

EVIDENCE-BASED REVIEW OF STROKE REHABILITATION

Executive Summary (12th Edition)

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The Evidence-Based Review of Stroke Rehabilitation (EBRSR) reviews current practices in stroke rehabilitation.

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Executive Summary

The Stroke Rehabilitation Evidence-Based Review (SREBR) reviews techniques, therapies, devices, procedures and medications associated with stroke rehabilitation. The purpose of the Evidence-Based Review of Stroke Rehabilitation was to fulfil the 12th recommendation of The Stroke Rehabilitation Consensus Panel Report that supported the continuing review of stroke rehabilitation research with the *“purpose of maintaining timely and accurate information on effective stroke rehabilitation, identifying ideas for further research, supporting continuous peer-review and encouraging improved evidence-based practice.”* The aim of the SREBR was to:

- Be an up-to-date review of the current evidence in stroke rehabilitation.
- Provide a comprehensive and accessible review to facilitate best-practice.
- Provide specific conclusion based on evidence that could be used to help direct stroke care at the bedside and at home.

Since its original publication in April 2002, the SREBR has undergone eleven major revisions and now includes articles published up to August 2009. To date, we have included almost 956 randomized controlled trials (RCTs).

Methods

For the first edition of the SREBR a literature search using multiple databases (MEDLINE, EBASE, MANTIS, PASCAL and Sci Search) was used to

identify all potential trials published from 1970-2001, regardless of study design. The search was restricted to the English language and excluded animal studies. Search terms included, but were not restricted to: *“stroke”, “cerebrovascular accident”, “cerebrovascular disorder”, “rehabilitation”, “physiotherapy”, “occupational therapy”, “speech therapy”, “recreation therapy”*. The initial literature search identified approximately 2,500 abstracts.

From 2001 onwards, the individual authors of each of the modules have conducted their own searches. These searches, and the databases used, were individually tailored to identify potential trials within each subsection of every module. This approach was adopted as each author gained expertise, knowledge and familiarity with their subject matter. It no longer made sense to use a non-specific approach to identifying the broad range of interventions associated with stroke rehabilitation. We estimate that, as of the 12th edition of the SREBR, over 100 unique search strategies have been conducted. Depending on the breadth of the current evidence, searches may have been restricted to randomized controlled trials, since they are given the greatest emphasis when formulating conclusions.

Meta-analyses, systematic reviews and review articles were identified at this point and while they were not used in formulating conclusions, their content was included and studies cited within these works that were not identified in the original literature search, were also sought. The review was restricted to published works. Although the review was not confined

to the results from randomized controlled trials (RCT), these articles received priority when formulating conclusions.

Data Extraction and Quality Assessment Tool

Two abstractors, each blinded to the others' results reviewed each article independently. Reviewers collected data relating to the study methodology, identification of outcome measures, results, and final conclusions and also quantitatively evaluated the study's methodological quality using the Physiotherapy Evidence Database (PEDro) scale, developed by the Centre for Evidence-Based Physiotherapy (CEBP) in Australia.

The PEDro Scale consists of 10 quality ratings each receiving either a yes or no score:

1. Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received).
2. Allocation was concealed.
3. The groups were similar at baseline regarding the most important prognostic indicators.
4. There was blinding of all subjects.
5. There was blinding of all therapists who administered the therapy.
6. There was blinding of all assessors who measured at least one key outcome.
7. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups (*).

8. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat".
9. The results of between-group statistical comparisons are reported for at least one key outcome.
10. The study provides both point measures and measures of variability for at least one key outcome.

(For the purposes of this review, follow-up was considered adequate if all of the subjects that had been originally randomized could be accounted for at the end of the study period.*

The maximum score a study could receive was 10. Two independent raters reviewed each article. Scoring discrepancies were resolved through discussion

Formulating Conclusions Based on Levels of Evidence

The levels of evidence used to summarize the findings are based, in part on the Eastern Ontario/Queen's Evidence Based Report, which in turn were based on the levels of evidence used by the United States Agency for Health Care Policy and Research (AHCPR) Guidelines for Stroke Rehabilitation. There are many systems currently available to summarize a body of knowledge and establish levels of evidence. Some of these are increasingly complex, requiring a specialized body of knowledge for correct interpretation. With our focus on ease and

accessibility, we intentionally chose a system that was simple and straightforward.

Three levels of evidence were considered; 1a (strong), 1b (moderate) and 2 (limited). The following definitions of evidence were used:

- **Level 1a (Strong) ***: The findings were supported by the results of 2 or more RCTs of at least “fair” quality.
- **Level 1b (Moderate)**: The findings were supported by a single RCT of at least “fair” quality.
- **Level 2 (Limited)**: The findings were supported by at least one non-experimental study (non-randomized controlled trial, cohort studies etc.).
- **Level 3 (Consensus)**: In the absence of evidence, agreement by a group of experts on the appropriate treatment course. Consensus opinion is regarded as the lowest form of evidence. As such, it is arguably not considered evidence at all.
- **Level 4 (Conflicting)**: Disagreement between the findings of at least 2 RCTs. Where there were more than 4 RCTs and the results of only one was conflicting, the conclusion was based on the results of the majority of the studies, unless the study with conflicting results was of higher quality.

** In chapter 5, which examines the effectiveness of four different models of providing stroke care, sufficient studies and data were available to enable pooled. Therefore, we used the results obtained from **meta-analyses** to establish strong (Level 1a) evidence. It is our intention to expand the use of this approach, when formulating conclusions in future updates of the review, where meta-analyses are feasible. Meta-analyses, conducted by the authors of this review have also been included in modules 8,15,16,17 and 18.*

Using this system, conclusions were easily arrived at when the results of multiple studies were in agreement. However, interpretation became difficult when the study results conflicted. In cases where RCTs also differed in terms of methodological quality, the results of the study (or studies) with the higher PEDro score(s) were more heavily weighted to arrive at the final conclusions. However, there were still some instances where interpretation remained problematic. For instance, the authors needed to make a judgment when the results of a single study of higher quality conflicted with those of several studies of inferior quality. In these cases we attempted to provide a rationale for our decision and to make the process as transparent as possible. In the end the reader is encouraged to be a “critical consumer” of all of the material presented.

Levels of Evidence

The table below summarizes the levels of evidence, by module (updated September 2009).

	Strong	Moderate	Limited	Consensus	Conflicting	Totals
Module						
4	2	1	4	3	0	10
5	10	1	0	0	0	11
6	5	3	2	0	2	12
7	4	2	1	0	2	9
8	34	35	12	0	5	86
9	15	15	4	0	9	43
10	13	8	3	2	8	34
11	0	9	5	0	3	17
12	6	11	8	0	1	26
13	5	10	9	0	3	27
14	5	15	11	0	1	32
15	2	11	6	10	1	30
16	1	5	1	0	1	8
17	3	16	2	2	1	24
18	7	10	3	0	0	20
19	5	10	0	2	2	19
20	3	9	1	0	4	17
Totals	120	171	72	19	43	425

Modules

- 4) Triage process
- 5) Efficacy of stroke rehabilitation
- 6) Elements of stroke rehabilitation
- 7) Outpatient stroke rehabilitation
- 8) Secondary prevention of stroke
- 9) Mobility
- 10) Interventions for the upper extremity

- 11) Hemiplegic shoulder
- 12) Cognitive disorders and apraxia
- 13) Perceptual disorders
- 14) Aphasia
- 15) Dysphagia post stroke
- 16) Nutritional interventions
- 17) Medical complications
- 18) Depression
- 19) Community Reintegration
- 20) Miscellaneous treatments

The table below provides an overview of selected characteristics of studies reviewed within each of the 16 modules assessing stroke-related interventions.

Module	No. of RCTs	Mean "n" Of RCTs	Mean/Median PEDro Score	Total Number of non RCTs Reviewed
5	23	228	6.0/6	82
6	52	148	6.2/6	72
7	60	129	6.3/6	57
8	163	4,780	7.5/8	413
9	161	60	5.9/6	179
10	173	35	5.9/6	162
11	34	42	6.0/6	113
12	25	1616	7.3/7	242
13	37	48	5.02/5	155
14	39	58	6.1/6	76
15	11	56	5.4/6	127
16	7	56	5.3/6	71
17	41	148	6.5/7	248
18	38	73	7.2/7	152
19	38	170	5.7/6	223
20	66	152	6.4/6	67
Totals	968 *	487	6.2/6	2,439

(* Duplication of RCTs between modules accounts for the discrepancy between this figure and the number 956 cited within the text.)

The following brief summaries highlight the information provided in the SREBR and provide conclusions regarding treatments involved in stroke rehabilitation. The entire evidence-based review is available at:

<http://www.ebrsr.com>

Interdisciplinary Inpatient Stroke Rehabilitation

Acute Rehabilitation

There is strong evidence that acute stroke care is associated with a reduction in the odds of death or dependency and the need for institutionalization. There is strong evidence that specialized care is not associated with reductions in mortality, or length of hospital stay. There is strong evidence that acute stroke care is not associated with a

reduction in functional disability compared to alternative interventions.

Combined Acute and Rehabilitation

There is strong evidence that combined acute and rehabilitation stroke units are associated with a reduction in the odds of combined death/dependency, the need for institutionalization and length of hospital stay, but are not associated with reductions in mortality alone. There is strong evidence that combined stroke units are also associated with improved functional outcomes.

