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Stop stroke. Save lives. End Suffering.

Clinical Guidelines for Acute Stroke Management

National Stroke Foundation 2007



Australian Government

National Health and Medical Research Council

Clinical Guidelines for Acute Stroke Management

The following organisations have provided valuable input into the development of this document and the National Stroke Foundation gratefully acknowledges their endorsement of the Clinical Guidelines for Acute Stroke Management (2007):

Australian and New Zealand Society for Geriatric Medicine

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Australian Physiotherapy Association

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Dietitians Association of Australia

Occupational Therapy Australia

Royal Australian and New Zealand College of Radiologists

Speech Pathology Australia

Stroke Society of Australasia

The Council of Ambulance Authorities

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Australian Government

National Health and Medical Research Council

Disclaimer

This document is a general guide to appropriate practice, to be followed subject to the clinician's judgement and the patient's preference in each individual case. The guidelines are designed to provide information to assist decision-making and are based on the best evidence available at the time of development.

These guidelines can be downloaded from the NHMRC website: www.nhmrc.gov.au/publications.

Copies of the document can also be downloaded through the National Stroke Foundation website: www.strokefoundation.com.au.

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About the National Stroke Foundation

The National Stroke Foundation is a not-for-profit organisation that works with the public, government, health professionals, patients, carers and stroke survivors to reduce the impact of stroke on the Australian community.

Our challenge is to save 110,000 Australians from death and disability due to stroke over 10 years.

We will achieve this by:

- Educating the public about the risk factors and signs of stroke and promoting healthy lifestyles.
- Working with all stakeholders to develop and implement policy on the prevention and management of stroke.
- Encouraging the development of comprehensive and coordinated services for all stroke survivors and their families.
- Encouraging and facilitating stroke research.

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PREFACE

This second edition of the Clinical Guidelines for Acute Stroke Management represents a major undertaking which has significantly updated the first edition in both methodology and coverage. The current edition has been expanded with new information covering Transient Ischaemic Attack (TIA) assessment and management, and the economic implications of the guidelines. Greater details regarding early management of ischaemic and haemorrhagic stroke are also included in this update. It also includes a consumer rating, identifying aspects of care considered to be critical from a patient perspective that will complement the evidence ratings for each recommendation.

There is a growing evidence base for stroke care with significant new trials for many topics included in these guidelines including assessment of TIA, pharmacotherapy used in secondary prevention (cholesterol lowering and antiplatelet therapy), surgery for 'malignant' middle cerebral artery infarction to name a few. The last four years have also seen a greater focus on early recognition and faster, more efficient assessment which has necessitated ongoing collaboration between emergency service personnel, emergency department staff and specialist stroke unit teams. Focus on, and access to, thrombolysis has also advanced since the approval of rt-PA in Australia in 2003. While changes have been made, there

remains much we can improve on, particularly, access to key effective acute interventions such as stroke care units and rt-PA.

Evidence from a recent national survey demonstrates the number of stroke units in Australia is slowly increasing.¹ However, organised stroke care remains the cornerstone of effective stroke care and must remain the priority for implementation of these updated guidelines. Furthermore, for the first time patient data involved in acute stroke care has been audited nationally.¹ This is an exciting initiative that will provide more detailed assessment of the current care provided in acute stroke management and will enable more targeted quality improvement activities to be undertaken.

Although this edition highlights the advancement in knowledge, there still remains much work for researchers, with only 82 of the 148 recommendations underpinned by Level I or Level II evidence. Highlighted areas for further research have been included in this edition.

Finally, we are very grateful for the ongoing support and time from a wide range of dedicated experts. In particular special thanks goes to those involved on the expert working group who contributed much time and effort in developing these guidelines.



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KEY MESSAGES

This second edition of the Clinical Guidelines for Acute Stroke Management has been developed to provide a series of evidence-based recommendations related to acute stroke care. The guidelines should not be seen as an inflexible recipe for stroke care; rather, they provide a framework that is based on the best available evidence that can be adapted to local needs, resources and individual circumstances. Development of the guidelines has been undertaken by a multidisciplinary Expert Working Group (EWG) using methodology consistent with National Health and Medical Research Council (NHMRC) standards.²

This summary is designed to provide a quick overview of the recommendations presented in the guidelines. However, important information pertaining to the evidence supporting each recommendation as well as information about caveats to the recommendations is

included in a preamble to each section. Because of this, the recommendations should be read in conjunction with information in the body of the main document. Further information in relation to key sections is provided in tables of evidence in the supplement document.

Unlike previous stroke guidelines, each recommendation is given an overall grading based on the NHMRC interim levels of evidence pilot.³ In addition the levels of evidence of the key references for each guideline along with the actual reference are included. Where no Level I, II, III or IV evidence was available but there was sufficient consensus of the EWG, clinical practice points have been provided. A summary comparing the first and second editions is included below along with the levels of evidence and grading system.

	FIRST EDITION (2003)	SECOND EDITION (2007)
Total number of recommendations	96	148
Number of recommendations based on Level I or II studies	26 (27%)	82 (55%)
Number of recommendations based on Level III or IV studies	19 (20%)	14 (10%)
Number of recommendations based on consensus	51 (53%)	52 (35%)

Grading of Recommendations³

GRADE	DESCRIPTION
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

CLINICAL PRACTICE POINTS	
✓	Recommended best practice based on clinical experience and expert opinion.

Designations of Levels of Evidence According to Type of Research Question³

LEVEL	INTERVENTION	DIAGNOSIS	PROGNOSIS	AETIOLOGY	SCREENING
i	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies
ii	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
iii-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation	All or none	All or none	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
iii-2	A comparative study with concurrent controls: <ul style="list-style-type: none"> • Non-randomised, experimental trial • Cohort study • Case-control study • Interrupted time series with a control group 	A comparison with reference standard that does not meet the criteria required for Level II and III-1	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: <ul style="list-style-type: none"> • Non-randomised, experimental trial • Cohort study • Case-control study
iii-3	A comparative study without concurrent controls: <ul style="list-style-type: none"> • Historical control study • Two or more single arm study • Interrupted time series without a parallel control group 	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: <ul style="list-style-type: none"> • Historical control study • Two or more single arm study
iv	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

1. Organisation of Services

1.1: Stroke unit care

- a) All people with stroke should be admitted to hospital and be treated in a comprehensive stroke unit with an interdisciplinary team. (Grade A; Level I^{6, 19})
- b) Smaller hospitals should consider models of stroke unit care that adhere as closely as possible to the criteria for stroke unit care. Where possible, patients should receive care on geographically discrete units. (Grade B; Level I^{6, 21})

1.2: Organisation of services for TIA

All patients with suspected TIA should be managed in services that allow rapid assessment and treatment to be undertaken within 24-48 hours of symptom onset:

- > Those identified at high risk (ABCD² score < 4) should be admitted to a stroke unit (or where available referred to a specialist TIA clinic if the person can be assessed within 24-48 hours) to facilitate rapid assessment and treatment; (✓)
- > Those identified at low risk (ABCD² score ≤ or = 4) may be managed in the community by a general practitioner, private specialist or where possible referred to a specialist TIA clinic and seen within 7-10 days. (✓)

1.3: Organisation of care for rural centres

- a) All health services caring for people with stroke should use networks which link large stroke specialist centres with smaller regional and rural centres. (Grade D; Level IV^{36, 37, 39, 42})
- b) These networks should assist to establish appropriate stroke units along with protocols governing rapid assessment, pathways for direct communication with stroke specialist centres ("telestroke" services), and rapid transfers. (Grade D; Level IV^{36, 37, 39, 42})

1.4: Care Pathways

All stroke patients admitted to hospital may be managed using an acute care pathway. (Grade C; Level II⁴⁴)

1.5: Inpatient care coordinator

A stroke coordinator may be used to foster coordination of services and assist in discharge planning. (✓)

1.6: Team meetings

The multidisciplinary stroke team should meet regularly (at least weekly) to discuss assessment of new patients, review patient management and goals, and plan for discharge. (Grade C, extrapolated from Level I¹⁸)

1.7: Family meetings

The stroke team should meet regularly with the person with stroke and the family/carer to involve them in management, goal setting and planning for discharge. (Grade C, extrapolated from Level I¹⁸)

1.8: Information and education

All stroke survivors and their families/carers should be provided with timely, up-to-date information in conjunction with opportunities to learn via education from members of the interdisciplinary team and other appropriate community service providers. Simple information provision alone is not effective. (Grade A; Level I^{51, 52})

1.9: Early Supported Discharge

- a) Health services with organised inpatient stroke services should provide comprehensive interdisciplinary community rehabilitation and support services for people with stroke and their family/carer. (Grade A; Level I⁶¹⁻⁶³)
- b) If interdisciplinary community rehabilitation services and carer support services are available, then early supported discharge should be offered for all stroke patients with mild to moderate disability. (Grade A; Level I^{61, 62})

1.10: Shared care

- a) All patients with stroke or TIA should have their risk factors reviewed and managed long term by a general practitioner with input and/or referral to a stroke physician for specialist review where available. (Grade C; Level II⁶⁸)
- b) Locally developed protocols and pathways should be used to efficiently link primary and secondary care for people with stroke or TIA, including rapid assessment and referrals, acute management, direct communication links, efficient discharge services and long term management. (✓)

- c) Rural practitioners should participate in networks linking them to regional or metropolitan centres with specialty in stroke care. (✓)

1.11: Standardised assessment

- a) Clinicians should use validated and reliable assessment tools or measures that meet the needs of the patient and guide clinical decision making. (✓)
- b) Clinicians should provide timely and efficient assessment of patients with acute stroke. Where possible a multidisciplinary assessment should be undertaken and documented within two days of admission. (✓)
- c) Assessment findings should be discussed at the team meeting and communicated to the patient and family/carer in a timely and appropriate manner. (✓)

1.12: Palliation and death

- a) A pathway for acute stroke palliative care may be used to improve palliation for people dying after acute stroke. (Grade D; Level IV⁷¹)
- b) An accurate assessment of imminent death should be made for patients with severe stroke or those who are deteriorating. Any assessment must consider prognostic risk factors along with the wishes of the patient and their family/carer. (✓)
- c) Acute stroke patients should have access to specialist palliative care services as needed. (✓)
- d) People with stroke who are dying, and their families, should have care that is consistent with the principles and philosophies of palliative care. (✓)

1.13: Stroke service improvement

- a) All acute stroke services should be involved in quality improvement activities that include regular audit and feedback ('regular' is considered at least every two years). (Grade B; Level I⁷⁷)
- b) Indicators based on nationally agreed standards of care should be used when undertaking any audit. Performance can then be compared to similar stroke services as described by the National Stroke Unit Program. (✓)

2. Pre-Hospital Care

- a) Ambulance services, health care professionals and the general public should receive education concerning the importance of early recognition of stroke, emphasising stroke is a medical emergency. (Grade C; Level III-3 & IV³⁹)
- b) Stroke patients should be given a high priority grouping by ambulance services. (Grade C; Level III-2^{83, 84})
- c) Ambulance services should be trained in the use of validated rapid pre-hospital stroke screening tools and incorporate such tools into protocols for all pre-hospital assessment of people with suspected stroke. (Grade B; Level III-2⁸⁶⁻⁸⁹)
- d) Ambulance services should preferentially transfer suspected patients to a hospital with stroke unit care. (✓)

3. Early Assessment and Diagnosis

3.1: Assessment of TIA

- a) All patients with suspected TIA should have a full assessment that includes assessment of stroke risk using the ABCD² tool at the initial point of health care contact whether first seen in primary or secondary care. (Grade B; Level II³⁵)
- b) The following investigations should be undertaken routinely for all patients with suspected TIA: full blood count, electrolytes, renal function, cholesterol level, glucose level, and electrocardiogram. (✓)
- c) Patients classified as high risk (ABCD² >4) should have an urgent CT brain ('urgent' is considered as soon as possible, but certainly within 24 hours). Carotid duplex ultrasound should also be undertaken urgently in patients with carotid territory symptoms who would potentially be candidates for carotid re-vascularisation. Patients classified as low risk (ABCD² ≤4) should have a CT brain and carotid ultrasound (where indicated) as soon as possible (i.e. within 48-72 hours). (Grade B; Level I^{35, 100, 102} & Level III-3⁹⁹)

3.2: Triage in emergency department

- a)** Diagnosis should be reviewed by a clinician experienced in the evaluation of stroke. (Grade C; Level III-3 ^{108, 111})
- b)** Emergency department staff should use a validated stroke screen tool to assist in rapid accurate assessment for all people with stroke. (Grade C; Level II ¹¹²)
- c)** Local protocols developed jointly by staff from pre hospital emergency services, the hospital emergency department and the stroke unit should be used for all people with suspected stroke. Such protocols should include early notification by paramedic staff, high priority transportation and triage, rapid referrals from ED staff to stroke specialists and rapid access to imaging. (Grade D; Level III-3 & IV ^{39, 83, 85})

3.3: Imaging

- a)** All patients with suspected stroke should have an urgent brain CT or MRI ('urgent' is considered as soon as possible, but certainly less than 24 hours). (Grade A; Level I diagnostic study ¹⁰⁰)
- b)** A repeat brain CT or MRI should be considered urgently when a patient's condition deteriorates. (✓)
- c)** All patients with carotid territory symptoms who would potentially be candidates for carotid re-vascularisation should have an urgent carotid duplex ultrasound. (Grade B; Level I ¹⁰²)
- d)** Further brain, cardiac or carotid imaging should be undertaken in selected cases including:
 - > Patients where initial assessment has not confirmed likely source of ischaemic event;
 - > Patients with a history of more than one TIA;
 - > Patients likely to undergo carotid surgery. (Grade B; Level I ^{100, 102} and Level III-2 ¹¹⁶)

3.4: Investigations

- a)** The following investigations should be obtained routinely in all patients – full blood picture, electrocardiogram, electrolytes, renal function, fasting lipids, erythrocyte sedimentation rate and/or C-reactive protein, and glucose. (✓)
- b)** Selected patients may require the following additional investigations: angiography, chest x-ray, syphilis serology, vasculitis screen and

prothrombotic screen. These tests should be performed as soon as possible after stroke onset, and in selected patients, some of these tests may need to be performed as an emergency procedure. (✓)

4. Acute Medical and Surgical Management

4.1: Ischaemic Stroke and TIA

4.1.2: Thrombolysis

- a)** Intravenous rt-PA in acute ischaemic stroke should only be undertaken in patients satisfying specific inclusion and exclusion criteria. (Grade A; Level I ^{120, 122})
- b)** Intravenous rt-PA in acute ischaemic stroke should be given under the authority of a specialist physician and interdisciplinary acute care team with expert knowledge of stroke management, experience in the use of intravenous thrombolytic therapy and with pathways and protocols available to guide medical, nursing and allied health acute phase management. Pathways or protocols must include guidance in acute blood pressure management. (Grade C; Level I ¹²⁰ & Level IV ¹²³)
- c)** Thrombolysis should only be undertaken in a hospital setting with appropriate infrastructure, facilities and networks. (✓)
- d)** A minimum set of de-identified data from all patients treated with thrombolysis should be recorded in a central register to allow monitoring, review, comparison and benchmarking of key outcomes measures over time. (Grade C; Level IV ¹²⁶)

4.1.3: Antithrombotic therapy

- a)** Aspirin (150-300mg) should be given as soon as possible after the onset of stroke symptoms (i.e. within 48 hours) if CT/MRI scan excludes haemorrhage. (Grade A; Level I ¹⁶⁰)
- b)** The routine use of anticoagulation (e.g. intravenous unfractionated heparin) in unselected patients following ischaemic stroke/TIA is not recommended. (Grade A; Level I ^{157, 158})

4.1.4: Blood pressure lowering therapy

- a)** If extremely high blood pressure (e.g. BP > 220/120) exists, instituting or increasing antihypertensive therapy may be started, but blood pressure should be cautiously reduced (e.g. by no more than 10-20%) and the patient observed for signs of neurological deterioration. (✓)
- b)** Pre-existing antihypertensive therapy may be continued (orally or via nasogastric tube) provided there is no symptomatic hypotension or other reason to withhold treatment. (✓)

4.1.5: Surgery for ischaemic stroke

- a)** Selected patients (e.g. 18-60 years where surgery can occur within 48 hours of symptom onset) with significant middle cerebral artery infarction should be urgently referred to a neurosurgeon for consideration of hemicraniectomy. (Grade A; Level I ¹⁶⁵)
- b)** There is currently insufficient evidence to make recommendations about the use of intracranial endovascular surgery. (Level I ¹⁶⁶)

4.2: Intracerebral haemorrhage (ICH)

- a)** The use of haemostatic drug treatment with rFVIIa is currently considered experimental and is not recommended for use outside a clinical trial. (Grade B; Level I ¹⁶⁹)
- b)** The routine use of surgery is not recommended for patients with supratentorial haematoma but may be considered in certain circumstances, including:
- > stereotactic surgery for patients with deep ICH; (Grade C; Level I ¹⁸¹)
 - > craniotomy for patients where haematoma is superficial (<1cm from surface). (Grade C; Level II ¹⁸⁰)
- c)** Surgical evacuation may be undertaken for cerebellar hemisphere haematomas >3cm diameter in selected patients. (✓)
- d)** In ICH patients who have a history of hypertension, mean arterial pressure should be maintained below 130 mm Hg. (✓)

4.3 General Acute Stroke Care

4.3.1: Physiological monitoring

Patients should have their neurological status (including Glasgow Coma Scale) and vital signs including pulse, blood pressure, temperature, oxygen

saturation, glucose, and respiratory pattern monitored and documented regularly during the acute phase, the frequency of such observations being determined by the patient's status. (Grade C, Level II ¹⁸⁵ and Level III-2 ^{186, 187})

4.3.2: Oxygen therapy

Patients who are hypoxic should be given oxygen supplementation. (✓)

4.3.3: Glycaemic control

- a)** Patients with hyperglycaemia should have their blood glucose level monitored and appropriate glycaemic therapy instituted to ensure euglycaemia, especially if the patient is diabetic. Hypoglycaemia should be avoided. (✓)
- b)** Intensive, early maintenance of euglycaemia is currently not recommended. (Grade B; Level II ¹⁹⁸)

4.3.4: Neuroprotective agents

The use of putative neuroprotectors should only be used if part of a randomised controlled trial. (Grade A; Level I&II ¹⁹⁹⁻²⁰²)

4.3.5: Complementary and alternative therapy

- a)** The routine use of the following complementary and alternative therapies are not recommended:
- > Acupuncture; (Grade B, Level I ^{216, 217})
 - > Ginkgo biloba extract or Dan shen agents; (Grade B, Level I ^{219, 220})
 - > Reiki therapy; (Grade C, Level II ²¹⁸)
 - > Other alternative therapies. (✓)
- b)** Health professionals should be aware of different forms of complementary and alternative therapies and be available to discuss these with stroke survivors and their families. (✓)

5. Assessment and Management of Consequences of Stroke

5.1: Dysphagia

- a)** Patients should be screened for swallowing deficits before being given food, drink or oral medications. Screening should be undertaken by personnel specifically trained in swallowing screening. (Grade C, Level I ^{225, 226})
- b)** Patients should be screened within 24 hours of admission. (✓)

- c) Patients who fail the swallowing screening should be referred to a speech pathologist for a comprehensive assessment. (✓)

5.2: Nutrition

- a) Close monitoring of hydration status and appropriate fluid supplementation should be used to treat or prevent dehydration. (Grade B; Level I ²⁵⁰)
- b) All patients with acute stroke should be screened for malnutrition. (Grade B; Level II ²⁶⁰)
- c) Those who are at risk of malnutrition, including those with dysphagia, should be referred to a dietitian for assessment and ongoing management. Assessment of nutritional status should include the use of validated nutrition assessment tools or measures. (✓)
- d) Nutritional supplementation should be offered to people whose nutritional status is poor or deteriorating. (Grade A; Level I ²⁵²)
- e) NG feeding is the preferred method during the first month post stroke for people who do not recover a functional swallow. (Grade B; Level II ²⁵⁶)
- f) Food intake should be monitored for all people with acute stroke. (✓)

5.3: Early Mobilisation

- a) Patients should be mobilised as early and as frequently as possible. (Grade B; Level II ²⁶⁴)
- b) After assessment the physiotherapist should advise staff and carers of appropriate mobilising and transfer techniques. (✓)

5.4: Early therapy for difficulties with Activities of Daily Living (ADL)

- a) Patients with difficulties in occupational performance in daily activities should be treated by an occupational therapist or a specialist multidisciplinary team that includes an occupational therapist (Grade B; Level I ^{18, 268})
- b) Patients with confirmed difficulties in occupational performance in personal tasks, instrumental activities, vocational activities or leisure activities should have a management plan formulated and documented to address these issues. (✓)
- c) The occupational therapist should advise staff and carers on techniques and equipment to maximise

outcomes relating to functional performance in daily activities, sensorimotor, perceptual and cognitive capacities. (✓)

5.5: Cognition and perception

- a) All patients should be screened for cognitive and perceptual deficits using a validated screening tool. (✓)
- b) Patients identified during screening should undertake full assessment and management by an appropriately trained health professional. (✓)

5.6: Communication

- a) All patients should be screened for communication deficits using a validated screening tool. (Grade C, Level I ²⁹³)
- b) Those with suspected communication difficulties should receive formal assessment by a speech pathologist. (✓)
- c) Patients with communication difficulties should be treated as early and as frequently as possible. (Grade C, Level I ²⁹⁶ & Level III-2 ²⁹⁵)
- d) All written health information should be available in an aphasia friendly format. (Grade D, Level IV ²⁹⁸)
- e) The speech pathologist should advise staff and family/carers of appropriate communication techniques. (Grade C, Level II ^{299, 300})

5.7: Incontinence

- a) All patients with suspected continence difficulties should be assessed by trained personnel using a structured functional assessment. (Grade B; Level II ³⁰¹)
- b) A portable bladder ultrasound scan can be used to assist in diagnosis and management of urinary incontinence. (Grade B; Level I ³⁰²).
- c) Patients with confirmed continence difficulties should have a continence management plan formulated and documented. (Grade C; Level II ³⁰¹)
- d) The use of indwelling catheters should be avoided as an initial management strategy. (✓)
- e) A post discharge continence management plan should be developed with the patient and carer prior to discharge and should include how to access continence resources in the community. (✓)

5.8: Mood

- a) Patients with suspected altered mood (e.g. depression, anxiety, emotional lability) should be assessed by trained personnel using a standardised scale. (Grade B; Level II & Level III-1 68, 307, 309, 311, 314, 321)
- b) Patients with stroke may be managed using a case management model after discharge to reduce post stroke depression. If used, services should incorporate education of the recognition and management of depression, screening and assistance to coordinate appropriate interventions via a medical practitioner. (Grade C; Level II 68, 325)
- c) Routine use of antidepressants to prevent post-stroke depression is not currently recommended. (Grade B; Level I 317)
- d) Antidepressants may be used for people with emotional lability. (Grade B; Level I 315)
- e) Patients with depression or anxiety may be treated with antidepressants and/or psychological interventions to improve mood. (Grade B; Level I 316)

6. Prevention and Management of Complications

6.1: Cerebral Oedema

- a) Selected patients (e.g. 18-60 years with potential for surgery to occur within 48 hours of symptom onset) with significant middle cerebral artery infarction should be urgently referred to a neurosurgeon for consideration of hemicraniectomy. (Grade A; Level I 165)
- b) Corticosteroids are not recommended for management of patients with brain oedema and raised intracranial pressure. (Grade A; Level I 328)
- c) Osmotherapy and hyperventilation may be trialled while a neurosurgical consultation is undertaken, or for patients with deteriorating condition due to raised intracranial pressure. (Grade C; Level I for potential short term benefit of glycerol 172, Level IV for hyperventilation 329)

6.2: Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE)

- a) Early mobilisation and adequate hydration should be encouraged with all acute stroke patients to help prevent DVT and PE. (✓)

- b) Antiplatelet therapy should be used for people with ischaemic stroke to prevent DVT/PE. (Grade A; Level I 331)
- c) The following interventions may be used with caution for selected people with acute ischaemic stroke at high risk of DVT/PE:
 - > low molecular weight heparin or heparin in prophylactic doses; (Grade B; Level I 331, 334, 335 and Level II 336)
 - > thigh-length antithrombotic stockings. (Grade C; Level II 331, 338)

6.3: Pyrexia

Antipyretic therapy, comprising regular paracetamol and/or physical cooling measures, should be used routinely where fever occurs. (Grade C; Level II 212, 344)

6.4: Pressure care

- a) All patients unable to mobilise independently should have a pressure care risk assessment completed by trained personnel. (✓)
- b) All those assessed at high risk should be provided with a pressure relieving mattress as an alternative to a standard hospital mattress. (Grade B; Level I 345)

7. Secondary Prevention

7.1: Behaviour change

- a) Every person with stroke should be assessed and informed of their risk factors for a further stroke and possible strategies to modify identified risk factors. The risk factors and interventions include:
 - > smoking cessation: nicotine replacement therapy, bupropion or nortriptyline therapy, nicotine receptor partial agonist therapy and/or behavioural therapy should be considered; (Grade A; Level I 359-361, 363-366)
 - > improving diet: a diet that is low in fat (especially saturated fat) and sodium, but high in fruit and vegetables should be consumed; (Grade A; Level I 367-369, 372, 376 & II 370, 373-375)
 - > increasing regular exercise; (Grade C; meta-analysis of cohort studies in primary prevention demonstrate strong link between low exercise and stroke risk 386-388)

- avoiding excessive alcohol. (Grade C; meta-analysis of cohort studies in primary prevention demonstrate link between high alcohol intake and stroke risk ³⁹²)
- b)** Interventions should be individualised and may be delivered using behavioural techniques (such as educational or motivational counselling). (Grade A; Level I ^{362-366, 395, 396})

7.2: Blood pressure lowering

- a)** All patients after stroke or TIA, whether normotensive or hypertensive, should receive blood pressure lowering therapy, unless contraindicated by symptomatic hypotension. (Grade A; Level I ³⁹⁸)
- b)** Commencement of new blood pressure lowering therapy may occur prior to discharge or within the first week after stroke or TIA. (Grade B; Level II ^{400, 401} & Level III-3 ³⁹⁴)

7.3: Antiplatelet therapy

- a)** Long term antiplatelet therapy should be prescribed to all people with ischaemic stroke or TIA who are not prescribed anticoagulation therapy. (Grade A; Level I ⁴⁰²)
- b)** Low dose aspirin and modified release dipyridamole should be prescribed to all people with ischaemic stroke or TIA who do not have concomitant acute coronary disease. (✓ ^{406, 411})
- c)** Aspirin alone or clopidogrel alone may be used for people who do not tolerate aspirin plus dipyridamole therapy. Clopidogrel alone should be used for those who are intolerant of aspirin or in whom aspirin is contraindicated. (✓ ⁴⁰²)
- d)** The combination of aspirin plus clopidogrel is not recommended in the secondary prevention of cerebrovascular disease in patients who do not have acute coronary disease or recent coronary stent. (Grade A; Level II ^{408, 409})

7.4: Anticoagulation therapy

- a)** Anticoagulation therapy for long-term secondary prevention should be used in all people with ischaemic stroke or TIA who have atrial fibrillation, cardioembolic stroke from valvular heart disease, or recent myocardial infarction, unless a contraindication exists. (Grade A; Level I ^{119, 415})
- b)** Anticoagulation therapy for secondary prevention for those people with ischaemic stroke or TIA from

presumed arterial origin should not be routinely used as there is no evidence of additional benefits over antiplatelet therapy. (Grade A; Level I ⁴¹²)

- c)** The decision to commence anticoagulation therapy should be made prior to discharge. (Grade C; Level III-3 ³⁹⁴)
- d)** In patients with TIA, commencement of anticoagulation therapy should occur once CT or MRI has excluded intracranial haemorrhage as the cause of the current event. (✓)

7.5: Cholesterol lowering

- a)** Therapy with a statin should be used for all patients with ischaemic stroke or TIA. (Grade B; Level II ^{382, 418})
- b)** Patients with high cholesterol levels should receive dietary review and counselling by a specialist, trained clinician. (Grade B; Level I ^{395, 396})

7.6: Diabetes management

All acute stroke patients should have their glucose monitored. Patients with glucose intolerance or diabetes should be managed in line with national guidelines for diabetes. (✓)

7.7: Carotid surgery

- a)** Carotid endarterectomy should be undertaken in patients with non disabling carotid artery territory ischaemic stroke or TIA with ipsilateral carotid stenosis measured at 70-99% (NASCET criteria) if surgery can be performed by a specialist surgeon with low rates of perioperative mortality/morbidity. (Grade A; Level I ^{429, 430})
- b)** Carotid endarterectomy should be undertaken in select patients (considering age, gender and comorbidities) with non disabling carotid artery territory ischaemic stroke or TIA with ipsilateral carotid stenosis measured at 50-69% (NASCET criteria) if surgery can be performed by a specialist surgeon with very low rates of perioperative mortality/morbidity. (Grade A; Level I ^{429, 430})
- c)** Carotid endarterectomy may be undertaken in highly select patients (considering age, gender and comorbidities) with asymptomatic carotid stenosis of 60-99% if it can be performed by a specialist surgeon with very low rates of perioperative mortality/morbidity. (Grade A; Level I ^{429, 430})

8. Discharge Planning, Transfer of Care and Integrated Community Care

- d)** Eligible patients should undergo carotid endarterectomy as soon as possible after the event (ideally within 2 weeks). (Grade A; Level I ⁴³¹)
- e)** Carotid endarterectomy should only be performed by a specialist surgeon at centres where outcomes of carotid surgery are routinely audited. (Grade B; Level I ⁴²⁹)
- f)** Carotid endarterectomy is not recommended for those with <50% symptomatic stenosis or those with <60% asymptomatic stenosis. (Grade A; Level I ^{429, 432})
- g)** Carotid angioplasty and stenting should not routinely be considered for patients with symptomatic stenosis. However, it may be considered as an alternative in certain circumstances, that is in patients who meet criteria for carotid endarterectomy but are deemed unfit due to medical comorbidities (e.g. significant heart/lung disease, age >80yrs), or conditions that make them unfit for open surgery (e.g. high or low carotid bifurcation, carotid re-stenosis). (Grade B; Level I ⁴³⁷ & Level II ^{438, 439})

7.8: Patent foramen ovale (PFO)

- a)** All patients with an ischaemic stroke or TIA, and a PFO, should receive antiplatelet therapy as first choice. (Grade C; Level II ⁴⁴²)
- b)** Anticoagulation may also be considered taking into account other risk factors and the increased risk of harm. (Grade C; Level II ⁴⁴²)
- c)** Currently there is insufficient evidence to recommend PFO closure. (✓)

7.9: Concordance with medication

Interventions to promote adherence to medication regimes are often complex and should include one or more of the following:

- > information, reminders, self-monitoring, reinforcement, counselling, family therapy; (Grade B; Level I ⁴⁴⁶⁻⁴⁴⁸)
- > reduction in the number of daily doses; (Grade B; Level I ^{446, 447})
- > multi-compartment medication compliance device; (Grade C; Level I ^{449, 450})

8.1: Inpatient rehabilitation

If ongoing inpatient rehabilitation is needed, care should be provided in either a stroke rehabilitation unit or a general rehabilitation unit. (Grade A, Level I ^{6, 19})

8.2: Pre-discharge needs assessment

- a)** Before discharge, people with stroke and their carers should have the opportunity to identify and discuss their post-discharge needs (e.g. physical, emotional, social and financial) with relevant members of the interdisciplinary team. (✓)
- b)** Before discharge all patients should be assessed to determine the need for a home visit prior to discharge from hospital. (✓)
- c)** If needed, a home assessment should be carried out to ensure safety and community access. (Grade C; Level I ⁴⁵³)

8.3: Carer training

Relevant members of the interdisciplinary team should provide specific training for carers before the person's discharge home. This should include training, as necessary, in:

- > personal care techniques, communication strategies, physical handling techniques, ongoing prevention and other specific stroke-related problems; (Grade B; Level II ⁵⁶)
- > safe swallowing and appropriate dietary modifications. (✓)

8.4: Care plans

- a)** People with stroke, their carers, the general practitioner, and community care providers should be involved with the interdisciplinary team in the development of a care plan. (✓)
- b)** Care plans should be used and outline care in the community after discharge, including the development of self-management strategies, provision of equipment and support services, and outpatient appointments. (✓)

8.5: Discharge planner

- a)** A discharge planner may be used to coordinate a comprehensive discharge program for people with acute stroke. (Grade D; Level III-3 ⁴⁵⁷)

- b) The stroke survivor's general practitioner, other primary health professionals and community service providers should be involved in, and informed about, the discharge plans and agreed post-discharge management, as early as possible prior to discharge. (✓)

8.6: Community rehabilitation

Rehabilitation in the community is equally effective if delivered in the hospital via outpatients, or day hospital, or in the community, and should be offered to all stroke patients as needed.

(Grade A, Level I ^{63, 458, 459})

8.7: Post-discharge support

- a) Contact with and education by trained staff should be offered for all stroke survivors and carers after discharge. (Grade C; Level II ^{53, 54, 57, 59, 60, 463, 468-470})
- b) People with stroke and their carers should be provided with a contact person (in the hospital or community) for any post-discharge queries. (Grade D; Level I ⁴⁷¹ & Level II ^{53, 60})

8.8: Return to driving

The National Guidelines for Driving and relevant state guidelines should be followed when assessing fitness to drive following a stroke or TIA. In general, patients with TIA or minor stroke, especially those found to be at high risk, should be advised to delay returning to driving for at least 1- 4 weeks. (✓)

- > Urgent CT on admission is the most cost effective strategy for brain imaging in stroke patients. There are currently no cost-effectiveness data for the use of MRI in acute stroke.
- > Carer training is cost effective. However, more information is required to ascertain the implications for carers.
- > Carotid endarterectomy in recently symptomatic patients with high grade carotid stenosis appears highly cost-effective when performed with low perioperative morbidity and mortality but updated information is needed.
- > Warfarin is cost effective in selected high risk patients.
- > Blood pressure reduction for secondary stroke prevention is cost effective.
- > The combination antiplatelet therapy of dipyridamole plus aspirin was consistently found to be cost effective compared with aspirin alone. However, there is conflicting evidence for the cost effectiveness of clopidogrel.
- > Some brief lifestyle change interventions are cost effective in populations other than stroke (e.g. brief smoking cessation advice, QUIT lines/phone counselling, physical activity counselling) and such interventions should be applicable to people with stroke.

9. Cost and Socioeconomic Implications

- > Overall there are relatively few studies concerned with the economic implications of stroke care and even fewer for socioeconomic implications.
- > Stroke unit care is cost-effective.
- > There is insufficient evidence to determine the economic implications of care pathways alone.
- > Early supported discharge programs produce equivalent outcomes for patients at similar or potentially reduced costs, in particular for urban settings and in patients with moderate stroke severity.
- > Treatment with rt-PA has consistently been demonstrated to be cost effective.

In Australia, stroke affects approximately 53,000 people per year. Around half of these people are over the age of 75 and as the population ages the number of strokes occurring each year is expected to increase.⁴ The burden of stroke goes beyond the measured cost in Australia of \$1.3 billion per annum.⁵ The impact on individuals, families and the workforce is substantial. Of those who have a stroke, approximately a third will die within the first 12 months, a third will make a complete recovery and a third will be left with a disability that causes some reliance on others for assistance with activities of daily living. Effective early stroke treatment aims to promote maximum recovery and prevent costly complications and subsequent strokes. This guideline has been developed in response to the burden of stroke on individuals and the community as a whole. This guideline specifically addresses the important aspects of care for people in the acute phase of stroke recovery and the assessment and management of people with transient ischaemic attack (TIA).

Setting the scene: a consumer perspective

The process of developing the Clinical Guidelines for Acute Stroke Management has importantly included input and advice from stroke survivors and their family/carer. Their first-hand experience of stroke and stroke care can contribute much to our understanding of what we can do that will make a difference to the experience of people as they are recovering from a stroke. However, experience in implementation and from working with consumers suggests that recommendations that receive the main focus are those with the highest levels of evidence, or those that are more medically driven. Furthermore, many of the aspects of care that consumers consider critical to their care are unsupported by strong, clear evidence (e.g. discharge planning).

A novel approach has been undertaken during the development of these guidelines. During this process consumers indicated that almost all topics are viewed to be extremely important, especially discharge planning and transfer of care. Health professionals should be mindful not only of strength of the evidence but also of the needs and opinions of acute stroke patients when implementing the guidelines for acute

stroke management. Further information about the consumer perspective is found throughout the document as well as in Appendix A.

