impairment and stroke in south Madrid and southwest Stockholm. *Journal of Stroke and Cerebrovascular Diseases* 2005; 14(4):167-173.

Hartman-Maeir A, Soroker N, Oman SD, Katz N. Awareness of disabilities in stroke rehabilitation—a clinical trial. *Disability and Rehabilitation* 2003; 25(1):35-44.

Schindler I, Kerkhoff G, Karnath HO, Keller I, Goldenberg G. Neck muscle vibration induces lasting recovery in spatial neglect [see comment]. *Journal of Neurology, Neurosurgery & Psychiatry* 2002; 73(4):412-419.

Bragoni M, Altieri M, Di P, V, Padovani A, Mostardini C, Lenzi GL. Bromocriptine and speech therapy in non-fluent chronic aphasia after stroke. *Neurological Sciences* 2000; 21(1):19-22.

Paolucci S, Matano A, Bragoni M, Coiro P, De Angelis D, Fusco FR et al. Rehabilitation of left brain-damaged ischemic stroke patients: the role of comprehension language deficits. A matched comparison. *Cerebrovascular Diseases* 2005; 20(5):400-406.

Pedersen PM, Vinter K, Olsen TS. Improvement of oral naming by unsupervised computerised rehabilitation [References]. *Aphasiology* 2001; 15(2):151-169.

Whiting E, Chenery HJ, Chalk J, Copland DA. Dexamphetamine boosts naming treatment effects in chronic aphasia [References]. *Journal of the International Neuropsychological Society* 2007; 13(6):972-979.

Kiger M, Brown CS, Watkins L. Dysphagia management: an analysis of patient outcomes using VITALSTIM therapy compared to traditional swallow therapy. *Dysphagia* 2006; 21(4):243-253.

Seki T, Kurusu M, Tanji H, Arai H, Sasaki H. Acupuncture and swallowing reflex in poststroke patients. *Journal of the American Geriatrics Society* 2003; 51(5):726-727.

Excluded Studies from Review of Reviews

(1) Barclay GR, Stevenson T, Poluha W, Moffatt MEK, Taback SP. Force platform feedback for standing balance training after stroke. SO: Barclay-Goddard R, Stevenson T, Poluha W, Moffatt MEK, Taback SP Force platform feedback for standing balance training after stroke *Cochrane Database of Systematic Reviews: Reviews* 2004 2004;(4).

(2) Kwan J, Sandercock P. In-hospital care pathways for stroke. SO: Kwan J, Sandercock P In-hospital care pathways for stroke *Cochrane Database of Systematic Reviews: Reviews* 2004;(4).

(3) West C, Hesketh A, Vail A, Bowen A. Interventions for apraxia of speech following stroke. SO: West C, Hesketh A, Vail A, Bowen A Interventions for apraxia of speech following stroke *Cochrane Database of Systematic Reviews: Reviews* 2005;(4).

(4) -Outpatient-Service-. Therapy-based rehabilitation services for stroke patients at home. SO: Outpatient Service Trialists Therapy-based rehabilitation services for stroke patients at home *Cochrane Database of Systematic Reviews: Reviews* 2003;(1).

(5) Prvu Bettger JA, Stineman MG. Effectiveness of multidisciplinary rehabilitation services in postacute care: state-of-the-science. A review. [Review] [64 refs]. *Archives of Physical Medicine & Rehabilitation* 2007; 88(11):1526-1534.

(6) Legg L, Drummond A, Leonardi-Bee J, Gladman JR, Corr S, Donkervoort M et al. Occupational therapy for patients with problems in personal activities of daily living after stroke: systematic review of randomised trials [see comment]. [Review] [13 refs]. *BMJ* 2007; 335(7626):922.

(7) Shiflett SC. Does acupuncture work for stroke rehabilitation: what do recent clinical trials really show? [Review] [26 refs]. *Topics in Stroke Rehabilitation* 2007; 14(4):40-58.

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(13) Legg LA, Drummond AE, Langhorne P. Occupational therapy for patients with problems in activities of daily living after stroke. [Review] [74 refs]. *Cochrane Database of Systematic Reviews* 2006;(4):CD003585.

(14) Cicerone KD, Dahlberg C, Malec JF, Langenbahn DM, Felicetti T, Kneipp S et al. Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002 [see comment]. [Review] [117 refs]. *Archives of Physical Medicine & Rehabilitation* 2005; 86(8):1681-1692.

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(16) Smidt N, de Vet HC, Bouter LM, Dekker J, Arendzen JH, de Bie RA et al. Effectiveness of exercise therapy: a best-evidence summary of systematic reviews [see comment]. [Review] [133 refs]. *Australian Journal of Physiotherapy* 2005; 51(2):71-85.

(17) Hopwood V, Lewith GT. Does acupuncture help stroke patients become more independent? [Review] [12 refs]. *Journal of Alternative & Complementary Medicine* 2005; 11(1):175-177.

(18) Langhorne P, Taylor G, Murray G, Dennis M, Anderson C, Bautz-Holter E et al. Early supported discharge services for stroke patients: a meta-analysis of individual patients' data [see comment]. *Lancet* 2005; 365(9458):501-506.

(19) 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? [Review] [230 refs]. *Clinical Rehabilitation* 2004; 18(8):833-862.

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