Subacute Rehabilitation

There is strong evidence that specialized, interdisciplinary rehabilitation provided in the subacute phase of stroke is associated with reductions in mortality, or the

combined outcome of death or dependency, but is not associated with a reduced need for institutionalization or length of hospital stay, compared to conventional care on a general medical ward.

There is strong evidence that for the subset of more severe stroke patients, specialized stroke rehabilitation reduces mortality, but does not result in improved functional outcomes, nor does it reduce the need for institutionalization, compared to conventional care. There is strong evidence that for the subset of patients with moderately severe stroke, specialized rehabilitation improves functional outcomes but does not reduce mortality, compared to conventional care. There is strong evidence that for the subset of patients with mild stroke, specialized rehabilitation does not improve functional outcome or reduce mortality, compared to conventional care.

There is moderate evidence that patients with severe or moderately severe stroke who receive treatment on a stroke rehabilitation unit have a lower risk of being dependent or of having a poor outcome (death or dependency) compared with patients who receive little or no rehabilitation.

Mobile Stroke Teams

There is strong evidence that mobile stroke teams providing care within the hospital setting do not result in improved outcomes when compared to conventional care.

Elements of Stroke Rehabilitation

The Role of Rehabilitation in Recovery

There is *limited* evidence that the improvement in disability seen in stroke rehabilitation cannot be explained on the basis of natural recovery of the neurological impairment alone.

Remedial vs. Compensatory Rehabilitation

There is *limited* evidence that neurological impairment (remedial) focused rehabilitation results in longer lengths of hospital stay when compared to a functionally (compensatory) oriented rehabilitation approach.

Hemorrhagic Strokes

There is *limited* evidence that patients with hemorrhagic strokes improve more rapidly in rehabilitation than those with ischemic strokes.

Care Pathways in Stroke Rehabilitation

There is *strong* evidence that care pathways do not improve stroke rehabilitation outcomes. There is *moderate* evidence that care pathways do not, reduce hospital costs or decrease hospital lengths of stay.

Early Admission to Stroke Rehabilitation

There is *limited* evidence that early admission to stroke rehabilitation directly results in improved functional outcomes. There is *strong* evidence that early mobilization; a component of stroke unit care is associated with improved outcome. Stroke patients should be admitted to stroke rehabilitation units as soon as they are medically stable, until the results of an RCT determines otherwise.

Intensity of Therapy

There is *strong* evidence that greater intensity of therapy results in

improved functional outcomes over the short-term (4 weeks -6 months). However, the overall beneficial effect was modest. Most of the studies also found the positive benefits were not maintained consistently over time. There is *limited* evidence that the same therapy delivered more intensely over a shorter period of time results in improved functional outcomes and is cost effective. There is conflicting evidence as to whether language therapy is efficacious in treating aphasia post stroke. The positive trials provided more intense therapy over a relatively short period of time whereas the negative trials provided much less intense therapy over a much longer period of time.

Duration of Rehabilitation Gains

There is *strong* evidence that the relatively greater functional improvements made by patients rehabilitated on specialized stroke units when compared to general medical units are maintained over the short-term and long-term. There is strong evidence that functional outcomes achieved through stroke rehabilitation are maintained and actually improve for up to one year. There is moderate evidence that these same functional gains decline after five years.

Outpatient Stroke Rehabilitation

Early Supported Discharge

There is *strong* evidence that high-level stroke patients discharged early from an acute hospital unit can be as successfully rehabilitated in the community by an interdisciplinary stroke rehabilitation team. Such programs can reduce hospital lengths of stay by approximately one week. There is conflicting evidence that the costs associated with home

intervention are lower when compared to usual care. At present it is not known whether severe to moderate stroke patients can be managed exclusively with early supported discharge programs.

Outpatient Rehabilitation

There is *moderate* evidence that hospital-based outpatient rehabilitation improve outcomes when compared to routine care over the short-term. However, the benefits are not maintained long-term. In contrast, there is strong evidence that additional home-based rehabilitation does not result in improved functional outcomes when compared to routine care. There is conflicting evidence as to whether hospital-based or home-based outpatient rehabilitation therapies are superior. There is limited evidence that subgroups of stroke patients may benefit from different outpatient treatment approaches; for elderly frail stroke patients, day hospital services may reduce death and institutionalization, while for younger stroke patients, home-based outpatient therapy may improve functional and quality of life outcomes.

Secondary Prevention

Stroke and TIA

There is *limited* evidence that urgent assessment and initiation of treatment following TIA is associated with reduced 90-day risk for stroke. There is *moderate* evidence that treatment of patients using an accelerated protocol in an emergency department observation unit results in shorter lengths of stay and reduced costs, but does not result in increased risk for stroke when compared to inpatient admission for TIA.

Risk Factor Management Programs

There is *moderate* evidence based that a comprehensive, post-discharge care plan, which includes management of risk for future stroke, may have a positive effect on both risk management and stroke knowledge. There is *moderate* evidence that a pharmacist-led education intervention may improve management of blood pressure and lipid levels over time. There is *limited* evidence that a risk management program initiated during the acute admission for stroke TIA is associated with good patient adherence over time. There is *limited* evidence that a program designed to increase adherence to evidence-based guidelines for treatment of TIA and stroke is associated with improved quality of care.

Hypertension

There is *strong* evidence that a reduction in blood pressure is associated with a decreased risk of stroke particularly among patients with a previous history of intracerebral haemorrhage. There is *strong* evidence that the use of ACE-inhibitors, other than Captopril, is associated with a reduced risk of stroke. There is *strong* evidence that the addition of a Ca-antagonist to a regimen that may include ACE-inhibitors or β -blockers and a diuretic decrease the risk of stroke events in both diabetic and non-diabetic stroke patients. There is *moderate* evidence that, while the use of an ARB (telmisartan) is not inferior to an ACE-inhibitor (ramipril), combination therapy (ACE-inhibitor + ARB) is not associated with increased benefit in terms of reduction of risk and may be associated with increased symptoms of hypotension, syncope and renal dysfunction.

There is *strong* evidence that the addition of an ARB (telmisartan) to existing antihypertensive treatments is not associated with further reduction in risk for recurrent stroke. However, *post hoc* analysis of available data suggests that benefits associated with the addition of telmisartan may not be apparent for at least 6 months. Further study is required. There is *moderate* evidence that treatment with telmisartan is well-tolerated by individuals who are unable to tolerate ACE-inhibitors.

There is also *moderate* evidence that immediate treatment of blood pressure following stroke serves to reduce the risk of recurrent stroke. There is *moderate* evidence that antihypertensive therapy post-stroke is associated with a reduction of risk for functional disability and dependency. There is *moderate* evidence that the addition of telmisartan to an antihypertensive regimen is not associated with reduced risk for functional disability.

Although hypertension is the most significant risk factor for stroke, only a small percentage of persons with the condition achieve adequate control. It has been recommended that blood pressures should be maintained below 140/90 mm Hg for individuals with existing cerebrovascular disease. Treatment with an ACE inhibitor/diuretic combination is recommended

Management of Diabetes

Diet and medications should both be used to establish and maintain optimum glycemic control, to prevent microvascular complications. There is evidence, based on a systematic review and 2 meta-analyses, that improved glycemic control is

associated with reduced risk for macrovascular complications in both Type 1 and Type 2 diabetes. However, benefit in terms of reduced risk for stroke is less clear. There is also evidence from a recent meta-analysis that, while intensive treatment has cardiovascular benefits, it is not more effective than standard therapy in reducing risk for stroke in individuals with Type 2 diabetes. There is *strong* evidence that intensive glucose-lowering therapy is not more effective than standard therapy in reducing risk for macrovascular events in individuals with previous macrovascular disease.

There is *moderate* evidence, based on subgroup analysis of a single RCT of excellent quality, that the addition of pioglitazone to the treatment regimen of individuals with Type 2 diabetes and a history of previous stroke is associated with reduced risk for recurrent stroke. There is *strong* evidence that intensive glucose-lowering therapy is associated with increased episodes of hypoglycaemia.

There is *strong* evidence that treatment of hypertension among diabetic patients reduces the risk of stroke. There is *strong* evidence that calcium-channel blocker and ACE-inhibitor-based regimens provide no additional benefit over conventional therapies in terms of both blood pressure control and prevention of macrovascular events including stroke in individuals with Type 2 diabetes.

There is *conflicting* evidence with regard to the impact of treatment with statins on the risk for stroke in individuals with Type 2 diabetes mellitus. There is *strong* evidence that treatment with fibrates is associated with increased HDL

cholesterol and lower triglyceride concentrations. There is *strong* evidence that among individuals with Type 2 diabetes, treatment with fenofibrate is not associated with a reduction in risk for stroke. Neither statin nor fibrate trials have included many patients with both diabetes and a history of stroke or TIA. Therefore, further study within this group of patients is required.

Hyperlipidaemia

The relationship between hyperlipidemia and stroke is complex and has not been fully clarified. It seems likely that elevated concentrations of total serum cholesterol, triglycerides and LDL are associated with an increased risk of non-haemorrhagic stroke.