Acute stroke care

Acute care is characterised by a focus on rapid, thorough assessment and early management. Evidence continues to evolve and highlights the fact that the principles of rehabilitation should be similarly applied in the acute setting.⁶ Rehabilitation is a proactive, person-centred and goal-oriented process that should begin the first day after stroke. Its aim is to improve function and/or prevent deterioration of function, and to bring about the highest possible level of independence - physically, psychologically, socially and financially. Rehabilitation is concerned not only with physical recovery but also with reintegration of the person into the community. Furthermore, rehabilitation is a process that aims to maximise self-determination and optimise choices for those with stroke.

The central aspect of rehabilitation is the provision of a coordinated program by a specialised, interdisciplinary team of health professionals. This rehabilitation team involves combined and coordinated use of medical, nursing and allied health skills, along with social, educational and vocational services, to provide individual assessment, treatment, regular review, discharge planning and follow-up.

While the interdisciplinary team recognises the specialist contribution of each discipline, generally no mention has been made of their specific roles throughout the document. The following is provided as a summary of the main aspects of members of the team:

> **Doctors** coordinate comprehensive medical care (including consulting other medical specialists as needed), assist stroke survivors and their families in making informed choices and re-adjustments, and prevent complications and recurrent stroke. The doctor is often responsible for making sure the best available resources and services are offered to those affected by stroke. An inpatient medical team (commonly a specialist [e.g. in neurology, rehabilitation or geriatrics], registrar and junior medical officers) often work in conjunction with a general practitioner to provide care in hospital and in the community.

- > **Nurses** perform comprehensive nursing assessments and help manage aspects of patient care including observations, swallowing, mobility, continence, skin integrity, pain control and prevention of complications. Nurses also provide patient centred care and assist coordination of care, discharge planning, support and education. Nurses can provide specialist stroke care in the acute, rehabilitation and community context as well as deliver palliative and terminal nursing care.
- > **Physiotherapists** address recovery of sensorimotor function in the upper and lower limb, and work with clients and their families to aid recovery of functional mobility (e.g. walking) in both hospital and community environments. They also assist in the treatment of musculoskeletal problems or complications (e.g. shoulder pain) and respiratory problems.
- > **Occupational therapists** work with clients and their families/carers to optimise participation and independence for all daily occupations (including self-care, leisure and productivity). This is achieved by either working directly to address recovery of function (including motor, cognitive or perceptual function), or by adapting the task or the environment.
- > **Speech pathologists** work with people who have difficulties with communication, cognition and swallowing, and also train carers to facilitate activity and participation.
- > **Dietitians** work with clients, and their family/carer, who need medical nutrition therapy including texture modified diets and enteral feeding as well as those at risk of, or suffering from malnutrition. They also provide education and counselling for risk factor modification and management of co-morbidities.
- > **Social workers** provide support, counselling and information to those with stroke and their family/carer regarding options to optimise physical, emotional, social and spiritual well-being. They also assist in organising community resources.

The team may be expanded to include **psychologists** and/or **neuropsychologists, psychiatrists, pharmacists, ophthalmologists, orthoptists, podiatrists, orthotists, and therapy assistants** as well as general ward staff. The person with stroke and their family/carer should also be acknowledged as an important team member.

Australian Clinical Guidelines for Stroke Management

Scope of the Guidelines

The Australian Clinical Guidelines for Stroke Management have been developed as two documents.

This document, Clinical Guidelines for Acute Stroke Management, relates to assessment and early management for acute stroke or transient ischemic attack (TIA) and significantly updates the document which was released in September 2003. These Guidelines are intended for use by health professionals and policy makers who plan, organise and deliver care for people with stroke during the acute phase of recovery.

The second document, Clinical Guidelines for Stroke Rehabilitation and Recovery,⁷ encompasses all care after the acute phase and presents evidence-based recommendations for rehabilitation interventions and care in the community for stroke survivors and their families/carers. This document is available from the National Stroke Foundation website (www.strokefoundation.com.au) or the National Health and Medical Research Council (NHMRC) website (www.nhmrc.gov.au/publications).

The Clinical Guidelines for Acute Stroke Management should be used in conjunction with the Clinical Guidelines for Stroke Rehabilitation and Recovery, to underpin high quality, integrated stroke care across the continuum of care.

Focus of the Guidelines

The Clinical Guidelines for Acute Stroke Management specifically addresses the early assessment and management of stroke and TIA in adults only (i.e. does not specifically include care of children). “Early” is defined as the first seven days of care.

While stroke is discussed broadly in this document, it is recognised that there are different types of stroke. It is noted that haemorrhagic stroke (particularly subarachnoid haemorrhage) is often excluded from some studies. Furthermore, the early management of subarachnoid haemorrhage is specialised and as such it was decided that this guideline does NOT include recommendations on the care of those with this condition. A subsequent guideline should be developed to cover this condition. However,

intracerebral haemorrhage has been included and specifically discussed. Furthermore this guideline has been expanded from the first edition (2003) to include a number of new topics, for example, assessment and management of TIA.

Development of the Guidelines

The Clinical Guidelines for Acute Stroke Management have been developed according to processes prescribed by the NHMRC² under the direction of an interdisciplinary Expert Working Group (EWG) (see Appendix A). The draft 'Additional levels of evidence and grades for recommendations for developers of guidelines pilot program 2005-2007' has been used to assist in grading the recommendations along with specifying levels of evidence.³ Consultation from other individuals and organisations was also included in the development process in line with NHMRC standards. Details about the development methodology and consultation process are outlined in Appendix A.

Consumer versions of the Guidelines

Consumer versions of the Clinical Guidelines for Acute Stroke Management and Clinical Guidelines for Stroke Rehabilitation and Recovery documents have been developed through partnerships between the National Stroke Foundation and State Stroke Associations throughout Australia. Given the different needs of stroke survivors and their families at different stages of recovery, the two Clinical Guideline documents are presented as three books for consumers. These books are available through the National Stroke Foundation and State Stroke Associations.

Revision of the Guidelines

The National Stroke Foundation aims to combine, review and update the Clinical Guidelines for Acute Stroke Management along with the Clinical Guidelines for Stroke Rehabilitation and Recovery by 2010.

Using the Guidelines

The primary goal in developing guidelines is to help health care workers improve the quality and effectiveness of the care they provide. The guidelines should not be seen as an inflexible recipe for stroke care; rather, they provide a framework that is based on the best available evidence that can be adapted to local needs, resources and individual circumstances.

Guidelines are also different to clinical or care pathways (also referred to as critical pathways, care

paths, integrated care pathways, case management plans, clinical care pathways or care maps). Guidelines are an overview of the current best evidence translated into clinically relevant statements. On the other hand, care pathways are seen as a resource which applies the guidelines in a local setting based on local needs. Care pathways are based on best practice guidelines but provide a local link between the guidelines and their use.⁸

The guidelines and the preambles provide an overview of the evidence. Those wishing to implement it may need to find out more information, for example, the exact processes involved in use of a particular screening tool. Strategies planned to encourage this transfer of evidence into clinical practice may include, but are not limited to:

- > distribution via existing networks, key professional and lay organisations, publications in professional journals, and electronic access via the internet;
- > development and use of decision making tools and summary documents (e.g. care pathways);
- > educational meetings / conferences;
- > use of local opinion leaders;
- > audit, feedback and reminders;
- > use of networks.

In considering implementation of these Guidelines at a local level, health professionals are encouraged to identify the barriers and facilitators to evidence-based care within their environment to determine the best strategy for local needs. Further information regarding implementation is discussed in Appendix A.

Implications for service equity

In addition to providing an avenue to improve the health outcomes for people with stroke, these guidelines provide an opportunity to discuss and address the difficulty of equity in health. The impact of stroke is dependent on a number of socioeconomic characteristics including gender, culture/ethnicity, education, occupation, income, location of residence, and lifestyle. It is known, for example, that the incidence of stroke varies depending on different socioeconomic characteristics.⁹⁻¹⁷ One of these studies found access to some services during hospital care (e.g. physiotherapy, occupational therapy and speech pathology) differed depending on socioeconomic factors, even though there was universal access to health care.¹³ However, few

studies were identified during the development process regarding the impact of interventions for acute stroke. Further discussion about the socioeconomic impact of stroke is discussed in Section 9 of this document.

Access is one of the major barriers to equitable services and is influenced by geography, culture and spiritual beliefs. Particular challenges are therefore noted for rural and remote services where resources, particularly human resources, may be limited. Whilst it is recognised that residents in rural and remote areas may have difficulty accessing health care as readily as their urban counterparts the aim in all settings must be to develop local solutions that ensure optimal practice and quality outcomes that are based on the best available evidence using the available resources.

Careful consideration is also required for the differing needs of people with stroke. Appropriate resources may be required in a variety of languages and formats for people with stroke and their carers. The particular needs of people from Aboriginal and Torres Strait Islander and those from culturally and linguistically diverse backgrounds also require special attention and resources.¹⁷ Other groups of people (e.g. younger people with stroke) may also have specific needs that require particular resources or application of these guidelines.

Format

These guidelines are organised in nine sections to address issues deemed by the guideline developers as important in acute stroke care. The aim of the guidelines is to provide a logical framework from pre-hospital care through to discharge and follow up in the community.

The introduction to each topic provides justification for the recommendation. The guidelines are then presented in a box and are summarised according to the 'interim' NHMRC expanded levels of evidence which are listed below.³ Each recommendation is also graded according to the draft NHMRC grading system. The key references for each guideline are also included. Where no satisfactory Level I, II, III or IV evidence was available but there was sufficient consensus, clinical practice points based on expert opinion is provided by the EWG. The group tried at all times to organise each section as a logical flow from assessment to management. As such the order of the recommendations in each section is no indication of their importance.

Designations of Levels of Evidence According to Type of Research Question³

LEVEL	INTERVENTION	DIAGNOSIS	PROGNOSIS	AETIOLOGY	SCREENING
i	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies
ii	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
iii-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation	All or none	All or none	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)

cont.

Designations of Levels of Evidence According to Type of Research Question³ cont.

LEVEL	INTERVENTION	DIAGNOSIS	PROGNOSIS	AETIOLOGY	SCREENING
iii-2	A comparative study with concurrent controls: <ul style="list-style-type: none"> • Non-randomised, experimental trial • Cohort study • Case-control study • Interrupted time series with a control group 	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: <ul style="list-style-type: none"> • Non-randomised, experimental trial • Cohort study • Case-control study
iii-3	A comparative study without concurrent controls: <ul style="list-style-type: none"> • Historical control study • Two or more single arm study • Interrupted time series without a parallel control group 	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: <ul style="list-style-type: none"> • Historical control study • Two or more single arm study
iv	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Grading of Recommendations³

GRADE	DESCRIPTION
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

CLINICAL PRACTICE POINTS

✓	Recommended best practice based on clinical experience and expert opinion.
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1.1 Stroke unit care

The organisation of hospital services to provide stroke unit care is the single most important recommendation for acute stroke management. Stroke unit care should be the highest priority for clinicians and administrators to consider. There is overwhelming evidence that stroke unit care significantly reduces death and disability after stroke compared with conventional care in general wards for all people with stroke.⁶

Models of stroke care described in the literature include:

- acute stroke ward: acute unit in a discrete ward;
- comprehensive stroke unit care: combined acute and rehabilitation unit in a discrete ward;
- stroke rehabilitation unit: a discrete rehabilitation unit for people with stroke, who are transferred from acute care 1-2 weeks post stroke;
- mixed rehabilitation ward: rehabilitation provided on a ward managing a general caseload.

In Australia, most stroke units established to date have a primary focus on early (acute) care and early aspects of rehabilitation, with varying degrees of intensity and follow-up. However, the evidence for stroke unit care is clearest for units that can provide several weeks of rehabilitation (on a comprehensive stroke unit or stroke rehabilitation unit).^{6, 18, 19}

The stroke units that have been shown to deliver highly effective stroke care share a number of characteristics, including:

- location in a geographically discrete unit;
- comprehensive assessments;
- a coordinated interdisciplinary team;
- early mobilisation and avoidance of bed rest;
- staff who have a special interest in the management of stroke, and access to ongoing professional education and training;
- clear communication, with regular team meetings to discuss management (including discharge

planning) and other meetings as needed (e.g. family conferences);

- active encouragement of people with stroke and their carers/family members to be involved in the rehabilitation process.^{6, 18}

A mobile stroke team has been suggested as one strategy to improve processes of care for hospitals that do not currently have a dedicated stroke unit.²⁰ One robust systematic review found no clear benefit for mobile stroke teams. The only significant benefit related to a process outcome (documented OT assessment) with non significant trends reported for improved patient outcomes.²¹ Mobile stroke teams are generally not more effective than care on a general ward but are inferior to care on a stroke unit.²¹ Hence based on best available data mobile stroke teams are not the answer to regional hospitals or metropolitan hospitals without a stroke unit. In such situations it is recommended that a small (2-4 bed) geographically based stroke unit be established as part of a larger general ward. In larger hospitals, a comprehensive stroke unit is considered the best model for acute stroke patients.¹⁹ Mobile stroke teams should only be developed if part of a formal randomised controlled trial to establish an Australian evidence base.

Finally there is evidence that all patients should be admitted to a stroke unit in a hospital rather than avoid admission to hospital (“hospital at home”). Evidence from one robust systematic review found that hospital at home services had similar outcomes to general ward care but noted that general wards are inferior to stroke unit care.²² A subsequent study confirmed that stroke unit care is indeed superior to general hospital ward care and hospital at home services provided by a specialist stroke team.²³ Currently hospital at home services are not a common model used in Australia and hence efforts should be focused on providing organised inpatient stroke unit care.

1.1	STROKE UNIT CARE	GRADE	LEVEL	CONSUMER RATING
a)	All people with stroke should be admitted to hospital and be treated in a comprehensive stroke unit with an interdisciplinary team.	A	Level I ^{6, 19}	9.3/10
b)	Smaller hospitals should consider models of stroke unit care that adhere as closely as possible to the criteria for stroke unit care. Where possible, patients should receive care on geographically discrete units.	B	Level I ^{6, 21}	–

1.2 Organisation of services for transient ischaemic attack (TIA)

There are various models suggested for organising services for those with TIA. Such models include direct hospital admission to a stroke unit, rapid outpatient clinics for TIA, or management by a general practitioner.

Admission to hospital

While there is very strong evidence for admission to hospital and care on a stroke unit for all levels of stroke severity⁶ it is unclear if there are benefits for those with TIA and very minor stroke. Analyses undertaken revealed that mild strokes (presumably including TIA) did not appear to benefit from stroke unit care (compared to general ward) in terms of reduced risk of death alone or death or institutional care. However, mild stroke patients managed in stroke units reduced the risk of being dependent if they survived.⁶ Furthermore, hospital admission to a stroke unit increased the likelihood of undertaking necessary diagnostic tests (e.g. carotid ultrasound, MRI) and had higher adherence to protocols and processes of care consistent with best practice stroke care compared to conventional hospital ward.²⁴

While mild or recovering symptoms are one reason for not administering rt-PA initially, there is some indication of a correlation between TIA and a subsequent deterioration in symptoms in a significant minority of cases.²⁵⁻²⁷ Hence a short hospital admission may provide opportunity for administration of rt-PA should the patient deteriorate. One study found a policy of admission to hospital for 24 hours after TIA is cost neutral if considering rt-PA alone.²⁸

Rapid TIA clinic

No robust data were found to determine the outcomes of this model of care. One retrospective study in the UK found that a clinic was cost effective if all relevant investigations had been completed prior to the visit allowing informed decisions to be made at a “one stop” service.²⁹ Another case series reported a rapid assessment clinic was useful to screen for patients eligible for carotid surgery but found only a small number of patients (4.8%) underwent carotid surgery.³⁰ There is currently no national data for stroke or TIA care provided in emergency departments or outpatient clinics. Only 5% of hospitals surveyed in 2007 have a rapid assessment outpatient clinic for TIAs or mild stroke. Availability of such services was significantly more common where there was a stroke care unit.

There are no Australian data to indicate the average waiting times from referral to actually being seen in a clinic. Data from the UK indicate while 78% of hospitals have a neurovascular clinic only 34% are seen within 7 days with the average waiting time being 12 days.³¹ Local services have begun to provide earlier access to special clinics for people with stroke, especially for those assessed as having a lower risk of stroke. It is vital that any such service should provide timely access to routine investigations.

Management by primary care

The role of the GP in initial assessment and management of TIA and stroke in Australia is unclear. Information collected in one ongoing Australian study found that TIA represents only 0.1% of GP consultations.³² Furthermore, tests and imaging was requested in only a small number of contacts for people with stroke (full blood count 2%; lipid test 1%; CT brain 2%; Doppler ultrasound of carotid arteries 1%).³³ MRI is not available in some areas especially in rural and remote centres³⁴ and GPs are unable to request MRI. Often people will present to the GP several hours or even days after the event due to underestimation of the need for rapid assessment and management. Given the small numbers of people with stroke or TIA who normally present to the GP and the fact that TIA is often over diagnosed, it appears that GPs are best placed to provide initial screening and referral to specialist stroke services for full assessment and early management. Long term management of risk factors, however, is the primary role of GPs.

In conclusion, there is very little direct evidence to guide administrators and clinicians in the most appropriate organisation of services for people with TIA. It is clear, however, that whichever model is utilised it should focus on rapid assessment and early management and be based on local resources and needs. Similar to stroke services, development of networks between general practitioners and stroke centres would enable appropriate use of more intensive resources. Access to services should be determined on the basis of risk of stroke. While recognising its limitations, the ABCD² tool is a useful screening tool that should be used to determine high and low risk in patients with TIA (see assessment of TIA section 3.1).

ABCD² Tool³⁵

A	AGE: ≥60 years (1 point)
B	BLOOD PRESSURE: ≥ 140/90mm Hg (1 point)
C	CLINICAL FEATURES: unilateral weakness (2 points), speech impairment without weakness (1 point)
D	DURATION: >60mins (2 points), 10-59 mins (1 point); and
D	DIABETES (1 point)

1.2	ORGANISATION OF SERVICES FOR TIA	GRADE	LEVEL	CONSUMER RATING
	All patients with suspected TIA should be managed in services that allow rapid assessment and treatment to be undertaken within 24-48 hours of symptom onset:			
	<ul style="list-style-type: none"> Those identified at high risk (ABCD² score >4) should be admitted to a stroke unit (or where available referred to a specialist TIA clinic if the person can be assessed within 24-48 hours) to facilitate rapid assessment and treatment; Those identified at low risk (ABCD² score ≤ 4) may be managed in the community by a general practitioner, private specialist or where possible referred to a specialist TIA clinic and seen within 7-10 days. 	✓	–	–
		✓	–	–

1.3 Organisation of care for rural centres

In some areas, the number of people with stroke requiring care is not high enough to support a dedicated stroke unit and maintain staff expertise. Many aspects of good stroke unit care, such as an interdisciplinary team, starting rehabilitation from day one, and regular team meetings, can be introduced in hospitals too small to support a stroke unit.

A number of Level IV studies, based mainly in North America and Germany, have developed and evaluated the safety and feasibility of services that effectively link regional and rural centres to specialist stroke centres in order to increase the reach of effective acute stroke therapy.³⁶⁻⁴² These studies generally involved a networked model that incorporated the following aspects:

- standardised protocols for rapid assessment, transfers and initiation of acute stroke management (e.g. rt-PA);
- 24 hour access to stroke specialist centres either via a simple phone link or more detailed online link

that includes live video footage and CT reports (described generally as ‘telestroke’); and

- educational support for smaller sites.

Overall most studies reported an improvement in process outcomes (e.g. time from event to CT, number of people admitted within 24 hours) as well as an increase in percentage of people receiving rt-PA (without an increase in haemorrhage or mortality). It is also noted that many of the regional centres were encouraged and supported to set up small stroke units further improving outcomes and building on the strength of the networks. While more robust data are needed the use of a networked model seems a logical approach for Australia where geography is a considerable barrier to best practice stroke care.

The National Stroke Unit Program⁴³ describes the structure, process and clinical profile of different categories of stroke services that can be used to aid the development of an appropriate, local stroke service.

1.3	ORGANISATION OF CARE FOR RURAL CENTRES	GRADE	LEVEL	CONSUMER RATING
a)	All health services caring for people with stroke should use networks which link large stroke specialist centres with smaller regional and rural centres.	D	Level IV 36, 37, 39, 42	–
b)	These networks should assist to establish appropriate stroke units along with protocols governing rapid assessment, pathways for direct communication with stroke specialist centres (“telestroke” services), and rapid transfers.	D	Level IV 36, 37, 39, 42	–

1.4 Care pathways

Clinical pathways (also known as care pathways or critical pathways) are defined as a plan of care that aims to promote organised and efficient multidisciplinary stroke care based on the best available evidence and guidelines.⁴⁴ Care pathways are one way of promoting organised and efficient patient care and hence improve outcomes. The definition, structure and detail contained within the pathway may vary from setting to setting.⁴⁵

A robust systematic review on the use of care pathways found that such interventions can have both positive and negative effects and concluded that there was insufficient evidence to justify routine use of care pathways.⁴⁴ However, of the three RCTs and 12 non RCTs included only one RCT and 7 non RCTs were initiated in the acute phase (three of the non RCTs were initiated in the hyper acute phase in the emergency department). When the acute trials were considered separately no negative effects were found while benefits of some patient outcomes (reduced length of stay, fewer readmissions and fewer urinary tract infections) as well as improved process outcomes (access to neuroimaging) were found.

Of the other outcomes reported a large proportion demonstrated non significant trends in favour of care pathway intervention.⁴⁴

Several subsequent Level III-3 & IV studies have found improved efficiency in acute processes primarily focused on increasing the number of people eligible for thrombolysis (e.g. door to CT and door to IV thrombolysis times).⁴⁶⁻⁴⁸ One other Level III-3 study failed to find benefits of an acute pathway when implemented on a general medical ward.⁴⁹

Overall there is a small body of generally consistent evidence that suggests care pathways can improve the process of care in acute stroke management where a number of investigations are needed in a short period of time, particularly when thrombolysis is considered. In the clinical setting, care pathways can provide a useful resource to optimise early stroke care, especially in settings without organised stroke care or where staff are frequently changing.

1.4	CARE PATHWAYS	GRADE	LEVEL	CONSUMER RATING
	All stroke patients admitted to hospital may be managed using an acute care pathway.	C	Level II ⁴⁴	–

1.5 Inpatient care coordinator

The use of an inpatient stroke care coordinator is one of a number of strategies used to facilitate a coordinated approach to care. The coordinator is generally a member of the team and the role is often performed in addition to other clinical or management responsibilities. Exponents of this model suggest that a stroke coordinator is particularly useful for coordinating services and facilitating the involvement of the person with stroke and the carer in care planning, including planning for discharge or transfer of care. One RCT and two lower level trials regarding

a case managed care intervention in which one person coordinates inpatient acute stroke care have been included within the review on inpatient care pathways.⁴⁴ The RCT reported a reduction in length of stay (11v14 days) and therefore lower costs as well as a reduction in returns to emergency departments. While a care coordinator was only one component of care (usually in combination to protocols or pathways) it is logical that such a position aids the organisation of services noted in stroke unit care settings.

1.5	INPATIENT CARE COORDINATOR	GRADE	LEVEL	CONSUMER RATING
	A stroke coordinator may be used to foster coordination of services and assist in discharge planning.	✓	–	–

1.6 Team meetings

Ongoing communication between the members of the stroke team is a key element of an organised stroke service. Data from trials included in the Stroke Unit meta-analysis found that organised stroke units were characterised by formal weekly meetings of the multidisciplinary team along with one or more informal

meetings.¹⁸ While this evidence relates to the total stroke unit “package” rather than the individual elements of that package, team meetings appear essential to foster good communication and coordinated services.

1.6	TEAM MEETINGS	GRADE	LEVEL	CONSUMER RATING
	The multidisciplinary stroke team should meet regularly (at least weekly) to discuss assessment of new patients, review patient management and goals, and plan for discharge.	C	extrapolated from Level I ¹⁸	–

1.7 Family meetings

Ongoing communication between the stroke team and the family/carer, with early involvement, is also a key element of an organised stroke service. Communication is established through formal and informal meetings to discuss assessment results, management plans and to also plan for discharge. Formal family meetings that involve members of the

stroke team (or the whole team) may not occur in every individual case, however, it is apparent that organised stroke unit care incorporates processes that informs and involves the patient and their family in all aspects of care. As such informal meetings should occur when stroke team members relay or discuss assessment findings or management plans.¹⁸

1.7	FAMILY MEETINGS	GRADE	LEVEL	CONSUMER RATING
	The stroke team should meet regularly with the person with stroke and the family/carer to involve them in management, goal setting and planning for discharge.	C	extrapolated from Level I ¹⁸	9.3/10

1.8 Information and education

The provision of information and education is particularly important for those with stroke and their families. However, written information may only be provided to a small percentage of patients and family/carers and when provided may not be written in a suitable readability level or design.⁵⁰ Furthermore, information is often not retained by those with stroke and their families highlighting the need to provide individualised, flexible and targeted information at different stages of recovery with opportunities provided to enable interaction with relevant stroke team members.

The evidence for interventions to improve information and education provision, however, is difficult to interpret. Two systematic reviews concluded that information provided in an educational context, especially an active educational-counselling approach, improves knowledge better than information provided in a booklet or leaflet (which was found to be ineffective if simply provided alone).^{51, 52} However, it is unclear if increased knowledge about stroke translates

into improved recovery and adjustment for people with stroke and their carers.⁵² Subsequent trials have reported mixed benefits from education interventions in line with conclusions reached by the systematic reviews. That is, some trials reported psychosocial benefits (e.g. reduced anxiety)⁵³⁻⁵⁸ or improved knowledge and/or compliance with treatment^{59, 60} however, most did not demonstrate any impact on functional outcomes and most were based in rehabilitation units or in the community.

Numerous other trials have assessed interventions to educate people with stroke and their family/carer, particularly after discharge from hospital (see section 8.7). In most of these trials the intervention was multifactorial and it is difficult to gauge the effect of education or information provision alone. State Stroke Associations and the National Stroke Foundation are able to provide written information including consumer versions of these guidelines and fact sheets that could be used as part of a comprehensive education program.

1.8	INFORMATION AND EDUCATION	GRADE	LEVEL	CONSUMER RATING
	All stroke survivors and their families/carers should be provided with timely, up-to-date information in conjunction with opportunities to learn via education from members of the interdisciplinary team and other appropriate community service providers. Simple information provision alone is not effective.	A	Level I 51, 52	9.4/10

1.9 Early supported discharge

Early supported discharge (ESD) is a model that links inpatient care with community services. ESD services should be considered an extension of stroke unit care rather than an alternative to it. A key argument for ESD is that the home provides an optimum rehabilitation environment, since the goal of rehabilitation is to establish skills that are appropriate to the home setting. Stroke survivors have reported greater satisfaction following ESD than conventional care.

Meta-analysis has found that ESD services reduce the inpatient length of stay and adverse events (e.g. readmission rates), while increasing the likelihood of being independent and living at home.^{61, 62} Risks relating to carer strain might be expected with ESD, but there is too little evidence to demonstrate whether or not this is

the case.^{61, 62} ESD predominantly involves people with mild to moderate disability and thus this service should target this group of stroke survivors.^{61, 62} Given the potential for increased patient satisfaction and reduced pressure on acute resources such services should be developed to provide comprehensive early supported discharge and follow up, particularly in centres where inpatient organised stroke services currently exist as development of such services should be the first priority.

To work effectively, ESD services must have similar elements to those of organised stroke teams (see characteristics of stroke units above). Thus ESD should only be considered where there are adequate community services for rehabilitation and carer support.

1.9	EARLY SUPPORTED DISCHARGE	GRADE	LEVEL	CONSUMER RATING
a)	Health services with organised inpatient stroke services should provide comprehensive interdisciplinary community rehabilitation and support services for people with stroke and their family/carer.	A	Level I ⁶¹⁻⁶³	–
a)	If interdisciplinary community rehabilitation services and carer support services are available, then early supported discharge should be offered for all stroke patients with mild to moderate disability.	A	Level I ^{61, 62}	8.5/10

1.10 Shared care

The organisation of services which link primary care and hospital and community services is an increasingly important area for good stroke care. While initial assessment and rehabilitation should be undertaken in an inpatient stroke unit, long term follow up focussing on secondary prevention and support is undertaken in general practice. A national survey of risk factors in general practice found 70% of patients aged over 30 had one or more risk factors and 34% had two or more.⁶⁴ Hypertension was the risk factor with greatest prevalence (44%), followed by hypercholesterolaemia (43%) and current smoking (17%) and all risk factors except smoking were found to increase with age.⁶⁴ Studies have also found that there is under treatment of TIA and stroke risks⁶⁵⁻⁶⁷ and hence there is considerable scope to further improve management.

One RCT found a model of shared care between hospital based stroke specialists and general practice (using a third party coordinator) demonstrated some improvement in the management of secondary prevention and management (including prevention)

of depression.⁶⁸ Other studies of post discharge support, commonly provided by a specialist nurse, may also be utilised to improve the link between hospital and primary care, however, the sustainability of such a service has not been evaluated. As the general practitioner (GP) is the hub of community health provision it is important to develop clear links between primary and secondary care. Networks have been suggested to improve such a link with several Level 4 studies showing the benefits of networks for hospital services (see section 1.3). Such networks could collaboratively develop local protocols or pathways for acute management, efficient discharge services and long term management. As stroke or TIA is less than 0.5% of a typical GP workload³³ and specialist stroke units with educated and skilled staff have consistently demonstrated improved patient outcomes, it would seem sensible for GPs, especially those in rural centres, to develop such networks with specialist stroke centres. Local divisions of practice are well placed to help facilitate any networks between stroke specialist centres and local GPs.

1.10	SHARED CARE	GRADE	LEVEL	CONSUMER RATING
a)	All patients with stroke or TIA should have their risk factors reviewed and managed long term by a general practitioner with input and/or referral to a stroke physician for specialist review where available.	C	Level II ⁶⁸	–
b)	Locally developed protocols and pathways should be used to efficiently link primary and secondary care for people with stroke or TIA, including rapid assessment and referrals, acute management, direct communication links, efficient discharge services and long term management.	✓	–	–
c)	Rural practitioners should participate in networks linking them to regional or metropolitan centres with specialty in stroke care.	✓	–	–

1.11 Standardised assessment

Complete assessment requires the input from all members of the stroke team. Such assessments are foundational to identify deficits, set goals and plan for management. While there is some evidence to suggest a structured assessment helps to identify particular problems⁶⁹ there is little direct evidence guiding what should be included and when such assessments should be carried out. It is recommended that all assessments occur as soon as possible after admission (aiming for within two days of admission) with the stroke team working together so as not to over burden the patient by duplicating questions. Weekend cover and workforce shortages are a continual issue for many centres and such issues will reduce the timeliness of assessments. Although reassessment is useful to monitor recovery and assist in planning, the timing of such assessments should consider the needs of the patient along with the usefulness of the findings. Communication of assessment findings to the patient and family/carer is essential.

Any assessment needs to also consider the ability of the patient to actually provide informed consent for further management. Such ability may be compromised following stroke (e.g. global aphasia) and all members of the multidisciplinary team must consider the rights of the patient during any assessment and management planning.

There are a large number of assessment tools that have been developed for use in acute stroke management (examples include National Institutes of Health Stroke Scale, Modified Rankin Score, Scandinavian Stroke Scale). However, given the enormous variety of assessment tools and measures it is beyond the scope of this guideline to make specific recommendations regarding which measures or tools should be used in each circumstance. It is important that all staff carefully chose a specific tool based on the validity, reliability and availability of such tools and be trained in the use of the chosen tool. It is also important to balance the use of a detailed assessment (which may take considerable time) with the need to provide early and active interventions.

1.11	STANDARDISED ASSESSMENT	GRADE	LEVEL	CONSUMER RATING
a)	Clinicians should use validated and reliable assessment tools or measures that meet the needs of the patient and guide clinical decision making.	✓	–	–
b)	Clinicians should provide timely and efficient assessment of patients with acute stroke. Where possible a multidisciplinary assessment should be undertaken and documented within two days of admission.	✓	–	–
c)	Assessment findings should be discussed at the team meeting and communicated to the patient and family/carer in a timely and appropriate manner.	✓	–	–

1.12 Palliation and death

Approximately 20% of stroke patients die as a result of the stroke in the first 30 days.⁷⁰ Palliation can be a complex phase of care and requires careful consideration and service planning. Issues to consider include linking with specialist palliative care services for direct care, intermittent referral, or clinical support on a needs basis. Other issues to consider include clinical issues such as feeding, hydration and pain management. There is often uncertainty during the

acute phase after a severe stroke as it is hard to predict if a patient will improve or not. Carer support, counselling and multidisciplinary care are basic principles of palliative care and need to be considered. Early discussion of prognosis and palliation may be beneficial for some family members/carers. Practical end-of-life issues, such as the use of medical power of attorney and advanced directives, should also be discussed. Organ donation may be sensitively raised if

appropriate. Issues of bereavement may become part of the responsibility of the stroke team and formal mechanisms should be in place to ensure the patient, their family and caregivers have access to bereavement care, general counselling, information and support services.

Evidence to guide palliative care in stroke is lacking. Only one low level study was identified that developed and implemented a care pathway for palliative care in acute stroke. The study reported improved processes of care based on national standards.⁷¹

While there are a number of systematic reviews in this area (primarily for cancer), there are insufficient studies to support specific interventions.^{72, 73} There is evidence

from systematic reviews to suggest communication skills training can have a small beneficial effect on behaviour change in health professionals working with people with cancer.^{74, 75} Thus education and training may be provided to those caring for stroke patients and their families to assist in the care of non-complex patients where specialist services are not routinely involved.

People with stroke who are dying, their families and caregivers, should have care that is consistent with the principles and philosophies of palliative care in accordance with the "Standards for Providing Quality Palliative Care for All Australians". This includes an integration of the physical, psychological, spiritual, cultural and social needs of all those involved.⁷⁶

1.12	PALLIATION AND DEATH	GRADE	LEVEL	CONSUMER RATING
a)	A pathway for acute stroke palliative care may be used to improve palliation for people dying after acute stroke.	D	Level IV ⁷¹	–
b)	An accurate assessment of imminent death should be made for patients with severe stroke or those who are deteriorating. Any assessment must consider prognostic risk factors along with the wishes of the patient and their family/carer.	✓	–	–
c)	Acute stroke patients should have access to specialist palliative care services as needed.	✓	–	–
d)	People with stroke who are dying, and their families, should have care that is consistent with the principles and philosophies of palliative care.	✓	–	–

1.13 Stroke service improvement

Stroke unit care has been shown to involve higher rates of adherence to key processes of care.²⁴ Thus it is important to monitor key processes and patient outcomes to foster improved service delivery. One important strategy to improve quality of care involves the process of audit and feedback. Audit and feedback has been found to produce small to modest improvements from a large number of wide ranging studies.⁷⁷ Audit and feedback has also been successfully used locally and internationally to both prompt service improvement and demonstrate

improved services.^{78, 79} However, quality improvement activities often use a multifaceted strategy such as educational meetings, reminders, printed material, or opinion leaders with or without audit and feedback.^{77, 80}

Experience from the National Sentinel Audit of Stroke in the UK suggests benefits of a cycle of comprehensive audit at least every two years.⁷⁹ However, services may benefit from more frequent audit based on a smaller number of key indicators by providing the ability to monitor continuous quality improvement activities.

1.13	STROKE SERVICE IMPROVEMENT	GRADE	LEVEL	CONSUMER RATING
a)	All acute stroke services should be involved in quality improvement activities that include regular audit and feedback ('regular' is considered at least every two years).	B	Level I ⁷⁷	–
b)	Indicators based on nationally agreed standards of care should be used when undertaking any audit. Performance can then be compared to similar stroke services as described by the National Stroke Unit Program.	✓	–	–

2 PRE-HOSPITAL CARE

There is growing evidence that good early stroke management can reduce damage to the brain and minimise the effects of stroke. Because of this early recognition of stroke the subsequent response of individuals to having a stroke and the timing and method by which people are transferred to hospital are important to ensure optimal outcomes. In this hyperacute phase of care, the ambulance service provides a central, coordinating role. Stroke patients should not only receive a high triage priority but the system should facilitate early notification of the receiving hospital and ensure that the correct hospital is selected (i.e. one with organised stroke unit care) where a choice exists.