There is *strong* evidence that statins are an effective treatment intervention to lower cholesterol and reduce risk of stroke and TIA. There is *moderate* evidence that intensive treatment with atorvastatin will reduce risk of recurrent stroke in individuals with previous stroke but no previous history of coronary artery disease. However, there is also *moderate* evidence that intensive treatment with atorvastatin is associated with an increased risk of hemorrhagic stroke in individuals with previous stroke.

Recent AHA/American Stroke Association guidelines for the secondary prevention of stroke (Sacco et al. 2006) recommend the use of statins to lower cholesterol and suggest that, for individuals with CHD or symptomatic atherosclerotic disease, the target goal for cholesterol should be LDL-C <100 mg/dL and LDL-C <70mg/dL for *very high risk individuals with multiple risk factors*. However, the use of statin therapy even for those with no pre-existing

indications for statins, may be considered reasonable in order to reduce the risk for vascular events.

Infection

There is *limited* evidence that stroke is associated with infection and chlamydia pneumoniae infection in particular. There is *strong* evidence that the use of a chlamydia pneumoniae reactive antibiotic (in seropositive patients with coronary artery disease) has no significant effect on the risk of stroke.

Physical Activity

There is *limited* evidence that increasing physical activity is associated in a graded manner with reduction in risk of stroke (both ischemic and haemorrhagic). Even moderate levels of physical activity are associated with a significant stroke risk reduction (20%).

Diet

There is *strong* evidence that a low-fat, low-cholesterol diet rich in fruits, vegetables, legumes, and Ω -3 fatty acids is effective in reducing blood pressure and serum cholesterol in patients with previous angina, MI or risk factors for coronary artery disease. Inasmuch as reduction of blood pressure reduces stroke risk, a low fat, low sodium diet may be regarded as beneficial for this purpose.

There is *strong* evidence that consumption of a Mediterranean-type diet is associated with a reduction in coronary events. There is *moderate* evidence that a low-fat, low-cholesterol diet of the Mediterranean type reduces risk of cardiovascular outcomes including stroke.

Anti-oxidants

There is potentially *conflicting* evidence with regard to the effectiveness of a combination of antioxidants in retarding the progression of atherosclerosis as measured by the intima-media thickness (IMT) of the common carotid artery. There is *strong* evidence that the use of individual antioxidants has no beneficial effect in the prevention of stroke events. There is *moderate* evidence that the use of vitamin C and vitamin E, in combination, may reduce risk for stroke in higher risk individuals. There is *moderate* evidence that polyunsaturated fatty acid (PUFA) may reduce stroke risk.

Homocysteine

There is *limited* evidence that elevated homocysteine levels ($>15\mu\text{mol/L}$) are associated with increased risk of atherosclerotic vascular disease, including stroke, and that levels of folic acid, vitamin B6, and vitamin B12 are inversely related to plasma homocysteine levels. There is *strong* evidence that supplementation with folic acid and vitamins B6 and B12 is associated with significant reductions in plasma homocysteine levels (tHcy). There is *conflicting* evidence that vitamin B therapy is associated with decreasing carotid intima-media thickness (CIMT) in individuals with elevated vascular risk. Benefits in terms of vascular structure may be limited to individuals with CIMT $>1.0\text{mm}$. There is *moderate* evidence that treatment with folic acid, vitamins B6 and B12 is associated with reduced risk of stroke in individuals with vascular disease. However, there is *moderate* evidence that treatment with folic acid, vitamins B6 and B12 does not reduce stroke risk in individuals with previous stroke.

There is *moderate* evidence that homocysteine-lowering therapy with B vitamins has no impact on stroke severity or disability.

Smoking

Smoking increases the risk of both ischemic and haemorrhagic stroke in a positive dose-response manner. Recent *limited* evidence suggests that exposure to environmental smoke increases the risk of stroke. There is *limited* evidence that smoking cessation reduces the risk of a subsequent stroke.

Alcohol

There is *limited* evidence that light alcohol consumption (1 – 2 drinks per day) reduces the risk for ischemic stroke while heavy drinking (more than 5 drinks per day) and binge drinking increase it. There is *limited* evidence that alcohol consumption increases the risk for hemorrhagic stroke in a linear, dose-dependent fashion.

Behavioural Intervention

There is *moderate* evidence that multi-factorial behavioural intervention can substantially reduce the risk of stroke even within a high-risk population. An understanding of how behavioural change occurs is necessary to ensure optimization of promotion of healthy lifestyles.

Atherosclerosis and Noncardiac Embolism

ASA

There is *strong* evidence that ASA therapy reduces the risk for recurrent stroke. In patients with acute stroke, aspirin therapy reduces the risk for recurrent ischemic stroke or death by 13%. Aspirin reduces the risk for serious vascular events in patients

with a history of previous TIA or minor stroke by 22% with long-term therapy. Doses of 75 – 150 mg/day are sufficient to produce the most effect with least risk. Therapy should be initiated as soon as is safe following the onset of the stroke event and maintained over the long-term.

Theinopyridines (Ticlopidine and Clopidogrel)

There is *strong* evidence that theinopyridines are more effective than ASA in reducing the risk of vascular complications, particularly among patients with a history of prior TIA or stroke. However, ticlopidine is associated with a poor safety profile in terms of associated adverse events. There is *strong* evidence that treatment with clopidogrel is as effective as ticlopidine in terms of prevention of secondary vascular events, including stroke. There is *moderate* evidence that clopidogrel is similar to aspirin with regard to safety. There is *moderate* evidence that treatment with ticlopidine is associated with a significantly greater risk for adverse events, including hepatic dysfunction, than clopidogrel.

Combination Therapies

There is *moderate* evidence that clopidogrel in combination with ASA is more effective than ASA alone in preventing stroke among patients with unstable angina and non-Q-wave MI only. There is *moderate* evidence that combination therapy with clopidogrel and low-dose ASA is not more effective than ASA alone in reducing the risk for myocardial infarction, stroke or death from cardiovascular causes in individuals with cardiovascular disease or multiple risk factors. There is *moderate* evidence that, in patients with previous stroke or TIA treated within 24 hours of the

stroke event, clopidogrel in combination with ASA is not associated with reduced 90-day risk of stroke when compared to ASA alone.

There is *moderate* evidence that, in patients with previous stroke or TIA, clopidogrel combined with ASA is not more effective than clopidogrel alone in preventing recurrent stroke, myocardial infarction, vascular death or re-hospitalization for acute ischaemic events. There is *strong* evidence that dual antiplatelet therapy with clopidogrel and ASA is associated with a significantly increased risk for bleeding events, particularly in individuals with symptomatic cardiovascular disease.

There is *strong* evidence that clopidogrel used in combination with ASA is more effective in modifying platelet activity than ASA alone. There is *moderate* evidence that clopidogrel in combination with ASA provides more effective platelet inhibition than ASA in combination with dipyridamole.

There is *moderate* evidence that dipyridamole in combination with ASA is more effective than either agent used on its own in the prevention of recurrent stroke. There is *moderate* evidence that combined ASA+extended release dipyridamole therapy is not noninferior to clopidogrel monotherapy.

Triple Antiplatelet Therapy

There is *moderate* evidence that combination therapy using three antiplatelet agents (ASA, clopidogrel and dipyridamole) is associated with more bleeding and adverse events than ASA monotherapy.

Miscellaneous Antiplatelet Therapies

There is *strong* evidence that Triflusal is not inferior to ASA in the prevention of stroke and is associated with fewer bleeding incidents. There is *moderate* evidence that the use of Glycoprotein IIb/IIIa inhibitors (Lotrafiban) in the secondary prevention of stroke is associated with excessive bleeding incidents.

Anticoagulants for Secondary Prevention of Noncardioembolic Stroke

There is *strong* evidence that, in patients with previous noncardioembolic stroke, treatment with oral anticoagulant therapy of moderate intensity provides no significant advantage over treatment with antiplatelet therapy for the prevention of secondary events. There is *strong* evidence that treatment with oral anticoagulant therapy is associated with higher risk for adverse events. High intensity therapy is associated with significant risk of major bleeding events and intracerebral haemorrhage.

Cardiac Abnormalities

Atrial Fibrillation

Atrial Fibrillation has been associated with an increased risk of cardioembolic stroke. There is *strong* evidence that the use of anti-coagulation therapy, particularly with adjusted dose warfarin, substantially reduces the risk of primary and secondary stroke in individuals with atrial fibrillation. There is *strong* evidence that the use of patient decision aids is associated with increased patient knowledge. There is *moderate* evidence that, among patients with atrial fibrillation, this is associated with a temporary increase in the use of appropriate

warfarin-based therapy. There is *limited* evidence that strategies to increase adherence to treatment guidelines for anticoagulation during hospitalization following stroke may only be effective for current ECG-documented AF included in the primary admitting diagnosis. Improved strategies to increase knowledge regarding the benefits of long-term anticoagulation therapies in the secondary prevention of stroke may be required.

There is *strong* evidence that treatment with ASA 300 – 325 mg/day is associated with reduced risk of stroke when compared to no treatment in individuals with atrial fibrillation. However, anticoagulant therapy (dose-adjusted warfarin) is more effective in preventing strokes among individuals with atrial fibrillation than antiplatelet therapy (ASA).