Studies involving pre-hospital approaches have found:

- Education regarding the signs of stroke and the critical nature of stroke delivered to emergency medical service staff, emergency department staff and the general public increased the use of ambulance transport, decreased admission delays and improved the number of patients receiving thrombolysis.^{39, 81, 82} While it is unclear how often education should be provided to improve early recognition current practice suggested that local services should incorporate such education into routine, ongoing education at least annually.
- High priority by emergency medical services and early notification to hospital emergency departments improves efficient acute stroke management.⁸³⁻⁸⁵ However, this is one component

of a multifaceted strategy and it is difficult to determine the effect of this strategy alone.

- Preferential transportation to known stroke specialist centres, based on agreed local protocols, has been suggested in several low level studies.³⁹⁻⁴¹ Again, this is one component of a multifaceted strategy and it is difficult to determine the effect of this strategy alone. However, there are clear benefits for admission to a stroke unit. Hence, where practical (e.g. hospitals located within the same local area), ambulance services should transport patients with suspected stroke to hospitals with such organised services.
- Several validated pre-hospital screening tools have been developed, for example, the Los Angeles Prehospital Stroke Screen or the Melbourne Ambulance Stroke Screen (MASS).⁸⁶⁻⁸⁹
- Specific training for emergency medical services staff improves diagnostic accuracy and reduces pre-hospital delays.^{39, 83} For example, a one hour training session based on the only Australian tool, the MASS, increased the diagnostic accuracy of pre-hospital emergency service staff from 78 to 94%.⁸³
- Pre-hospital initiation by paramedics of intravenous magnesium sulphate has been shown to be feasible and safe in one small pilot study⁹⁰ and a subsequent RCT is ongoing.

2	PRE-HOSPITAL CARE	GRADE	LEVEL	CONSUMER RATING
a)	Ambulance services, health care professionals and the general public should receive education concerning the importance of early recognition of stroke, emphasising stroke is a medical emergency.	C	III-3 & IV ³⁹	9.5/10
b)	Stroke patients should be given a high priority grouping by ambulance services.	C	Level III-2 <small>83, 84</small>	9.6/10
c)	Ambulance services should be trained in the use of validated rapid pre-hospital stroke screening tools and incorporate such tools into protocols for all pre-hospital assessment of people with suspected stroke.	B	Level III-2 <small>86-89</small>	9.7/10
d)	Ambulance services should preferentially transfer suspected patients to a hospital with stroke unit care.	✓	–	–

The aim of assessment of a patient with suspected stroke or TIA is to confirm the diagnosis, identify and treat the cause, and guide relevant secondary prevention to prevent complications or stroke reoccurrence. Appropriate diagnosis of stroke and immediate referral to a stroke team is vital given advances in hyperacute treatments. Strong working relationships are required between emergency department staff and the stroke team to improve timely assessment and early management.

Section 3 as a whole was given a consumer rating of 9.7/10.

3.1 Assessment of TIA

There are strong similarities between minor ischaemic stroke and TIA and hence principles of assessment and management should follow that outlined for people with ischaemic stroke including secondary prevention. This section discusses aspects of care that are specific for people with TIA. The organisation of care for people with TIA is discussed in section 1.2.

Definition and prognosis

TIA is defined as “rapidly developed clinical signs of focal or global disturbance of cerebral function lasting fewer than 24 hours, with no apparent non-vascular cause” although revision of this definition has been suggested to shorten the timeframe to 1 hour as TIAs rarely last longer than this timeframe.⁹¹ More recent data have highlighted a higher and earlier risk of subsequent stroke with TIA than previously reported (2.5-5% at 2 days; 5-10% at 30 days; 10-20% at 90 days).⁹²⁻⁹⁸ It is noted that approximately half of the early risk is seen within the first 48 hours necessitating early diagnostic workup and earlier treatments to prevent further events. Given the significant cost and impact of stroke it is clear that attention is needed to improve the efficiency of diagnosis and management of TIA and thus prevent subsequent stroke.

Assessment

As with stroke, an accurate clinical assessment should be followed by routine investigations such as a full blood picture, electrolytes, renal function, cholesterol level, glucose level, and electrocardiogram (see section 3.4). Imaging should also be undertaken. The presence of new CT changes within 48 hours after TIA

was found to predict stroke risk in a retrospective prognostic study, however, such changes were only identified in a small number of cases (4%).⁹⁹ As with ischaemic stroke, CT is useful to exclude differential diagnosis that could mimic TIA and should be used to exclude subdural haematoma or brain tumour and should be undertaken early in all patients.¹⁰⁰ Magnetic resonance diffusion weighted imaging (MR-DWI) is the imaging strategy of choice for patients with suspected TIA with studies detecting ischaemic changes in 16-67% of those with TIA signifying infarction.¹⁰¹ MR-DWI may also assist risk stratification and direct management; although further large studies are needed to confirm that an infarction detected by MR-DWI is a clear prognostic indicator of stroke.¹⁰¹

The presence of symptomatic carotid disease increases risk of stroke in patients with TIA.⁹⁴ Carotid investigations should therefore be carried out urgently when an arterial source is suspected and carotid surgery considered (see section 3.3 and 7.6).¹⁰²

Risk factor assessment and stratification

Five factors have been identified as risks for early stroke after TIA including age (>60years), diabetes mellitus, longer symptom duration (> 10 mins), motor or speech symptoms of TIA, and high blood pressure (> 140/90mmHg).³⁵

Two simple risk stratification tools for TIA have been validated in different populations.^{35, 103, 104} These two risk tools have recently been combined and validated with the combined tool (ABCD²) found to be more predictive than either of the two tools alone.³⁵

The combined tool has a maximum score of 7 and is described below.

ABCD² Tool³⁵

- A** AGE: ≥ 60 years (1 point)
- B** BLOOD PRESSURE: ≥ 140/90mm Hg (1 point)
- C** CLINICAL FEATURES: unilateral weakness (2 points), speech impairment without weakness (1 point)
- D** DURATION: >60mins (2 points), 10-59 mins (1 point); and
- D** DIABETES (1 point)

Scores 6-7 indicate a high risk (8.1% 2-day risk; 21% of TIA cohorts in validation studies); Scores 4-5 indicate a moderate risk (4.1% 2-day risk; 45% total TIA cohorts); and 0-3 indicate low risk (1% 2-day risk; 34% of TIA cohorts).³⁵ Based on studies looking at the original ABCD tool, a cut off of 4 has been suggested to differentiate high and low risk¹⁰³ and this more

simple scoring has been agreed by the working group to be used in these guidelines using the ABCD² tool. Hence those with >4 are designated HIGH risk and those ≤4 are LOW risk.

ABCD² Tool interpretation¹⁰³
>4 = HIGH risk; ≤4 = LOW risk

3.1	ASSESSMENT OF TIA	GRADE	LEVEL
a)	All patients with suspected TIA should have a full assessment that includes assessment of stroke risk using the ABCD ² tool at the initial point of health care contact whether first seen in primary or secondary care.	B	Level II ³⁵
b)	The following investigations should be undertaken routinely for all patients with suspected TIA: full blood count, electrolytes, renal function, cholesterol level, glucose level, and electrocardiogram.	–	–
c)	Patients classified as high risk (ABCD ² >4) should have an urgent CT brain ('urgent' is considered as soon as possible, but certainly within 24 hours). Carotid duplex ultrasound territory symptoms who would potentially be candidates for carotid re-vascularisation. Patients classified as low risk (ABCD ² ≤4) should have a CT brain and carotid ultrasound (where indicated) as soon as possible (i.e. within 48-72 hours).	B	Level I ^{35, 100, 102} & Level III-3 ⁹⁹

3.2 Triage in emergency department

Although there is little direct evidence it is essential to undertake a good medical assessment including accurate history and assessment of presenting symptoms. Assessment of acute stroke using stroke specific scales varies widely. The more commonly used acute assessment scales, for example, the National Institutes of Health Stroke Scale (NIHSS), only measure stroke impairment or severity but such scales have prognostic value.^{106, 107} Such scales also require experience and formal training and as such, other tools have been developed for use by staff not as familiar with stroke.

Studies aimed at improving the organisation of services to provide rapid and accurate assessment in emergency departments have found the following:

- A small number of studies have found a high diagnostic accuracy (approximately 90% sensitivity) by emergency medical staff.¹⁰⁸⁻¹¹⁰ However the selection of hyperacute therapy often depends on an accurate diagnosis to be confirmed by a stroke

specialist and approximately 20-30% of cases are incorrectly diagnosed as stroke or TIA¹¹¹ suggesting the need for a close working relationship between emergency department staff and stroke specialists.¹¹⁰

- Of the diagnostic screening tools specifically used in emergency departments that have been developed to aid the triage process, only the ROSIER scale has been adequately studied. The scale has been found to sensitively identify stroke mimics thereby helping emergency department staff make appropriate referral to the stroke team.¹¹²
- The use of pathways or protocols has been found to reduce hospital delays for acute care in several, mostly non-randomised, studies.^{44, 46-48, 113} Such tools ensure that patients receive appropriate and timely medical and nursing assessments along with crucial investigations (refer to discussion on care pathways, section 1.4).

- A notification system between emergency medical services staff, emergency department staff and the stroke team has also been found to reduce intrahospital delays and improve patient related outcomes (those benefiting from receiving thrombolysis).^{39, 83-85}
- One non-randomised study reported benefits from a process of reorganisation of services that included establishing a nurse led triage team specifically for neurological patients, improved prenotification by ambulance staff of patients eligible for rt-PA, and

introducing a small CT unit within the emergency department for priority imaging.⁸⁵ While the proximity of the CT unit was seen as a key component in this study it is optimistic to consider this a feasible strategy for most departments.

- Education of emergency department staff has also been undertaken as part of a multidimensional strategy with improvements noted in processes of care (for example, reduced delays to CT and increased numbers receiving thrombolysis).^{39, 81, 82}

3.2	TRIAGE IN EMERGENCY DEPARTMENT	GRADE	LEVEL
a)	Diagnosis should be reviewed by a clinician experienced in the valuation of stroke.	C	Level III-3 108, 111
b)	Emergency department staff should use a validated stroke screen tool to assist in rapid accurate assessment for all people with stroke.	C	Level II ¹¹²
c)	Local protocols developed jointly by staff from pre hospital emergency services, the hospital emergency department and the stroke unit should be used for all people with suspected stroke. Such protocols should include early notification by paramedic staff, high priority transportation and triage, rapid referrals from ED staff to stroke specialists and rapid access to imaging.	D	Level III-3 & IV ^{39, 83, 85}

3.3 Imaging

A. Brain imaging

Stroke and TIA are clinical diagnoses with brain imaging available to confirm cerebral ischaemia or haemorrhage and exclude stroke mimics. One robust systematic review reported the most cost effective strategy in acute stroke is for all patients to undergo immediate imaging.¹⁰⁰ Recent studies have found that MRI is more sensitive than CT for ischaemic changes and is as sensitive as CT in identifying acute haemorrhagic change.^{114, 115} CT is sensitive to ICH in the acute phase but not after 8-10 days when MRI should be used to differentiate ICH and ischaemic stroke.¹⁰⁰ Thus to confirm diagnosis and differentiate ICH from ischaemic stroke, MRI is now considered the imaging strategy of choice. Consideration of several factors including longer imaging time and limited availability of MRI scanners in many centres compared to CT, however, limits the application of MRI as a

routine strategy and it is likely that CT will remain the imaging modality of first choice for the foreseeable future.

B. Carotid Imaging

In patients with carotid territory symptoms and where a large artery disease is suspected, carotid imaging studies should be performed. A recent robust systematic review comparing non invasive tests to conventional intra arterial angiography found that non invasive methods provide good accuracy, in particular contrast enhanced magnetic resonance angiography (CEMRA), in patients with 70-99% stenosis. Other methods (Doppler ultrasound, Magnetic Resonance angiography, Computed Tomography Angiography) were found to be less accurate than CEMRA but still reasonably good with CTA found to have the lowest accuracy.¹⁰² It was noted that CEMRA is a relatively new test and not all patients would have access to

this test. Doppler ultrasound is widely available and useful in most centres. Non invasive measures for symptomatic events were much less accurate for patients with 50-70% stenosis, however, too few data exist and no clear conclusions can be made.¹⁰² Carotid surgery is most beneficial early after non-severely disabling stroke (see section 7.7) and hence carotid imaging should be undertaken as part of the initial diagnostic workup in selected patients.

C. Cardiac imaging

Echocardiography may be considered to determine a potential cardioembolic source in selected patients

(e.g. history of cardiac abnormalities or an abnormal electrocardiogram where there are no current indications for anticoagulation or in patients with stroke of unknown origin after standard diagnostic workup).¹¹⁶ Transthoracic echocardiography (TTE) is less invasive but less sensitive than transesophageal echocardiography (TEE) in detecting sources of cardiac emboli in patients with TIA or stroke.¹¹⁶ TEE also appears more useful than TTE in assisting clinical decision making (i.e. aid decision whether to commence anticoagulation or not).¹¹⁷

3.3	IMAGING	GRADE	LEVEL
a)	All patients with suspected stroke should have an urgent brain CT or MRI ('urgent' is considered as soon as possible, but certainly less than 24 hours).	A	Level I diagnostic study ¹⁰⁰
b)	A repeat brain CT or MRI should be considered urgently when a patient's condition deteriorates.	✓	–
c)	All patients with carotid territory symptoms who would potentially be candidates for carotid re-vascularisation should have an urgent carotid duplex ultrasound.	B	Level I ¹⁰²
d)	Further brain, cardiac or carotid imaging should be undertaken in selected cases including: <ul style="list-style-type: none"> • Patients where initial assessment has not confirmed likely source of ischaemic event; • Patients with a history of more than one TIA; • Patients likely to undergo carotid surgery. 	B	Level I ^{100, 102} and Level III-2 ¹¹⁶

3.4 Investigations

Once clinical diagnosis has been made, investigations are used to confirm the diagnosis and to determine the potential cause of the event, specifically if there is a cardiac or arterial source. Routine investigations should include full blood count, electrolytes, renal function, cholesterol and glucose levels and electrocardiogram although direct evidence is lacking for each of these investigations. If clinical history, imaging and routine investigations do not adequately

diagnose the underlying cause then further investigations may be warranted. Many tests exist and need to be considered based on individual patient needs. For example, thrombophilia screening may be needed when the clinical history identifies a family history of thrombosis (particularly for those <50 years old). Some tests should be regularly repeated to allow for careful monitoring in the acute period (see section 4.3.1).

3.4	INVESTIGATIONS	GRADE	LEVEL
a)	The following investigations should be obtained routinely in all patients – full blood picture, electrocardiogram, electrolytes, renal function, fasting lipids, erythrocyte sedimentation rate and/or C-reactive protein, and glucose.	✓	–
b)	Selected patients may require the following additional investigations: angiography, chest x-ray, syphilis serology, vasculitis screen and prothrombotic screen. These tests should be performed as soon as possible after stroke onset, and in selected patients, some of these tests may need to be performed as an emergency procedure.	✓	–

Section 4 as a whole was given a consumer rating of 10/10.

4.1 Ischaemic stroke and TIA

4.1.1 Early management of TIA

Management of TIA involves early risk factor management to prevent further ischaemic events. An initial policy of commencing aspirin as soon as haemorrhage has been excluded on CT or MRI is recommended early after ischaemic event (see Section 4.1.3). While there is a lower long term risk of stroke in those with TIA and AF compared to previous stroke and AF¹¹⁸ there is strong evidence for the long term use of anticoagulation in patients with concomitant AF.^{118, 119} Other secondary prevention management is the same as that outlined for those with stroke (see Section 7).

4.1.2 Thrombolysis

Two systematic reviews have been undertaken to determine the benefits of thrombolysis in acute ischaemic stroke.^{120, 121} Four different agents have been evaluated: streptokinase, recombinant pro-urokinase, recombinant tissue plasminogen activator (rt-PA) and urokinase. Most of the data are from trials of intravenous thrombolysis involving rt-PA. Results found:

- Thrombolysis in all trials and all agents combined results in a significant reduction in the composite end-point of death or disability;
- Thrombolysis (all agents pooled) shows a net benefit, but is associated with a definite risk of intracerebral haemorrhage and increased mortality at the end of 3 or 6 month follow-up.
- Heterogeneity between the trials was evident and no clear evidence for one agent, dose or route was found. There was indirect evidence that rt-PA may have more benefit and less hazard.
- Therapy appears most beneficial if provided in experienced centres in highly selected patients. Widespread use of thrombolytic therapy in routine

clinical practice in non organised stroke care is not recommended.¹²⁰

Subsequent pooled analysis from the rt-PA trials confirm that treatment with intravenous rt-PA has a clear net benefit in reducing the odds of death or dependency if given within 3 hours.¹²² Cases treated within 3 hours showed 30% greater odds of functional independence with a 12% absolute difference between the rt-PA treatment group and placebo treated patients (number needed to treat of approximately 8).¹²² Treatment given between 3-6 hours from stroke onset also appears promising and further trials are underway (e.g. IST-3, ECASS-III).

Subsequent phase IV studies have generally demonstrated similar outcomes to the major phase III studies.¹²³ Protocol deviation has been identified across one network of hospitals as a potential reason for poorer clinical outcomes in routine practice as compared to the outcomes obtained in the treatment arms of the randomised trials.¹²⁴ However, an audit and quality improvement process in these same hospitals subsequently demonstrated a reduction in protocol violations (50% down to 19.1% following the quality improvement) and an associated decline in adverse events from 15.7% to 6.4%.¹²⁵ Close monitoring of outcomes, audit and quality improvement activities are, therefore, strongly recommended for all centres delivering rt-PA. The international "Safe Implementation of Thrombolysis in Stroke" (SITS) register is available to support data collection, audit and benchmarking across centres and across countries. Recent safety and clinical outcome data from the European arm of the SITS registry suggests lower adverse events than those seen in the clinical trials of rt-PA.¹²⁶ Current Australian data are comparable to the international data and are shown in the table below.

OUTCOME	AUSTRALIA*	WORLDWIDE SITS	PHASE III tPA DATA**
Independent at 3 months	51.4%	49.9%	50.1%
Symptomatic ICH	1.0%	1.7%	8.6%
Mortality	14.1%	13.9%	15%

Table 1. Safe Implementation of Thrombolysis in Stroke (SITS) register. Summary as of end of June 2007 * 393 total cases entered ** Phase III tPA data¹²²

Intravenous rt-PA was licensed by the Australian Therapeutic Goods Administration for use in acute ischaemic stroke in October 2003. While it is not feasible for all hospitals to deliver stroke thrombolysis due to local resources, a number of Australian hospitals with organised stroke care and acute stroke

units have demonstrated an ability to safely administer rt-PA.^{127, 128} Table 2 outlines the patient selection criteria for the safe and effective delivery of rt-PA. These criteria are adapted from the inclusion and exclusion criteria for the NINDS rt-PA trial.¹²⁹

Patient Selection Criteria	
Indications	
1	Onset of ischaemic stroke within the preceding 3 hours.
2	Measurable and clinically significant deficit on NIH Stroke Scale examination.
3	Patient's computed tomography (CT) does not show haemorrhage or non-vascular cause of stroke.
4	Patient's age is >18 years.
Contraindications: ABSOLUTELY Do NOT administer tPA if any of these statements are true:	
1	Uncertainty about time of stroke onset (e.g. patients awaking from sleep)
2	Coma or severe obtundation with fixed eye deviation and complete hemiplegia.
3	Only minor stroke deficit which is rapidly improving.
4	Seizure observed or known to have occurred at onset of stroke.
5	Hypertension: systolic blood pressure \geq 185mmHg; or diastolic blood pressure $>$ 110mmHg on repeated measures prior to study.
6	Clinical presentation suggestive of subarachnoid haemorrhage even if the CT scan is normal.
7	Presumed septic embolus.
8	Patient having received heparin with the last 48 hours and has elevated PTT or has a known hereditary or acquired haemorrhagic diathesis (e.g. PT or APTT greater than normal).
9	INR $>$ 1.5.
10	Platelet count is $<$ 100,000 μ L.
11	Serum glucose is $<$ 2.8mmol/l or $>$ 22.0 mmol/l.
RELATIVE Contraindications: If any of the following statements is true, use tPA with caution. In each situation careful consideration of the balance of the potential risks and benefits must be given:	
1	Severe neurological impairment with NIH Stroke Scale score $>$ 22.
2	Age $>$ 80 years.
3	CT evidence of extensive middle cerebral artery (MCA) territory infarction (sulcal effacement or blurring of gray-white junction in greater than 1/3 of MCA territory).
4	Stroke or serious head trauma within the past 3 months where the risks of bleeding are considered to outweigh the benefits of therapy.
5	Major surgery within the last 14 days.
6	Patient has known history of intracranial haemorrhage, subarachnoid haemorrhage, known intracranial arteriovenous malformation or previously known intracranial neoplasm that, in the opinion of the clinician, the increased risk of intracranial bleeding would outweigh the potential benefits of treatment.
7	Suspected recent (within 30 days) myocardial infarction.
8	Recent (within 30 days) biopsy of a parenchymal organ or surgery that, in the opinion of the responsible clinician, would increase the risk of unmanageable (e.g. uncontrolled by local pressure) bleeding.
9	Recent (within 30 days) trauma with internal injuries or ulcerative wounds.
10	Gastrointestinal or urinary tract haemorrhage within the last 30 days or any active or recent haemorrhage that, in the opinion of the responsible clinician, would increase the risk of unmanageable (e.g. by local pressure) bleeding.
11	Arterial puncture at noncompressible site within the last 7 days.
12	Concomitant serious, advanced or terminal illness or any other condition that, in the opinion of the responsible clinician would pose a risk to treatment.

Table 2: Patient selection criteria for potential eligibility for rt-PA

Based on the evidence, intravenous rt-PA therapy is beneficial for select patients but should be delivered in well equipped and skilled emergency departments and/or stroke care units with adequate expertise and infrastructure for monitoring, rapid assessment and investigation of acute stroke patients. Collaboration between clinicians in pre-hospital emergency services, emergency medicine, neurology and neuroradiology is recommended to foster prompt identification of potentially eligible patients, expert patient selection along with audit and quality improvement initiatives.

There are a significant number of other studies (a non exhaustive number of references are noted below), most of which are small Level III or IV studies (only a few are Level II studies) that have evaluated the following either alone or in combination with intravenous thrombolysis:

- the use of other agents (e.g. tenecteplase, reteplase, desmoteplase).¹³⁰⁻¹³³ While some agents appear promising, others have failed to show clear benefits. Further data are needed and until so the use of such agents should only be considered within a clinical trial setting.
- intra-arterial (IA) thrombolysis.^{121, 134-141} Only one moderate sized RCT has been completed which reported benefits of IA thrombolysis with prourokinase.¹⁴⁰ Many non controlled studies and a couple of very small RCTs also report benefits (either using IA therapy alone or in addition to IV rt-PA). Use of IA thrombolysis requires considerable resources and while it may be promising (particularly for basilar artery thrombosis and middle artery

thrombosis seen within 6 hours who are either not eligible for IV rt-PA or who do not respond to IV rt-PA) its widespread implementation within Australia is currently limited. Further robust, large studies are needed.

- ultrasound assisted therapy in addition to intravenous thrombolysis.¹⁴²⁻¹⁴⁶ This is an evolving field and robust evidence is needed before this experimental approach could be considered in routine clinical care.
- mechanical thrombolysis.¹⁴⁷⁻¹⁵³ Recanalisation rates have been found to be similar between trials using the MERCI device and IV and IA thrombolysis. As with IA thrombolysis the use of mechanical retrieval devices is limited to a small number of centres with adequate resources and expertise. Further studies are needed (along with appropriate approval) before clear recommendations for Australian centres can be made.
- anticoagulation or antiplatelet agents.^{135, 154, 155}

Advanced MR and CT imaging techniques may identify ischaemic but potentially viable brain tissue beyond the 3 hour time window. These techniques are currently under evaluation as a means of selecting patients likely to benefit from intravenous rt-PA and other thrombolytic therapies at treatment windows out to 9 hours after symptom onset. While some of the patient selection techniques and other forms of thrombolysis appear promising, data from large, RCTs evaluating long-term functional outcomes are needed before definitive recommendations can be made.

4.1.2	THROMBOLYSIS	GRADE	LEVEL
a)	Intravenous rt-PA in acute ischaemic stroke should only be undertaken in patients satisfying specific inclusion and exclusion criteria	A	Level I ^{120, 122}
b)	Intravenous rt-PA in acute ischaemic stroke should be given under the authority of a specialist physician and interdisciplinary acute care team with expert knowledge of stroke management, experience in the use of intravenous thrombolytic therapy and with pathways and protocols available to guide medical, nursing and allied health acute phase management. Pathways or protocols must include guidance in acute blood pressure management.	C	Level I ¹²⁰ & Level IV ¹²³
c)	Thrombolysis should only be undertaken in a hospital setting with appropriate infrastructure, facilities and networks.	✓	–
d)	A minimum set of de-identified data from all patients treated with thrombolysis should be recorded in a central register to allow monitoring, review, comparison and benchmarking of key outcomes measures over time.	C	Level IV ¹²⁶

4.1.3 Antithrombotic therapy

Evidence predominantly from two large trials found improved outcomes when aspirin (160-300mg) is commenced within 48 hours in patients with ischaemic stroke.¹⁵⁶ While there is a small increase in intracranial haemorrhage there is a definite net benefit for use of this therapy.

Anticoagulation (e.g. intravenous unfractionated heparin) has a potentially more potent antithrombotic effect and demonstrates greater protection from clots in the leg or lungs (see section 6.2), however, the harm of increased bleeding negates any such benefits when compared with aspirin even in patients with cardioembolic stroke.^{157, 158}

Uncommon presentations may lead to consideration of early anticoagulation in special circumstances. Patients with arterial dissection may be one such case. Arterial dissection involves a tear developing along the inner lining of the artery which is then prone to clotting and causing stroke. Dissection is rare (2.5% of all strokes) but is more frequent in patients under 45 years old (5-22%).¹⁵⁹ There is currently no RCT evidence for the choice of antithrombotic therapy with lower level studies suggesting no difference in outcomes between antiplatelet and anticoagulation therapy with only a small number (0.5%) of ICH in such patients.¹⁵⁹

4.1.3	ANTITHROMBOTIC THERAPY	GRADE	LEVEL
a)	Aspirin (150-300mg) should be given as soon as possible after the onset of stroke symptoms (i.e. within 48 hours) if CT/MRI scan excludes haemorrhage.	A	Level I ¹⁶⁰
b)	The routine use of anticoagulation (e.g. intravenous unfractionated heparin) in unselected patients following ischaemic stroke/TIA is not recommended.	A	Level I ^{157, 158}

4.1.4 Blood pressure lowering therapy

While there is strong evidence for lowering blood pressure for secondary prevention (see section 7.2), acute blood pressure therapy (i.e. within first 48 hours) remains controversial with both high and low blood pressure found to negatively affect patient outcomes.^{161, 162} It is unclear from a limited number of small studies if therapy to lower (or raise) blood pressure clearly improves patient outcomes and what

agent should be used although large RCTs are underway.^{161, 163, 164} In the absence of clear data there was consensus that in patients with severe hypertension, commencing or increasing blood lowering therapy should be considered. Close monitoring with or without therapy is also recommended (see section 4.3.1).

4.1.4	BLOOD PRESSURE LOWERING THERAPY	GRADE	LEVEL
a)	If extremely high blood pressure (e.g. BP > 220/120) exists, instituting or increasing antihypertensive therapy may be started, but blood pressure should be cautiously reduced (e.g. by no more than 10-20%) and the patient observed for signs of neurological deterioration.	✓	–
b)	Pre-existing antihypertensive therapy may be continued (orally or via nasogastric tube) provided there is no symptomatic hypotension or other reason to withhold treatment.	✓	–

4.1.5 Surgery for ischaemic stroke

Hemicraniectomy for ischaemic stroke should be considered for large middle cerebral artery (MCA) infarcts where prognosis is poor, so called “malignant infarction”. A meta-analysis of three RCTs found benefits (reduced mortality and improved functional outcomes for those surviving) of decompressive surgery in conjunction with medical therapy compared with medical therapy alone.¹⁶⁵ Such benefits were seen in selected patients only who fulfilled clear inclusion criteria (e.g. those between 18- 60 years old who can undertake surgery within 48 hours of symptom onset, with clinical deficits suggesting significant MCA involvement).¹⁶⁵ Given the prognosis

for patients with ‘malignant’ or significant middle artery occlusion an urgent referral to a neurosurgical consultant is strongly recommended.

One recent robust systematic review failed to find any RCTs for the use of angioplasty and stenting for intracranial artery stenosis.¹⁶⁶ Evidence from case series with three or more cases, demonstrated an overall perioperative rate of stroke of 7.9%, perioperative death of 3.4%, and perioperative stroke or death of 9.5%. Robust data are required before clear conclusions can be made regarding this intervention.

4.1.5	SURGERY FOR ISCHAEMIC STROKE	GRADE	LEVEL
a)	Selected patients (e.g. 18-60 years where surgery can occur within 48 hours of symptom onset) with significant middle cerebral artery infarction should be urgently referred to a neurosurgeon for consideration of hemicraniectomy.	A	Level I ¹⁶⁵
b)	There is currently insufficient evidence to make recommendations about the use of intracranial endovascular surgery.	–	Level I ¹⁶⁶

4.2 Intracerebral haemorrhage (ICH)

In general the treatment of ICH is similar to that for ischaemic stroke (e.g. rapid assessment, routine investigations, and prevention of complications). This section addresses medical and surgical management that is specific for patients with ICH.

Medical management

Haematoma growth is predictive of mortality and poor outcomes after ICH.¹⁶⁷ Despite a phase II trial of a haemostatic agent, recombinant activated factor VII (rFVIIa), showing reduction in haematoma growth and reduced disability and mortality at 3 months¹⁶⁸ a subsequent trial, the FAST trial, not yet published, while also showing significant reduction in haematoma growth at 24 hours, did not confirm the earlier findings of a clinical benefit. At this time the use of rFVIIa in the treatment of intracerebral haemorrhage should be considered experimental and further trials are needed before recommendations on the usefulness in routine clinical practice can be made.¹⁶⁹

Neuroprotective agents that have been tested have found no clear benefits in patients with ICH.¹⁷⁰ Citicoline has been evaluated in a very small phase I study and further, larger studies are needed.¹⁷¹ Corticosteroids, glycerol and

Mannitol have all failed to demonstrate benefits in patients with ICH.¹⁷²⁻¹⁷⁴

While there is consensus that ICH, due to anticoagulation, should be urgently reversed there is no clear consensus about which strategies to choose due to the lack of good quality data.^{175, 176} Traditional approaches include administration of prothrombin complex concentrate (PCC), fresh-frozen plasma (FFP), or vitamin K (if used in addition to other strategies).^{175, 176} Off-label use of rFVIIa alone or in combination with FFP has also been reported in small Level IV studies but is viewed as experimental only.^{177, 178}

Management of acute blood pressure is particularly important, however, currently no randomised studies have been completed to guide treatment. One Level IV study with only 27 patients reported a protocol of keeping blood pressure below 160/90mmHg was feasible and safe with a low percentage of haematoma growth.¹⁷⁹ Until more robust data becomes available it is generally accepted that blood pressure lowering in ICH patients with a history of hypertension is indicated only to keep mean arterial blood pressure (MAP) below 130mmHg (MAP=diastolic BP +1/3(systolic-diastolic BP)).

Surgical management

Surgical management decisions have been clarified over the last few years with the STICH trial finding no clear benefits for routine surgery over conservative management.¹⁸⁰ A subsequent systematic review, that included the STICH trial, confirmed that there is no overall benefit.¹⁸¹ However, subgroup analysis found two specific groups of patients who may benefit from surgery: patients with deep ICH if stereotactic surgery is used,

and patients with superficial (<1cm from surface) haematoma when craniotomy is performed.^{180, 181} There is currently no prospective RCT to guide surgery for those with cerebellar ICH. Again, there is general agreement that surgery should be considered if cerebella haematomas are >3cm in diameter or where hydrocephalus occurs, although advanced age and coma reduce favourable outcomes and need to be considered.¹⁸²

4.2	INTRACEREBRAL HAEMORRHAGE (ICH)	GRADE	LEVEL
a)	The use of haemostatic drug treatment with rFVIIa is currently considered experimental and is not recommended for use outside a clinical trial.	B	Level I ¹⁶⁹
b)	The routine use of surgery is not recommended for patients with supratentorial haematoma but may be considered in certain circumstances, including: <ul style="list-style-type: none"> • stereotactic surgery for patients with deep ICH; • craniotomy for patients where haematoma is superficial (<1cm from surface) 	C C	Level I ¹⁸¹ Level II ¹⁸⁰
c)	Surgical evacuation may be undertaken for cerebellar hemisphere haematomas >3cm diameter in selected patients.	✓	–
d)	In ICH patients who have a history of hypertension, mean arterial pressure should be maintained below 130 mm Hg.	✓	–

4.3 General acute stroke care

This section addresses acute care that is the same for ischaemic and haemorrhagic stroke. Early physiological changes including hypertension, hypotension, hyperglycaemia, fever, and hypoxia have all been shown to be associated with poor outcomes after stroke and general measures should be initiated to monitor and manage such changes in the acute phase.^{161, 183, 184}

4.3.1 Physiological monitoring

One small RCT¹⁸⁵ and two non randomised trials^{186, 187} have found that monitoring in the first 2 days after

stroke enhances the benefits of conventional stroke unit care. However the intensity (e.g. continuous or every 2-6 hours) and duration (e.g. 24-72 hours) of such monitoring is still unclear and further larger studies including cost effectiveness data are required. However, it is clear that due to the current focus on hyperacute management regular monitoring is needed that reflects individual patient needs as well as balancing the need for early rehabilitation to commence.

4.3.1	PHYSIOLOGICAL MONITORING	GRADE	LEVEL
	Patients should have their neurological status (including Glasgow Coma Scale) and vital signs including pulse, blood pressure, temperature, oxygen saturation, glucose, and respiratory pattern monitored and documented regularly during the acute phase, the frequency of such observations being determined by the patient's status.	C	Level II ¹⁸⁵ & Level III-2 ^{186, 187}

4.3.2 Oxygen therapy

One systematic review of hyperbaric oxygen therapy concluded that there is insufficient evidence to demonstrate clear benefits.¹⁸⁸ One preliminary study of normobaric oxygen therapy found short term improvements in stroke severity scales but no difference in patient outcomes at 3 months.¹⁸⁹

Many centres represented in the stroke unit trials data had management policies for oxygen therapy¹⁸ and until further evidence is available there is consensus that in patients found to be hypoxic oxygen therapy should be provided.

4.3.2	OXYGEN THERAPY	GRADE	LEVEL
	Patients who are hypoxic should be given oxygen supplementation.	✓	–

4.3.3 Glycaemic control

Hyperglycaemia after stroke is commonly found in 1/3 of patients although reported prevalence varies between 8-83% depending on the cohort and definition.¹⁹⁰ Observational data indicates that hyperglycaemia fluctuates in the first 72 hours in non diabetic as well as diabetic patients even with current best practice.¹⁹¹ Observational data also demonstrates poorer outcomes for non diabetic patients with hyperglycaemia¹⁹⁰ and the prevalence of undetected diabetes ranges from 16-24% of patients.^{192, 193} Patients with glucose intolerance after stroke is also common (approximately

25%)^{193, 194} and linked to higher stroke recurrence (see section 7.6).¹⁹⁵ Given these facts, acute monitoring and management appear important although evidence is scarce. Two pilot studies found glucose infusion to be safe and feasible.^{196, 197} However, a recent large follow up of one study investigating aggressive maintenance of euglycaemia via glucose-potassium-insulin infusion failed to demonstrate benefits.¹⁹⁸ There is consensus that management should be commenced in patients with hyperglycaemia, however, further data are needed to determine the most appropriate management strategies.

4.3.3	GLYCAEMIC CONTROL	GRADE	LEVEL
a)	Patients with hyperglycaemia should have their blood glucose level monitored and appropriate glycaemic therapy instituted to ensure euglycaemia, especially if the patient is diabetic. Hypoglycaemia should be avoided.	✓	–
b)	Intensive, early maintenance of euglycaemia is currently not recommended.	B	Level II ¹⁹⁸

4.3.4 Neuroprotective agents

A large number of neuroprotective agents have been studied in clinical trials, however, none have demonstrated clear robust benefits and hence cannot be recommended for routine use.¹⁹⁹⁻²⁰² One robust RCT of NXY-059 was found to have some benefits (reduced disability at 90 days), but it did not significantly improve other outcome measures (e.g. neurological functioning as measured by the NIHSS score).²⁰³ The follow up trial has not been published in full, however, the summary of results was released and failed to confirm the beneficial effects seen in the earlier trial. At this stage, NXY-059 cannot be recommended for routine use.