There is *moderate* evidence that oral anticoagulation therapy is more effective than ASA+clopidogrel in the prevention of stroke in individuals with atrial fibrillation. There is *moderate* evidence that treatment with ASA+clopidogrel is associated with reduced risk for stroke when compared to ASA monotherapy in individuals who are not eligible for oral anticoagulation. There is *moderate* evidence that the use of ASA+clopidogrel is associated with increased risk for bleeding events compared with ASA monotherapy. Risk for major bleeding events with ASA+clopidogrel is similar to that reported for oral anticoagulation with vitamin-K antagonists.

There is *moderate* evidence that the antiplatelet Indobufen may be as effective as warfarin, but is associated

with a reduced risk of bleeding events. There is also *strong* evidence that treatment with the direct thrombin inhibitor ximelagatran/melagatran is not inferior to treatment with warfarin. However, ximelagatran has been withdrawn from the market and its development terminated due to safety concerns.

Other Cardiac Abnormalities

A variety of cardiac abnormalities increase the risk of cardioembolic strokes. As demonstrated in the previous discussion of atrial fibrillation, there is *strong* evidence that this risk is decreased with anticoagulation therapy, primarily adjusted-dose warfarin. There is additional *moderate* evidence to support the effectiveness of anticoagulant therapy in reducing the risk of stroke subsequent to myocardial infarction.

Carotid Artery Occlusion

Reperfusion Interventions

There is *strong* evidence that carotid endarterectomy is an effective and durable means by which to reduce the risk of stroke in individuals with symptomatic carotid artery stenosis of 70 – 99%. While there is *strong* evidence that the procedure is effective in reducing the risk of stroke in individuals with asymptomatic stenosis of $\geq 60\%$, the risks associated with the procedure outweigh the benefit if they exceed 3%. Recent guidelines include recommendations for the use of CEA for the treatment of carotid stenosis of $>50\%$. Use of CEA for the treatment of asymptomatic carotid stenosis (60-99%) is not recommended.

There is *moderate* evidence that early CEA is not associated with increased

risk for stroke or death. Pooled analysis suggests that benefits associated with CEA may decrease as time from the qualifying ischemic event increases.

There is *moderate* evidence that nursing-led coordinated case management following carotid endarterectomy is associated with short-term improvements in knowledge of stroke warning signs and self-reported lifestyle and dietary changes.

Based on the results of 2 recent meta-analyses of CAS and CEA, there is *no clear evidence* to support the equivalence of the two procedures in the treatment of carotid artery stenosis. In both analyses, there is evidence that the risk for stroke and death at 30 days post procedure may be greater among individuals treated with carotid artery stenting when compared to endarterectomy, particularly among symptomatic patients. Interpretation of the evidence is complicated by factors such as diversity of enrolment, interventionalist experience, ongoing evolution of technology and early trial stoppages.

Although CAS has not been proven to be noninferior to CEA based on 30-day risk for stroke and death, there is *strong* evidence that long-term risk for stroke is similar between treatments, once the 30-day period has passed uneventfully.

There is *conflicting* evidence that the use of cerebral protection devices reduces the risk for embolic complications associated with CAS.

Current treatment guidelines recommend CAS for carefully selected

groups of patients only. There is *limited* evidence that the risk for 30-day complications increase with age and the presence of symptoms.

Mobility/Lower Extremity

Remedial vs. Compensatory Rehabilitation

There is *strong* evidence that the Bobath approach is not superior to other therapy approaches. There is *conflicting* evidence that the Motor Learning Approach is superior to the Bobath approach for achieving improvements in functional outcome. There is *moderate* evidence that a Motor Learning Approach reduces length of hospital stay.

Intensity of Training

There is *strong evidence* that enhanced therapy is associated with improvements in gait. There is *strong evidence* that these improvements are achieved and maintained for up to three months, but not sustained for longer periods of time.

Strength Training and Cardiovascular Conditioning

There is *strong* evidence that strength training increases walking distance post stroke. There is *moderate* evidence that progressive strength training can improve ADL function. Collectively, this constitutes strong evidence that strength training increases walking distance. There is strong evidence that while cardiovascular training post stroke improves level of physical fitness and gait performance it does not result in additional improvement in ADL performance.

Electrical Stimulation

There is *moderate* evidence that transcutaneous electrical

neurostimulation treatment improves gait speed and muscle strength. There is *strong* evidence that functional electrical stimulation and gait retraining results in improvements in hemiplegic gait.

Assistive Devices

There is *moderate* evidence that a quad cane is more effective than a standard cane for reducing postural sway. There is limited evidence that walking with a cane can improve hemiplegic gait. There is *limited* evidence that use of canes is associated with improved functional mobility.

Treadmill Training and Partial Weight Support

There is *conflicting* evidence that treadmill training alone (without partial weight support) is better than conventional therapy. There is *conflicting* evidence that partial body weight support results in improved walking and motor recovery when compared to conventional therapy. There is *moderate* evidence that partial body weight support is of no greater benefit than aggressive braced assisted walking. Treadmill training when combined with other gait specific activities improves gait.

EMG-Biofeedback

There is *strong* evidence that EMG biofeedback training improves gait and standing post stroke.

Balance Training

There is *strong* evidence that balance training post stroke improves outcome. There is *conflicting* evidence as to what form of balance training yields the most effective result. There is *conflicting* evidence that falls prevention programs are effective following stroke.

Ankle Foot Orthoses

There is *limited* evidence that ankle foot orthoses alone improve various parameters of gait in hemiplegic strokes. There is *moderate* evidence that ankle foot orthoses combined with posterior tibial nerve deinnervation improves gait outcomes in hemiplegic strokes.

Task-Specific Training

There is *strong* evidence that task-specific gait training improves gait post stroke.

Deinnervation of Spastic Muscles

There is *strong* evidence that deinnervating lower extremity muscles with Botulinum toxin reduces spasticity but *conflicting* evidence as to whether such deinnervation impacts on functional outcomes.

Anti-Spastic Medications

There is *conflicting* evidence that Dantrolene sodium is effective in treating post-stroke spasticity compared to placebo. There is *moderate* evidence that ketazolam, diazepam and tolperisone are more effective when compared to placebo in treating post-stroke spasticity. There is *limited* evidence that Tizanidine is not superior to oral Baclofen. There is *moderate* evidence that intrathecal baclofen can reduce spasticity in the chronic stages of stroke. There is *moderate* evidence that Tolperisone reduces spasticity.

Upper Extremity Interventions

Neurodevelopmental Techniques

There is *strong* evidence that neurodevelopmental techniques are not superior to other therapeutic approaches. There is *moderate* evidence that compared to Bobath,

Motor Relearning Programme may be more beneficial to short-term motor functioning, but not to long-term motor functioning.

Additional/Enhanced Therapy

There is *conflicting* evidence that enhanced therapies improve short-term upper extremity function. There is *conflicting* evidence that specialized programs improve reaching.

Repetitive Task Specific Therapy

There is *conflicting* evidence that repetitive task-specific training techniques improves measures of upper extremity function. There is *conflicting* evidence that bilateral arm training is superior to unilateral training.

Sensorimotor Training

There is *conflicting* evidence that sensorimotor training improves upper extremity function, compared to traditional techniques. However, there is *moderate* evidence that patients with right hemiparesis do benefit from sensorimotor training. There is *strong* evidence that sensorimotor training with robotic devices improves upper extremity functional outcomes, and motor outcomes of the shoulder and elbow. There is *strong* evidence that robotic devices do not improve motor outcomes of the wrist and hand.

Mental Imagery

There is *strong* evidence that mental practice can improve motor and ADL performance following stroke.

Virtual Reality

There is *moderate* evidence that virtual reality treatment improves locomotor function in the chronic stages of stroke.

Constraint Induced Movement Therapy

There is *conflicting* evidence of benefit of CIMT in comparison to traditional therapies in the acute stage of stroke. There is *strong* evidence of benefit of CIMT and modified CIMT in comparison to traditional therapies in the chronic stage of stroke. Benefits appear to be confined to stroke patients with some active wrist and hand movements, particularly those with sensory loss and neglect.

Hand Splinting

There is *strong* evidence that hand splinting does not improve motor function or reduce contracture formation. There is *moderate* evidence that daily stretches do not prevent the development of contractures.

Spasticity Treatment

Botulinum Toxin

There is *strong* evidence that treatment with botulinum toxin significantly decreases spasticity in the upper extremity in stroke survivors and that this is associated with decreased spasticity, increased range of motion, with subsequent improvements in upper extremity function. There is *moderate* evidence that electrical stimulation combined with botulinum toxin injection is associated with reductions in muscle tone.

Combination of Botulinum Toxin and Physical Therapy

There is *strong* evidence that a combination of physiotherapy and Botulinum Toxin Injection is associated with improved upper extremity function.

Physical Therapy

There is *moderate* evidence that physical therapy by itself can reduce spasticity. There is *moderate* evidence that a nurse-led stretching program can help to increase range of motion in the upper extremity and reduce pain in the chronic stage of stroke.

Other Treatments

There is *moderate* evidence that the centrally acting muscle relaxant, Tolperisone and shock wave therapy can both reduce spasticity following stroke. There is *limited* evidence that treatment with ethyl alcohol improves elbow and finger PROM and can decrease spasticity in the upper extremity in stroke survivors.

EMG/Biofeedback

There is *strong* evidence that EMG/Biofeedback therapy is not superior to other forms of treatment.

Functional Electrical Stimulation (FES)

There is *strong* evidence that FES treatment improves upper extremity function.

Treatment to Reduce Hand Edema

There is *moderate* evidence that intermittent pneumatic compression does not reduce hand edema following stroke. There is *limited* evidence that both neuromuscular nerve stimulation and continuous passive motion help to reduce hand edema compared to limb elevation.

Painful Hemiplegic Shoulder

Shoulder Subluxation

Shoulder subluxation occurs early in the course of recovery as a consequence of early flaccidity of supporting shoulder musculature, but

not scapular rotation. Shoulder subluxation may be a cause of shoulder pain but current evidence suggests it is not the primary cause of the pain.

Spastic Contracted Shoulder

There is a significant correlation between spasticity and a painful frozen or contracted shoulder. There appears to be an important role for the subscapularis muscle and to a lesser extent pectoralis major musculature, which develops greater tonic activity with subsequent muscle imbalance.

Shoulder Pain and Functional Outcome

There is an association between hemiplegic shoulder pain and poorer functional outcomes, which may simply reflect an association with more severe strokes.

Positioning/Support

There is *consensus* evidence that proper positioning of the hemiplegic shoulder helps to avoid subluxation. However, there is *moderate* evidence that prolonged positioning does not negatively influence active and passive range of motion or level of pain. There is *limited evidence* that shoulder slings prevent subluxation associated with hemiplegic shoulder pain, although the superiority of a specific device has not been established. There is *conflicting* evidence that strapping the hemiplegic shoulder reduces the development of pain. There is *moderate* evidence that strapping does not improve upper limb function or range of motion.

Exercise

There is *moderate* evidence that the use of overhead pulleys is associated with increases in hemiplegic shoulder

pain and should be avoided. In contrast, there is *moderate evidence* that a gentle range of motion program by a therapist results in less hemiplegic shoulder pain.

Corticosteroid Injections

There is *moderate evidence* that corticosteroid injections do not improve shoulder pain or range of motion in hemiplegic patients. There is *limited evidence* that oral non-steroidal anti-inflammatories can reduce pain during therapy sessions.

Botulinum Toxin

There is *limited evidence* that botulinum toxin can reduce pain in the hemiplegic shoulder.

Functional Electrical Stimulation (FES)

There is *conflicting evidence* that FES improves muscle function, pain, subluxation and range of motion of the hemiplegic shoulder.

Motor Block & Surgical Resection of Shoulder Muscles

There is limited evidence that surgically resecting the subscapularis and pectoralis tendons improves outcomes in stroke patients with painful hemiplegic shoulder. As well, there is moderate evidence that motor blocks of the suprascapular and pectoralis muscles treat muscle imbalance, pain and decreased range of motion of the hemiplegic shoulder. There is *conflicting evidence* that motor blocks of the pectoralis major muscle reduces spastic shoulder pain or improves passive range of motion of the hemiplegic shoulder.

Aromatherapy

There is *moderate evidence* that aromatherapy combining with acupressure can reduce pain

associated with painful hemiplegic shoulder.

Complex Regional Pain Syndrome (type 1)

CRPS is a poorly understood clinical entity. Most cases improve with time. There is *moderate evidence* that oral corticosteroids improves CRPS for at least the first 4 weeks. There is *limited evidence* that passive range of motion exercises can prevent the development of CRPS.

Modified Imagery Program

There is *moderate evidence* that a modified imagery program can reduce the pain associated with shoulder-hand syndrome.

Cognitive Disorders and Apraxia

Cognitive Impairment and Hypertension

There is *conflicting evidence* that treatment of hypertension is associated with reduced risk for cognitive decline and dementia following stroke. Further trials in which cognition is the primary study outcome are required.

There is *moderate evidence* that treatment of hypertension may reduce the risk for cognitive decline or dementia in patients with history of previous stroke or TIA when compared to placebo. There is no evidence that one particular antihypertensive agent is superior to another for the prevention of cognitive decline.

Cognitive Rehabilitation

Remediation of Attention Deficits

There is *limited evidence* that computer-assisted training of attention tasks may improve performance of specific attention tasks. There is *moderate evidence*

that daily attention training is associated with recovery of the N140 component of somatosensory evoked potentials. There is *moderate* evidence that visual attention retraining using the Useful Field of View is more effective than conventional computerized visuoperceptual training in improving the on-road driving performance of individuals who have experienced stroke and have right-sided lesions.

Remediation of Memory Deficits

There is *strong* evidence that compensatory strategies are effective in improving memory outcomes post brain injury. Strategies include imagery-based training and the use of assistive, electronic devices. Further studies among individuals who have experienced stroke are required.

There is *moderate* evidence that an intensive, computerized training program may result in improvements in both working memory and attention.

Remediation of Executive Functioning and Problem-Solving Deficits

There is *little evidence* regarding remediation of executive functioning and problem solving post-stroke. There is *limited* evidence that analogical problem-solving skills training may increase problem-solving skills and performance of extended activities of daily living.

Multi-modal Interventions

There is little evidence regarding the use of multi-modal interventions following stroke. Based on a single, small study, there is *limited* evidence that a multi-modal, home-based cognitive rehabilitation program may be beneficial in terms of cognitive

function and instrumental activities of daily living.

Alternative Therapies

There is *moderate* evidence that electro-acupuncture and high-intensity low-frequency TENS have no effect on cognitive functioning following stroke.

There is *moderate* evidence that self-regulated music listening therapy may have a positive impact on verbal memory and focussed attention in individuals with left hemisphere stroke.

Pharmacotherapy

Aspirin

ASA is commonly used in the treatment of vascular dementia. There is *moderate* evidence that ASA is effective in stabilizing and/or improving cognitive outcomes in patients with multi-infarct dementia.

Cholinesterase Inhibitors

There is *strong* evidence that donepezil taken for 24 weeks improves cognitive function in patients with probable or possible vascular dementia. There is *limited* evidence that treatment with rivastigmine is associated with more stable cognitive performance and improved behavioural outcomes among patients with subcortical vascular dementia. There is *moderate* evidence that treatment with galantamine is associated with improvements in cognitive and functional ability. However, the benefits associated with treatment with galantamine are more clearly demonstrated among patients with mixed dementia than vascular dementia.

Nimodipine

There is *moderate* evidence that treatment with nimodipine is beneficial for memory. There is also *moderate* evidence that treatment with nimodipine may slow cognitive deterioration and improve semantic and phonetic fluency among patients with subcortical vascular dementia.

Memantine

There is *strong* evidence that treatment with memantine is associated with stabilization or improvement of cognitive function.

Pentoxifylline

There is *strong* evidence that treatment with pentoxifylline is associated with cognitive benefit in patients with multi-infarct dementia.

Citicoline

There is *moderate* evidence that long-term treatment with citicoline has no effect on cognitive function.

Milnacipran

There is *moderate* evidence that, in individuals with post stroke depression, treatment with milnacipran has positive effects on cognition.

Post Stroke Delirium

Prevention of Delirium Post Stroke

There is limited evidence that a multi-component approach to the management of known risk factors is associated with reduced incidence and duration of delirium. However, this has not been demonstrated within the stroke population.

Treatment of Delirium Post Stroke

There is *limited* evidence that increased knowledge and awareness of risk and precipitating factors along

with individualized care is associated with reduced duration of delirium, shorter lengths of stay, and reduced mortality. There is *limited* evidence that short-term use of rivastigimine may reduce post-stroke delirium. Further research is required.

Post Stroke Apraxia

There is *strong* evidence that strategy training is effective in the treatment of apraxias post-stroke. Training effects may include improvement in performance of activities of daily living that appear to be sustained over time. There is *strong* evidence that gesture training is associated with improvement in ideomotor apraxia. Improvements may extend to activities of daily living and these effects may be sustained for at least 2 months following the end of treatment.

Perceptual Disorders

Treatment of Perceptual Deficits

There is *strong* evidence that perceptual training interventions improve perceptual functioning. There is *moderate* evidence that a transfer of training approach is no more effective than a functional approach to perceptual training.

Treatment of Neglect

Visual Scanning

There is *strong* evidence that treatment utilizing primarily enhanced visual scanning techniques improves visual neglect post-stroke with associated improvements in function.

Computer-based Rehabilitation

There is *moderate* evidence that computer-based visual scanning training does not remediate visual

neglect. There is *limited* evidence that virtual reality training may help to improve awareness of neglected space.

Limb Activation

There is *strong* evidence that limb activation therapies improve neglect. Little information is available with regard to duration of effect or the effect of treatment on functional ability.

Sensory Stimulation Interventions

There is *conflicting* evidence that external sensory stimulation interventions are beneficial in the treatment of neglect. There is *moderate* evidence that use of electrical somatosensory stimulation as a supplement to visual scanning training is associated with greater benefit than visual scanning training alone.

Feedback Strategies

There is *strong* evidence that the use of feedback strategies is beneficial in the treatment of neglect. More study is required to establish the degree to which treatment effects generalize to other behaviours and to determine the durability of effect.

Prismatic Adaptation

There is *strong* evidence that treatment with prisms is associated with an increase in visual perception scores in stroke patients with homonymous hemianopsia and visual neglect. There is *moderate* evidence that these improvements are not associated with improvement in ADL scores.