Other groups of agents including colony stimulating factors (including erythropoietin, granulocyte colony

stimulating factor and analogues),^{204, 205} theophylline, aminophylline, caffeine and analogues,²⁰⁶ have too few data and further trials are required before clear conclusions can be made.

A number of trials have found potential benefits from initial small trials, for example albumin,²⁰⁷ Edaravone ²⁰⁸ and arundic acid (ONO2506) ²⁰⁹ but larger trials are required to confirm the preliminary study results. Similarly, a large number of mainly lower level studies have assessed the feasibility of reducing body temperature (via physical cooling or acetaminophen) as an acute intervention and while physical cooling looks promising, larger RCTs are needed before such interventions can be recommended.^{210, 211, 212-215}

4.3.4	NEUROPROTECTIVE AGENTS	GRADE	LEVEL
The use of putative neuroprotectors should only be used if part of a randomised controlled trial.		A	Level I&II 199-202

4.3.5 Complementary and alternative therapy

Complementary and alternative therapies cover a range of practices including acupuncture, homoeopathy, traditional Chinese medicine, aromatherapy, music therapy, Reiki therapy, conductive education, naturopathy, reflexology and osteopathy. Evidence suggests:

- Acupuncture is relatively safe (1.5% severe adverse events) but there is no clear evidence of benefit in either acute or subacute stroke care.^{216, 217} Further robust studies are needed.
- Reiki therapy was not found to be beneficial in one small RCT.²¹⁸
- Ginkgo biloba extract and Dan shen agents have some reported benefits, however, trials have

methodological limitations and hence no clear conclusions can be made.^{219, 220} Further robust studies are needed.

- No robust trials for other therapies were found and hence no conclusions can be made. Herbal preparation may develop harmful interactions with certain medications and should be discussed with relevant health professionals.

Since complementary medicine may relate to particular cultural backgrounds or other belief systems, health professionals should be aware of, and sensitive to, the needs and desires of the stroke survivor and the family/carer. Health professionals should be willing to discuss the effectiveness of therapy and different options of care within the context of the current health care system.

4.3.5	COMPLEMENTARY AND ALTERNATIVE THERAPY	GRADE	LEVEL
a)	The routine use of the following complementary and alternative therapies are not recommended: <ul style="list-style-type: none"> • Acupuncture; • Ginkgo biloba extract or Dan shen agents; • Reiki therapy; • Other alternative therapies. 	B B C	Level I ^{216, 217} Level I ^{219, 220} Level II ²¹⁸
b)	Health professionals should be aware of different forms of complementary and alternative therapies and be available to discuss these with stroke survivors and their families.	✓	–

5 ASSESSMENT AND MANAGEMENT OF THE CONSEQUENCES OF STROKE

Section 5 as a whole was given a consumer rating of 9.8/10.

5.1 Dysphagia

The incidence of dysphagia varies widely, depending on the timing and method of evaluation, but is very common (27–50%) in acute stroke.²²¹ Dysphagia is also associated with an increased risk of complications, such as aspiration pneumonia, dehydration and malnutrition.²²¹ Prompt screening, accurate assessment and early management are therefore needed to prevent these complications and promote recovery of functional swallow.

Studies involving assessment and management of dysphagia in acute stroke have found:

- ▶ The adherence to a formal dysphagia screening protocol reduces the incidence of pneumonia in acute stroke patients.^{222, 223} Another study implementing evidence based acute care involving dysphagia screening, referral and assessment demonstrated improved process and patient outcomes.²²⁴ Further studies, however, are needed to clarify what are the key factors that improve outcomes including which screening tool is most useful.
- ▶ Three systematic reviews were all unable to conclude which screening tool used for bedside assessment was most useful due to variability in the studies.²²⁵⁻²²⁷ While most tests had sensitivities of 70-90% some were much lower, with the lowest reported to be 42%.^{225, 227} Specificity was almost always lower with ranges from 22-67% in one review²²⁵ and 59-91% in another.²²⁷ Screening should be undertaken routinely before providing food or drink to patients. Ideally such screening would be undertaken within the first 24 hours of hospital admission.
- ▶ Subsequent studies of bedside clinical screening have demonstrated similar sensitivities with other bedside tests.²²⁸⁻²³³ The best was found to be the 50ml water swallow test in combination with oxygen saturations (with sensitivity reported between 87-100%).^{228, 230, 232}
- ▶ Screening tests are used to identify patients with possible dysphagia. Screening tools may also be used by a speech pathologist as part of a comprehensive assessment to thoroughly examine the patient. However, screening tools have been developed for use by non specialist staff who always undertakes essential training prior to using such tools.²²⁵ Overall more methodological robust studies are required to clarify which test is preferred.
- ▶ The gag reflex is not a valid screen for dysphagia.²²⁵
- ▶ Videofluoroscopic modified barium swallow (VMBS) study may be considered the reference standard to confirm swallowing dysfunction and presence of aspiration, however, several limiting factors have been noted including: the relatively complex, time consuming and resource intensive nature of the test; small exposure to radiation; and patients may have difficulty sitting upright in a chair for the test. In addition, the results of the test can be difficult to interpret and variation among individual raters may occur.²²⁷ There is currently no agreed criterion for when a VMBS study is required and local policies should be developed that take into consideration local resources and the potential limitations noted above.
- ▶ Fiberoptic endoscopic evaluation of swallowing (FEES) has also been used as a reference standard in studies assessing screening tools²³⁰⁻²³² and has been found to have similar sensitivity and specificity compared with VMBS.²³⁴ FEES is portable (possibly allowing more immediate access and time saving), requires less staff and is therefore cheaper, and reduces radiation exposure.²³⁴ While speech pathologists currently coordinate and conduct VMBS studies, FEES can only be conducted by specialists with recognised training and credentialing and as such it is not yet commonly available in Australia.
- ▶ One recent robust trial found more patients receiving a behavioural intervention (i.e. swallowing compensatory strategies plus dietary modification, either high or low intensity therapy) returned to a normal diet at 6 months or recovered swallowing at 6 months, than those receiving usual care.²²¹ While this study suggests potential benefits for more

intense therapy, further high quality trials are needed. This study strengthens rather than alters the recommendations for management of those with dysphagia outlined in the Clinical Guidelines for

Stroke Rehabilitation and Recovery. No other significant studies were found and readers are directed to that document for details regarding management strategies.

5.1	DYSPHAGIA	GRADE	LEVEL
a)	Patients should be screened for swallowing deficits before being given food, drink or oral medications. Screening should be undertaken by personnel specifically trained in swallowing screening.	C	Level I ^{225, 226}
b)	Patients should be screened within 24 hours of admission.	✓	–
c)	Patients who fail the swallowing screening should be referred to a speech pathologist for a comprehensive assessment.	✓	–

5.2 Nutrition

Dehydration is common after stroke due to consequences of stroke such as swallowing impairment, immobility and communication difficulties. Malnutrition is also common with Australian data indicating that 16-19% of patients are malnourished on admission.^{235, 236} Previous observational studies have shown that dehydration and malnutrition increases in the first week of hospitalisation and are associated with poor outcomes post stroke, including increased complications and mortality, a fact confirmed by more recent studies.²³⁵⁻²³⁷

Currently there is no universally accepted gold standard for the assessment of nutritional status in the acute stroke patient. Malnutrition is typically diagnosed based on objective nutrition parameters (biochemical, anthropometric or immunological markers), for example serum albumin, weight or skin folds, however, these are imperfect measures which are impacted by factors secondary to stroke. Validated nutritional screening tools have also been developed and should be used in patients with acute stroke on admission and at regular intervals throughout admission. This would appear logical given the poor prognosis of those with malnutrition. A number of validated nutrition assessment tools, including the Subjective Global Assessment (SGA) along with the associated patient generated SGA, Malnutrition Screening Tool (MST), Malnutrition Universal Screening Tool (MUST) and Mini Nutritional Assessment (MNA), have been used in studies of acute hospitalised patients including those with stroke.^{235, 236, 238-241} Such validated tools should be used alone or in addition to objective nutritional parameters in the assessment of nutritional

status.

Studies relating to hydration and nutrition post stroke have found the following:

- Suboptimal fluid intake leads to negative outcomes^{242, 243} and is particularly problematic in people with dysphagia.^{244, 245} As a result it may be necessary to increase fluid intake via the intravenous, subcutaneous or enteral route (using a nasogastric [NG] tube or percutaneous endoscopic gastrostomy [PEG]). There is no clear evidence to suggest one route is more beneficial than the other when addressing adequate hydration levels.²⁴⁶
- There are very few robust observational studies found that report nutritional intake of acute hospitalised stroke patients. The identified studies suggest that nutritional intake is suboptimal.^{247, 248} Furthermore, there is suggestion that the nutritional needs of those with haemorrhagic strokes may be higher than previously calculated and therefore these patients may be at particular risk of malnutrition.²⁴⁹
- Simple strategies such as making fluid accessible, offering preferred fluids and providing supervision during meals have been found to increase fluid intake in elderly people who are able to take fluids orally.^{250, 251}
- One systematic review found oral nutritional supplementation of patients deemed to be undernourished at baseline reduces infectious complications and mortality when compared with placebo/standard care.²⁵² A subsequent RCT of oral liquid supplementation in addition to a normal hospital

diet reduced non-elective readmissions to hospital in a generalised population. Only 2.3-5.5% of those included were stroke patients.²⁵³ Given the observational data regarding poorer outcomes it is considered good practice for staff to monitor food intake along with fluid intake to maximise nutrition and outcomes for people with acute stroke.

- A prospective observational study also found early nutritional support (via tube feeding) improved outcomes compared to standard care for severe stroke patients.^{254, 255} The FOOD trial found no significant difference in death and disability or incidence of pneumonia for patients provided with early NG enteral feeding compared with intravenous or subcutaneous fluids (without nutrition).²⁵⁶ However, there was a non significant trend for those who received early NG tube feeding to have a reduced risk of death but an increased likelihood of being severely disabled.²⁵⁶ Unfortunately this trial was underpowered to detect such changes.
- There is conflicting evidence for the preferred method of enteral feeding for those with dysphagia. In by far the largest and most robust study, NG tube feeding in the first month after stroke was associated with increased functional recovery and was more likely to be associated with normal feeding 6 months after stroke when compared with PEG feeding.²⁵⁶ Three other much smaller studies reported benefits of PEG feeding compared with NG feeding.²⁵⁷⁻²⁵⁹ Given the FOOD trial paper is almost 10 times larger than other trials and much more robust, it is prudent to base decisions on the data from this study suggesting NG is preferred in the acute phase for those requiring enteral feeding.
- Implementation of locally developed evidence-based guidelines for nutritional support using opinion leaders and educational programmes linked to audit and feedback improved adherence to guidelines by staff and reduced patient complications (infections).²²⁴

5.2	NUTRITION	GRADE	LEVEL
a)	Close monitoring of hydration status and appropriate fluid supplementation should be used to treat or prevent dehydration.	B	Level I ²⁵⁰
b)	All patients with acute stroke should be screened for malnutrition.	B	Level II ²⁶⁰
c)	Those who are at risk of malnutrition, including those with dysphagia, should be referred to a dietitian for assessment and ongoing management. Assessment of nutritional status should include the use of validated nutrition assessment tools or measures.	✓	–
d)	Nutritional supplementation should be offered to people whose nutritional status is poor or deteriorating.	A	Level I ²⁵²
e)	NG feeding is the preferred method during the first month post stroke for people who do not recover a functional swallow.	B	Level II ²⁵⁶
f)	Food intake should be monitored for all people with acute stroke.	✓	–

5.3 Early mobilisation

Observational data suggests acute stroke patients spend significant time inactive in bed.²⁶¹ Complications of immobility may account for up to 51% of deaths in the first 30 days after ischaemic stroke, with over 62% of complications occurring in the first week.²⁶² Although the true contribution of immobility to complications and death is difficult to quantify, there is evidence that bed rest for many conditions does more harm than good (see also Section 6.2).²⁶³

Early mobilisation (i.e. sitting out of bed, standing and walking) has been described as an important component of stroke unit care¹⁸ and there is indirect evidence supporting the practice.²⁶⁴ Currently however, there is limited direct evidence for the benefit of commencing mobilisation very early after stroke. Meta-analysis has demonstrated the benefits of greater intensity of physical rehabilitation in the first few months after stroke,²⁶⁵ however, there were no trials of acute (< 6 days) rehabilitation included in this review. A systematic review

of very early versus delayed mobilisation after stroke is currently underway ²⁶⁶ as is the large AVERT Phase III trial which is testing whether very early mobilisation (within 24 hours of stroke onset) reduces death and disability, reduces complications after stroke, improves quality of life and is cost effective compared with standard stroke unit care.²⁶⁷

Due to the early risk of falls and potential for manual handling issues for both the patient and staff an early assessment by a physiotherapist and appropriate advice communicated to the stroke team, especially to nursing staff, is prudent.

5.3	EARLY MOBILISATION	GRADE	LEVEL
a)	Patients should be mobilised as early and as frequently as possible.	B	Level II ²⁶⁴
b)	After assessment the physiotherapist should advise staff and carers of appropriate mobilising and transfer techniques.	✓	–

5.4 Early therapy for difficulties with occupational performance in daily activities (Activities of Daily Living, ADL)

Assessment and management of occupational performance in daily activities fall into two areas:

- Occupational performance in basic self-maintenance tasks such as showering, toileting, dressing, and eating.
- Occupational performance in domestic and community tasks such as home maintenance tasks, management of financial affairs and community access, including driving.

A recent robust systematic review found patients who receive occupational therapy interventions reduce the likelihood of a poor outcome and increase personal activity of daily living scores.²⁶⁸ It is unclear what specific factors contribute to this benefit especially in the acute

period. Included studies have been undertaken during subacute care in hospital or in the community with very little data in the acute phase of care although early OT involvement was typical of units described in the stroke unit trialist collaboration.¹⁸

Based on assessment findings, interventions targeting specific areas such as occupational performance in daily activities, upper limb function, cognition, perception and participation in the community including driving should be tailored to each patient. No recent studies have been found that alter the recommendations for such topics outlined in the Clinical Guidelines for Stroke Rehabilitation and Recovery and readers are directed to that document for details.

5.4	EARLY THERAPY FOR DIFFICULTIES WITH ACTIVITIES OF DAILY LIVING (ADL)	GRADE	LEVEL
a)	Patients with difficulties in occupational performance in daily activities should be treated by an occupational therapist or a specialist multidisciplinary team that includes an occupational therapist.	B	Level I ^{18, 268}
b)	Patients with confirmed difficulties in occupational performance in personal tasks, instrumental activities, vocational activities or leisure activities should have a management plan formulated and documented to address these issues.	✓	–
c)	The occupational therapist should advise staff and carers on techniques and equipment to maximise outcomes relating to functional performance in daily activities, sensorimotor, perceptual and cognitive capacities.	✓	–

5.5 Cognition and perception

Cognitive and perceptual impairment commonly involves attention, memory, orientation, language, executive functions, neglect, apraxia and agnosia. Cognitive and perceptual impairment and dementia are common after stroke (up to 60% have cognitive impairment and up to 30% develop dementia within the first 12 months)²⁶⁹⁻²⁷² and there is overlap between these impairments making it hard to delineate between them.

Early screening for cognitive impairment is important although no gold standard currently exists.^{273, 274} Non linguistic tests should be considered where communication deficits are present as language based assessments are inadequate in these patients.²⁷⁴ A more detailed assessment conducted by a trained team member (e.g. occupational therapist, neuropsychologist, or speech pathologist) can clarify the type of impairments and guide the team in providing the most appropriate rehabilitation interventions. Adequate screening and assessment for cognitive impairment is important to determine a patient's capacity to participate in the recovery process and make important decisions (i.e. post discharge accommodation and follow up, financial decisions) and should assist the stroke team to care and communicate with the person with stroke and their family/carer.

Neglect is the most common cognitive impairment reported in 20-40% of acute stroke patients (more commonly in those with right-sided lesions), however, the exact incidence is hard to ascertain due to variability in studies and a lack of inclusion of patients with communication deficits.²⁷⁵⁻²⁷⁷ Currently there are a

significant number of screening and assessment tools used for neglect but there is no universally agreed gold standard.^{275, 278, 279} This may account for the low numbers of patients found to be assessed in the acute phase of care in one overseas audit.²⁸⁰ However, as neglect is associated with increased falls risk and poor functional outcome, screening should be carried out in all patients and those identified followed up with a comprehensive assessment.²⁷⁹

Correspondingly, apraxia is a relatively common cognitive impairment, particularly after a stroke affecting the left hemisphere. As with neglect, there are a number of screening and assessment tools used to detect the presence of apraxia, however, there is no universally agreed gold standard.^{281, 282} The presence of apraxia may have a significant effect on the capacity to complete functional activities, therefore, screening should be completed on all patients. Those identified with a diagnosis of apraxia should be followed up by comprehensive evaluation and intervention.²⁸³⁻²⁸⁶

Assessment and treatment on a stroke unit was found to improve outcomes for those with perceptual difficulties compared with care provided on a conventional ward.²⁸⁷ Specific management of cognitive and perceptual deficits is outlined in the Clinical Guidelines for Stroke Rehabilitation and Recovery, and no significant research has been undertaken in the last few years that changes the recommendations. Little research has been undertaken in the acute period and it is unclear if outcomes are improved with early treatment. Further studies are needed.

5.5	COGNITION AND PERCEPTION	GRADE	LEVEL
a)	All patients should be screened for cognitive and perceptual deficits using a validated screening tool. (Consensus opinion)	✓	–
b)	Patients identified during screening should undertake full assessment and management by an appropriately trained health professional.	✓	–

5.6 Communication

Communication deficits after stroke are common with aphasia, the most common deficit, found in 30% of first-ever ischemic strokes.²⁸⁸ Other communication disorders post stroke includes dyspraxia and dysarthria. There is a higher mortality rate for people with

aphasia.²⁸⁹ The prognosis for recovery from aphasia is generally moderate to good with most patients improving and approximately 40% having a full recovery within one year post stroke.^{290, 291}

The first step in planning management for people with aphasia is the identification and diagnostic process. The presence of aphasia may be determined through a screening process prior to a full assessment that will guide management. An audiology assessment may also be useful as hearing loss is particularly common in the elderly population and can impact on assessment.²⁹²

Reviews of studies evaluating assessment and management techniques have found the following:

- One systematic review examined six screening tools and found the Frenchay Aphasia Screening Test was the most thoroughly evaluated and widely used measure with sensitivity of 87% and specificity of 80%.²⁹³ The Frenchay Aphasia Screening Test was developed in the UK to be used by non speech pathologists and includes references specific to European countries. This must be taken into account when using the tool in the Australian setting. Likewise, while there was a range of other screening tests reported in the literature, further evaluation of their reliability, validity and practical application is needed.²⁹³
- A large number of more detailed assessment tools have been described in the literature and these are often used not only to diagnose aphasia but also to guide management choices. However, no gold standard test is universally acknowledged. While it is not within the scope of this guideline to discuss these tests in detail it is noted that all detailed assessment tools are normally administered and interpreted by a speech pathologist trained in the use of such tools.
- Evidence for therapy for communication deficits is limited with most trials having methodological shortcomings and small numbers.²⁹⁴ It is also noted that during the acute phase, therapy often focuses on dysphagia and communication therapy is often delayed. However, evidence from reviews of RCT and non randomised trials seems to indicate that therapy is more effective when intense therapy is commenced early.^{295, 296} Evidence of interventions for aphasia, verbal dyspraxia and dysarthria remain consistent with that included in the Clinical Guidelines for Stroke Rehabilitation and Recovery and readers are directed to that document for details.
- While it is important to provide information to patients and carers, communication deficits need to be carefully considered. One study found that the reading level for those with aphasia was well below the level of that provided in written material.⁵⁰ Small case series studies have found that modifying written materials using aphasia-friendly principles significantly improves the comprehension of the materials for people with aphasia.^{297, 298}
- Although evidence is scarce, augmentative and alternative communication devices should be considered for those with severe aphasia⁷ although it may not be appropriate for all aphasic patients (e.g. those with receptive difficulties).
- Small RCTs have demonstrated some benefits in training others (volunteers or family members) in supportive communication techniques.^{299, 300} However, even if carers are not formally trained in specific techniques it is good practice for speech pathologists to advise them on the communication deficits found on assessment and strategies to improve communication between the patient and their family/carer.

5.6	COMMUNICATION	GRADE	LEVEL
a)	All patients should be screened for communication deficits using a validated screening tool.	C	Level I ²⁹³
b)	Those with suspected communication difficulties should receive formal assessment by a speech pathologist.	✓	–
c)	Patients with communication difficulties should be treated as early and as frequently as possible.	C	Level I ²⁹⁶ & Level III-2 ²⁹⁵
d)	All written health information should be available in an aphasia friendly format.	D	Level IV ²⁹⁸
e)	The speech pathologist should advise staff and family/carers of appropriate communication techniques.	C	Level II ^{299, 300}

5.7 Incontinence

Dysfunction of the bladder and/or bowel is common soon after stroke and may be caused by a combination of stroke-related impairments (e.g. weakness, cognitive or perceptual impairments). Incontinence is associated with complications (e.g. depression) and prolonged recovery and is a major factor for many patients and their carers.³⁰¹

Urinary Incontinence

Several types of urinary incontinence occur after stroke and hence assessment is important to identify distinct aetiology to enable commencement of targeted interventions. Methods of diagnostic assessment have been described as a five step sequential process:³⁰²

1. clinical history-taking, including history of incontinence before the stroke, nature, duration and reported severity of symptoms and exacerbating factors including diet, fluid and medications;
2. validated scales that measure the severity of symptoms and impact of symptoms on quality of life;
3. physical examination, including abdominal, perineal (pelvic floor strength), rectal, neurological and measurement of body mass index (BMI);
4. simple investigations, including urinalysis, midstream specimen of urine (MSSU), measurement of post void residual volume (PVRV), provocation stress test, frequency–volume charts and pad tests;
5. advanced investigations, including urodynamics tests such as cystometry, urethral pressure measurement, pressure–flow studies, videourodynamics and ambulatory monitoring.

Clinical history alone provided high sensitivity (92%) but low specificity (56%) in determining a diagnosis of incontinence when compared to urodynamic testing.³⁰² Post-void bladder scanning may also be useful to guide assessment and management and has generally high specificity (84–89%) and sensitivity (82–86%) compared with urodynamics.³⁰² Therefore all patients with stroke should have at least a clinical history taken. If incontinence is identified after obtaining the clinical history then a physical examination and simple investigations should be undertaken. Advanced investigations are not justified routinely but may be considered later for those whose incontinence has not resolved.

In general there is a lack of evidence for effective interventions, particularly in the acute phase.

- One robust systematic review³⁰¹ noted two particular studies that demonstrated benefits. One study found a structured functional approach to assessment and management, compared with a traditional neurodevelopmental approach in early rehabilitation increased the likelihood of being continent at discharge. The other study demonstrated benefits of care provided by a specialist continence nurse compared with GP care once in the community.³⁰¹ This review found trials of physical, behavioural, complementary and anticholinergic drug interventions were inconclusive and more robust data are needed to guide continence care after stroke.³⁰¹
- A second systematic review focused on behavioural approaches to manage urinary incontinence. This review found only modest evidence of the benefits for urge suppression along with pelvic floor exercises, however, more robust data are needed.³⁰³

Faecal Incontinence

Faecal incontinence has been found to occur in 30% of acute stroke patients however only 11% are incontinent at 3–12 months post stroke.³⁰⁴ Toilet access and constipating drugs are two modifiable risk factors after stroke. Constipation is also common post stroke as is reported to be up to 66% in one community based study.³⁰⁴ The research base for management for faecal incontinence and constipation is extremely limited and is based on patients in rehabilitation and community settings and further research in the acute phase is needed although efforts should be made to effectively manage any problems in the acute phase in order to prevent further complications.

Evidence in this updated edition only reinforced the recommendations outlined in the Clinical Guidelines for Stroke Rehabilitation and Recovery and readers are directed to that document for more detail about management of bladder and bowel dysfunction following stroke. However, it is noted that extrapolated evidence from stroke unit trials suggest bladder and bowel care, especially avoidance of urinary catheters and treatment for constipation, are important components of best practice stroke care.¹⁸

5.7	INCONTINENCE	GRADE	LEVEL
a)	All patients with suspected continence difficulties should be assessed by trained personnel using a structured functional assessment.	B	Level II ³⁰¹
b)	A portable bladder ultrasound scan can be used to assist in diagnosis and management of urinary incontinence.	B	Level I ³⁰²
c)	Patients with confirmed continence difficulties should have a continence management plan formulated and documented.	C	Level II ³⁰¹
d)	The use of indwelling catheters should be avoided as an initial management strategy.	✓	–
e)	A post discharge continence management plan should be developed with the patient and carer prior to discharge and should include how to access continence resources in the community.	✓	–

5.8 Mood

Mood is frequently affected following a stroke. Depression is the most common mood disturbance with a meta-analysis of observational studies finding approximately one third of patients have depression after stroke.³⁰⁵ Depression is common in the acute, medium and long term.³⁰⁵ Anxiety and emotionalism may also occur, either separately or in combination. While some people with mood disturbances may recover spontaneously over a few months, others may have problems that persist despite active interventions.³⁰⁵ Physical disability, stroke severity and cognitive impairment are reported to predict depression, however, methodological limitations to current studies do not allow for accurate predictive models to be developed.³⁰⁶

Assessment can be difficult due to the complex interaction of stroke specific deficits (especially aphasia or cognitive impairments) and the normal adjustment needed to a potentially devastating situation. Assessment of abnormal mood may occur via psychiatric interview using standard diagnostic criteria such as the Diagnostic and Statistical Manual of Mental Disorders (e.g. DSMIV), psychiatric rating scales (e.g. Hamilton Depression rating scale, Geriatric depression scale) or a self-rating mood scale (e.g. Patient Health Questionnaire 9-item depression scale [PHQ-9]). Rating scales and single simple screening questions have been found to have adequate sensitivity but generally lack specificity and hence are useful for screening rather than to diagnose depression (although they are not as

useful for anxiety).³⁰⁷⁻³¹² It is not always clear what contribution the physical symptoms of stroke make to the total score on a rating scale.³¹³ Scales specifically for people with aphasia have also been developed.³¹⁴

Treatment options include pharmacological therapy, or psychological therapy, which includes counselling and problem-solving interventions. The heterogeneity and methodological shortcomings of trials make it difficult to reach conclusions on interventions to prevent or to manage depression after stroke.^{315, 316} While most studies focussed on prevention of depression start early after stroke, studies for treating depression are almost always in the subacute and chronic phases of recovery. Studies have found the following:

- Routine prophylactic use of pharmacotherapy was not effective in preventing depression, however, individual psychotherapy improved scores on mood scales, but it is unclear if it prevents post-stroke depression.³¹⁷ Subsequent small studies have found conflicting results for routine pharmacotherapy and further large robust studies are needed.^{318, 319} Subsequent studies of psychotherapy have reported benefits in terms of improved mood and life satisfaction.^{320, 321}
- A robust systematic review found pharmacotherapy improved scores on mood scales, but clear benefit in remission of post-stroke depression and improvement of functional outcomes has not been shown.³¹⁶ Subsequent trials have also failed to demonstrate consistent, clear benefits.³²²⁻³²⁴

- One systematic review found pharmacotherapy was of benefit to people with emotionalism.³¹⁵
- Case management models of care that focused on education, screening, management and links with primary care physician and/or stroke physician were found to be beneficial in reducing depression.^{68, 325}
- No randomised controlled trials (RCTs) have been undertaken to evaluate electroconvulsive therapy (ECT) for stroke, and a robust systematic review of ECT in an elderly population with depression was unable to draw any conclusions due to the lack of good quality evidence.³²⁶

Although depression is common, there remain many challenges regarding assessment and management. For example, there are no clear data to suggest how long therapy should continue after a stroke, at what dosage, what rate of side effects may be expected or what is the best process for ending treatment. Patients and carers should be informed that mood problems after stroke are common and encouraged to contact a healthcare professional should any mood changes persist for two weeks or longer and interfere with daily activities.

5.8	MOOD	GRADE	LEVEL
a)	Patients with suspected altered mood (e.g. depression, anxiety, emotional lability) should be assessed by trained personnel using a standardised scale.	B	Level II & Level III-1 68, 307, 309, 311, 314, 321
b)	Patients with stroke may be managed using a case management model after discharge to reduce post stroke depression. If used, services should incorporate education of the recognition and management of depression, screening and assistance to coordinate appropriate interventions via a medical practitioner.	C	Level II ^{68, 325}
c)	Routine use of antidepressants to prevent post-stroke depression is not currently recommended.	B	Level I ³¹⁷
d)	Antidepressants may be used for people with emotional lability.	B	Level I ³¹⁵
e)	Patients with depression or anxiety may be treated with antidepressants and/or psychological interventions to improve mood.	B	Level I ³¹⁶

6 PREVENTION AND MANAGEMENT OF COMPLICATIONS

Section 6 as a whole was given a consumer rating of 9.8/10.

6.1 Cerebral oedema

Cerebral oedema in the infarcted or peri-lesional brain tissue often leads to early deterioration and death.³²⁷

Studies to reduce cerebral oedema and raised intracranial pressure have found the following:

- A recent meta-analysis of RCTs found benefits (reduced mortality and improved functional outcomes for those surviving) of decompressive surgery in conjunction with medical therapy compared with medical therapy alone (see also section 4.1.5).¹⁶⁵ Given the prognosis for patients with 'malignant' or significant middle artery occlusion, mainly due to the effect of cerebral oedema, an urgent referral to a neurosurgical consultant is recommended.
- One robust systematic review found corticosteroids have no benefit and may cause harm and are therefore not recommended.³²⁸
- Another robust systematic review found osmotherapy using glycerol reduces short term mortality but no long term differences were noted and hence its use should be considered in selected cases (e.g. while assessing use of decompressive surgery).¹⁷²
- Hyperventilation has not been rigorously tested in stroke but short term effects have been found in patients with traumatic brain injury.³²⁹

6.1	CEREBRAL OEDEMA	GRADE	LEVEL
a)	Selected patients (e.g. 18-60 years with potential for surgery to occur within 48 hours of symptom onset) with significant middle cerebral artery infarction should be urgently referred to a neurosurgeon for consideration of hemicraniectomy.	A	Level I ¹⁶⁵
b)	Corticosteroids are not recommended for management of patients with brain oedema and raised intracranial pressure.	A	Level I ³²⁸
c)	Osmotherapy and hyperventilation may be trialled while a neurosurgical consultation is undertaken, or for patients with deteriorating condition due to raised intracranial pressure.	C	Level I for potential short term benefit of glycerol ¹⁷² , Level IV for hyperventilation ³²⁹

6.2 Deep Venous Thrombosis (DVT) or Pulmonary Embolism (PE)

DVT and the associated complication of PE, are significant risks in the first few weeks post stroke with PE accounting for 5% of deaths after stroke (third most common cause).³³⁰ Risk factors reported in the literature include reduced mobility, stroke severity, age, dehydration, increasing time between stroke and the

introduction of preventive measures, haemorrhagic stroke and cryptogenic ischaemic stroke.³³¹ While there is often a high number of DVTs found in studies (15-80%), many of these are asymptomatic. Clinically apparent incidence is low for both DVT (<1-10%) and PE (<1-6%).³³¹

- In high-risk populations, duplex or triplex ultrasound techniques are useful to confirm or rule out suspected DVT (sensitivity 91-92%, specificity 94%).³³² However, use of the Wells Score to categorise the risk and the D-Dimer prior to ultrasound has been found to be the most cost effective testing strategy.³³²
 - There is limited evidence to guide treatment decisions in patients with acute ischaemic or haemorrhagic stroke, who may be at particularly high risk of bleeding complications related to anticoagulant therapy.³³³
 - Observational data suggests acute stroke patients spend significant time inactive.²⁶¹ Early mobilisation is not supported by direct evidence, however, studies of stroke unit care that encourage early mobilisation have been found to have lower rates of DVT¹⁸ and early mobilisation has been identified as one of the most important factors contributing to better outcomes with stroke unit care (see Section 5.3).²⁶⁴
 - Hydration, similarly, has not been evaluated in trials, but studies have found dehydration to be strongly associated with DVT²⁴² and early hydration, a component of stroke unit care, could be expected to provide some protection against DVT.
 - Routine antiplatelet therapy (using aspirin) has modest benefits for acute ischaemic stroke and has also been shown to have modest preventative qualities for DVT (NNT>300) and PE prophylaxis (NNT>1000).³³¹
 - Heparin and low molecular weight heparin (LMWH) have both been shown to prevent DVT and PE after ischaemic stroke.^{331, 334, 335} Evidence from these studies also demonstrated that early use of such treatment is consistently associated with increased risk of cerebral haemorrhage when used in the first few days or weeks after the onset of ischaemic stroke.^{331, 334}
 - LMWH is at least as effective as unfractionated heparin (UFH) in preventing DVT, and may be more effective in preventing overall rates of VTE.^{336, 337} However, LMWH is associated with an increase in bleeding complications and there is insufficient evidence to determine whether LMWH has any advantage (or disadvantage) compared to standard heparin for clinically important end-points such as symptomatic VTE, intracranial haemorrhage, major extracranial haemorrhage and mortality.^{331, 334, 336, 337}
 - The routine use of low molecular weight heparin or standard heparin in unselected patients is not recommended as the risks offset the benefits. LMWH may be more effective than UFH although the risk of bleeding also appears to be higher. The benefits of prophylactic UFH or LMWH may outweigh the risks for certain subgroups, for example, those with leg paresis, who are immobile, those with a prior history of DVT or PE, those with an inherited thrombophilic tendency or those who are morbidly obese.³³¹ LMWH may be more convenient to administer (often once a day dosing), but dosing precautions (such as for patients with renal failure) should prophylactic anticoagulant therapy be considered.
- The evidence for physical methods of preventing DVT is less clear:
- Two systematic reviews concluded there is currently insufficient evidence of the effectiveness of physical methods to prevent DVT.^{331, 338} One trial of note included in the more recent review assessed the use of intermittent pneumatic compression (IPC) in conjunction with elastic stockings. The study reported a reduced incidence of asymptomatic DVT for patients with ICH in an ICU setting. However, the study was too small to detect clinical/symptomatic DVT differences in the groups and a higher number discontinued treatment in the intervention group.³³⁹
 - Graduated compression (antithrombotic) stockings do reduce the incidence of post-surgical DVT,^{338, 340, 341} but the evidence for people with stroke is inconclusive.³³⁸ Potential benefits in those at high risk of DVT need to be weighed up against risks, which include acute limb ischaemia (especially in stroke survivors with diabetes), peripheral neuropathy, and peripheral vascular disease. Results of the ongoing CLOTS trial should further assist therapy decisions in this area.

6.2	DEEP VEIN THROMBOSIS (DVT) AND PULMONARY EMBOLISM (PE)	GRADE	LEVEL
a)	Early mobilisation and adequate hydration should be encouraged with all acute stroke patients to help prevent DVT and PE.	✓	–
b)	Antiplatelet therapy should be used for people with ischaemic stroke to prevent DVT/PE.	A	Level I ³³¹
c)	The following interventions may be used with caution for selected people with acute ischaemic stroke at high risk of DVT/PE: <ul style="list-style-type: none"> • low molecular weight heparin or heparin in prophylactic doses; • thigh-length antithrombotic stockings. 	B C	Level I ^{331, 334, 335} & Level II ³³⁶ Level II ^{331, 338}

6.3 Pyrexia

Pyrexia is associated with poorer outcomes after stroke.³⁴² The most common causes of pyrexia are chest or urinary infections.³⁴³ A number of trials have evaluated different techniques for reducing body temperature as a means of neuroprotection in the

acute phase rather than specifically responding to pyrexia (see section 4.3.4). Paracetamol and physical cooling for those with pyrexia have been found to be modestly effective therapies to reduce temperature in acute stroke.^{212, 344}

6.3	PYREXIA	GRADE	LEVEL
	Antipyretic therapy, comprising regular paracetamol and/or physical cooling measures, should be used routinely where fever occurs.	C	Level II ^{212, 344}

6.4 Pressure care

Pressure ulcers are defined as “areas of localised damage to the skin and underlying tissue due to pressure, shear or friction”.³⁴⁵ One large multicentre trial reported 1% of patients developed pressure ulcers during acute stroke admission.²⁶⁰ Age, stroke severity, immobility, incontinence, nutritional status and diabetes are contributing risk factors. The skin of those deemed at high risk should be examined initially and reviewed as regularly as needed based on individual factors.

Pressure care policies are a common characteristic of stroke unit care.¹⁸ Risk assessment scales, such as the Braden, Norton or Waterlow Risk Assessment scales, have only modest sensitivity and specificity but may be more useful than clinical judgement alone.³⁴⁶

There is no evidence that the use of risk assessment scales reduces the incidence of pressure ulcers.³⁴⁶

Four main strategies for the treatment of pressure ulcers not specific to stroke involve:

1. local treatment of the wound using wound dressings and other topical applications;
2. pressure relief using beds, mattresses or cushions, or by repositioning the patient;
3. treating concurrent conditions which may delay healing, e.g. poor nutrition, infection;
4. use of physical therapies such as electrical stimulation, electromagnetic, ultrasound, laser therapy.³⁴⁷

Evidence for such interventions includes the following:

- There is insufficient research evidence to guide decisions about which dressings or topical agents are most effective in pressure ulcer management.³⁴⁸
- One systematic review found foam alternatives to the standard hospital mattress were shown to reduce the incidence of pressure ulcers in people at risk.³⁴⁵ However, included trials varied greatly in quality and comparisons were difficult. The relative merits of alternating and constant low pressure devices, and of the different alternating pressure devices or seat cushions for pressure ulcer prevention are unclear. Sheepskin overlays appear promising based on one trial of orthopaedic patients. Air filled vinyl boots (with integral foot cradle) were found to be ineffective or even harmful (i.e. increased pressure sores).³⁴⁵
- No evidence was found for the effects of repositioning as a pressure relieving strategy.
- One systematic review was not able to draw any firm conclusions on the effect of enteral and parenteral nutrition on the prevention and treatment of pressure ulcers.³⁴⁹ One subsequent trial of nutritional support reported no difference in complications of pressure sores for those receiving nutritional supplementation.²⁶⁰ However, supplementation was only recommended in the small number of patients with malnutrition and further large trials would be needed to confirm or deny any benefits of nutritional support in this subgroup.
- There is not enough evidence to clearly determine if physical therapies are beneficial.^{347, 348}

A management plan is useful for those assessed at an increased risk of developing pressure ulcers. Such a plan needs to be tailored to each individual situation in response to identified risk factors. Careful monitoring should also be incorporated with the frequency determined by individual factors.

6.4	PRESSURE CARE	GRADE	LEVEL
a)	All patients unable to mobilise independently should have a pressure care risk assessment completed by trained personnel.	✓	–
b)	All those assessed at high risk should be provided with a pressure relieving mattress as an alternative to a standard hospital mattress.	B	Level I ³⁴⁵

6.5 Pain

Pain from any cause can affect people with stroke due to reduced movement as a result of the stroke, pre-existing disease or stroke specific pain (central post-stroke pain). No recent studies have been found that alter the recommendations outlined in the Clinical Guidelines for Stroke Rehabilitation and Recovery and readers are directed to that document for details.

However, it is important to note that during the acute phase, particular emphasis should be directed at prevention of post stroke shoulder pain, including the prevention of shoulder subluxation, as shoulder pain once present can be particularly problematic and no clear interventions currently exist.⁷

6.6 Falls

Falling is common in acute hospital settings. No recent studies have been found that alter the recommendations outlined in the Clinical Guidelines for Stroke Rehabilitation and Recovery and readers are directed to that document for details. Further

information regarding generic guidelines for falls prevention and management in the elderly is also available³⁵⁰ and should be considered for acute stroke patients.

- 7.1 Behaviour change to prevent another stroke has been given a Consumer Rating of 9.7/10.**
- 7.2 -7.8 Medical or surgical treatments to prevent another stroke has been given a Consumer Rating of 9.6/10.**
- 7.9 Concordance with medication to prevent another stroke has been given a Consumer Rating of 9.6/10.**

A person with stroke has an accumulated risk of subsequent stroke of 43% over 10 years with an annual rate of approximately 4%.³⁵¹ The rate of strokes after TIA is significantly higher (up to 20% after 3 months) suggesting greater opportunities to prevent stroke after TIA.³⁵ Secondary prevention therefore relates to both stroke and TIA. Data from overseas highlight the current underutilisation of secondary prevention strategies for people with stroke and TIA.^{35, 352, 353} Long term management of risk factors is the primary role of GPs and good communication between secondary and primary care is important (see section 1.10 Shared care).

7.1 Behaviour change

Evidence on behaviour change strategies targeting lifestyle factors to prevent recurrence of stroke is limited and often derived from cohort studies of primary prevention.

➤ Smoking increases the risk of both ischaemic and haemorrhagic stroke due to vascular narrowing and changes in blood dynamics.³⁵⁴⁻³⁵⁶ While no RCTs have been conducted, observational studies have found the risk from smoking decreases after quitting with the risk disappearing altogether after 5 years.^{357, 358} Several Cochrane systematic reviews have been undertaken related to different therapies for smoking cessation. Nicotine replacement therapy is beneficial and doubles the chances of smoking cessation.³⁵⁹ Some antidepressants (i.e. bupropion and nortriptyline but not selective serotonin reuptake inhibitors) aid long-term smoking cessation.³⁶⁰ Varenicline (a nicotine receptor partial agonist) has recently been developed for long-term smoking cessation with a threefold success rate compared with non drug quit attempts.³⁶¹ Varenicline has also been found to be more beneficial than the antidepressant bupropion.³⁶¹ A number of behavioural therapies delivered by different health professionals in different settings have demonstrated modest effects for smoking

cessation in general populations and should be provided via an individualised approach either in a group or on a one-to-one basis.³⁶²⁻³⁶⁵ One good example of such behavioural therapies involves telephone counselling, which improved smoking cessation rates particularly when three or more call backs are made.³⁶⁶

- Diet has an impact on a number of risk factors and can provide additional benefits to pharmacological interventions in people with vascular disease. Reducing dietary salt in people with cardiovascular disease (especially in those with high blood pressure) modestly reduces blood pressure and may therefore be beneficial to prevent stroke.³⁶⁷⁻³⁷¹ A meta-analysis of cohort studies found a diet high in fruit and vegetables (>5 servings per day) reduced the risk of stroke.³⁷² Similarly, a diet that is low in fat but high in fruit and vegetables has been shown to be effective in risk reduction for those with cardiovascular disease.^{370, 373-375} Similar dietary modification has also been shown to be beneficial for those with dyslipidemia³⁷⁶⁻³⁷⁸ and obesity (to assist in controlling hypertension).³⁷⁹ Supplementary antioxidants and vitamins, however, have not been found to reduce stroke.³⁸⁰⁻³⁸² One recent large RCT of a general dietary intervention (intended to be low in fat and high in vegetables, fruits and grains) in women 50-79 years old noted a significant reduction in diastolic blood pressure and low-density lipoprotein cholesterol.³⁸³ However, no difference in stroke incidence or coronary heart disease was found. The authors suggested a more individual, targeted approach may be needed.³⁸³ Recommendations for dietary intake are available from other guidelines and provide useful information based on cardiovascular disease and general populations.^{384, 385}
- There is strong evidence from meta-analysis of cohort studies that exercise has a protective effect on stroke.³⁸⁶⁻³⁸⁸ However, for secondary stroke prevention, there is currently a lack of direct

evidence on interventions to increase fitness.³⁸⁹ Exercise has clear benefits for reducing hypertension in at-risk people³⁹⁰ and improving glycemic control for those with type 2 diabetes.³⁹¹ Thus increasing exercise, particularly aerobic exercise, could be expected to reduce the risk of further stroke.

- Excessive alcohol consumption increases the risk of stroke,³⁹² so reducing alcohol levels could be expected to modify the risk of further strokes. However, light alcohol intake was found to be protective of stroke events.³⁹² The NHMRC Dietary Guidelines for Australian Adults 2003 recommend limiting alcohol consumption to a daily level of 2 standard drinks for men and 1 standard drink for women.³⁸⁴
- A multifactorial behavioural intervention strategy may be required that targets several risk factors. One study found a program of initiating tailored

secondary prevention, including lifestyle interventions, while in hospital lead to improved rates of adherence both prior to discharge and 3 months after discharge.^{393, 394} Every stroke survivor was given lifestyle advice and good adherence was achieved regarding diet (78%), exercise (70%) and smoking cessation (83% of previous smokers had quit).³⁹⁴ Other educational interventions have also reported improved adherence to dietary advice.^{59, 60} Systematic reviews have also found behaviour techniques, for example dietary or motivational counseling, provided by a specialist, trained clinician is effective at changing behaviour in primary care setting.^{395, 396} Lifescripts is a national initiative, which provides tools for primary care clinicians promoting risk factor management (see <http://www.health.gov.au/internet/wcms/Publishing.nsf/Content/health-publth-strateg-lifescrpts-index.htm>).

7.1	BEHAVIOUR CHANGE	GRADE	LEVEL
a)	Every person with stroke should be assessed and informed of their risk factors for a further stroke and possible strategies to modify identified risk factors. The risk factors and interventions include: <ul style="list-style-type: none"> • smoking cessation: nicotine replacement therapy, bupropion or nortriptyline therapy, nicotine receptor partial agonist therapy and/or behavioural therapy should be considered; • improving diet: a diet that is low in fat (especially saturated fat) and sodium, but high in fruit and vegetables should be consumed; • increasing regular exercise; (meta-analysis of cohort studies in primary) prevention demonstrate strong link between low exercise and stroke risk • avoiding excessive alcohol. (meta-analysis of cohort studies in primary) prevention demonstrate link between high alcohol intake and stroke risk 	A	Level I 359-361, 363-366
		A	Level I 367-369, 372, 376 & II 370, 373-375
		C	386-388
		C	392
b)	Interventions should be individualised and may be delivered using behavioural techniques (such as educational or motivational counselling).	A	Level I 362-366, 395, 396

7.2 Blood pressure lowering

High blood pressure is the major risk factor for both first and subsequent stroke. In general effective blood pressure management requires that blood pressure is maintained below acceptable limits (i.e. lower than 140/90 mm Hg).³⁹⁷ However, reduction in blood pressure, irrespective of initial blood pressure, has been shown to reduce the recurrence of stroke and

combined vascular events including myocardial infarction.³⁹⁸ Reducing blood pressure is particularly important for patients who have diabetes where levels should be below 130/85 mm Hg.³⁹⁷ Currently the most direct evidence available in secondary stroke prevention is for the use of an ACE inhibitor or for combination therapy with an ACE inhibitor and a

diuretic.³⁹⁸ A subsequent trial compared an angiotensin receptor blocker (ARB) with a calcium antagonist. Both agents were found to reduce blood pressure, although the ARB was significantly more effective in reducing mortality and all cardiovascular and cerebrovascular events, including all recurrent events.³⁹⁹ It is noted that in this study only 1/3 used monotherapy for blood pressure lowering and of the 2/3 using combination therapy 46% were using a diuretic and 33% were using a Beta blocker with no difference in combination therapy between groups.³⁹⁹ Only approximately 3% of patients commenced therapy within 1 week and no subgroup analysis was performed for this aspect.

The timing of commencing therapy remains unclear. Hyperacute therapy (within first 48 hours) is discussed separately as it relates to acute medical treatment

rather than secondary prevention (see section 4.1.4). However, two recent small studies in those with mild stroke or TIA without major carotid disease, found blood pressure lowering therapy (with an angiotensin II receptor antagonist or ACE inhibitor) was safe when commenced 2-4 days after stroke, although follow up was short (2 weeks).^{400, 401} Another study found a program of initiating secondary prevention medications, including blood pressure lowering therapy, while in hospital lead to improved rates of adherence both prior to discharge and 3 months after discharge.³⁹⁴

Lifestyle change including diet and exercise, by themselves or in conjunction with pharmacotherapy, can also be used to reduce blood pressure (see section 7.1).

7.2	BLOOD PRESSURE LOWERING	GRADE	LEVEL
a)	All patients after stroke or TIA, whether normotensive or hypertensive, should receive blood pressure lowering therapy, unless contraindicated by symptomatic hypotension.	A	Level I ³⁹⁸
b)	Commencement of new blood pressure lowering therapy may occur prior to discharge or within the first week after stroke or TIA.	B	Level II ^{400, 401} & Level III-3 ³⁹⁴

7.3 Antiplatelet therapy

There is evidence from 21 RCTs in 23,000 patients with previous ischaemic stroke or TIA that, compared with control, antiplatelet therapy significantly reduces the risk of subsequent serious vascular events including stroke, MI or vascular death (17.8% compared with 21.4%).⁴⁰² Antiplatelet therapy may have adverse effects, particularly a small risk of haemorrhage, but the benefits outweigh the risks.⁴⁰³ Although the benefits of antiplatelet therapy are well known and treatment can commence soon after stroke (see section 4.1.3), under treatment is common.⁴⁰⁴

The evidence for antiplatelet therapy indicates:

- Aspirin remains the most readily available, cheapest and most used anti-platelet agent. Aspirin reduces the risk of serious vascular events by about 13% in patients with previous ischaemic stroke or TIA.⁴⁰⁵

Aspirin at lower doses (75-150mg) is just as effective as higher doses (300-1300mg) and is associated with a lower risk of gastrointestinal adverse effects.⁴⁰² The lowest therapeutic dose of aspirin remains unclear, but the DUTCH TIA trial showed that in more than 3,000 patients with TIA, 30 mg was as effective as 283 mg in preventing serious vascular events.⁴⁰⁵

- Combination therapy with extended release dipyridamole (200mg bd) plus aspirin is more effective than aspirin alone (relative risk reduction [RRR] 18%).⁴⁰⁶ The main adverse effect of combination therapy is headache (34% ceased medication compared with 17% for aspirin alone over 5 years).⁴⁰⁶
- Dipyridamole alone at any dose is no more effective than aspirin.⁴⁰⁷

- Clopidogrel (75mg) is modestly more effective than aspirin in the prevention of major vascular events (RRR 8.7%).⁴⁰²
- The combination of low dose aspirin (75-162mg) plus clopidogrel (75mg) has no net benefit compared with clopidogrel alone (RRR 6%) or aspirin alone (RRR 7%) because any long-term benefits with combination therapy are offset by an increase in bleeding (1.7-2.6% v 1.3%).^{408, 409}
- Like clopidogrel, ticlopidine is modestly more effective than aspirin in prevention of vascular events.⁴¹⁰ Ticlopidine is associated with less gastrointestinal complications than aspirin, but an excess of skin rash and diarrhoea.⁴¹⁰ Ticlopidine is currently only available for those intolerant of aspirin

or with aspirin failure. Because it can cause neutropenia and thrombocytopenia, careful monitoring is required after commencement. However, its role has been superseded by clopidogrel which has a similar mechanism of action and similar efficacy, but without the serious haematological adverse effects.

When selecting antiplatelet therapy, individual patient factors (e.g. comorbidities - especially acute coronary disease, tolerance, stroke recurrence while on antiplatelet agent) should be considered and management tailored accordingly. Ongoing trials are directly comparing clopidogrel with combined aspirin-dipyridamole (e.g. PROfESS). The results of these studies will further guide choice of agents.

7.3	ANTIPLATELET THERAPY	GRADE	LEVEL
a)	Long term antiplatelet therapy should be prescribed to all people with ischaemic stroke or TIA who are not prescribed anticoagulation therapy.	A	Level I ⁴⁰²
b)	Low dose aspirin and modified release dipyridamole should be prescribed to all people with ischaemic stroke or TIA who do not have concomitant acute coronary disease.	✓	406, 411
c)	Aspirin alone or clopidogrel alone may be used for people who do not tolerate aspirin plus dipyridamole therapy. Clopidogrel alone should be used for those who are intolerant of aspirin or in whom aspirin is contraindicated.	✓	402
d)	The combination of aspirin plus clopidogrel is not recommended in the secondary prevention of cerebrovascular disease in patients who do not have acute coronary disease or recent coronary stent.	A	Level II ^{408, 409}

7.4 Anticoagulation therapy

There is evidence from robust systematic reviews involving a number of RCTs against the routine use of anticoagulant therapy in people with non-cardioembolic ischaemic stroke or TIA.^{157, 412}

Two subsequent studies of note have been reported in the last few years confirming this conclusion. One trial comparing oral coagulation (INR 2-3) and aspirin (30-325mg) found no difference in outcomes and was stopped early due to results of the other arm of the trial which found aspirin inferior to combined aspirin and dipyridamole.⁴¹³ However, this trial was not sufficiently powered to detect benefits of anticoagulation compared with aspirin and other issues have been raised including the open trial

method and variable aspirin dosage. Another trial of warfarin (INR 2-3) compared to aspirin (1300mg) for those with significant intracranial artery stenosis was also stopped early due to safety concerns for those receiving warfarin.⁴¹⁴

However, in people with non-rheumatic atrial fibrillation and a recent TIA or minor ischaemic stroke, the benefits of anticoagulants outweigh the risks and anticoagulants are more effective than antiplatelet therapy for long-term secondary prevention.^{119, 415} They should therefore be prescribed unless there is a major contraindication (e.g. poor compliance, major bleeding risk).

There remains uncertainty about the ideal time to commence therapy and no clear data are available to inform this decision. Trials generally enrolled patients after 1 or 2 weeks to reduce the risk of haemorrhage (only 12% of patients in the recent ESPRIT trial were enrolled within 1 week). One Level III-3 trial commenced appropriate anticoagulation prior to discharge from acute hospital care in 100% of cases

while all were still adhering to this therapy at 3 months post discharge.³⁹⁴ In patients with TIA, anticoagulation therapy should be commenced as soon as imaging has excluded intracerebral haemorrhage or a stroke mimic as the cause of the symptoms. Aspirin or other antiplatelet therapy should be used between acute event and time when anticoagulation is commenced.

7.4	ANTICOAGULATION THERAPY	GRADE	LEVEL
a)	Anticoagulation therapy for long-term secondary prevention should be used in all people with ischaemic stroke or TIA who have atrial fibrillation, cardioembolic stroke from valvular heart disease, or recent myocardial infarction, unless a contraindication exists.	A	Level I ^{119, 415}
b)	Anticoagulation therapy for secondary prevention for those people with ischaemic stroke or TIA from presumed arterial origin should not be routinely used as there is no evidence of additional benefits over antiplatelet therapy.	A	Level I ⁴¹²
c)	The decision to commence anticoagulation therapy should be made prior to discharge.	C	Level III-3 ³⁹⁴
d)	In patients with TIA, commencement of anticoagulation therapy should occur once CT or MRI has excluded intracranial haemorrhage as the cause of the current event.	✓	–

7.5 Cholesterol lowering

There is conflicting evidence regarding the link between elevated cholesterol and stroke subtypes, as epidemiology studies suggest that higher cholesterol is associated with a higher risk of ischaemic stroke but a lower risk of haemorrhagic stroke.⁴¹⁶ However, trials of cholesterol lowering interventions have not demonstrated increased rates of haemorrhagic strokes.⁴¹⁷ Two large RCTs have now demonstrated that statin therapy is beneficial for people with stroke or TIA.^{382, 418} While the earlier Heart Protection Study failed to demonstrate reductions in secondary stroke events, the more recent SPARCL study has demonstrated a modest reduction in subsequent stroke events with a statin.⁴¹⁸ Meta Analysis of trials demonstrate that benefits occur within 12 months of commencing therapy and are related to low-density lipoprotein (LDL) cholesterol reduction.^{417, 419} Meta-Analysis also suggest statins have a good

safety profile and are not associated with liver toxicity.^{420, 421} One study reported higher rates of adherence for statin therapy commenced prior to discharge from hospital.⁴²²

Lifestyle change strategies involving dietary modification have been shown to lower cholesterol levels in those with cardiovascular risks and should be used as an alternative, or in addition, to pharmacotherapy (see section 7.1) Currently the Pharmaceutical Benefits Scheme (PBS) states that dietary advice and interventions should be undertaken either prior or alongside drug therapy to reduce cholesterol and be reviewed annually. Systematic reviews including a wide range of patient groups have found benefits in behavioural interventions (e.g. motivational counselling or dietary counselling) delivered by specialist or trained clinicians, to positively change dietary patterns and lower cholesterol.^{395, 396}

7.5	CHOLESTEROL LOWERING	GRADE	LEVEL
a)	Therapy with a statin should be used for all patients with ischaemic stroke or TIA.	B	Level II ^{382, 418}
b)	Patients with high cholesterol levels should receive dietary review and counselling by a specialist, trained clinician.	B	Level I ^{395, 396}

7.6 Diabetes management

Diabetes and glucose intolerance post stroke have been found to be independent risk factors for subsequent strokes.^{195, 423, 424} Hyperglycaemia in the first few days after stroke is very common and levels fluctuate (see section 4.3.3). However, assessment of glucose tolerance after stroke or TIA would allow identification and subsequent management for patients with undiagnosed diabetes or glucose intolerance, hence providing additional secondary

prevention measures for stroke recurrence. Evidence for the management of diabetes is primarily based on primary prevention. Important aspects of care include careful blood pressure control, aggressive cholesterol control and glycemic control with behavioural (e.g. diet and exercise) and pharmacotherapy. National guidelines for the management of diabetes are available and relevant recommendations should be followed.⁴²⁵⁻⁴²⁸

7.6	DIABETES MANAGEMENT	GRADE	LEVEL
	All acute stroke patients should have their glucose monitored. Patients with glucose intolerance or diabetes should be managed in line with national guidelines for diabetes.	✓	–

7.7 Carotid surgery

Carotid endarterectomy

Carotid disease detected early by non-invasive imaging (see section 3.3) usually requires independent verification either by repeated non-invasive methods or traditional cerebral angiography before undergoing carotid surgery.¹⁰² If carotid disease is confirmed there is well established, robust evidence for the use of carotid endarterectomy (CEA) as the management of choice, particularly for symptomatic patients with ipsilateral moderate to severe stenosis (> 50% [NASCET criteria]).^{429, 430} Benefits are greatest among those with more severe stenosis, those >75 years of age, men, patients with recent stroke (rather than TIA), and those who undergo surgery early.^{430, 431} For stabilised patients the greatest benefit was found if surgery was undertaken within 2 weeks (NNT=5) with less effect at 12 or more weeks (NNT=125).⁴³¹

However, surgery is not without risks that need to be considered and discussed with the patient and their family/carer. For example, gender, age and comorbidity should be carefully considered in patients with symptomatic stenosis between 50% and 69%, as the absolute benefit of surgery is less than that for more severe degrees of stenosis.^{430, 431} There is no net benefit of CEA for those with symptomatic stenosis <50%.⁴²⁹

While the low risk of stroke in patients with asymptomatic carotid stenosis 60-99% can be lowered further by surgery the overall effect of surgery is small.⁴³² CEA for asymptomatic carotid stenosis is more beneficial for men than women, and for younger rather than older patients.⁴³² There is no clear benefit for patients with different degrees of stenosis >60% while there is no net benefit of CEA for those with

asymptomatic stenosis <60%.⁴³² Careful selection of patients considered at high risk of stroke is therefore needed to justify surgery in those with asymptomatic stenosis.⁴³²

It is important that centres undertaking CEA participate in ongoing, independent and systematic audits of surgical complication rates⁴³³ as this often determines the balance between benefits and harms, particularly for those with 50-69% stenosis. The evidence suggests low complication rates are needed (<6%) in patients with 70-99% stenosis to achieve net benefits. So extremely low rates (<3%) are suggested where centres are considering CEA for patients with symptomatic stenosis of 50-69% or asymptomatic stenosis 60-99%.^{429, 432}

Treatment with antiplatelet therapy (predominantly aspirin monotherapy) either commencing prior to or after CEA has been shown to reduce stroke recurrence although no effect was found for other outcomes.⁴³⁴ Combination therapy of clopidogrel and aspirin has been found to be beneficial using surrogate markers in two studies, however, no patient outcomes have been reported^{435, 436} and further studies are needed.

Carotid angioplasty and stenting

Endovascular surgery has been explored as an alternative to CEA, particularly in selected patients (significant heart or lung disease, >80 years, high or low carotid bifurcation or carotid re-stenosis after CEA). One systematic review found a reduction in cranial neuropathies with no other difference in benefits between the two approaches.⁴³⁷ Two of the five trials included in the review were stopped early raising safety concerns. Two subsequent trials have not added significant clarity to the debate. One trial reported similar results to the review with no difference between treatments.⁴³⁸ However, the other trial was stopped early due to safety concerns in those undergoing stenting.⁴³⁹

While many factors that may account for the inconsistencies have been discussed, further trials and analysis are needed before endovascular surgery can be routinely considered compared with CEA or if any particular subgroup should undergo one or the other treatment. Two ongoing trials will assist in answering such questions: the International Carotid Stenting Study (ICSS) and the Carotid Revascularisation Endarterectomy versus Stenting Trial (CREST).

7.7	CAROTID SURGERY	GRADE	LEVEL
a)	Carotid endarterectomy should be undertaken in patients with non disabling carotid artery territory ischaemic stroke or TIA with ipsilateral carotid stenosis measured at 70-99% (NASCET criteria) if surgery can be performed by a specialist surgeon with low rates of perioperative mortality/morbidity.	A	Level I ^{429, 430}
b)	Carotid endarterectomy should be undertaken in select patients (considering age, gender and comorbidities) with non disabling carotid artery territory ischaemic stroke or TIA with ipsilateral carotid stenosis measured at 50-69% (NASCET criteria) if surgery can be performed by a specialist surgeon with very low rates of perioperative mortality/morbidity.	A	Level I ^{429, 430}
c)	Carotid endarterectomy may be undertaken in highly select patients (considering age, gender and comorbidities) with asymptomatic carotid stenosis of 60-99% if it can be performed by a specialist surgeon with very low rates of perioperative mortality/morbidity.	A	Level I ^{429, 430}
d)	Eligible patients should undergo carotid endarterectomy as soon as possible after the event (ideally within 2 weeks).	A	Level I ⁴³¹
e)	Carotid endarterectomy should only be performed by a specialist surgeon at centres where outcomes of carotid surgery are routinely audited.	B	Level I ⁴²⁹
f)	Carotid endarterectomy is not recommended for those with <50% symptomatic stenosis or those with <60% asymptomatic stenosis.	A	Level I ^{429, 432}

cont.

7.7	CAROTID SURGERY cont.	GRADE	LEVEL
g)	Carotid angioplasty and stenting should not routinely be considered for patients with symptomatic stenosis. However, it may be considered as an alternative in certain circumstances, that is in patients who meet criteria for carotid endarterectomy but are deemed unfit due to medical comorbidities (e.g. significant heart/lung disease, age >80yrs), or conditions that make them unfit for open surgery (e.g. high or low carotid bifurcation, carotid re-stenosis).	B	Level I ⁴³⁷ & Level II ^{438, 439}

7.8 Patent foramen ovale

Patent foramen ovale (PFO) is more common in those with cryptogenic stroke, especially those <55 years.⁴⁴⁰ While much debated, PFO has not been found to increase the risk of subsequent stroke or death in cryptogenic stroke, however, it may increase such risks if present in combination with an atrial septal aneurysm.⁴⁴⁰

Two systematic reviews ^{440, 441} have identified only one RCT ⁴⁴² for medical management that compared warfarin (INR 1.4-2.8) to aspirin (325mg). The study was not designed to evaluate superiority between agents, however, no differences in recurrent stroke or

death rates over 2 years were found.⁴⁴² Warfarin use was found to have higher rates of minor bleeding.⁴⁴²

No RCT has compared surgical closure to standard medical care and Level IV data are conflicting. One systematic review involving 10 studies suggests surgery is beneficial compared to medical care,⁴⁴¹ however, 3 other subsequent studies failed to find any difference in stroke recurrence and reported non significant increase in harms.⁴⁴³⁻⁴⁴⁵ Until clear evidence exists from RCTs no recommendation can be made on the surgical closure of PFO.

7.8	PFO	GRADE	LEVEL
a)	All patients with an ischaemic stroke or TIA, and a PFO, should receive antiplatelet therapy as first choice.	C	Level II ⁴⁴²
b)	Anticoagulation may also be considered taking into account other risk factors and the increased risk of harm.	C	Level II ⁴⁴²
c)	Currently there is insufficient evidence to recommend PFO closure.	✓	–

7.9 Concordance with medication

Failure to take prescribed medication is a major barrier to optimal secondary prevention.

Three robust reviews have found only modest effects for interventions to improve adherence with medications in people with chronic illness, although the interventions were not tested specifically in the stroke population. Studies have found the following:

- Simplification of drug dose regimens, information/education, motivation, counselling,

family therapy, support and reminders, and complex or combined interventions were useful in promoting adherence to prescription regimes.⁴⁴⁶⁻⁴⁴⁸

- Education alone or informing people about adverse drug effects did not change adherence.⁴⁴⁸
- The use of multi-compartment packaging or other reminder packing strategies to promote adherence has conflicting evidence. One systematic review found benefits of compliance among non-adherent

adults living at home with diabetes, however, no benefits were noted for those with hypertension.⁴⁴⁹ However, the other more robust review found improvements in number of pills taken in four of the five included studies, but only modest clinical benefits were reported in one of the three trials for those with hypertension.⁴⁵⁰

- > One study found a program of initiating tailored secondary prevention medications while in hospital lead to improved rates of adherence both prior to discharge and 3 months after discharge.³⁹⁴ While only small numbers are reported, making it difficult

to establish secondary incidence, commencing strategies early may be a key to improving medication adherence and improve secondary prevention along with regular follow up.

The available studies suggest there is no single intervention that is proven to work across all patients, conditions and settings. Hence, specific interventions should be tailored to each individual's situation after stroke. Information specific to general practice has been developed and provides further practical advice.⁴⁵¹ However, further studies specific to stroke are needed.

7.9	CONCORDANCE WITH MEDICATION	GRADE	LEVEL
Interventions to promote adherence to medication regimes are often complex and should include one or more of the following: <ul style="list-style-type: none"> - information, reminders, self-monitoring, reinforcement, counselling, family therapy; - reduction in the number of daily doses; - multi-compartment medication compliance device; 		B B C	Level I ⁴⁴⁶⁻⁴⁴⁸ Level I ^{446, 447} Level I ^{449, 450}

8

DISCHARGE PLANNING, TRANSFER OF CARE AND INTEGRATED COMMUNITY CARE

Good discharge planning is crucial for successful reintegration into the community as well as effective and efficient use of limited hospital resources. While it is known that the transfer of responsibility for management from inpatient to the community can be difficult, insufficient attention and resources are often provided for this process. One group that is of particular concern is younger stroke survivors (i.e. <65 years) who may require residential care post-discharge. Whilst the ideal discharge outcome may in fact be to an inpatient rehabilitation facility this is not always feasible in all geographical locations. Careful consideration needs to be given to discharge destinations (other than a rehabilitation facility) to ensure the person is in appropriate accommodation and is able to receive necessary services.⁴⁵² Discharge planning relies on effective communication between team members, the person with stroke, family/carers, and community service providers including general practitioners. Important aspects of care during this phase including team meetings, family meetings, information/education and shared care have been discussed under organisation of care and should also be considered when planning discharge or transfer of care (see Sections 1.5, 1.6, 1.7 & 1.10). Other important aspects of care to consider during acute care include return to work, leisure and sexuality. While such topics should be discussed with relevant stroke patients, these topics are covered in the Clinical Guidelines for Stroke Rehabilitation and Recovery and readers are referred to that document for recommendations.

8.1 Ongoing inpatient care

The evidence suggested that organised stroke unit care is most effective when a number of weeks of rehabilitation are offered.^{6, 19} Furthermore, all patient types benefit from rehabilitation (probably more so those who are severely affected by stroke).⁶ If the acute stroke services are unable to provide necessary ongoing rehabilitation then alternative rehabilitation services, ideally on a stroke rehabilitation unit, need to be considered and organised. While prognostic studies have described different attributes that impact on rehabilitation and recent imaging can predict the amount of damage and areas where recovery may be possible there is no generic criteria for selecting those who require ongoing, active rehabilitation. Hence, the decision as to who should be provided with continued inpatient or outpatient rehabilitation is a complex decision that requires input from the whole stroke team taking into consideration the needs and wishes of those with stroke and their families. Often rehabilitation will be undertaken in a different part of the hospital or a different site altogether. Evidence for hospital based rehabilitation is still consistent with that in the Clinical Guidelines for Stroke Rehabilitation and Recovery that describes high level evidence for inpatient rehabilitation care and community rehabilitation services.

8.1	INPATIENT REHABILITATION	GRADE	LEVEL	CONSUMER RATING
	If ongoing inpatient rehabilitation is needed, care should be provided in either a stroke rehabilitation unit or a general rehabilitation unit.	A	Level I ^{6, 19}	9.4/10

8.2 Pre-discharge needs assessment

A pre and/or post-discharge needs assessment examines, for example, the social, emotional, physical and financial needs of the person with stroke and his/her family/carer. Assessment of discharge needs should start as soon as possible after admission. Any cognitive or behavioural issues identified should be

discussed and management incorporated into any discharge plan (e.g. monitoring of mood). The circumstances and capacity of the carer and family should also be explored, ideally with the person with stroke, to identify any community care supports needed. The needs assessment should identify who

requires a home visit. Factors to consider include the reported environmental barriers at home, specific physical and/or cognitive impairments, risk of falls and the needs and desires of the patient and the family. The need for home modifications or assistive equipment may also be determined, and appropriate modifications and/or assistive equipment recommended.

There is no stroke-specific evidence regarding the effectiveness of this approach, and very little evidence in other populations. One systematic review included four RCTs regarding the use of an Occupational Therapy home visit.⁴⁵³ No clear evidence was found

on the effectiveness of pre-discharge home visits for people with stroke, or indeed for older people preparing to go home. However, such interventions may influence quality of life, number of falls and patient autonomy.⁴⁵³ Home assessment and modification has been found to reduce falls in elderly people in the community^{454, 455} but it is unclear if this same benefit exists for stroke patients discharged from an acute hospital. Further robust studies are therefore required to determine which sub-groups benefit from home visits, since this is a time consuming and costly intervention.

8.2	PRE-DISCHARGE NEEDS ASSESSMENT	GRADE	LEVEL	CONSUMER RATING
a)	Before discharge, people with stroke and their carers should have the opportunity to identify and discuss their post-discharge needs (e.g. physical, emotional, social and financial) with relevant members of the interdisciplinary team.	✓	–	9.5/10
b)	Before discharge all patients should be assessed to determine the need for a home visit prior to discharge from hospital.	✓	–	–
c)	If needed, a home assessment should be carried out to ensure safety and community access.	C	Level I ⁴⁵³	–

8.3 Carer training

Carers often report feeling inadequately trained, poorly informed, and dissatisfied with the extent of support available after discharge. Evidence from a recent, high quality trial suggests that carers benefit from undertaking training prior to discharge in a range of

activities related to care, including personal care techniques, communication, physical handling and transfers, ongoing prevention of functional decline and other specific stroke-related problems.⁵⁶

8.3	CARER TRAINING	GRADE	LEVEL	CONSUMER RATING
	Relevant members of the interdisciplinary team should provide specific training for carers before the person's discharge home. This should include training, as necessary, in: <ul style="list-style-type: none"> personal care techniques, communication strategies, physical handling techniques, ongoing prevention and other specific stroke-related problems; safe swallowing and appropriate dietary modifications. 	B	Level II ⁵⁶	9.5/10
		✓	–	9.5/10

8.4 Care plans

A care plan is normally completed prior to discharge and identifies appropriate management strategies to guide care after the stroke survivor returns to the community. Care plans are based on the needs identified in the pre-discharge assessment, and are useful in building self-management strategies for those with stroke. All team members, including the person with stroke, the family/carer, the general practitioner, and community-based service providers are ideally involved in developing and documenting an agreed plan that takes into account the complex adjustments

needed, especially when changing settings or care. A formal family meeting or conference is often used to develop such a plan.

Evidence for discharge planning (one component of the total care planning process) is unclear.⁴⁵⁶ This suggests care plans are often one component of a complex service delivery (e.g., early supported discharge or inpatient integrated pathway). In many of the trials it is difficult to determine the evidence for this specific component.

8.4	CARE PLANS	GRADE	LEVEL	CONSUMER RATING
a)	People with stroke, their carers, the general practitioner, and community care providers should be involved with the interdisciplinary team in the development of a care plan.	✓	–	9.7/10
b)	Care plans should be used and outline care in the community after discharge, including the development of self-management strategies, provision of equipment and support services, and outpatient appointments.	✓	–	9.7/10

8.5 Discharge planner

Effective communication regarding inpatient management and future management plans remains an important part of good stroke care. Discharge planning may be coordinated by one member of the team (e.g. inpatient care coordinator) or it may be undertaken by someone who coordinates discharges for multiple teams (or the whole hospital). One lower level trial involving a comprehensive discharge planning program for people with craniotomy or stroke, coordinated by a discharge planner, reduced length of stay and readmissions, but did not change

function or patient satisfaction.⁴⁵⁷ Two relevant systematic reviews were identified, however, neither review provided clear conclusions.^{44, 456}

Any person coordinating discharge should provide the person with stroke and their family/carer with appropriate information regarding the details of any community services, possible waiting times, costs and contact details prior to discharge. Good pre-discharge care planning addresses these communication issues and supports effective transfer of care.