Eye-patching and Hemi-spatial Glasses

There is *strong* evidence that the use of right half-field eyepatches improves

left visual neglect. There is *moderate* evidence that monocular, opaque patching to improve neglect produces inconsistent results. There is *conflicting* evidence that the use of bilateral half-field eye patches improves functional ability.

Caloric/Vestibular Stimulation

There is *limited* evidence that caloric stimulation has a transient, positive effect on visuospatial neglect. Its applicability as a treatment intervention has not been evaluated.

Vestibular Galvanic Stimulation

There is very *limited* evidence that galvanic stimulation is as effective as caloric stimulation in improving neglect. Its effectiveness as part of a treatment intervention has not been assessed.

Optokinetic Stimulation

There is *limited* evidence that optokinetic stimulation improves personal position sense in patients with neglect. There is *conflicting* evidence regarding the possible benefit associated with the use of optokinetic stimulation as an adjunct to scanning therapy. There is *moderate* evidence that the addition of optokinetic stimulation to a neglect-specific rehabilitation program has no effect on functional outcome.

Trunk Rotation Therapy

There is *moderate* evidence that trunk rotation therapy does not result in improvement of unilateral spatial neglect or performance of activities of daily living. In addition, there is *moderate* evidence that trunk rotation therapy in combination with half-field eye patching is similarly ineffective. There is *moderate* evidence that trunk rotation when combined with visual

scanning is of benefit in the treatment of spatial neglect.

Neck Muscle Vibration

There is *moderate* evidence that neck muscle vibration therapy in association with visual exploration training is effective in improving both symptoms of neglect and performance of ADLs. There is *limited* evidence that muscle therapy alone is associated with reduction of neglect. The effect of treatment may be sustained for periods in excess of one year.

TENS Treatment

There is *moderate* evidence that TENS treatments used in conjunction with exploration/scanning training results in improvements on tests of neglect, reading and writing.

Dopaminergic Medications

There is *limited* evidence that dopamine agonist therapy reduces the symptoms of neglect. There is *limited* evidence that carbidopa L-dopa improves both neglect and functional ability.

Repetitive Transcranial Magnetic Stimulation

There is *limited* evidence, based on 3 very small, preliminary studies, that treatment with repetitive transcranial magnetic stimulation to the posterior parietal cortex on the undamaged side results in improved spatial awareness for up to 6 weeks following the end of treatment. Further investigation is required.

Transcranial Direct Current Stimulation

There is *moderate* evidence that anodal transcranial direct current stimulation is associated with improvement on tests of neglect.

Aphasia Post Stroke

Language Therapy

There is *conflicting* evidence whether speech and language therapy (SLT) is efficacious in treating aphasia following stroke. The failure to identify a consistent benefit appears to be due, in part, to the low intensity of SLT applied in the negative studies. The most comprehensive meta-analysis concluded that language therapy for aphasia had a significant positive impact on aphasia recovery in the acute phase and to a lesser extent during the chronic phase. It also revealed that improvement was tied to more intensive therapy and that severe aphasics benefited the most.

Trained Volunteers

There is *strong* evidence that trained volunteers can provide speech and language therapy and achieve similar outcomes to speech- language pathologists. This could serve as an effective adjunct to speech-language pathologists' treatment.

Group Aphasia Therapy

There is *moderate* evidence that group intervention results in improvements on communicative and linguistic measures among patients with chronic aphasia. There is *limited* evidence that participation in group therapy results in improved communication. There is *moderate* evidence that group therapy results in less improvement in graphic (writing) elements of aphasia when compared to individualized therapy.

Community-Based Therapy Programs

There is *limited* evidence that a community-based program improves language outcomes at both the impairment and disability level

independent of severity, setting, diagnostic type or stage of aphasia. There is *moderate* evidence that an in-home program administered by trained volunteers improves language outcomes at the impairment and functional levels.

Conversation Partners

There is *moderate* evidence that the technique of training conversation partners, Supported Conversation for Adults with Aphasia (SCA), is associated with enhanced conversation skills. There is *limited* evidence that training conversation partners is associated with increased well-being and social participation in addition to positive communication outcomes.

Family and Patient Education

There is *moderate* evidence that group-based caregiver education is associated with temporary improvement in caregiver stress, but not with improved use or effectiveness of functional communication strategies. There is *limited* evidence that participation in educational seminars results in improved knowledge, participation in social activities and family adjustment. Further examination of the role of education is warranted. There is *limited* evidence that participation in community-based programs improves the psychological well-being of patients and their families.

Computer-Based Therapy

There is *strong* evidence that computer-based interventions can improve language skills assessed at the impairment level. There is *limited* evidence that improvements made via computer-based interventions generalize to functional communication.

Filmed Language Instruction

There is *moderate* evidence that supplementary, filmed language instruction is of no benefit to aphasic patients.

Forced-Use Aphasia Therapy

There is *moderate* evidence that forced-use aphasia therapy results in greater language performance in chronic aphasics over a short period of time. There is *limited* evidence that communication gains made following constraint-induced language therapy may be sustained over time.

Repetitive Transcranial Magnetic Stimulation

There is *limited* evidence that treatment with slow rTMS to the anterior portion of R Broca's homologue is associated with improved naming performance in patients with chronic, nonfluent aphasia.

Direct Current Stimulation

There is *limited* evidence that cathodal direct current stimulation applied over Broca's area may be associated with improvement in picture naming.

Deficit-Specific Therapy

There is *moderate* evidence that task-specific semantic therapy improves semantic activities and that task-specific phonological therapy improves phonologic activities. There is *limited* evidence that phonological and semantic cueing improve naming accuracy and word retrieval abilities. There is *moderate* evidence that intensive "ecological" language therapy is associated with improvement across language modalities. There is *limited* evidence that target-specific therapy demonstrates no benefit for patients

suffering from global aphasia. There is *limited* evidence that specific therapy for alexia improves language function.

Drug Treatments

There is *strong* evidence of a significantly positive impact of the drug Piracetam on aphasia recovery in stroke patients also receiving language therapy over the short-term. There is *limited* physiological evidence that piracetam serves to increase activation of language processing regions within the brain. There is *strong* evidence that Bromocriptine does not improve aphasia recovery post stroke. There is *moderate* evidence that treatment with levodopa as an adjunct to speech and language therapy has a positive effect on some language functions such as verbal fluency and repetition. There is *moderate evidence* that dextroamphetamine improves aphasia recovery when combined with language therapy. There is *moderate* evidence that Dextran 40 when given to acute stroke patients results in worse outcomes than the non-treatment control. Bifemelane, a cholinergic treatment, has not been sufficiently studied to draw any meaningful conclusions. There is *moderate* evidence that the use of Moclobemide does not enhance aphasia recovery. There is also *moderate* evidence that the use of donepezil may have a positive effect on global language function. However, this improvement was reported only during active treatment and may not extend to everyday communication. There is *moderate* evidence that use of memantine may be beneficial in the treatment of chronic aphasia. Combination therapy using constrain-induced language therapy and memantine may result in

greater benefit than either therapy used independently.

Dysphagia and Aspiration Following Stroke

Incidence of Dysphagia/Aspiration

The incidence of dysphagia appears to be quite high following acute stroke, with between one-third to two-thirds of all stroke patients affected. VMBS studies are the “gold standard” for diagnosing dysphagia and aspiration. The incidence of aspiration in the acute phase of stroke varies from 21-42% and decreases to less than 12% by 3 months post stroke. Between one-third and one-half of patients who aspirate following stroke are silent aspirators.

Aspiration and Pneumonia

Aspiration appears to be associated with an increase in the incidence of pneumonia. The risk of developing pneumonia appears to be proportional to the severity of aspiration.

Assessment of Dysphagia

There is *consensus* opinion that acute stroke survivors should be NPO until swallowing ability has been determined. There is *consensus* opinion that a trained assessor should screen all acute stroke survivors for swallowing difficulties as soon as they are able. There is *consensus* opinion that a speech and language therapist should assess all stroke survivors who fail swallowing screening and identify the appropriate course of treatment. There is *consensus* opinion that an individual trained in low-risk feeding strategies should provide feeding assistance or supervision to all stroke survivors. There is *consensus* opinion that a dietician should assess the nutrition and hydration status of all

stroke patients who fail swallowing screening. There is *limited* evidence that individual's with dysphagia should feed themselves to reduce the risk of aspiration. There is *consensus* opinion that dysphagic stroke patients typically require diets with modified food and liquid textures. There is *moderate* evidence that dysphagia screening protocols can reduce the incidence of pneumonia.

Feeding Assistance

There is *consensus* opinion that an individual trained in low-risk feeding strategies should provide feeding assistance or supervision to all stroke survivors.

Dietary Modifications

Although dietary modifications have been used to help reduce the incidence of aspiration and their consequences, the evidence to support their use is lacking. For patients on modified diets there is *consensus* opinion that a dietitian should be consulted to ensure that the modified diet is nutritionally adequate and appropriate, and to consult the stroke survivor or substitute decision-maker, to ensure that the modified diet is as appealing as possible.

Thermal Stimulation

There is *moderate* evidence that thermal stimulation does not improve swallowing function post stroke.

Dysphagia Therapy

There is *moderate* evidence that a short course (two weeks) of formal dysphagia therapy does not improve clinical outcomes. There is *moderate* evidence that a one-month dysphagia intervention program does not improve the likelihood of returning to a normal diet by six months. However, there is also *moderate* evidence that

such a program may reduce the likelihood of chest infections and death or institutionalization.