8.5	DISCHARGE PLANNER	GRADE	LEVEL	CONSUMER RATING
a)	A discharge planner may be used to coordinate a comprehensive discharge program for people with acute stroke.	D	Leve I III-3 ⁴⁵⁷	–
b)	The stroke survivor's general practitioner, other primary health professionals and community service providers should be involved in, and informed about, the discharge plans and agreed post-discharge management, as early as possible prior to discharge.	✓	–	–

8.6 Community rehabilitation

Often rehabilitation will need to continue after discharge (either as part of an early supported discharge program or general community rehabilitation) and can be undertaken in various settings depending on availability of transport, patient wishes and family/carer and local resources. Evidence for community based rehabilitation is still consistent with that in the Clinical Guidelines for Stroke

Rehabilitation and Recovery which described high level evidence for community rehabilitation services for people with stroke. The needs identified by the stroke team and the patient/family/carer (via the pre-discharge needs assessment) and availability of local community services will determine which option is preferred.

8.6	COMMUNITY REHABILITATION	GRADE	LEVEL	CONSUMER RATING
	Rehabilitation in the community is equally effective if delivered in the hospital via outpatients, or day hospital, or in the community, and should be offered to all stroke patients as needed.	A	Level I ^{63, 458, 459}	9.4/10

8.7 Post discharge support

The level of services available following discharge from hospital can be poor, and people with stroke and their families often report being dissatisfied with the information, support services and therapy available.⁴⁶⁰

A number of follow-up services have been evaluated including:

- social work;^{461, 462}
- specialist nurse support;^{53, 54, 57, 59, 60, 463}
- the Stroke Transition After Inpatient Care (STAIR) program;⁴⁶⁴
- stroke family care worker;⁴⁶⁵
- mental health worker;⁴⁶⁶
- home visits by physician or physiotherapist;⁴⁶⁷ and
- stroke family support organisers.⁴⁶⁸⁻⁴⁷⁰

Such services are usually multidimensional and can include emotional and social support, assistance with referral to other services, and the provision of

information to people with stroke and their families.

The evidence is difficult to interpret and no one service has been shown to be clearly beneficial. Studies suggest modest advantage when providing tailored education although no clear functional benefits have been found and further studies are needed. A simple approach often incorporated into other multidimensional interventions is the use of telephone contact after discharge. While one recent systematic review failed to demonstrate consistent benefits from a range of non stroke populations,⁴⁷¹ two stroke related studies involving 3 telephone calls from a nurse in the first 3-5 months post discharge provided some benefits.^{53, 60} As the early post discharge period is consistently reported by stroke survivors and their family/carers to be a difficult time, the provision of simple and relevant services appears important.

8.7	POST-DISCHARGE SUPPORT	GRADE	LEVEL	CONSUMER RATING
a)	Contact with and education by trained staff should be offered for all stroke survivors and carers after discharge.	C	Level II ^{53, 54, 57, 59, 60, 463, 468-470}	–
b)	People with stroke and their carers should be provided with a contact person (in the hospital or community) for any post-discharge queries.	D	Level I ⁴⁷¹ & Level II ^{53, 60}	–

8.8 Return to driving after stroke or TIA

The issue of returning to driving can be confusing and the topic is often raised by the patient or their family/carer, especially for patients with minor stroke or TIA. Currently there are National Guidelines for Driving⁴⁷² as well as state or local guidelines. The current National Guidelines describe conditions for unconditional licences and where conditional licences exist. Patients with stroke automatically have a conditional licence and are not to return to driving for a minimum of 1 month if there are significant neurological, perceptual or cognitive deficits. A physician assessment should be undertaken before returning to drive and where necessary (where stroke deficits are deemed to potentially impact on driving) a driver assessment. There is currently no restriction in place for those with first TIA, however, restrictions apply when the person has had two or more TIAs. In such cases a conditional licence may be granted taking into account the opinion of the treating doctor/GP, and the nature of the driving task, and subject to periodic review if the aetiology of the TIAs has been identified, the underlying cause removed,

and the person has had a 6 month period free of attacks.⁴⁷²

State based guidelines describe the responsibilities of the patient, the treating doctor or both. In general they recommend a period without driving. The ABCD² tool may assist to screen those at high risk after TIA and to inform the decision and advice provided to patients and their families. Those with a high risk should clearly be advised to avoid driving given the higher risk of stroke within the first few weeks.

In all cases, people with stroke who held a driving licence pre-stroke should be provided with written information about returning to drive including legal obligations and necessary assessments. This information should be provided prior to discharge from hospital or preferably within the first visit in the case of those not admitted to hospital.

Further discussion about assessment and management of driving after stroke is found in the Clinical Guidelines for Stroke Rehabilitation and Recovery.

8.8	RETURN TO DRIVING	GRADE	LEVEL	CONSUMER RATING
	The National Guidelines for Driving and relevant state guidelines should be followed when assessing fitness to drive following a stroke or TIA. In general, patients with TIA or minor stroke, especially those found to be at high risk, should be advised to delay returning to driving for at least 1- 4 weeks.	✓	–	9.7/10

Introduction

This section presents a review of the cost and socioeconomic implications of providing evidence based stroke care supported by the recommendations contained within this guideline. The Guidelines project officer conducted a separate systematic review for this section. The search strategy included a focus on cost-effectiveness studies that considered both the costs and health outcomes associated with an intervention. The key search terms used were consistent with those used for the previous searches with adjustments made to focus on economic implications. The search strategy used is available from the NSF. Overall, 1,438 potential papers were identified with reference to the primary subjects (recommendation headings) in this guideline. The abstracts were scrutinised for omissions and appropriate papers were retrieved and reviewed. As the breadth of topics was wide and the methods used quite disparate, a narrative review was deemed the most appropriate way to summarise the cost and socioeconomic evidence. There was also a preference to include studies undertaken in Australia, therefore if similar work had been undertaken elsewhere this was often discarded, unless the results were relevant to the findings in Australia. This is because it is often difficult to extrapolate from international studies to the Australian context given differences in health services provision and funding, target populations and interventions, such as drug dosages.

The discussion related to the cost-effectiveness evidence is presented to reflect the structure of the document. It should be noted that this guideline includes many consensus recommendations or recommendations based on levels of evidence below Level II for a number of 'micro' clinical practice issues (e.g. physiological monitoring and oxygen therapy). As such, it is not possible to analyse the implications of these sorts of recommendations, as they in fact often form part of a larger package or program of care, for which there is Level I evidence (for example, stroke units). Furthermore, there is limited cost-effectiveness evidence available for many acute stroke care interventions and often these types of studies have not been conducted. Therefore, evidence and discussion for the main (strongest) recommendations in this guideline will be provided. This review is also an

extension to the work recently prepared for assessing the potential economic implications of the Stroke Rehabilitation and Recovery Guidelines.⁷

There are two important points to keep in mind when reviewing the data presented in relation to cost-effectiveness. Firstly, an intervention can be cost-effective without being cost saving and secondly what constitutes a cost-effective intervention is a value judgement. In previous Australian policy decisions, \$30,000-\$50,000 per Disability Adjusted Life Year (DALY) recovered has been considered to represent value-for-money in the health sector.⁴⁷³

Evidence related to socioeconomic implications is sparser than the cost-effectiveness evidence. Where relevant references to socioeconomic implications were identified these will be highlighted. Overall, we know that there are disparities between people with different socioeconomic status. Socioeconomic status and its definition can vary depending on both the wealth of a country and that of the individuals within that country. In addition, the socio-economic status of countries and individuals does not tend to shift readily. The most disadvantaged people in society in terms of occupational status, level of education and financial resources tend to have the greatest burden of health risks which cluster and accumulate over time.⁴⁷⁴ Evidence suggests that socioeconomic factors appear to outweigh classic risk factors in predicting stroke trends and it has been estimated that about 68% of the variation in stroke mortality rates can be explained by differences in gross domestic product (GDP) between countries.⁴⁷⁵

In Australia, evidence from the North East Melbourne Stroke Incidence study (NEMESIS) indicates that stroke incidence rates increase among people with increasing levels of social disadvantage.¹⁵ People with the highest level of disadvantage were estimated to have about a 60% increased risk of stroke compared to those with the lowest level of disadvantage. Accounting for socioeconomic status is therefore an important aspect to consider when exploring the potential expected benefits of prevention interventions, as these may be over or underestimated for different populations.

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9.1 Organisation of care

9.1.1 Stroke Unit Care

To date there has been one systematic review identified that included three studies comparing the costs and outcomes of stroke units to that of general wards.⁴⁷⁶ All three studies were based in Europe (UK, Sweden and Germany) and included costs of community and outpatient care. All three studies found modest cost savings (3-11%) using stroke unit care, however, the figures failed to reach significance. The authors concluded that there was “some” evidence for the costs to be at least equivalent to conventional care.

More recently, an Australian prospective cohort study comprising 468 patients from Melbourne has been published.⁴⁷⁷ The investigators determined that care delivered in geographically localised units was cost-effective compared with general medical wards or mobile stroke (inpatient) teams and that the additional cost in providing stroke units compared with general medical wards was found to be justified given the greater health benefits in terms of delivering best practice processes of care and avoiding severe complications. When compared to general medical care costs (\$12,251), costs for mobile teams were significantly higher (\$15,903 $p=0.024$), but borderline for stroke units (\$15,383 $p=0.08$). This was primarily explained by the greater use of specialist medical services. The incremental cost-effectiveness of stroke unit over general wards was \$AUD9,867 per patient achieving thorough adherence to clinical processes and \$AUD16,372 per patient with severe complications avoided, based on costs to 28 weeks.

These findings generally accord with international studies, such as that conducted by Patel et al (2004).⁴⁷⁸ This is the first Australian study to detail the costs and cost-effectiveness of different acute care models, and it provides important information to underpin increased investment in stroke units.

Further, other work by Moodie et al (2004) has demonstrated that when modelled over the lifetime of a cohort of first-ever stroke patients, stroke units when compared to general medical care, produced considerable gains in terms of health benefits with these additional benefits associated with additional costs. There was an additional lifetime cost of \$1,288 per DALY recovered, or alternatively \$20,172 per stroke averted or \$13,487 per premature death averted. It was determined that the stroke unit intervention was cost-effective given the small additional costs per extra unit of benefit gained.⁴⁷⁹

Currently, only 19% of public hospitals report providing stroke unit care⁴⁸⁰ and there is clustering of stroke units in large urban centres. Stroke units improve outcomes for people with stroke (see section 1.1). Further economic modelling work has predicted that if access to stroke units was improved to 80% from a baseline of 25%, then more than 8,374 DALYs could be recovered.⁴⁸¹ Although this literature does not specifically indicate the real costs of setting up a stroke unit, there is evidence that health services should be organised to provide stroke unit care and that considerable gains in terms of health benefits could be achieved.

9.1.2 Care Pathways and Clinical Practice Guidelines

The effectiveness of care pathways in stroke management is variable and the effects on length of stay and costs are inconclusive.^{44, 482} To date there has not been a cost-effectiveness study for care pathways in stroke, but there is evidence that the setting of use may be important.

The study (pre-post audit design) conducted by Read and Levy (2006) has shown that implementation of pathways in regional Queensland can assist in improving adherence to important processes of care, such as early access to allied health, improved use of antithrombotic agents in eligible cases at discharge and estimation of blood glucose levels.⁴⁸³ Similar studies conducted in Victoria have also indicated improved adherence to some important processes of care with use of care pathways or clinical management plans.^{20, 24, 484} More recent evidence may suggest better effectiveness in acute settings than rehabilitation settings.⁴⁵ It also appears that factors, such as the experience of the specialist team in managing stroke, may be important, with the use of such plans more effective in settings that have newly organised stroke services.

There has been one study conducted in Italy that has examined whether adherence to clinical practice guidelines influences the cost of acute stroke care. Non-compliance with guidelines was shown to be associated with increased costs (for every unit of non-compliance there was a 1.38% increase in hospital costs).⁴⁸⁵ Locally, evidence published from the SCOPES study indicates that greater adherence to important clinical processes of care occur more often in stroke units and there is also a reduction in severe complications, which when these measures are used as proxies of health outcome indicate that these units are more cost-effective than other care modalities.⁴⁷⁷ In SCOPES, hospitals with

stroke units that used care pathways were more likely to complete them.²⁴ In most studies it is difficult to separate out the specific benefits of care pathways from other aspects of organised services, such as team meetings and experienced staff. Therefore, the fundamental conclusion from this review is that organised management for stroke that provides evidence-based clinical care, with or without care pathways, should be cost-effective.

9.1.3 Early Supported Discharge (ESD)

One systematic review identified eight trials evaluating the economic implications of ESD compared with conventional care.⁴⁷⁶ Two studies were conducted in Australia with the remainder from Hong Kong (one), Canada (one), Sweden (two) and the UK (two). All but one of the studies compared ESD using home-based services to conventional services (noted to be either hospital rehabilitation or mix of hospital and community rehabilitation). Of the eight studies included, six studies were noted as having medium or high methodological quality. These studies reported a trend for reduced costs of between 4-30% with ESD, however, this cost saving was found to be statistically significant in only one of the six studies. The authors concluded that there was “moderate” evidence that ESD services provided care at modestly lower total costs than conventional care. However, the heterogeneity of the ESD care provided was noted along with the uncertain impact of ESD care on hospital readmission and informal carers. The review also concurred with the previous summary (section 1.9) that ESD favours stroke survivors with mild or moderate disability.

One subsequent UK trial-based study assessed the outcomes and costs of early domiciliary care compared to hospital based care.⁴⁷⁸ A societal perspective for costs was used based on 1997/8 prices. Mean costs for health care and social care costs over 12 months were £6840 for domiciliary care compared to £11,450 for stroke units. In terms of Quality Adjusted Life Years (QALYs) these were less for domiciliary care when compared to stroke unit care (0.221 v 0.297). Cost-effectiveness was calculated using incremental cost-effectiveness ratios (ICERs) for avoiding an additional 1% of deaths or institutionalisation that ranged from £496 (without informal costs) to £1033 (with highest estimate of informal costs) for stroke unit care compared with domiciliary care. Based on each additional QALY gained the costs ranged from £64,097 to £136,609. Hence in this study, health outcomes were

lower using this ESD model in comparison to inpatient stroke unit care, but ESD was found to be cheaper. A separate randomised controlled trial of unselected hospital cases undertaken in Norway has also indicated that an early supported discharge program provided after 2 weeks in a stroke unit (as an alternative to inpatient rehabilitation) offered a cost neutral or cheaper option over a 12 month period. In particular, ESD was more cost-effective in cases of moderate stroke, rather than very mild or severe stroke.⁴⁸⁶

Data specific to the Australian context was included in the previous review and warrant further discussion. The data from a meta-analysis of ESD (12 trials, N=1277, search date March 2001) were used to apply costs from the Australian health system.⁴⁸⁷ Hospital costs were taken from the Australian National Hospital Cost Data for 1998/1999, domiciliary rehabilitation costs were taken from a single study of domiciliary rehabilitation care (Adelaide stroke study) and costs related to other community services were taken from the Australian Department of Health and Family Services Report, 1996/1997.⁴⁸⁷ Using a cost minimisation analysis (i.e. health outcomes were found to be equivalent) ESD was found to be 15% lower regarding overall mean costs (\$A16016 v \$18350). Cost estimates were based over a 12-month period and did not include any indication of set up costs. It was highlighted that the included studies were all based in urban centres confirming the view that ESD should only be considered where appropriate resources are available to provide effective domiciliary care. A small shift of costs from the secondary sector to the primary sector was noted (more GP visits with ESD care), however, no difference was found in the cost of routine community and outpatient services. Overall, ESD was found to provide a cost saving alternative to conventional care and the authors concluded that it therefore should be considered for certain subgroups of people with stroke

The above studies provide limited evidence regarding the cost-effectiveness of ESD in Australia. It can be concluded that ESD may offer an alternate option to inpatient care and produces equivalent outcomes for patients at similar or potentially reduced costs, in particular for urban settings and in cases with moderate severity strokes.

9.2 Specific interventions for the management of stroke

9.2.1 Intravenous thrombolysis

The use of intravenous recombinant tissue plasminogen activator (rt-PA) for treatment of eligible patients with acute ischaemic stroke has been consistently demonstrated to be cost-effective, independent of differences in included costs, modelling assumptions and the health care environments within which cost-effectiveness evaluations (CEAs) have been undertaken. A descriptive review of three comprehensive evaluations of rt-PA from the United States, Canada and the United Kingdom has been undertaken.⁴⁸⁸ This review found that rt-PA was cost-effective in all three studies, with health benefits and cost savings over a 30-year time horizon. A more recent cost-effectiveness analysis incorporating European individual patient data has shown consistent findings.⁴⁸⁹ In the Australian setting, Moodie and colleagues investigated the cost-effectiveness of intravenous rt-PA using a comprehensive stroke economic model, “A Model of Resource Utilization, Costs and Outcomes for Stroke (MORUCOS).⁴⁷⁹ Data obtained from NEMESIS were used to describe the ‘base case’ against which the use of intravenous rt-PA was compared. Disability-adjusted life years (DALYs) were used to measure health gains. Using this modelling approach, rt-PA was found to be both effective and cost-saving.

9.2.2 Aspirin within 48 hours of stroke

There are limited data on the cost-effectiveness of aspirin within 48 hours of stroke. Economic modelling for Australia suggests that the treatment is cost-effective and the incremental cost/DALY lifetime benefit of treating one additional first-ever case of stroke with aspirin as an acute therapy is about \$1,847.⁴⁹⁰ In contrast to other Level I recommendations in this guideline that have been compared using the same economic model, this result was less favourable to the cost-effectiveness results of stroke units (\$1,390), warfarin as primary and secondary prevention and intravenous rt-PA (these later two interventions being highly effective and cost saving). Although not cost saving, it should be noted that both stroke unit care and aspirin within 48 hours could be applied to many more patients than rt-PA and warfarin. Further, the stroke unit intervention represents a composite of these interventions as they are not independent and it is expected that patients treated in stroke units also receive these evidence-based therapies as required. In terms of ‘value’ each of these interventions would be considered highly cost-effective as they are much lower than the \$30,000-\$50,000 per DALY

recovered threshold expressed as representing value-for-money in the health sector.

9.2.3 Imaging modalities

CT and MRI in stroke

One systematic review of economic evaluations identified 3 studies that assessed the cost-effectiveness of CT scanning in acute stroke patients.⁴⁹¹ The authors of this review concluded that immediate CT scanning (versus no CT scanning or later CT scanning) may reduce the cost of stroke care by shortening or avoiding inpatient stays. The absolute difference between scanning immediately, within 24 hours, or within 48 hours was minimal. These findings were sensitive to inpatient costs, the availability of non-hospital stroke care and the ability to effectively use saved bed-days. Although the authors’ conclusions are based on the UK data¹⁰⁰ it is likely that this finding is applicable to the Australian setting. Currently there are no data regarding the cost-effectiveness of MRI in subgroups of stroke patients.

Carotid imaging

One cost-effectiveness study has provided evidence that carotid duplex ultrasound is the most efficient single examination strategy to detect high grade carotid stenosis in symptomatic patients suitable for carotid endarterectomy.⁴⁹² This study used Markov modelling and incorporated both published data from randomised trials and data from a multicentre cohort study (n=350) performed to assess the diagnostic accuracy. The addition of magnetic resonance angiography slightly increased effectiveness but at disproportionately high costs.⁴⁹² A more recent detailed cost-effectiveness study of the assessment of carotid stenosis conducted in the UK provided evidence that non-invasive assessment of carotid stenosis, including use of ultrasound as the first or repeat test, could be used in place of intra-arterial angiography to select patients who are likely to benefit from carotid endarterectomy. However, the findings from the economic model were sensitive to the accuracy of non-invasive testing and to the cost and timing of surgery.¹⁰²

9.2.4 Rapid assessment clinics and management of Transient Ischaemic Attack

The cost-effectiveness of rapid assessment clinics and clinics to enable the outpatient management of ‘low-risk’ TIA has not been evaluated in terms of cost-effectiveness to our knowledge.

9.2.5 Carer training

One study was identified that assessed the economic outcome of training carers.⁴⁹³ Evidence was based on one RCT conducted in the UK. The study has been discussed previously (see section 8.3). Costs were based at 2001-2 prices and included health and other formal care costs as well as informal costs. Providing carer training during inpatient rehabilitation reduced total costs (mean saving of £4043), primarily reflecting savings due to earlier discharge from inpatient care, while also improving health outcomes. No difference in QALYs in carers were found, however, the authors suggested that this was likely to be influenced by the insensitivity of the outcome measure used (EuroQol five-dimensional questionnaire).

Since the burden of providing both formal and informal care after stroke in Australia is significant,⁴⁹⁴ inpatient rehabilitation services in Australia should be encouraged to introduce formal carer training as part of their care. Further cost-effectiveness studies in this area are needed that include appropriate assessment of the impact on carers.

9.2.6 Stroke prevention

There are few economic evaluation studies available for secondary prevention based on Australian data in stroke. The majority of the literature related to the cost effectiveness of prevention interventions relates to carotid surgery and pharmacological therapies, which may include stroke outcomes, but are not always stroke specific.

Carotid endarterectomy in symptomatic patients with high-grade stenosis

There has been one systematic review of health economic studies that have assessed the costs and benefits of carotid endarterectomy and associated preoperative arterial imaging.⁴⁹⁵ The authors of this review identified 21 studies for inclusion but only three were true cost-effectiveness studies. All three studies were set in the United States in the early 1990s and used modelling techniques incorporating data from published, randomised clinical trials. Although carotid endarterectomy was cost-effective in these evaluations, the authors of the review pointed to significant differences in the estimated costs and benefits between these studies and among the included partial economic evaluations. An important observation is that the use of trial data about peri-operative morbidity and mortality is likely to overestimate the benefits of carotid endarterectomy when applied in the

real world situation. Nevertheless, it is very likely that carotid endarterectomy in recently symptomatic patients with high grade carotid endarterectomy is highly cost-effective when performed with low perioperative morbidity and mortality.⁴⁹⁶

Pharmacological therapies

Moodie (2004) has investigated the cost-effectiveness of anti-thrombotic (warfarin) treatment for people with atrial fibrillation as a primary and secondary prevention measure.⁴⁷⁹ This investigator determined that 1,851 DALYs could be recovered with a cost/DALY saved of \$480. This finding was based on the 1997 Australian population modelled using MORUCOS, an economic model with resource utilisation data derived from the North East Melbourne Stroke Incidence Study. One published systematic review has identified three studies assessing the cost-effectiveness of anticoagulation for primary prevention in people with atrial fibrillation (AF).⁴⁹⁷ Warfarin was more cost-effective than aspirin for people with two or more stroke risk factors, in addition to those with chronic non-valvular AF in one study. Warfarin was also found to be cost-effective for people with only one other stroke risk factor costing US\$8000 per QALY. However, warfarin use for people with no other stroke risk factors, apart from AF, was not cost effective with costs of US\$370,000 per QALY. A second study confirmed these findings. The third study found anticoagulation for AF caused by mitral stenosis to be cost effective with costs of only US\$3700 per QALY.

Economic benefits of a specific blood pressure medication (ramipril) for people at high risk of heart disease and stroke has been studied.⁴⁹⁸ This Australian study reported a potential reduction of 9,188 strokes over 5 years. The incremental cost-effectiveness result, estimated as a cost per life-year saved, was \$17,214 based on a combined cardiovascular death endpoint.

Six international studies were identified that assessed the cost-effectiveness of antiplatelet therapy in secondary stroke prevention. Two studies compared a combination of dipyridamole plus aspirin to aspirin alone.^{499, 500} One study compared clopidogrel to aspirin.⁵⁰¹ The other three studies compared all three therapy options.⁵⁰²⁻⁵⁰⁴ The studies predicted costs in the UK, USA and France over a period of 2 years, 5 years or over a lifetime. The combination therapy of dipyridamole plus aspirin was found to be cost effective compared with aspirin alone in all five studies. However, there was conflicting evidence for

the cost effectiveness of clopidogrel. Two studies reporting no cost effectiveness using clopidogrel.^{502, 503} Two other studies found clopidogrel was cost effective and reported ICERs of US\$31,200 and US\$26,580 per QALY saved.^{501, 504}

An economic model based on data obtained in the Heart Protection Study has provided evidence that cholesterol lowering using simvastatin 40mg daily is cost-effective, not only among the population of patients enrolled in this trial (aged 40-80 years with coronary disease, other occlusive arterial disease or diabetes) but also for people with an annual risk of major vascular events of 1% or more, independent of the age of commencement of statin treatment.⁵⁰⁵ Cost-effectiveness estimates remained favourable when proprietary (£4.87) versus generic simvastatin (£29.69) prices were assumed. Simvastatin treatment was cost saving or cost less than £2500 per life year gained across the range of scenarios assessed.⁵⁰⁵

Lifestyle (non-pharmacological) prevention interventions

Cost-effectiveness studies undertaken for lifestyle changes are limited in that they have not been undertaken for stroke specifically and most consider primary prevention measures. However, in the available studies, smoking cessation has been reported to cost between £270-1500 per QALY saved depending on the intervention (e.g. advice from GP or nicotine replacement strategies).⁵⁰⁶ The use of quit lines or telephone counselling are also cost effective.^{507, 508} One large systematic review identified only five economic evaluations for lifestyle interventions (e.g. dietary modifications and/or exercise) aimed at reducing obesity in those with diabetes.⁵⁰⁹ Such interventions were found to be cost effective when viewed over a 5 year or longer period. One study in the UK suggested the costs saved far outweigh the costs spent on exercise in those over 45 years old.⁵¹⁰ There have also been several studies reporting the cost-effectiveness of physical activity counselling or activities highlighting that interventions can offer value for money over usual care for sedentary adults.⁵¹¹⁻⁵¹³ Clearly, stroke specific studies are needed to assess the potential cost-effectiveness of lifestyle change interventions as well as other prevention interventions.

Several other authors have also highlighted the usefulness of multiple risk assessment models for improving the effectiveness and/or efficiency of treatment to prevent cardiovascular disease.^{396, 514-518} This is prefaced on the fact that risk factors are continuous and arbitrary cut-

points for treatment do not discriminate well between those who will and will not have an event. Murray et al (2003) showed that combination pharmacological treatment for people with a 35% risk of a cardiovascular event over 10 years was cost-effective and would result in the recovery of 63 million DALYs worldwide.⁵¹⁵ There has been one recent comparative evaluation of five international guidelines from English speaking countries including Australia using the treatment recommendations within these guidelines and modelled for 'best practice'. It was reported that the cost per cardiovascular event prevented was lowest in older patients and very high in those aged less than 35 years. It was also expressed that clinical practice guidelines that used 'absolute risk' criteria as the principle determinant of treatment, were more cost-effective than those recommending management for thresholds of single risk factors.⁵¹⁴ In consideration of risk assessment, all persons who have experienced a stroke or TIA would be considered at high risk of another vascular event. Therefore, use of anti-platelet therapy, cholesterol lowering and BP lowering in eligible high-risk patients could be considered cost-effective.

Conclusions

In conclusion, there is good evidence of cost-effectiveness for the most clinically effective and important stroke prevention and treatment strategies recommended in this guideline. In particular, the findings from a recent modelling exercise in the Australian setting indicate that more widely accessible, evidence-based stroke care could produce substantial economic and health-related benefits and would require only modest investment. The authors suggested that if there was improved access of eligible stroke patients to effective acute care (stroke units and intravenous thrombolysis) and secondary prevention (BP lowering, warfarin for AF, aspirin in ischaemic stroke and carotid endarterectomy), as well as improved management of BP and AF as primary prevention in the Australian population, then about \$1.06 billion could be recovered as potential cost offsets with recovery of more than 85,000 DALYs.⁴⁸¹ Therefore, clinical guidelines such as these which promote improved treatment and prevention of stroke are an important contribution to achieving such increased access and the cost-effective use of health resources in this country.

APPENDIX A: Guideline development process report

Development of Clinical Guidelines for Acute Stroke Management

The Clinical Guidelines for Acute Stroke Guidelines have been developed by the National Stroke Foundation according to processes prescribed by the National Health and Medical Research Council (NHMRC) toolkit series under the direction of an interdisciplinary Expert Working Group (EWG). The EWG has worked through a collaborative process, and networked with a number of formal and informal groups and individuals from around Australia and overseas.

Expert Working Group

The National Stroke Foundation is extremely grateful to the following members of the working group who were responsible for the development of these guidelines:

Dr Alan Barber

Neurologist, Auckland City Hospital

Dr Christopher Beer

Senior Lecturer, University of Western Australia and Geriatrician/Clinical Pharmacologist Royal Perth and Mercy Hospitals and Swan Health Service

Prof Justin Beilby

Executive Dean, Faculty of Health Sciences and Professor of General Practice, University of Adelaide

Assoc Prof Julie Bernhardt

Physiotherapist, National Stroke Research Institute

Prof Christopher Bladin

Neurologist, Box Hill Hospital

Ms Brenda Booth

Consumer, Working Aged Group with Stroke, NSW

Dr Julie Cichero

Speech Pathologist, Private Practice & University of Queensland

Ms Louise Corben

Occupational Therapy, Monash Medical Centre & Bruce Lefroy Centre Murdoch Children's Research Institute

Dr Denis Crimmins (chair)

Neurologist, Gosford Hospital

Dr Richard Gerraty

Neurologist, Alfred Hospital and Monash University

Mr Kelvin Hill

Manager, Guidelines Program, National Stroke Foundation

Dr Erin Lalor

Chief Executive Officer, National Stroke Foundation

Assoc Prof Christopher Levi

Neurologist, John Hunter Hospital

Prof Richard Lindley

Professor of Geriatric Medicine, University of Sydney and Westmead Hospital

Prof Sandy Middleton

School of Nursing (NSW & ACT), Australian Catholic University

Ms Fiona Simpson

Dietitian and Senior Research Fellow, Royal North Shore Hospital Sydney

The members of the expert working group assisted in:

- Reviewing the framework of existing guidelines;
- Identifying, reviewing and classifying relevant literature;
- Developing the draft clinical guidelines;
- Providing feedback gained through the consultation process;
- Developing a plan for communication, dissemination and implementation; and
- Developing recommendations for periodically updating the guidelines.

All members of the working group completed and signed a declaration of potential conflicts of interest with development of these guidelines. Most had no perceived conflicts. The reasons provided for potential conflicts primarily involved receiving money from non commercial and commercial organisations specifically for undertaking clinical research. This was expected given the expertise of members of the working group in clinical research. Only a small number of members had received financial support from commercial companies for providing consultancy or lecturing.

Additional expertise and significant input was gratefully received from the following people:

Ms Anne Parkhill

Information Manager, Aptly

Independent consultant who undertook the systematic database searches during the process.

Ms Dominique Cadilhac

Manager Public Health Division, National Stroke Research Institute

Assoc Prof Helen Dewey

Neurologist and Associate Director,
National Stroke Research Institute and the
Austin Hospital

Consultants from the National Stroke Research Institute who were responsible for writing section 9 (Economic and socioeconomic implications) of these guidelines.

Additional people who kindly contributed to the guidelines development process during the appraisal and drafting process included:

Dr Michael Briffa

Palliative Care Specialist, Royal Adelaide Hospital

Prof Stephen Davis

Neurologist, Royal Melbourne Hospital

Dr Petrea Cornwell

Speech Pathology, University of Queensland

Dr Maree Hackett

Senior Research Fellow, the George Institute for International Health

Prof Graeme Hankey

Neurologist, Royal Perth Hospital

Dr Tami Howe

Speech Pathology, University of Queensland

Prof Linda Worrall

Speech Pathology, University of Queensland

The NSF kindly acknowledges the support of the University of Sydney who allowed access to their database of electronic journals used to source relevant articles during the development process.

Systematic searches and literature review

The systematic identification of relevant literature was conducted according to NHMRC standards between July and November 2006. Previous international and national stroke guidelines were identified and evaluated using the AGREE tool. Guidelines developed by the Royal College of Physicians in the UK in 2004 were deemed the most recent and robust guidelines and hence were used as a basis for updating the literature searches. An external consultant was used to undertake all the electronic database searches.

Question formulation

89 clinical questions were developed by the EWG to address interventions relevant to acute stroke care.

The questions generally queried the effects of a specific intervention and were developed in three parts: the intervention, the population and the outcomes. An example is “What is the effect of anticonvulsant therapy on reducing seizures in people with post-stroke seizures?” In this example, anticonvulsant therapy is the intervention, reduction of post-stroke seizures is the outcome, and the population is people with post-stroke seizures.

Finding relevant studies

For this guideline searching, there could be no single search coverage for all 89 questions: some sections of the guidelines need updating only from 2003, some are topics not previously addressed in the guidelines, some have already been well researched by other reputable guidelines authorities while some have no comprehensive meta-Analysis relating to them.

In order to have some structure to the searching and to make filtering of the references more manageable, the questions were searched and stored in separate Endnote libraries by broad topics;

1. Organisation of care
2. Discharge planning, transfer of care and integrated community care
3. Pre hospital care
4. Early diagnostic assessment
5. Management in the emergency phase
6. Assessment and management of consequences of stroke
7. Prevention and management of complications
8. Early secondary prevention
9. Palliation and death
10. TIA

Each reference within the library was then marked with the questions for which it was relevant.

For Australasian Medical Index, EMBASE, Medline and Medline in-process & other non-indexed citations searching was conducted in four broad steps;

- a) Terms for the patient group (P) were abridged from the Cochrane Collaboration’s Stroke Group.
- b) Where appropriate, intervention or other factor terms were added.
- c) Relevant evidence filters (Cochrane sensitive filter or Medline diagnostic filter) were applied to the basic search strategies.

d) If the search was for an update only to NSF or other authoritative meta-Analysis, the references were limited to years 2003 onwards.

For brevity, search strategies are not included here but are available from the NSF. Table 3 outlines the number of articles found for each 10 topic areas listed above.

Table 3: Results of database search for selected studies

TOPIC OUTLINE	AUSTRALASIAN MEDICAL INDEX	CLINICAL EVIDENCE	COCHRANE LIBRARY	EMBASE	MEDLINE	MEDLINE IN-PROCESS & OTHER NON-INDEXED CITATIONS
1	105	All stroke	554	157	749	16
2	112	management	19	47	96	4
3	53	section	43	50	264	8
4	58		1994	637	1855	1
5	139		2170	1012	1920	195
6	558		961	2635	2685	97
7	91		1051	200	658	24
8	133		225	1931	4441	130
9	23		3	185	24	–
10	15		2208	949	1171	–

A total of 28,656 potential articles resulted. A systematic process for choosing relevant articles occurred. At first, relevant systematic reviews were initially identified. Where no systematic review was found, primary studies were then searched. This initial process was conducted by one member of the working group and revealed 1341 articles. Final decision to include and review articles was made by two members of the working group after abstracts were scrutinised. Reference lists of identified articles and other guidelines were then used to identify further trials. The table of contents of a number of key journals for the last 6 months was also conducted. The following journals were chosen: Stroke, Cerebrovascular Disease, Lancet (and Lancet

Neurology), and Archives of Physical Medicine and Rehabilitation. For a number of topics a general internet search was then undertaken (using the “google” search engine). Finally, where possible, experts in the field were contacted to review the identified studies and suggest other new studies not identified. Hand searching continued until May 2007 and significant studies were included.

In addition to the initial searches the economic literature was searched with a total of 1484 references retrieved after deduplication (see table 4). Again one person sorted these and selected 70 potentially relevant articles. These abstracts were scrutinised for omissions by two people and appropriate papers were retrieved and reviewed (n=30).

Table 4: Results of database search for economic studies

ELECTRONIC DATABASE	REFERENCES RETRIEVED
Australasian Medical Index	25
Econlit	85
EMBASE	1026
Health Technology Assessment database	22
Medline	178
Medline in-process & other non-indexed citations	8
NHS Economic Evaluation Database	140

Appraising and selecting studies

A standardised appraisal process was used based on that outlined by Scottish Intercollegiate Guidelines Network (SIGN). Where available, appraisals already undertaken by the Stroke Therapy Evaluation Program (STEP) team were used to avoid duplication. The standardised appraisal form assesses the level of evidence (design and issues of quality), size of effect, relevance, applicability (benefits/harms) and generalisability of studies. Examples of completed checklists can be found on the STEP website (www.effectivestrokecare.org). Where Level I or II evidence was unavailable the search was broadened to include lower levels of evidence. Evidence for diagnostic and prognostic studies was also appraised using the SIGN methodology.

Summarising and synthesising the evidence

Details of relevant studies were summarised in evidence tables which form a supplement to this document. The supplement is available for download from the NSF website (www.strokefoundation.com.au).

For each question the evidence was collated using the draft NHMRC “Assessing the body of evidence form”. The recommended grading matrix was used to guide the strength or grading of the recommendation. For each question, the working group discussed and agreed on draft recommendations. The body of evidence matrix along with the draft recommendation gradings are shown below.

Body of evidence assessment matrix³

COMPONENT	A	B	C	D
	Excellent	Good	Satisfactory	Poor
Volume of evidence	several Level I or II studies with low risk of bias	one or two Level II studies with low risk of bias or a SR/multiple Level III studies with low risk of bias	Level III studies with low risk of bias, or Level I or II studies with moderate risk of bias	Level IV studies, or Level I to III studies with high risk of bias
Consistency	all studies consistent	most studies consistent and inconsistency may be explained	some inconsistency genuine uncertainty around clinical question	evidence is inconsistent
Clinical impact	very large	substantial	moderate	slight or restricted
Generalisability	population/s studied in body of evidence are the same as the target population for guideline	population/s studied in body of evidence are similar to the target population for the guideline	population/s studied in body of evidence different to target population for the guideline but it is clinically sensible to apply this evidence to target population*	population/s studied in body of evidence different to target population and hard to judge whether it is sensible to generalise to target population
Applicability	directly applicable to Australian healthcare context	applicable to Australian healthcare context with few caveats	probably applicable to Australian healthcare context with some caveats	not applicable to Australian healthcare context

NHMRC Draft grade of recommendation matrix³

GRADE	DESCRIPTION
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

Consultation

Public consultation was undertaken, with the draft document circulated to relevant professional bodies, interested individuals, consumers and consumer organisations over one month from mid April to the third week in May 2007. A public notice was also published in The Australian (April 19, 2007). Feedback received during consultation was considered by the EWG and the draft document amended. A formal letter of reply was sent to all individuals and organisations that provided feedback during this period outlining the response taken by the EWG.

Over 180 individual comments covering a wide range of topics were made from 34 individuals, groups or organisations. Contentious topics included antiplatelet therapy (secondary prevention), thrombolysis and DVT prevention and these sections were reviewed and updated. Additional information was also included regarding assessment and management of

hyperglycaemia, aspects of thrombolysis, faecal incontinence and apraxia. Other minor rewording or reformatting was made throughout the document in response to comments received. In response to the major issues received during consultation an independent expert was asked to review the key studies for the topics in question, in addition to other selected topics, and to advise the working group if the EWG had accurately interpreted and applied the evidence. Independent appraisals of the key studies along with an overall judgement about the appropriateness of the interpretation were provided. Only one recommendation was significantly changed based on this review with the vast majority of recommendations deemed to be in line with the evidence base.

Several prompted questions were also asked and the response noted in table 5.

Table 5: General questions and responses during public consultation

QUESTION	% RESPONSES "YES"
Did you find the document was easy to use and could you find relevant information quickly?	90%
Was it clear what evidence each guideline is based on?	71%
Is there sufficient detail provided in each recommendation to allow you to undertake the recommendation?	38%
Is it clear what sequence the recommendations should be applied?	52%
Do the guidelines permit clear indicators to determine if the recommendations are met?	52%
Does the guideline document provide enough detailed information while being concise?	71%
Are these guidelines consistent with what you understand as best practice?	57%

Given the small sample size each response was checked for clarifying comments if noted "No" and these were followed up where possible. All the recommendations with Level I evidence or those graded as an 'A' were checked and modified to ensure the recommendations were actionable. The sequencing of the recommendations was also reviewed and modified where appropriate.

The following professional organisations and individuals who were involved during the consultation process included:

Dr John Fink
Neurologist, Christchurch Hospital

Ms Ellen McMaster
Physiotherapist, Private Practice, NSW

Prof Stephen Davis
Neurologist, Royal Melbourne Hospital & Melbourne University

Prof Anthony Cross
On behalf of ACEM, Scientific committee Consumer Stroke Association, ACT

Prof Mark Nelson
GP, University Tasmania

Prof Nicholas Glasgow
GP, Australian National University

Chris Ellis
Physiotherapist, Dandenong Hospital

Mr David Hodge
Ambulance NSW

Ms Bronwyn Thomas

Physiotherapist, The Children's Hospital, Westmead

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Ms Fiona Couchman

Palliative Care Australia

Deran Bagdadi

Pfizer Global Pharmaceuticals

Ms Tennille Rowland

Occupational Therapist, Royal Brisbane and Women's Hospital

Ms Jane Levy

Principal Project Officer, Clinical Practice Improvement Centre, QLD Health

Dr Glen Adams, Marian Gandy, & Dr Paul Slade

Briston-Myers Squibb Pharmaceuticals

Dr Brian Draper

Hospital Chair, Faculty of Psychiatry of Old Age

Ms Lisa-Jane Moody

Audiology Dept, Geelong Hospital

Ms Lisa Allwell & Prof David Clarke

Beyondblue: the national depression initiative

Ms Lisa Hopper, Cristie Field, Kelly Carter

Speech Pathology, Gosford Hospital

Ms Jo James

Dietitian, Flinders Medical Centre

Ms Colette Bennett

Diabetes Centre, St Vincent's Hospital (Sydney)

Ms Nicole Pond, Brigid Horan, Julie Elliot,

Sharon Lawrence, Perryn Carroll,

Jenny Pomplun & Renae Hamilton

Hunter New England Health Hospitals

Ms Sarah Whitney, Kate Hanrahan,

Kate Schuj & Danielle Buckley

Royal Prince Alfred Hospital

Dr Owen Davies

Repatriation General Hospital, Flinders Medical Centre

Dr Ashish Soman & Dr Gordon Hirsch

Sanofi-Aventis Australia/NZ

Ms Rosemary Bryant

Royal College of Nursing, Australia

Dr Grantham

On behalf of Council of Ambulance Associations inc.

Mr Daniel De Stefanis

On behalf of allied health team, Stroke Unit, Royal Melbourne Hospital

Dr Annie McCluskey

Senior Lecturer (OT), University of Sydney

Dr John Litt & Ms Kathryn Rigby

On behalf of RACGP National Quality Committee

Ms Sharon Downie

Occupational Therapist, Monash Medical Centre

Dr Nancy Huang

On behalf of members of the National Blood Pressure and Vascular Disease Advisory Committee (NBPVDAC)

Consumer Involvement

Stroke guidelines are often large, complex documents which provide significant challenges for consumers. Specific challenges in this patient population include a typically older age and stroke specific impairments both of which have been found to reduce patient's reading ability, concentration and cognitive function. However, consumer input has been a key component in the development process of the current guidelines.

A consumer was included in the EWG and has been involved in every phase of the development process, including the development of the clinical questions to guide the literature searching. In addition a number of consumer organisations were specifically sent the draft document and asked to provide any comments reflecting the views of consumers. Finally a two part structured consultation process was also undertaken by an independent team from the University of Queensland on behalf of the National Stroke Foundation to understand the views of consumers on the current document. The first phase discovered the views of consumers on the best process to engage consumers and receive feedback on the guidelines. Based on the results of this qualitative data, consumers from a wide range of locations, stroke severities, carer/survivor mix, and other demographics were collected.

A total of 44 consumers were involved in two different phases. The key outcome from the first phase (involving one focus group of 13 stroke survivors and carers) was that consumers felt they were not qualified to provide detailed feedback on certain topics (e.g. medical recommendations) but simply wanted what was considered the best medical treatment. However, consumers were very focused on those areas that were more lifestyle or less medically focussed especially discharge planning. Hence the total numbers of recommendations of the draft guidelines were reduced to 18 questions in 7 broad areas with appropriate lay terminology.

The key outcome from the second phase (involving 2 focus groups [n=22] and 9 telephone interviews) was that almost all topics were viewed to be extremely

important to consumers. The average ratings (10 being extremely important) by stroke survivors and carers are provided where appropriate throughout the main text and are noted in table 6 below.

Furthermore, the consultation process was useful to gain consumer views and all consumers were grateful for the opportunity to input into the process. The results highlight that limited evidence should not necessarily determine the priorities for implementing these guidelines.

A report undertaken by the NSF in 2007 regarding consumer views of support after stroke which relates to good stroke care is available and recommended to further understand the needs of stroke survivors and carers.⁵¹⁹

Table 6: Consumer consultation of modified acute stroke topics

QUESTION	RATING (/10)
1. Organisation of Stroke care	
1.1 Care for stroke patients should take place in 'stroke units'.	9.3
1.2 The 'stroke unit team' should meet regularly with the stroke patient and their family or carer. This meeting helps to involve the stroke patient and their family or carer in managing and planning care.	9.3
1.3 Stroke patients may be managed at home if special health services and health professional support is available. These services and support mean some stroke patients can leave hospital earlier and recover successfully at home.	8.5
2. Getting to hospital	
2.1 Health professionals and the public should get education about how to recognise stroke early. That education needs to make it clear that stroke is a medical emergency.	9.5
2.2 Stroke needs to be considered a medical emergency. It needs to be given a high priority by ambulance services.	9.6
2.3 Ambulance staff should be trained to recognise stroke (for example, they should use an easy and standard test).	9.7
3. Arriving at hospital	9.7
4. Early treatment	10
5. General treatment including prevention and management of complications	9.8
6. Preventing another stroke	
6.1 Stroke patients are to be given information about healthy lifestyle and how to risk reduce risk factors.	9.7
6.2 Medical treatments (including drugs or surgery) are to be used when appropriate to help prevent another stroke.	9.6
6.3 Medical drugs are given for a reason. They work best when taken properly. Health professionals should help stroke patients and their families with medical drugs. For example, they should make sure the right drugs are taken at the right time and in the right way.	9.6

cont.

Table 6: Consumer consultation of modified acute stroke topics cont.

QUESTION	RATING (/10)
7. Leaving hospital	
7.1 Stroke survivors and their families need to be assessed before leaving the hospital (this means before going home or before moving to rehabilitation). This assessment may look at a range of needs and concerns (for example, physical, emotional, social, sexual, and financial).	9.5
7.2 Health care professionals (including the local doctor), the stroke survivor, and their family/carer should all be involved in developing a plan. This plan is about stroke care after hospital.	9.7
7.3 Stroke survivors and their families need to be; <ul style="list-style-type: none"> • given information • given an opportunity to discuss the information • offered information throughout recovery 	9.4
7.4 The stroke survivor should be assessed for ongoing rehabilitation. This rehabilitation may be provided in hospital or in the community.	9.4
7.5 Health professionals should provide training for family/carers before the stroke survivor leaves hospital.	9.5
7.6 Stroke survivors and their families/carers should be given information and advice about driving again after a stroke.	9.7

Revision of the Guidelines

The National Stroke Foundation aims to combine, review and update the Clinical Guidelines for Acute Stroke Management along with the Clinical Guidelines for Stroke Rehabilitation and Recovery by 2010 after which time the current recommendations outlined in this document will be superseded.

Implementation

Reviewing the evidence and developing evidence-based recommendations for care involves only the first steps to ensuring that evidence-based care is available. Following publication of the Clinical Guidelines for Acute Stroke Management, the guidelines must be disseminated to all those who provide care of relevance to acute stroke care, who may then identify ways in which the guidelines may be taken up at a local level.

Strategies by which guidelines may be disseminated and implemented include:

- distribution of education materials - for example: mailing of guidelines to stroke clinicians via existing stroke networks will be undertaken. Concise guidelines (in particular for General Practitioners) are also planned with GP networks utilised to circulate this new information. Guidelines documents will also be sent to all appropriate universities, colleges, associations, societies and other professional organisations.
- educational meetings - for example: interdisciplinary conferences or internet based 'webconferences' are planned. Resources will be developed to aid workshop facilitators identify barriers and solutions in the implementation phase.
- educational outreach visits - A peer support model using sites viewed as 'champions' in aspects of acute stroke management may be used in collaboration with national audit results.
- local opinion leaders: Educational resources will utilise key opinion leaders. It is also planned to have local champions facilitate workshops in their local areas.
- audit and feedback. Data from the first national audit of acute stroke will be fundamental to the implementation of these guidelines. A copy of relevant indicators covering organisation of care and clinical care will be available from the NSF along with key reports.
- reminders. Electronic reminders will be used once local teams have identified key areas of improvement and commenced planned strategies.

A systematic review of the above dissemination and implementation strategies found that there was difficulty in interpreting the evidence of the effectiveness of these interventions due to methodological weaknesses, poor reporting of the study setting and uncertainty about the generalisability of the results.⁸⁰ However most of the strategies appear to have modest effectiveness in implementing evidence based care but it is unclear if single interventions are any better or worse than multiple interventions.⁸⁰ Thus all of the above strategies may be used where appropriate for implementation of the Clinical Guidelines for Acute Stroke Management. Specific strategies will also be considered when targeting general practice in line with the RACGP Guidelines for “Putting prevention into practice”.⁴⁵¹ Implementation of these stroke Guidelines may also be supported by existing resources and networks.

These include:

- the Stroke Services in Australia report, which outlines how stroke services may be organised in different parts of Australia and the resources that may be needed to do this (available at www.strokefoundation.com.au);
- the Stroke Care Pathway, which provides a checklist addressing key processes of care as outlined in both documents (Acute, and Rehabilitation and Recovery) and a guide to developing local protocols (available from www.strokefoundation.com.au or www.health.vic.gov/acute-agedcare);
- other specific workshop resources to aid implementation (e.g. CD Rom or self directed workbook); and
- various networks including Stroke Services NSW, QLD Stroke collaborative and other state and local networks.

APPENDIX B: Priorities for Research

The guidelines reflect the current evidence base and its limitations. For some interventions, there is good evidence for or against their use; however, many other interventions in current use are not discussed because there is neither good quality evidence on their effectiveness, nor sufficient consensus in the field concerning their potential benefits. The substantial gaps in the evidence base highlight the need for practitioners to build quality research studies into their clinical practice.

Much research has been undertaken within the acute phase of care particularly around hyperacute pharmacotherapy. Areas of ongoing research include thrombolysis, acute blood pressure management, early TIA management, antiplatelet agent choice for secondary prevention, and early mobilisation.

Areas in which research is particularly needed include (but are not limited to):

- implementation strategies of proven evidence based acute stroke care
- components of stroke units e.g. inpatient stroke care coordinator, organisation of nursing care, early mobilisation etc
- management of hyperglycaemia
- management of intracerebral haemorrhage
- acute blood pressure management
- effective neuroprotection
- management of thrombolysis (e.g. increasing access to thrombolysis, refining eligibility criteria, timeframes for thrombolysis and IA and mechanical thrombolysis techniques)
- post-discharge follow up services
- pre-discharge needs assessment (including home visits)
- optimum organisation of care for people with TIA
- cognitive and perceptual difficulties (screening, assessment and management)
- bladder and bowel management in the acute phase
- mood (screening and management) in the acute phase
- acute pathways or processes to improve efficiency in early acute phase care
- screening tools in general

GLOSSARY AND ABBREVIATIONS

Activities of daily living: The basic elements of personal care such as eating, washing and showering, grooming, walking, standing up from a chair and using the toilet.

Activity: The execution of a task or action by an individual. Activity limitations are difficulties an individual may have in executing activities.

Agnosia: The inability to recognise sounds, smells, objects or body parts (other people's or one's own) despite having no primary sensory deficits.

Aphasia: Impairment of language, affecting the production or comprehension of speech and the ability to read and write.

Apraxia: Impaired planning and sequencing of movement that is not due to weakness, incoordination, or sensory loss.

Atrial fibrillation: Rapid, irregular beating of the heart.

Augmentative and alternative communication: Non-verbal communication, e.g. through gestures or by using computerised devices.

Deep vein thrombosis: Thrombosis (a clot of blood) in the deep veins of the leg, arm, or abdomen.

Disability: A defect in performing a normal activity or action (e.g. inability to dress or walk).

Dysarthria: Impaired ability to produce clear speech due to the impaired function of the speech muscles.

Dysphagia: Difficulty swallowing.

Dysphasia: Reduced ability to communicate using language (spoken, written or gesture).

Dyspraxia of speech: Inability to produce clear speech due to impaired planning and sequencing of movement in the muscles used for speech.

Emotionalism: An increase in emotional behaviour - usually crying, but sometimes laughing that is outside normal control and may be unpredictable as a result of the stroke.

Enteral tube feeding: Delivery of nutrients directly into the intestine via a tube.

Executive function: Cognitive functions usually associated with the frontal lobes including planning, reasoning, time perception, complex goal-directed behaviour, decision making and working memory.

Family support / liaison worker: A person who assists stroke survivors and their families to achieve improved quality of life by providing psychosocial support and information, referrals to other stroke service providers.

Impairment: A problem in the structure of the body (e.g. loss of a limb) or the way the body or a body part functions (e.g. hemiplegia).

Infarction: Death of cells in an organ (e.g. the brain or heart) due to lack of blood supply.

Inpatient stroke care coordinator: A person who works with people with stroke and with their carers to construct care plans and discharge plans and to help coordinate the use of health care services during recovery in hospital.

Interdisciplinary team: The entire rehabilitation team, made up of doctors, nurses, therapists, social workers, psychologists etc.

Ischaemia: An inadequate flow of blood to part of the body due to blockage or constriction of the arteries that supply it.

Neglect: The failure to attend or respond to, or make movements towards one side of the environment.

Participation: Involvement in a life situation.

Participation restrictions: are problems an individual may experience in involvement in life situations.

Percutaneous endoscopic gastrostomy (PEG): A form of enteral feeding in which nutrition is delivered via a tube that is surgically inserted into the stomach through the skin.

Phonological deficits: Language deficits characterised by impaired recognition and/or selection of speech sounds.

Pulmonary embolism: Blockage of the pulmonary artery (which carries blood from the heart to the lungs) with a solid material, usually a blood clot or fat, that has travelled there via the circulatory system.

Rehabilitation: Restoration of the disabled person to optimal physical and psychological functional independence.

Risk factor: A characteristic of a person (or people) that is positively associated with a particular disease or condition.

Stroke unit: A section of a hospital dedicated to comprehensive rehabilitation programs for people with a stroke.

Stroke: Sudden and unexpected damage to brain cells that causes symptoms that last for more than 24 hours, in the parts of the body controlled by those cells. It happens when the blood supply to part of the brain is suddenly disrupted, either by blockage of an artery or by bleeding within the brain.

Task-specific training: Training that involves repetition of a functional task or part of the task.

Transient ischaemic attack (TIA): Stroke-like symptoms that last less than 24 hours. While TIA is not actually a stroke, it has the same cause. A TIA may be the precursor of a stroke, and people who have had a TIA require urgent assessment and treatment to prevent stroke.

Abbreviations

AAC: Augmentative and alternative communication

ADL: Activities of daily living

AF: Atrial fibrillation

CEA: Carotid endarterectomy

CEMRA: Contrast enhanced magnetic resonance angiography

CT: Computed tomography

DVT: Deep vein thrombosis

ESD: Early supported discharge

EWG: Expert Working Group

DALY: Disability adjusted life years

FEES: Fiberoptic endoscopic examination of swallowing

FFP: Fresh frozen plasma

GP: General Practitioner

ICH: Intracranial haemorrhage

ICU: Intensive care unit

INR: International normalised ratio

IPC: Intermittent pneumatic compression

IV: Intravenous

LMWH: Low molecular weight heparin

M/A: Meta analysis

MAP: Mean arterial blood pressure

MCA: Middle cerebral artery

MBS: Modified barium swallow

MR-DWI: Magnetic resonance diffusion weighted imaging

MRI: Magnetic Resonance Imaging

NG: Nasogastric

NHMRC: National Health and Medical Research Council

NNT: Numbers needed to treat

OBS: Observational study

OT: Occupational therapist

PE: Pulmonary embolism

PEG: Percutaneous endoscopic gastrostomy

QALYs: Quality adjusted life years

RCT: Randomised controlled trial

rFVIIa: recombinant activated factor VII

rt-PA: Recombinant tissue plasminogen activator

RRR: Relative risk reduction

SR: Systematic review

STAIR: Stroke transition after inpatient care

STEP: Stroke Therapy Evaluation Program

TIA: Transient ischaemic attack

TTE: Transthoracic echocardiography

TEE: Transesophageal echocardiography

UK: United Kingdom

UFH: Unfractionated heparin

REFERENCES

- 1 National Stroke Foundation. National Stroke Audit. Organisational Report: Acute Services. Melbourne: 2007.
- 2 National Health and Medical Research Council. A guide to the development and evaluation of clinical practice guidelines. Canberra: NHMRC. 1999.
- 3 National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines, PILOT PROGRAM 2005 - 2007 (accessible at http://www.nhmrc.gov.au/consult/_files/levels_grades05pdf). 2005.
- 4 National Stroke Foundation. National Stroke Foundation Website (accessed on June 26 at www.strokefoundation.com.au). 2007
- 5 Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, et al. Lifetime cost of stroke subtypes in Australia: findings from the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2003 Oct;34(10):2502-7.
- 6 Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. *The Cochrane Database of Systematic Reviews* 2001, Issue 3 Art No: CD000197 DOI: 10.1002/14651858CD000197 2001.
- 7 National Stroke Foundation. Clinical Guidelines for Stroke Rehabilitation and Recovery. Melbourne; 2005.
- 8 Campbell H HR, Bradshaw N, Porteous M. Integrated care pathways. *BMJ*. 1998;316(7125):133-7.
- 9 Engstrom G, Jermtorp I, Pessah-Rasmussen H, Hedblad B, Berglund G, Janzon L. Geographic distribution of stroke incidence within an urban population: Relations to socioeconomic circumstances and prevalence of cardiovascular risk factors. *Stroke*. 2001;32(5):1098-103.
- 10 Arrich J, Lalouschek W, Mullner M. Influence of socioeconomic status on mortality after stroke: Retrospective cohort study. *Stroke*. 2005;36(2):310-4.
- 11 Gillum RF, Mussolino ME. Education, poverty, and stroke incidence in whites and blacks: The NHANES I Epidemiologic Follow-up Study. *Journal of Clinical Epidemiology*. 2003;56(2):188-95.
- 12 Jakovljevic D, Sarti C, Sivenius J, Torppa J, Mahonen M, Immonen-Raiha P, et al. Socioeconomic status and ischemic stroke: The FINMONICA stroke register. *Stroke*. 2001;32(7):1492-8.
- 13 Kapral MK, Wang H, Mamdani M, Tu JV. Effect of socioeconomic status on treatment and mortality after stroke. *Stroke*. 2002;33(1):268-73.
- 14 Kunst AE, Del Rios M, Groenhof F, Mackenbach JP. Socioeconomic inequalities in stroke mortality among middle-aged men. An international overview. *Stroke*. 1998;29(11):2285-91.
- 15 Thrift AG, Dewey HM, Sturm JW, Paul SL, Gilligan AK, Srikanth VK. Increasing stroke incidence with increasing levels of socioeconomic disadvantage. *Australasian Epidemiologist*. 2004;11(3):52-3.
- 16 Wolfe CDA, Rudd AG, Howard R, Coshall C, Stewart J, Lawrence E, et al. Incidence and case fatality rates of stroke subtypes in a multiethnic population: The South London stroke register. *Journal of Neurology Neurosurgery and Psychiatry*. 2002;72(2):211-6.
- 17 Thrift AG, Hayman N. Aboriginal and Torres Strait Island peoples and the burden of stroke. *International Journal of Stroke*. 2007;2:57-9.
- 18 Langhorne P, Pollock A. What are the components of effective stroke unit care? *Age and Ageing*. 2002 Sep;31(5):365-71.
- 19 Foley N, Salter K, Teasell R. Specialized stroke services: A meta-analysis comparing three models of care. *Cerebrovascular Diseases*. 2007;23(2-3):194-202.
- 20 van der Walt A, Gilligan AK, Cadilhac DA, Brodtmann AG, Pearce DC, Donnan GA. Quality of stroke care within a hospital: Effects of a mobile stroke service. *Medical Journal of Australia*. 2005;182(4):160-3.
- 21 Langhorne P, Dey P, Woodman M, Kalra L, Wood-Dauphinee S, Patel N, et al. Is stroke unit care portable? A systematic review of the clinical trials. *Age and Ageing*. 2005;34(4):324-30.
- 22 Langhorne P, Dennis MS, Kalra L, Shepperd S, Wade DT, Wolfe CDA. Services for helping acute stroke patients avoid hospital admission. *Cochrane Database of Systematic Reviews* 1999, Issue 3. Art. No.: CD000444. DOI: 10.1002/14651858.CD000444.
- 23 Kalra L, Evans A, Perez I, Knapp M, Donaldson N, Swift CG. Alternative strategies for stroke care: a prospective randomised controlled trial. *Lancet*. 2000;Sep 9;356(9233): 894-9.
- 24 Cadilhac DA, Ibrahim J, Pearce DC, Ogden KJ, McNeill J, Davis SM, et al. Multicenter comparison of processes of care between stroke units and conventional care wards in Australia. *Stroke*. 2004;35(5):1035-40.
- 25 Johnston SC, Easton JD. Are patients with acutely recovered cerebral ischemia more unstable? *Stroke*. 2003;34(10):2446-50.
- 26 Smith EE, Abdullah AR, Petkovska I, Rosenthal E, Koroshetz WJ, Schwamm LH. Poor outcomes in patients who do not receive intravenous tissue plasminogen activator because of mild or improving ischemic stroke. *Stroke*. 2005;36(11):2497-9.
- 27 Aslanyan S, Weir CJ, Johnston CS, Krams M, Grieve AP, Lees KR. The association of post-stroke neurological improvement with risk of subsequent deterioration due to stroke events. *European Journal of Neurology*. 2007;14(1):1-6.
- 28 Nguyen-Huynh MN, Johnston SC. Is hospitalization after TIA cost-effective on the basis of treatment with tPA? *Neurology*. 2005;65(11):1799-801.
- 29 Blight A, Pereira AC, Brown MM. A single consultation cerebrovascular disease clinic is cost effective in the management of transient ischaemic attack and minor stroke (Provisional record). *Journal of the Royal College of Physicians of London*. 2000;34(5):452-5.

- 30 Widjaja E, Salam SN, Griffiths PD, Kamara C, Doyle C, Venables GS. Is the rapid assessment stroke clinic rapid enough in assessing transient ischaemic attack and minor stroke? *J Neurol Neurosurg Psychiatry*. 2005;76:145-6.
- 31 Royal College of Physicians of London. National Sentinel Audit of Stroke 2006. Organisational Audit Report.
- 32 Senes S, Britt H. A general practice view of cardiovascular disease and diabetes in Australia. Canberra: Australian Institute of Health and Welfare and University of Sydney. 2001.
- 33 Senes S. How we manage stroke in Australia. Canberra: Australian Institute of Health and Welfare. 2006.
- 34 Miller G, Valenti L, Charles J. Use of diagnostic imaging in Australian general practice. *Australian family physician*. 2006;35(5):280-1.
- 35 Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, Elkins JS, Bernstein AL, et al. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. *Lancet*. 2007;369(9558):283-92.
- 36 Audebert HJ, Kukla C, Clarmann von Claranau S, Kuhn J, Vatankeh B, Schenkel J, et al. Telemedicine for safe and extended use of thrombolysis in stroke: the Telemedic Pilot Project for Integrative Stroke Care (TEMPIS) in Bavaria. *Stroke*. 2005 Feb;36(2):287-91.
- 37 Audebert HJ, Kukla C, Vatankeh B, Gotzler B, Schenkel J, Hofer S, et al. Comparison of tissue plasminogen activator administration management between Telestroke Network hospitals and academic stroke centers: the Telemedical Pilot Project for Integrative Stroke Care in Bavaria/Germany. *Stroke*. 2006 Jul;37(7):1822-7.
- 38 Hess DC, Wang S, Hamilton W, Lee S, Pardue C, Waller JL, et al. REACH: clinical feasibility of a rural telestroke network. *Stroke*. 2005;36(9):2018-20.
- 39 Kwan J, Hand P, Sandercock P. Improving the efficiency of delivery of thrombolysis for acute stroke: a systematic review. *Qjm*. 2004 May;97(5):273-9.
- 40 Silverman IE, Beland DK, Chhabra J, McCullough LD. The "drip-and-ship" approach: starting IV t-PA for acute ischemic stroke at outside hospitals prior to transfer to a regional stroke center. *Connecticut Medicine*. 2005 Nov-Dec;69(10):613-20.
- 41 Rymer MM, Thurtchley D, Summers D, America Brain and Stroke Institute Stroke T. Expanded modes of tissue plasminogen activator delivery in a comprehensive stroke center increases regional acute stroke interventions. *Stroke*. 2003 Jun;34(6):e58-60.
- 42 Wang DZ, Rose JA, Honings DS, Garwacki DJ, Milbrandt JC. Treating acute stroke patients with intravenous tPA: The OSF Stroke Network experience. *Stroke*. 2000;31(1):77-81.
- 43 National Stroke Foundation. Stroke Services in Australia - National Stroke Unit Program Policy Document. Available from <http://www.strokefoundation.com.au/health-professionals>
- 44 Kwan J, Sandercock P. In-hospital care pathways for stroke. *The Cochrane Database of Systematic Reviews* 2004, Issue 4 Art No: CD002924pub2 DOI: 101002/14651858CD002924pub2. 2004.
- 45 Kwan J. Care pathways for acute stroke care and stroke rehabilitation: From theory to evidence. *Journal of Clinical Neuroscience*. 2007;14(3):189-200.
- 46 Asimos AW, Norton HJ, Price MF, Cheek WM. Therapeutic yield and outcomes of a community teaching hospital code stroke protocol. *Academic Emergency Medicine*. 2004 Apr;11(4):361-70.
- 47 Mehdiratta M, Woolfenden AR, Chapman KM, Johnston DC, Schulzer M, Beckman J, et al. Reduction in IV t-PA door to needle times using an Acute Stroke Triage Pathway. *Canadian Journal of Neurological Sciences*. 2006 May;33(2):214-6.
- 48 Sattin JA, Olson SE, Liu L, Raman R, Lyden PD. An expedited code stroke protocol is feasible and safe. *Stroke*. 2006;37(12):2935-9.
- 49 Taylor WJ, Wong A, Siegert RJ, McNaughton HK. Effectiveness of a clinical pathway for acute stroke care in a district general hospital: an audit. *BMC Health Serv Res*. 2006;6:16.
- 50 Hoffmann T, McKenna K. Analysis of stroke patients' and carers' reading ability and the content and design of written materials: Recommendations for improving written stroke information. *Patient Education and Counseling*. 2006;60(3):286-93.
- 51 Bhogal SK, Teasell RW, Foley NC, Speechley MR. Community reintegration after stroke. *Topics in Stroke Rehabilitation*. 2003;10(2):107-29.
- 52 Forster A, Smith J, Young J, Knapp P, House A, Wright J. Information provision for stroke patients and their caregivers. *The Cochrane Database of Systematic Reviews* 2001, Issue 2 Art No: CD001919 DOI: 101002/14651858CD001919 2001.
- 53 Boter H. Multicenter randomized controlled trial of an outreach nursing support program for recently discharged stroke patients. *Stroke; a journal of cerebral circulation*. 2004;35(12):2867-72.
- 54 Burton C GB. Expanding the role of the stroke nurse: a pragmatic clinical trial. *Journal of Advanced Nursing*. 2005 Dec;52(6):640-50.
- 55 Clark MS, Rubenach S, Winsor A. A randomized controlled trial of an education and counselling intervention for families after stroke. *Clinical Rehabilitation*. 2003;17(7):703-12.
- 56 Kalra L, Evans A, Perez I, Melbourn A, Patel A, Knapp M, et al. Training carers of stroke patients: randomised controlled trial. *British Medical Journal*. 2004;328(7448):1099.

- 57 Larson J, Franzén Dahlin A, Billing E, Arbin M, Murray V, Wredling R. The impact of a nurse-led support and education programme for spouses of stroke patients: a randomized controlled trial. *Journal of clinical nursing*. 2005;14(8):995-1003.
- 58 Smith J, Forster A, Young J. A randomized trial to evaluate an education programme for patients and carers after stroke. *Clinical Rehabilitation*. 2004;18(7):726-36.
- 59 Nir Z, Weisel-Eichler A. Improving knowledge and skills for use of medication by patients after stroke: evaluation of a nursing intervention. *American Journal of Physical Medicine & Rehabilitation*. 2006;85(7):582-92.
- 60 Middleton S, Donnelly N, Harris J, Ward J. Nursing intervention after carotid endarterectomy: a randomized trial of Co-ordinated Care Post-Discharge (CCPD). *Journal of advanced nursing*. 2005;52(3):250-61.
- 61 Early Supported Discharge Trialists. Services for reducing duration of hospital care for acute stroke patients. *Cochrane Database of Systematic Reviews*. 2005, Issue 2. Art. No.: CD000443. DOI: 10.1002/14651858.CD000443.pub2.
- 62 Larsen T, Olsen TS, Sorensen J. Early home-supported discharge of stroke patients: a health technology assessment. *International Journal of Technology Assessment in Health Care*. 2006;22(3):313-20.
- 63 Outpatient Service Trialists. Therapy-based rehabilitation services for stroke patients at home. *The Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002925. DOI: 10.1002/14651858.CD002925.
- 64 Sturm JW, Davis SM, O'Sullivan JG, Vedadhagi ME, Donnan GA. The Avoid Stroke As Soon As Possible (ASAP) general practice stroke audit. *Medical Journal of Australia*. 2002;176(7):312-6.
- 65 Mead GE, Murray H, McCollum CN, O'Neill PA. How do general practitioners manage patients at risk from stroke? *British Journal of Clinical Practice*. 1996 Dec;50(8):426-30.
- 66 Peterson GM, Boom K, Jackson SL, Vial JH. Doctors' beliefs on the use of antithrombotic therapy in atrial fibrillation: identifying barriers to stroke prevention. *Internal Medicine Journal*. 2002 Jan-Feb;32(1-2):15-23.
- 67 Touze E, Cambou JP, Ferrieres J, Vahanian A, Coppe G, Leizorovicz A, et al. Antithrombotic management after an ischemic stroke in French primary care practice: results from three pooled cross-sectional studies. *Cerebrovascular Diseases*. 2005;20(2):78-84.
- 68 Joubert J, Reid C, Joubert L, Barton D, Ruth D, Jackson D, et al. Risk factor management and depression post-stroke: the value of an integrated model of care. *Journal of clinical neuroscience*. 2006;13(1):84-90.
- 69 Wikander B, Ekelund P, Milsom I. An evaluation of multidisciplinary intervention governed by functional independence measure (FIMSM) in incontinent stroke patients. *Scand J Rehabil Med*. 1998 Apr;30(1):15-21.
- 70 Thrift AG, Dewey HM, Macdonell RA, McNeil JJ, Donnan GA. Stroke incidence on the east coast of Australia: the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2000 Oct;31(9):2087-92.
- 71 Jack C, Jones L, Jack BA, Gambles M, Murphy D, Ellershaw JE. Towards a good death: The impact of the care of the dying pathway in an acute stroke unit. *Age and Ageing*. 2004;33(6):625-6.
- 72 Goodwin DM, Higginson IJ, Edwards AG, Finlay IG, Cook AM, Hood K, et al. An evaluation of systematic reviews of palliative care services. *J Palliat Care*. 2002 Summer;18(2): 77-83.
- 73 Forte AL, Hill M, Pazder R, Feudtner C. Bereavement care interventions: a systematic review. *BMC Palliative Care*. 2004;Jul 36; 3(1):3.
- 74 Fellowes D, Wilkinson S, Moore P. Communication skills training for health care professionals working with cancer patients, their families and/or carers. *The Cochrane Database of Systematic Reviews* 2004, Issue 2 Art No: CD003751 DOI: 101002/14651858CD003751pub2. 2004.
- 75 Gysels M, Richardson A, Higginson IJ. Communication training for health professionals who care for patients with cancer: a systematic review of effectiveness. *Support Care Cancer*. Oct;12(10):692-700.
- 76 Palliative Care Australia. Standards for Providing Quality Palliative Care for all Australians. 2005 [Available from: <http://www.pallcare.org.au/Portals/9/docs/Standards%20Palliative%20Care.pdf>]
- 77 Jamtvedt G, Young JM, Kristoffersen DT, O'Brien MA, Oxman AD. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane database of systematic reviews*. 2006, Issue 2. Art. No.: CD000259. DOI: 10.1002/14651858.CD000259.pub2.
- 78 Cadilhac D, Pearce D, Donna GA. Evaluation of the New South Wales Greater Metropolitan Transition Taskforce Stroke Unit Initiative 2003/2004: Final report: National Stroke Research Institute; 2004.
- 79 Irwin P, Hoffman A, Lowe D, Pearson M, Rudd AG. Improving clinical practice in stroke through audit: Results of three rounds of National Stroke Audit. *Journal of Evaluation in Clinical Practice*. 2005;11(4):306-14.
- 80 Grimshaw G, Eccles M, Thomas R, MacLennan G, Ramsay C, Fraser C, et al. Toward Evidence-Based Quality Improvement Evidence (and its Limitations) of the Effectiveness of Guideline Dissemination and Implementation Strategies 1966-1998. *J Gen Intern Med*. 2006;21:S14-20.
- 81 Wojner-Alexandrov AW, Alexandrov AV, Rodriguez D, Persse D, Grotta JC. Houston paramedic and emergency stroke treatment and outcomes study (HoPSTO). *Stroke*. 2005 Jul;36(7):1512-8.
- 82 Moser DK, Kimble LP, Alberts MJ, Alonzo A, Croft JB, Dracup K, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: A scientific statement from the American Heart Association Council on Cardiovascular Nursing and Stroke Council. *Circulation*. 2006;114(2):168-82.