Feeding Tubes

There is *consensus* opinion that enteral tube feeding be used in stroke patients who are high-risk dysphagics or who cannot meet their nutritional need orally. Enteral feeding should be considered after a stroke survivor has been NPO for 48 hours. There is *consensus opinion* that if dysphagia is severe and expected to last more than 6 weeks, a gastrostomy or jejunostomy feeding tube may be indicated. There is *strong* evidence that intragastric feeding devices are associated with fewer mechanical failures compared to nasogastric feeding tubes. There is *moderate* evidence that the risk of developing pneumonia is higher among ventilated patients fed by a naso-gastric tube compared with a gastrostomy tube. Based on the results from one large, international trial, there is *moderate* evidence that the type of feeding tube (nasogastric or gastro-enteric) does not affect the odds of death or the combined outcome of death or poor functional outcome.

Alternative Interventions

There is *moderate* evidence that Nifedipine, transcranial magnetic stimulation and black pepper oil can be used to improve specific aspects of swallowing following stroke. There is *moderate* evidence that selective decontamination of the digestive tract can help to reduce the incidence of pneumonia. There is *limited* evidence that head rotation, lingual exercises and EMG treatment can be used to improve swallowing function post stroke.

Nutritional Interventions Following Stroke

Nutritional Status

The incidence of malnutrition varies from 8 to 49% post stroke, depending on the timing of the assessment and the criteria used to define malnutrition. Unfortunately, there is no "gold standard" for the assessment of nutritional status. There is an absence of literature examining the nutrient intakes of stroke patients. Therefore, there is *no evidence* to suggest that nutrient intake following stroke is altered, although data extrapolated from a mixed geriatric population suggests that energy and protein intakes may be reduced.

Changes in Body Metabolism

There is *limited* evidence that stroke does not result in short term elevations of metabolic rate. There is evidence that an acute phase response accompanies stroke, although its contribution to the development of malnutrition is unclear. There is an absence of literature to confirm or refute the development of significant gastrointestinal impairments following stroke.

Feeding Tubes

There is *strong* evidence that intragastric feeding is associated with fewer complications than nasogastric feeding. The one-year survival rate of patients with gastrostomy feeding tubes varies widely from 16% to 70%. On average, feeding tubes are placed within the first month following stroke. Among patients with feeding tubes discharged to the community, Aspiration pneumonia was reported in 6-18% of patients.

Total Parenteral Nutrition

There have been *no studies* that have evaluated the efficacy of Total Parenteral Nutrition (TPN) in the treatment of stroke patients.

Oral Supplementation

There is *moderate* evidence that oral supplementation improves the energy and protein intakes of stroke patients. There is *conflicting* evidence that oral sip supplementation improves functional outcomes in stroke patients. There is *moderate* evidence that routine oral sip supplementation does not reduce the incidence of death or dependency following stroke; however, it can improve energy and protein intakes and improve their nutritional parameters.

Medical-Nursing Complications Post Stroke

Bladder & Bowel Management

There is *moderate* evidence that a functionally oriented rehabilitation approach results in significantly less bladder incontinence than a Bobath conventional approach. There is *moderate* evidence that prompted voiding significantly reduced the number of total incontinent episodes. The use of indwelling catheters in stroke patients has not been well studied. There is consensus opinion that indwelling catheters should be limited to those patients with intractable urinary retention, skin breakdown, continuous wetness and the need for urinary monitoring. There is *moderate* evidence that a nursing evaluation/intervention program can be effective in reducing constipation long-term following stroke. There is *moderate* evidence that a morning bowel routine is more effective than an evening bowel routine.

Deep Vein Thrombosis (DVT)

The incidence of DVT which are both clinically apparent and silent may be 30% or higher acutely post stroke. This rate may fall to 10% or lower in patients in the sub-acute phase of stroke receiving rehabilitation. There is *strong* evidence that anticoagulation significantly reduces the incidence of deep vein thrombosis (DVT), when compared to placebo. There is *strong* evidence that low molecular weight heparin is better than unfractionated heparin in reducing DVTs. There is *moderate* evidence that heparin is no better than pneumatic compression in preventing DVTs. There is *strong* evidence that graded compression stockings do not reduce the risk of proximal DVT. There is *moderate* evidence that intermittent pneumatic calf compression devices reduce the risk of the development of DVTs.

Seizures

There is no research specific to the treatment of post stroke seizures. There is *consensus opinion* that patients who have experienced seizures post stroke should be given preventative anticonvulsant medication to prevent seizure reoccurrence.

Osteoporosis

There is *moderate* evidence that vitamins D and K and sunlight therapy reduces osteoporosis in hemiplegic stroke patients. There is also *moderate* evidence that Ipiflavone was more effective than vitamin D in reducing osteoporosis in hemiplegic stroke patients. There is *strong* evidence that treatment with bisphosphonates (risedronate and etidronate) can preserve bone mineral density following stroke. There is *moderate* evidence that risidronate,

and a combination of folate and vitamin B₁₂, can prevent hip fracture in elderly women following stroke.

Central Pain States

There is *conflicting* evidence that amitriptyline treatment results in pain reduction in central pain states post stroke. There is *moderate* evidence that lidocaine treatment results in short-term pain relief. There is *moderate* evidence that intravenous morphine reduces some components of post stroke pain in a minority of patients. There is *moderate* evidence that Lamotrigine may be an alternative to tricyclic antidepressants in the treatment of central pain. There is *limited* evidence that selective serotonin reuptake inhibitor fluoxetine treatment is useful for the management of CPSP relatively early following stroke. There is *moderate* evidence that high-strength μ -opioid agonist levorphanol is effective in reducing pain in post-stroke patients. There is *limited* evidence that motor cortex stimulation can provide long-term effective pain relief.

Post Stroke Depression

Location of Lesion

There remains a wide diversity of findings in studies looking at the relationships between stroke location and depression. Not all studies have confirmed this relationship and more recent meta-analyses have failed to establish a definitive relationship between the site of the brain lesion and depression.

Depression, Functional Deficits, Cognition and Mortality

The negative effect of depression underscores the need for early detection and treatment of post-stroke

depression. Identification and treatment of post-stroke depression early in the acute phase may serve to enhance functional recovery. Early attention to issues of social withdrawal or impaired social functioning may help deter later depression and provide an opportunity for patients to resume pre-stroke activities. Post-stroke depression appears to have a negative impact on cognition; however, this relationship is poorly understood. The presence of depressive symptomatology post stroke has been associated with an increased risk for mortality.

Prevention of Post Stroke Depression

There is *strong* evidence that early initiation of antidepressant therapy in non-depressed stroke patients is associated with reduced risk for the development of post-stroke depression. While treatment over a period of one year was associated with significant reduction in risk, further study is required to assess both duration of treatment and optimal timing for the initiation of therapy.

Care Provision and the Prevention of PSD

There is *strong* evidence that ongoing, individualized contact and support provided via various care provision models is associated with less deterioration of mental health following stroke.

Pharmacologic Treatment of Post Stroke Depression

Heterocyclics

There is *strong* evidence that heterocyclic antidepressants improve depression post stroke. Side effects of heterocyclic antidepressants are frequent in elderly stroke patients.

Serotonin Reuptake Inhibitors

Based on the results of meta-analysis, there is *strong* evidence that selective serotonin reuptake inhibitors are effective in the treatment of post-stroke depression. Further placebo studies should be conducted using a blinded administrator and an optimal treatment duration in order to address methodological differences across current studies.

Selective Noradrenaline Reuptake Inhibitors

There is *moderate* evidence that reboxetine, a selective noradrenaline reuptake inhibitor, is effective in reducing retarded post-stroke depression.

Serotonin and Noradrenaline Reuptake Inhibitors

There is *limited* evidence suggesting that venlafaxine is a safe and effective treatment for post-stroke depression.

Gamma Aminobutyric Acid Compounds (GABA)

There is *moderate* evidence that the GABA compound, nefiracetam, is not more effective than placebo in the treatment of post-stroke depression.

Methylphenidate

There is *moderate evidence* that methylphenidate is more effective than placebo in improving depression and functional recovery post stroke. Methylphenidate acts more quickly than more traditional antidepressants.

Care Management for Post-Stroke Depression

There is *moderate* evidence that an active care management program including patient education and ongoing monitoring may enhance effectiveness of pharmacologic treatment for post stroke depression.

Alternative Medicine

There is *moderate* evidence that treatment with the herbal preparation, Free and Easy Wanderer Plus (FEWP) may be as effective as fluoxetine in the treatment of post-stroke depression

Pharmacologic Treatment, Functional Recovery and Mortality

There is *strong* evidence that pharmacologic treatment of depression is associated with improved functional recovery post stroke. There is *moderate* evidence that early treatment with antidepressants post stroke is associated with improved long-term survival.

Non-pharmacologic Treatment of Post Stroke Depression

Electroconvulsive Therapy (ECT)

There is *limited evidence* that ECT is a safe and effective treatment in post stroke patients.

Repetitive Transcranial Magnetic Stimulation

There is *moderate* evidence that repetitive transcranial magnetic stimulation is an effective, well-tolerated treatment for drug-resistant post-stroke depression.

Cognitive Behavioral Therapy

There is *moderate evidence* that cognitive behavioural therapy is ineffective as a treatment for post-stroke depression. There is *moderate* evidence that the provision of a brief psychosocial intervention in addition to antidepressant therapy may be more effective than antidepressant therapy alone in terms of depressive symptomatology, functional ability and social participation.

Music Therapy

There is *limited evidence* that music therapy improves post-stroke depression.

Speech Therapy

There is *moderate evidence* that speech therapy does not improve post-stroke depression or overall psychological wellbeing.

Physical Activity

There is *strong* evidence that exercise training does not provide significant benefit in terms of reduction in depressive symptomatology over time

Guidelines for Treatment of Post-Stroke Depression

Current guidelines recommend both screening and appropriate assessment of depression in patients with stroke. Treatment with an appropriate antidepressant is recommended for a period of approximately 6 months, given evidence of treatment effectiveness. Treatment (and subsequent withdrawal) should be monitored closely by an appropriately trained healthcare professional.

Post Stroke Emotionalism

In the first 6 months following stroke, post-stroke emotionalism affects approximately one-quarter of stroke survivors. There is *strong* evidence that antidepressant medication, and SSRIs in particular, are an effective treatment for post-stroke emotionalism.

Community Reintegration

Social Support

The presence and size of social support networks as well as the perceived effectiveness of social support networks have a positive

influence on physical recovery and quality of life post stroke. Higher levels of support are associated with greater functional gains, less depression and improved mood and social interaction. The size and perceived effectiveness of social support networks are important predictors of discharge destination.

There is *strong* evidence that social work interventions providing counselling along with information and education for stroke patients and their families are not associated with improvements on measures of independence or social activity.

There is *moderate* evidence that a specialized social support intervention that includes the stroke patient's social support network is not effective in improving perceived social support or functional recovery.

There is *moderate* evidence, based on one RCT examining a pilot project, that attendance at a day service is associated with improved participation in leisure activities.

There is *strong* evidence that home-based support and care management interventions are not associated with improved social activity, mood, quality of life or physical independence.

There is *moderate* evidence that participation in a social worker-led program of care coordination featuring frequent, regularly-scheduled contact may result in improved mental health.

There is *strong* evidence that involvement with a Family Support Organiser is associated with increased knowledge about stroke and satisfaction with services.

There is *conflicting* evidence that social support interventions are associated with a reduction in caregiver burden or strain.

There is *moderate* evidence that active case management may result in improved social activity. Further study is required.

Effects of Caregiving

Commonly identified effects of caregiving on the caregiver include increasing psychological distress, decreased social contact and activity, increased risk for depression, increased carer stress, strain or burden and an overall decrease in quality of life. Decreased social contact and activity in itself may contribute to increased carer strain, increased risk of depression and decreased life satisfaction.

Reports concerning the influence of patient characteristics vary with the effect in question. However, age, severity of stroke and stroke-related impairments, functional status and cognitive status have been reported as influencing caregiver outcomes.

Positive consequences of caregiving include improved appreciation of life, feeling needed or appreciated and development of a more positive outlook. Maintaining a positive attitude has been identified as an important coping strategy.

Support provided by caregiving peers may have a positive effect on the caregiver. There is *moderate* evidence that participation in an online program providing information and support through contact with both a nurse and other caregivers has no impact on depression or life satisfaction. There is *moderate*

evidence that a program of group-based education and support may improve stroke-related knowledge but has no impact on psychological health.

Family Functioning

Perceived family dysfunction is common post stroke. Family function affects treatment adherence, performance of ADLs and social activity. Stroke patients do better with well-functioning families characterized by effective communication, good problem solving or adaptive coping, and strong emotional interest in each other.

Education/Information Provision

There is *strong* evidence of a positive benefit associated with the provision of information and education through a variety of intervention types. Education sessions may have a greater effect on outcome than the provision of information materials alone. There is *strong* evidence that skills training is associated with a reduction in depression. There is *moderate* evidence that training in basic nursing skills improves outcomes of depression, anxiety and quality of life for both the caregiver and the stroke patient.

Although the receipt of information is of great importance to stroke patients and their families/caregivers, relatively few receive adequate information about topics they perceive to be important. Caregivers rarely receive adequate training in skills they require to care for the stroke survivor. Healthcare professionals involved in stroke care may acknowledge the importance of education for patients and carers; however, relatively few provide adequate information based upon the information needs of the recipients. In addition, written

materials should be suited to the educational/reading level of the intended recipient.

Social and Leisure Activities

Deterioration in social and leisure activities is common post-stroke and is greatest in women, the young and those who are better educated. Perceptions about how others view their disabilities and perceptions about how they will be able to cope post-stroke may influence the degree of social isolation experienced.

Leisure Therapy

When considered individually, there appears to be *conflicting* evidence as to the benefit of leisure therapy post-stroke and following discharge. However, a recent meta-analysis using pooled data from the same RCTs reported a modest improvement in leisure activity associated with leisure therapy.

There is *moderate* evidence that participation in a leisure education program focused on awareness and competency development is associated with improvement in number and duration of activities and reduction in depressive symptoms. There is moderate evidence that, in a group of high-functioning individuals, group-based exercise has no more impact than relaxation on instrumental activities of daily living.

Sexual Activity

A decrease in sexual activity is common post-stroke, although there is general agreement that sexual drive is still present. The main barriers to sexual activity are physical impairments and psychological factors, in particular a changed body image and lack of communication. Hypersexuality post-stroke is rare and

not well understood. There were no studies of treatment of sexual dysfunction identified. There is *consensus opinion* that sexual issues should be discussed during rehabilitation and addressed again after transition to the community when the stroke survivor and significant other are ready.

Driving

Patients for whom there is concern about their ability to drive need to be identified and proper assessment and treatment initiated. Determination of ability to drive should not rely solely on neuropsychologic testing or road test evaluation. Rather, a 2-step process is recommended in which the patient is first screened for readiness to participate in an on-road evaluation. There is *moderate* evidence that a visual attention-retraining program does not improve the driving performance of patients with stroke. In addition, there is *moderate* evidence that a simulator training program involving the use of appropriate adaptations and driving through complex scenarios similar to real life is associated with improvement in driving fitness and successful on road evaluation. Further research is required to identify interventions that would help improve driving abilities post stroke.

Return to Work

A substantial proportion of stroke survivors who were employed prior to the stroke event do not return to work. Factors influencing return to work include the degree of physical and cognitive impairment, age, educational level and type of pre-stroke employment. There is *consensus opinion* that stroke survivors who worked prior to their stroke should be encouraged, if their

condition permits, to be evaluated for their potential to return to work.

Miscellaneous Treatments

Acupuncture

There is *conflicting* evidence that acupuncture reduces spasticity, improves independence in ADL or enhances motor recovery following stroke. There is *moderate* evidence that acupressure/aromatherapy can reduce hemiplegic shoulder pain.

Transcutaneous Electrical Nerve Stimulation (TENS)

There is *conflicting* evidence that TENS improves a variety of motor recovery, spasticity and ADLs.

Reiki Treatment

There is *moderate* evidence that Reiki Treatment does not improve functional outcomes.

Massage Therapy

There is *moderate* evidence that massage therapy reduces pain and anxiety levels post-stroke.

Medications

Amphetamines

There is *strong* evidence that amphetamines do not improve motor recovery and/or functional outcomes, particularly when combined with physiotherapy. Although amphetamines exert an anti-depressant effect, it is uncertain the extent to which this effect influences recovery. However, there is *moderate* evidence that amphetamines improve certain elements of language recovery, when combined with language therapy.

Piracetam

There is a *strong* evidence of a significant impact of Piracetam on aphasia recovery in stroke patients also receiving speech and language therapy over the short-term. There is *limited evidence* that Piracetam increases activation of language processing regions within the brain. However, there is moderate evidence that Piracetam does not improve performance of ADL.

Bromocriptine

There is *strong* evidence that Bromocriptine does not improve aphasia recovery post stroke.

Selegiline

There is *moderate* evidence that Selegiline improves stroke impairment scores, but not functional outcomes.

Levodopa

There is *moderate* evidence that Levodopa improves short-term motor recovery following stroke.

Dextran 40

There is *moderate* evidence that Dextran 40 results in poorer functional outcome, compared to non-treatment control patients.

Bifemelane

Bifemelane in the treatment of language recovery has not been sufficiently studied to draw any meaningful conclusions.

L-Threodops (L-threo-3,4-dihydroxyphenylserine)

There is *moderate* evidence that L-DOPS improves short-term functional outcome post stroke.

Almitrine + Raubasine

There is *moderate* evidence that Almitrine + Raubasine improves functional outcome post stroke.

Repetitive Transcranial Magnetic Stimulation (rTMS)

There is *strong* evidence that rTMS helps short-term motor recovery in the chronic stage of stroke in the upper extremity. There is *conflicting* evidence that rTMS helps to relieve chronic pain following stroke.

Motor Cortex Stimulation (MCS)

There is *limited* evidence that MCS can reduce central post stroke pain for up to 10 years post stroke. There is *moderate* evidence that MCS can improve upper limb function following stroke.

Hyperbaric Oxygen Therapy

There is *strong* evidence that hyperbaric oxygen therapy does not improve neurological status.