- 83 Bray JE, Martin J, Cooper G, Barger B, Bernard S, Bladin C. An interventional study to improve paramedic diagnosis of stroke. *Pre-hospital Emergency Care*. 2005 Jul-Sep;9(3):297-302.
- 84 Belvis R, Cocho D, Marti-Fabregas J, Pagonabarraga J, Aleu A, Garcia-Bargo MD, et al. Benefits of a Pre-hospital stroke code system: Feasibility and efficacy in the first year of clinical practice in Barcelona, Spain. *Cerebrovascular Diseases*. 2005;19(2):96-101.
- 85 Lindsberg PJ, Happola O, Kallela M, Valanne L, Kuisma M, Kaste M. Door to thrombolysis: ER reorganization and reduced delays to acute stroke treatment. *Neurology*. 2006;67(2):334-6.
- 86 Bray JE, Martin J, Cooper G, Barger B, Bernard S, Bladin C. Paramedic identification of stroke: community validation of the Melbourne ambulance stroke screen. *Cerebrovascular Diseases*. 2005;20(1):28-33.
- 87 Kidwell CS, Starkman S, Eckstein M, Weems K, Saver JL. Identifying stroke in the field: Prospective validation of the Los Angeles Pre-hospital Stroke Screen (LAPSS). *Stroke*. 2000;31(1):71-6.
- 88 Nor AM, McAllister C, Louw SJ, Dyker AG, Davis M, Jenkinson D, et al. Agreement between ambulance paramedic- and physician-recorded neurological signs with Face Arm Speech Test (FAST) in acute stroke patients. *Stroke*. 2004 Jun;35(6):1355-9.
- 89 Kothari RU, Pancioli A, Liu T, Broderick J. Cincinnati Pre-hospital Stroke Scale: reproducibility and validity. *Annals of Emergency Medicine*. 1999 Apr;33(4):373-8.
- 90 Saver JL, Kidwell C, Eckstein M, Starkman S, Investigators F-MPT. Pre-hospital neuroprotective therapy for acute stroke: results of the Field Administration of Stroke Therapy-Magnesium (FAST-MAG) pilot trial. *Stroke*. 2004 May;35(5):e106-8.
- 91 Albers GW, Caplan LR, Easton JD, Fayad PB, Mohr JP, Saver JL, et al. Transient ischemic attack - Proposal for a new definition. *New England Journal of Medicine*. 2002;347(21):1713-6.
- 92 Coull AJ, Lovett JK, Rothwell PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: Implications for public education and organisation of services. *British Medical Journal*. 2004;328(7435):326-8.
- 93 Daffertshoter M, Mielke O, Pullwitt A, Felsenstein M, Hennerici M. Transient ischemic attacks are more than "ministrokes". *Stroke*. 2004;35(11):2453-8.
- 94 Eliasziw M, Kennedy J, Hill MD, Buchan AM, Barnett HJM. Early risk of stroke after a transient ischemic attack in patients with internal carotid artery disease. *Canadian Medical Association Journal*. 2004;170(7):1105-9.
- 95 Kleindorfer D, Panagos P, Pancioli A, Khoury J, Kissela B, Woo D, et al. Incidence and Short-Term Prognosis of Transient Ischemic. Attack in a Population-Based Study. *Stroke*. 2005;36(4):720-4.
- 96 Hill MD, Yiannakoulias N, Jeerakathil T, Tu JV, Svenson LW, Schopflocher DP. The high risk of stroke immediately after transient ischemic attack: A population-based study. *Neurology*. 2004;62(11):2015-20.
- 97 Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. *Journal of the American Medical Association*. 2000;284(22):2901-6.
- 98 Lovett JK, Dennis MS, Sandercock PA, Bamford J, Warlow CP, Rothwell PM. Very early risk of stroke after a first transient ischemic attack. *Stroke*. 2003;34(8):e138-40.
- 99 Douglas VC, Johnston CM, Elkins J, Sidney S, Gress DR, Johnston SC. Head Computed Tomography Findings Predict Short-Term Stroke Risk after Transient Ischemic Attack. *Stroke*. 2003;34(12):2894-8.
- 100 Wardlaw JM, Keir SL, Seymour J, Lewis S, Sandercock PA, Dennis MS, et al. What is the best imaging strategy for acute stroke? *Health Technology Assessment (Winchester, England)*. 2004 Jan;8(1):iii, ix-x, 1-180.
- 101 Redgrave JNE, Coutts SB, Schulz UG, Briley D, Rothwell PM. Systematic review of associations between the presence of acute ischemic lesions on diffusion-weighted imaging and clinical predictors of early stroke risk after transient ischemic attack. *Stroke*. 2007;38(5):1482-8.
- 102 Wardlaw JM, Chappell FM, Stevenson M, De Nigris E, Thomas S, Gillard J, et al. Accurate, practical and cost-effective assessment of carotid stenosis in the UK. *Health Technology Assessment (Winchester, England)*. 2006 Aug;10(30):1-200.
- 103 Bray JE, Coughlan K, Bladin C. Can the ABCD Score be dichotomised to identify high-risk patients with transient ischaemic attack in the emergency department? *Emergency Medicine Journal*. 2007;24(2):92-5.
- 104 Tsvigoulis G, Spengos K, Manta P, Karandreas N, Zambelis T, Zakopoulos N, et al. Validation of the ABCD score in identifying individuals at high early risk of stroke after a transient ischemic attack: A hospital-based case series study. *Stroke*. 2006;37(12):2892-7.
- 105 Cucchiara BL, Messe SR, Taylor RA, Pacelli J, Maus D, Shah Q, et al. Is the ABCD score useful for risk stratification of patients with acute transient ischemic attack? *Stroke*. 2006 Jul;37(7):1710-4.
- 106 Adams Jr HP, Davis PH, Leira EC, Chang KC, Bendixen BH, Clarke WR, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). *Neurology*. 1999;53(1):126-31.
- 107 Muir KW, Weir CJ, Murray GD, Povey C, Lees KR. Comparison of neurological scales and scoring systems for acute stroke prognosis. *Stroke*. 1996;27(10):1817-20.
- 108 Kothari RU, Brott T, Broderick JP, Hamilton CA. Emergency physicians: Accuracy in the diagnosis of stroke. *Stroke*. 1995;26(12):2238-41.

- 109 Ferro JM, Pinto AN, Falcao I, et al. Diagnosis of stroke by the non-neurologist: a validation study. *Stroke*. 1998;29:1106-9.
- 110 Morgenstern LB, Lisabeth LD, Mecozi AC, Smith MA, Longwell PJ, McFarling DA, et al. A population-based study of acute stroke and TIA diagnosis. *Neurology*. 2004;62(6):895-900.
- 111 Martin PJ, Young G, Enevoldson TP, Humphrey PR. Overdiagnosis of TIA and minor stroke: experience at a regional neurovascular clinic. *Qjm*. 1997 Dec;90(12):759-63.
- 112 Nor AM, Davis J, Sen B, Shipsey D, Louw SJ, Dyker AG, et al. The Recognition of Stroke in the Emergency Room (ROSIER) scale: development and validation of a stroke recognition instrument. *Lancet Neurol*. 2005;Nov;4(11):727-34.
- 113 Suzuki M, Imai A, Honda M, Kobayashi K, Ohtsuka S. Role of a critical pathway for door-to-CT-completion interval in the management of acute ischemic stroke patients in the emergency room. *Keio J Med* 2004;Dec;53(4):247-50.
- 114 Kidwell CS, Chalela JA, Saver JL, Starkman S, Hill MD, Demchuk AM, et al. Comparison of MRI and CT for detection of acute intracerebral hemorrhage. *JAMA*. 2004 Oct 20;292(15):1823-30.
- 115 Chalela JA, Kidwell CS, Nentwich LM, Luby M, Butman JA, Demchuk AM, et al. Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison. *Lancet*. 2007;369(9558):293-8.
- 116 Kapral MK, Silver FL, Feightner JW, Goldbloom R, Wayne Elford R, Labrecque M, et al. Preventive health care, 1999 update: 2. Echocardiography for the detection of a cardiac source of embolus in patients with stroke. *Canadian Medical Association Journal*. 1999;161(8):989-95.
- 117 De Bruijn SFTM, Agema WRP, Lammers GJ, Van Der Wall EE, Wolterbeek R, Holman ER, et al. Transesophageal echocardiography is superior to transthoracic echocardiography in management of patients of any age with transient ischemic attack or stroke. *Stroke*. 2006;37(10):2531-4.
- 118 Hart RG, Pearce LA, Koudstaal PJ. Transient Ischemic Attacks in Patients With Atrial Fibrillation. Implications for Secondary Prevention: The European Atrial Fibrillation Trial and Stroke Prevention in Atrial Fibrillation III Trial. *Stroke*. 2004;35:948-51.
- 119 Saxena R, Koudstaal PJ. Anticoagulants for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischaemic attack. *The Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD000185.pub2. DOI: 10.1002/14651858.CD000185.pub2.
- 120 Wardlaw JM, del Zoppo G, Yamaguchi T. Thrombolysis for acute ischaemic stroke. *The Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD000213. DOI: 10.1002/14651858.CD000213.
- 121 Mielke O, Wardlaw J, Liu M. Thrombolysis (different doses, routes of administration and agents) for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2004, Issue 4 Art No:CD000514DOI: 101002/14651858CD000514pub2. 2004.
- 122 The ATLANTIS ECASS and NINDS rt-PA Study Group Investigators. Association of outcome with early stroke treatment: Pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet*. 2004;363(9411):768-74.
- 123 Graham GD. Tissue plasminogen activator for acute ischemic stroke in clinical practice: a meta-analysis of safety data. *Stroke*. 2003 Dec;34(12):2847-50.
- 124 Katzan IL, Furlan AJ, Lloyd LE, Frank JL, Harper DL, Hinchey JA, et al. Use of tissue-type plasminogen activator for acute ischemic stroke: The Cleveland area experience. *Journal of the American Medical Association*. 2000;283(9):1151-8.
- 125 Katzan IL, Hammer MD, Furlan AJ, Hixson ED, Nadzam DM. Quality improvement and tissue-type plasminogen activator for acute ischemic stroke a Cleveland update. *Stroke*. 2003;34(3):799-800.
- 126 Wahlgren N, Ahmed N, Davalos A, Ford GA, Grond M, Hacke W, et al. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet*. 2007;369(9558):275-82.
- 127 Szoek CE, Parsons MW, Butcher KS, Baird TA, Mitchell PJ, Fox SE, et al. Acute stroke thrombolysis with intravenous tissue plasminogen activator in an Australian tertiary hospital. *Medical Journal of Australia*. 2003 Apr 7;178(7):324-8.
- 128 Bray JE, Coughlan K, Bladin C. Thrombolytic therapy for acute ischaemic stroke: Successful implementation in an Australian tertiary hospital. *Internal Medicine Journal*. 2006;36(8):483-8.
- 129 The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue Plasminogen Activator for Acute Ischaemic Stroke. *The New England Journal of Medicine*. 1995;333:1581-87.
- 130 Hacke W, Albers G, Al-Rawi Y, Bogousslavsky J, Davalos A, Eliasziw M, et al. The Desmoteplase in Acute Ischemic Stroke Trial (DIAS): A phase II MRI-based 9-hour window acute stroke thrombolysis trial with intravenous desmoteplase. *Stroke*. 2005;36(1):66-73.
- 131 Haley EC, Jr., Lyden PD, Johnston KC, Hemmen TM, Investigators TNKIS. A pilot dose-escalation safety study of tenecteplase in acute ischemic stroke. *Stroke*. 2005 Mar;36(3):607-12.
- 132 Hu HH, Teng MM, Hsu LC, Wong WJ, Wang LM, Luk YO, et al. A pilot study of a new thrombolytic agent for acute ischemic stroke in Taiwan within a five-hour window. *Stroke*. 2006 Mar;37(3):918-9.

- 133 Furlan AJ, Eyding D, Albers GW, Al-Rawi Y, Lees KR, Rowley HA, et al. Dose Escalation of Desmoteplase for Acute Ischemic Stroke (DEDAS): Evidence of safety and efficacy 3 to 9 hours after stroke onset. *Stroke*. 2006;37(5):1227-31.
- 134 Broderick J. Combined Intravenous and Intra-Arterial Recanalization for Acute Ischemic Stroke: The Interventional Management of Stroke Study. *Stroke*. 2004;35(4):904-11.
- 135 Eckert B, Kucinski T, Neumaier-Probst E, Fiehler J, Rother J, Zeumer H. Local intra-arterial fibrinolysis in acute hemispheric stroke: effect of occlusion type and fibrinolytic agent on recanalization success and neurological outcome. *Cerebrovascular Diseases*. 2003;15(4):258-63.
- 136 Flaherty ML, Woo D, Kissela B, Jauch E, Pancioli A, Carrozzella J, et al. Combined IV and intra-arterial thrombolysis for acute ischemic stroke.[summary for patients in *Neurology*. 2005 Jan 25;64(2):E1-2; PMID: 15668403]. *Neurology*. 2005 Jan 25;64(2):386-8.
- 137 Ducrocq X, Bracard S, Taillandier L, Anxionnat R, Lacour JC, Guillemin F, et al. Comparison of intravenous and intra-arterial urokinase thrombolysis for acute ischaemic stroke. *Journal of Neuroradiology*. 2005 Jan;32(1):26-32.
- 138 Inoue T, Kimura K, Minematsu K, Yamaguchi T, Japan Multicenter Stroke Investigator's C. A case-control analysis of intra-arterial urokinase thrombolysis in acute cardioembolic stroke. *Cerebrovascular Diseases*. 2005;19(4):225-8.
- 139 Macleod MR, Davis SM, Mitchell PJ, Gerraty RP, Fitt G, Hankey GJ, et al. Results of a multicentre, randomised controlled trial of intra-arterial urokinase in the treatment of acute posterior circulation Ischaemic stroke. *Cerebrovascular Diseases*. 2005;20(1):12-7.
- 140 Furlan A, Higashida R, Weschler L, Gent M, Rowley H, Kase C, et al. Intraarterial Pro-Urokinase for acute ischaemic stroke. The PROACT II Study: A randomised controlled trial. *JAMA*. 1999;282:2003-11.
- 141 Lindsberg PJ, Mattle HP. Therapy of basilar artery occlusion: a systematic analysis comparing intra-arterial and intravenous thrombolysis. *Stroke*. 2006;37(3):922-8.
- 142 Eggers J, Koch B, Meyer K, Konig I, Seidel G. Effect of ultrasound on thrombolysis of middle cerebral artery occlusion. *Annals of Neurology*. 2003 Jun;53(6):797-800.
- 143 Daffertshofer M, Gass A, Ringleb P, Sitzer M, Sliwka U, Els T, et al. Transcranial low-frequency ultrasound-mediated thrombolysis in brain ischemia: increased risk of hemorrhage with combined ultrasound and tissue plasminogen activator: results of a phase II clinical trial. *Stroke*. 2005 Jul;36(7):1441-6.
- 144 Alexandrov AV, Molina CA, Grotta JC, Garami Z, Ford SR, Alvarez Sabin J, et al. Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke. *The New England Journal of Medicine*. 2004;351(21):2170-8.
- 145 Molina CA, Ribo M, Rubiera M, Montaner J, Santamarina E, Delgado-Mederos R, et al. Microbubble administration accelerates clot lysis during continuous 2-MHz ultrasound monitoring in stroke patients treated with intravenous tissue plasminogen activator. *Stroke*. 2006 Feb;37(2):425-9.
- 146 Yamanome T, Sasoh M, Kubo Y, Nishikawa Y, Endoh H, Satoh N, et al. Transcranial Doppler enhanced thrombolysis for embolic occlusion of major cerebral arteries. *Interventional Neuroradiology*. 2003;9(SUPPL. 1):129-32.
- 147 Berlis A, Lutsep H, Barnwell S, Norbash A, Wechsler L, Jungreis CA, et al. Mechanical thrombolysis in acute ischemic stroke with endovascular photoacoustic recanalization. *Stroke*. 2004 May;35(5):1112-6.
- 148 Bergui M, Stura G, Daniele D, Cerrato P, Berardino M, Bradac GB. Mechanical thrombolysis in ischemic stroke attributable to basilar artery occlusion as first-line treatment. *Stroke*. 2006;37(1):145-50.
- 149 Noser EA, Shaltoni HM, Hall CE, Alexandrov AV, Garami Z, Cacayorin ED, et al. Aggressive mechanical clot disruption: A safe adjunct to thrombolytic therapy in acute stroke? *Stroke*. 2005;36(2):292-6.
- 150 Smith WS, Sung G, Starkman S, Saver JL, Kidwell CS, Gobin YP, et al. Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. *Stroke*. 2005 Jul;36(7):1432-8.
- 151 Smith WS. Safety of mechanical thrombectomy and intravenous tissue plasminogen activator in acute ischemic stroke. Results of the multi Mechanical Embolus Removal in Cerebral Ischemia (MERCI) trial, part I. *American Journal of Neuroradiology*. 2006 Jun-Jul;27(6):1177-82.
- 152 Flint AC, Duckwiler GR, Budzik RF, Liebeskind DS, Smith WS. Mechanical thrombectomy of intracranial internal carotid occlusion: pooled results of the MERCI and Multi MERCI Part I trials. *Stroke*. 2007;38(4):1274-80.
- 153 Gobin YP, Starkman S, Duckwiler GR, Grobelny T, Kidwell CS, Jahan R, et al. MERCI 1: A phase 1 study of mechanical embolus removal in cerebral ischemia. *Stroke*. 2004;35(12):2848-53.
- 154 Mikulik R, Dufek M, Goldemund D, Reif M. A pilot study on systemic thrombolysis followed by low molecular weight heparin in ischemic stroke. *European Journal of Neurology*. 2006 Oct;13(10):1106-11.
- 155 Mangiafico S, Cellerini M, Nencini P, Gensini G, Inzitari D. Intravenous glycoprotein IIb/IIIa inhibitor (tirofiban) followed by intra-arterial urokinase and mechanical thrombolysis in stroke. *American Journal of Neuroradiology*. 2005;26(10):2595-601.
- 156 Sandercock P, Gubitza G, Foley P, Counsell C. Antiplatelet therapy for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2003, Issue 2. Art. No.: CD000029. DOI: 10.1002/14651858.CD000029.

- 157 Gubitz G, Sandercock P, Counsell C. Anticoagulants for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No.: CD000024. DOI: 10.1002/14651858.CD000024.pub2.
- 158 Paciaroni M, Agnelli G, Micheli S, Caso V. Efficacy and safety of anticoagulant treatment in acute cardioembolic stroke: A meta-analysis of randomized controlled trials. *Stroke*. 2007;38(2):423-30.
- 159 Lyrer P, Engelter S. Antithrombotic drugs for carotid artery dissection. *Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD000255. DOI: 10.1002/14651858.CD000255.
- 160 Sandercock P, Gubitz G, Foley P, Counsell C. Antiplatelet therapy for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2003, Issue 2. Art. No.: CD000029. DOI: 10.1002/14651858.CD000029.
- 161 Mistri AK, Robinson TG, Potter JF. Pressor therapy in acute ischemic stroke: systematic review. *Stroke*. 2006 Jun;37(6):1565-71.
- 162 Willmot M, Leonardi-Bee J, Bath P. High Blood Pressure in Acute Stroke and Subsequent Outcome: A Systematic review. *Hypertension*. 2004;43:18-24.
- 163 Gray LJ, Sprigg N, Rashid PA, Willmot MR, Bath PMW. Effect of Nitric Oxide Donors on Blood Pressure and Pulse Pressure in Acute and Subacute Stroke. *Journal of Stroke and Cerebrovascular Diseases*. 2006;15(6):245-9.
- 164 Blood pressure in Acute Stroke Collaboration (BASC). Interventions for deliberately altering blood pressure in acute stroke. *Cochrane Database of Systematic Reviews* 2001, Issue 3. Art. No.: CD000039. DOI: 10.1002/14651858.CD000039.
- 165 Vahedi K, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurology*. 2007;6(3):215-22.
- 166 Cruz-Flores S, Diamond AL. Angioplasty for intracranial artery stenosis. *Cochrane Database of Systematic Reviews*. 2006, Issue 3. Art. No.: CD004133. DOI: 10.1002/14651858.CD004133.pub2.
- 167 Davis SM, Broderick J, Hennerici M, Brun NC, Diringner MN, Mayer SA, et al. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. *Neurology*. 2006;66(8):1175-81.
- 168 Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringner MN, et al. Recombinant activated factor VII for acute intracerebral hemorrhage. *New England Journal of Medicine*. 2005;352(8):777-85+851.
- 169 You H, Al-Shahi R. Haemostatic drug therapies for acute primary intracerebral haemorrhage. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD005951. DOI: 10.1002/14651858.CD005951.pub2. 2006.
- 170 Haley EC, Thompson JL, Levin B, Davis S, Lees KR, Pittman JG, et al. Gavestinel does not improve outcome after acute intracerebral hemorrhage: an analysis from the GAIN International and GAIN Americas studies. *Stroke*. 2005;36(5):1006-10.
- 171 Secades JJ, Alvarez-Sabin J, Rubio F, Lozano R, Davalos A, Castillo J, et al. Citicoline in intracerebral haemorrhage: a double-blind, randomized, placebo-controlled, multi-centre pilot study. *Cerebrovascular Diseases*. 2006;21(5-6):380-5.
- 172 Righetti E, Celani MG, Cantisani T, Sterzi R, Boysen G, Ricci S. Glycerol for acute stroke. *Cochrane Database of Systematic Reviews* 2004, Issue 2. Art. No.: CD000096. DOI: 10.1002/14651858.CD000096.pub2.
- 173 Misra UK, Kalita J, Ranjan P, Mandal SK. Mannitol in intracerebral hemorrhage: A randomized controlled study. *Journal of the Neurological Sciences*. 2005;234(1-2):41-5.
- 174 Feigin VL, Anderson N, Rinkel GJE, Algra A, van Gijn J, Bennett DA. Corticosteroids for aneurysmal subarachnoid haemorrhage and primary intracerebral haemorrhage. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD004583. DOI: 10.1002/14651858.CD004583.pub2.
- 175 Aguilar MI, Hart RG, Kase CS, Freeman WD, Hoeben BJ, Garcia RC, et al. Treatment of warfarin-associated intracerebral hemorrhage: Literature review and expert opinion. *Mayo Clinic Proceedings*. 2007;82(1):82-92.
- 176 Steiner T, Rosand J, Diringner M. Intracerebral hemorrhage associated with oral anticoagulant therapy: Current practices and unresolved questions. *Stroke*. 2006;37(1):256-62.
- 177 Freeman WD, Brott TG, Barrett KM, Castillo PR, Deen Jr HG, Czervionke LF, et al. Recombinant factor VIIa for rapid reversal of warfarin anticoagulation in acute intracranial hemorrhage. *Mayo Clinic Proceedings*. 2004;79(12):1495-500.
- 178 Brody DL, Aiyagari V, Shackelford AM, Diringner MN. Use of recombinant factor VIIa in patients with warfarin-associated intracranial hemorrhage. *Neurocritical Care*. 2005;2(3):263-7.
- 179 Qureshi AI, Mohammad YM, Yahia AM, Suarez JI, Siddiqui AM, Kirmani JF, et al. A prospective multicenter study to evaluate the feasibility and safety of aggressive antihypertensive treatment in patients with acute intracerebral hemorrhage. *Journal of Intensive Care Medicine*. 2005 Jan-Feb;20(1):34-42.
- 180 Mendelow AD, Gregson BA, Fernandes HM, Murray GD, Teasdale GM, Terence Hope D, et al. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): A randomised trial. *Lancet*. 2005;365(9457):387-97.
- 181 Teernstra OP, Evers SM, Kessels AH. Meta Analysis in treatment of spontaneous supratentorial intracerebral haematoma. *Acta Neurochirurgica*. 2006 May;148(5):521-8.

- 182 The European Stroke Initiative Writing Committee and the Writing Committee for the EUSI Executive Committee. Recommendations for the Management of Intracranial Haemorrhage – Part I: Spontaneous Intracerebral Haemorrhage. *Cerebrovasc Diseases*. 2006;22:294-316.
- 183 Diez-Tejedor E, Fuentes B. Homeostasis as basis of acute stroke treatment: Stroke units are the key. *Cerebrovascular Diseases*. 2005;20(SUPPL. 2):129-34.
- 184 Sprigg N, Gray LJ, Bath PM, Boysen G, De Deyn PP, Friis P, et al. Relationship between outcome and baseline blood pressure and other haemodynamic measures in acute ischaemic stroke: Data from the TAIST trial. *Journal of Hypertension*. 2006;24(7):1413-7.
- 185 Sulter G, Elting JW, Langedijk M, Maurits NM, De Keyser J. Admitting acute ischemic stroke patients to a stroke care monitoring unit versus a conventional stroke unit: a randomized pilot study. *Stroke*. 2003 Jan;34(1):101-4.
- 186 Silva Y, Puigdemont M, Castellanos M, Serena J, Suner RM, Garcia MM, et al. Semi-intensive monitoring in acute stroke and long-term outcome. *Cerebrovascular Diseases*. 2005;19(1):23-30.
- 187 Cavallini A, Micieli G, Marcheselli S, Quaglini S. Role of monitoring in management of acute ischemic stroke patients. *Stroke*. 2003 Nov;34(11):2599-603.
- 188 Bennett MH, Wasiak J, Schnabel A, Kranke P, French C. Hyperbaric oxygen therapy for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD004954. DOI: 10.1002/14651858.CD004954.pub2.
- 189 Singhal AB, Banner T, Roccatagliata L, Koroshetz WJ, Schaefer PW, Lo EH, et al. A pilot study of normobaric oxygen therapy in acute ischemic stroke. *Stroke*. 2005;36(4):797-802.
- 190 Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke*. 2001;32(10):2426-32.
- 191 Allport L, Baird T, Butcher K, Macgregor L, Prosser J, Colman P, et al. Frequency and temporal profile of poststroke hyperglycemia using continuous glucose monitoring. *Diabetes Care*. 2006;29(8):1839-44.
- 192 Gray CS, Scott JF, French JM, Alberti KG, O'Connell JE. Prevalence and prediction of unrecognised diabetes mellitus and impaired glucose tolerance following acute stroke. *Age and Ageing*. 2004;33(1):71-7.
- 193 Kernan WN, Viscoli CM, Inzucchi SE, Brass LM, Bravata DM, Shulman GI, et al. Prevalence of abnormal glucose tolerance following a transient ischemic attack or ischemic stroke. *Arch Intern Med*. 2005;165(2):227-33.
- 194 Matz K, Keresztes K, Tatschl C, Nowotny M, Dachenhausen A, Brainin M, et al. Disorders of glucose metabolism in acute stroke patients: an underrecognized problem. *Diabetes Care*. 2006;29(4):792-7.
- 195 Vermeer SE, Sandee W, Algra A, Koudstaal PJ, Kappelle LJ, Dippel DW, et al. Impaired glucose tolerance increases stroke risk in nondiabetic patients with transient ischemic attack or minor ischemic stroke. *Stroke*. 2006;37(6):1413-7.
- 196 Walters MR, Weir CJ, Lees KR. A randomised, controlled pilot study to investigate the potential benefit of intervention with insulin in hyperglycaemic acute ischaemic stroke patients. *Cerebrovascular Diseases*. 2006;22(2-3):116-22.
- 197 Scott JF, Robinson GM, French JM, O'Connell JE, Alberti KGMM, Gray CS. Glucose potassium insulin infusions in the treatment of acute stroke patients with mild to moderate hyperglycemia: The glucose insulin in stroke trial (GIST). *Stroke*. 1999;30(4):793-9.
- 198 Gray CS, Hildreth AJ, Sandercock PA, O'Connell JE, Johnston DE, Cartlidge NE, et al. Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK). *Lancet Neurology*. 2007;6(5):397-406.
- 199 Ladurner G, Kalvach P, Moessler H. Neuroprotective treatment with Cerebrolysin in patients with acute stroke: A randomised controlled trial. *Journal of Neural Transmission*. 2005;112(3):415-28.
- 200 Lees KR, Muir KW, Ford I, Reid L, Mendelow AD, Sandercock PAG, et al. Magnesium for acute stroke (Intravenous Magnesium Efficacy in Stroke trial): Randomised controlled trial. *Lancet*. 2004;363(9407):439-45.
- 201 Krams M, Lees KR, Hacke W, Grieve AP, Orgogozo JM, Ford GA. Acute Stroke Therapy by Inhibition of Neutrophils (ASTIN): An Adaptive Dose-Response Study of UK-279,276 in Acute Ischemic Stroke. *Stroke*. 2003;34(11):2543-8.
- 202 Muir KW, Lees KR. Excitatory amino acid antagonists for acute stroke. *Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD001244. DOI: 10.1002/14651858.CD001244.
- 203 Lees KR, Zivin JA, Ashwood T, Davalos A, Davis SM, Diener HC, et al. NXY-059 for acute ischemic stroke. *The New England Journal of Medicine*. 2006;354(6):588-600.
- 204 Bath PM, Sprigg N. Colony stimulating factors (including erythropoietin, granulocyte colony stimulating factor and analogues) for stroke. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: CD005207. DOI: 10.1002/14651858.CD005207.pub3.
- 205 Shyu WC, Lin SZ, Lee CC, Liu DD, Li H. Granulocyte colony-stimulating factor for acute ischemic stroke: A randomized controlled trial. *Canadian Medical Association Journal*. 2006;174(7):927-33.
- 206 Bath PMW. Theophylline, aminophylline, caffeine and analogues for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No.: CD000211. DOI: 10.1002/14651858.CD000211.pub2.

- 207 Palesch YY, Hill MD, Ryckborst KJ, Tamariz D, Ginsberg MD. The ALIAS Pilot Trial: a dose-escalation and safety study of albumin therapy for acute ischemic stroke--II: neurologic outcome and efficacy analysis. *Stroke*. 2006 Aug;37(8):2107-14.
- 208 Otomo E, Tohgi H, Kogure K, Hirai S, Takakura K, Terashi A, et al. Effect of a novel free radical scavenger, edaravone (MCI-186), on acute brain infarction: Randomized, placebo-controlled, double-blind study at multicenters. *Cerebrovascular Diseases*. 2003;15(3):222-9.
- 209 Pettigrew LC, Kasner SE, Albers GW, Gorman M, Grotta JC, Sherman DG, et al. Safety and tolerability of arundic acid in acute ischemic stroke. *Journal of the Neurological Sciences*. 2006;251(1-2):50-6.
- 210 De Georgia MA, Krieger DW, Abou-Chebl A, Devlin TG, Jauss M, Davis SM, et al. Cooling for acute ischemic brain damage (COOL AID): A feasibility trial of endovascular cooling. *Neurology*. 2004;63(2):312-7.
- 211 Jian S, Yongming Q, Zhihua C, Yan C. Feasibility and safety of moderate hypothermia after acute ischemic stroke. *Int J Dev Neurosci*. 2003;21(6):353.
- 212 Dippel DWJ, van Breda EJ, van der Worp HB, van Gemert HMA, Meijer RJ, Kappelle LJ, et al. Effect of paracetamol (acetaminophen) and ibuprofen on body temperature in a cute ischemic stroke PISA, a phase II double-blind, randomized, placebo-controlled trial. *BMC Cardiovascular Disorders*. 2003;3(-):2.
- 213 Lyden PD, Allgren RL, Ng K, Akins P, Meyer B, Al-Sanani F, et al. Intravascular cooling in the treatment of stroke (ICTuS): Early clinical experience. *Journal of Stroke and Cerebrovascular Diseases*. 2005;14(3):107-14.
- 214 Kasner SE, Wein T, Piriawat P, Villar Cordova CE, Chalela JA, Krieger DW, et al. Acetaminophen for altering body temperature in acute stroke: a randomized clinical trial. *Stroke*. 2002;33(1):130-4.
- 215 Wang H, Olivero W, Lanzino G, Elkins W, Rose J, Honings D, et al. Rapid and selective cerebral hypothermia achieved using a cooling helmet. *Journal of Neurosurgery*. 2004 Feb;100(2):272-7.
- 216 Wu HM, Tang JL, Lin XP, Lau J, Leung PC, Woo J, et al. Acupuncture for stroke rehabilitation. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD004131. DOI: 10.1002/14651858.CD004131.pub2.
- 217 Zhang SH, Liu M, Asplund K, Li L. Acupuncture for acute stroke. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD003317. DOI: 10.1002/14651858.CD003317.pub2.
- 218 Shifflett SC, Nayak S, Bid C, Miles P, Agostinelli S. Effect of Reiki treatments on functional recovery in patients in poststroke rehabilitation: a pilot study. *J Altern Complement Med*. 2002 Dec;8(6):755-63.
- 219 Wu B, Liu M, Zhang S. Dan Shen agents for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: CD004295. DOI: 10.1002/14651858.CD004295.pub3.
- 220 Zeng X, Liu M, Yang Y, Li Y, Asplund K. Ginkgo biloba for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD003691. DOI: 10.1002/14651858.CD003691.pub2.
- 221 Carnaby G, Hankey GJ, Pizzi J. Behavioural intervention for dysphagia in acute stroke: a randomised controlled trial. *Lancet Neurology*. 2006 Jan;5(1):31-7.
- 222 Hinchey JA, Shephard T, Furie K, Smith D, Wang D, Tonn S. Formal dysphagia screening protocols prevent pneumonia. *Stroke*. 2005;36(9):1972-6.
- 223 Odderson IR, Keaton JC, McKenna BS. Swallow management in patients on an acute stroke pathway: quality is cost effective. *Archives of Physical Medicine and Rehabilitation*. 1995;76:1130-3.
- 224 Perry L, McLaren S. Nutritional support in acute stroke: the impact of evidence-based guidelines. *Clinical Nutrition*. 2003 Jun;22(3):283-93.
- 225 Perry L, Love CP. Screening for dysphagia and aspiration in acute stroke: A systematic review. *Dysphagia*. 2001;16(1):7-18.
- 226 Martino R, Pron G, Diamant N. Screening for oropharyngeal dysphagia in stroke: Insufficient evidence for guidelines. *Dysphagia*. 2000;15(1):19-30.
- 227 Ramsey DJ, Smithard DG, Kalra L. Early assessments of dysphagia and aspiration risk in acute stroke patients. *Stroke*. 2003;34(5):1252-7.
- 228 Smith HA, Lee SH, O'Neill PA, Connolly MJ. The combination of bedside swallowing assessment and oxygen saturation monitoring of swallowing in acute stroke: A safe and humane screening tool. *Age and Ageing*. 2000;29(6):495-9.
- 229 Nishiwaki K, Tsuji T, Liu M, Hase K, Tanaka N, Fujiwara T. Identification of a simple screening tool for dysphagia in patients with stroke using factor analysis of multiple dysphagia variables. *Journal of Rehabilitation Medicine*. 2005;37(4):247-51.
- 230 Lim SHB, Lieu PK, Phua SY, Seshadri R, Venketasubramanian N, Lee SH, et al. Accuracy of bedside clinical methods compared with fiberoptic endoscopic examination of swallowing (FEES) in determining the risk of aspiration in acute stroke patients. *Dysphagia*. 2001;16(1):1-6.
- 231 Leder SB, Espinosa JF. Aspiration risk after acute stroke: Comparison of clinical examination and fiberoptic endoscopic evaluation of swallowing. *Dysphagia*. 2002;17(3):214-8.
- 232 Chong MS, Lieu PK, Sitoh YY, Meng YY, Leow LP. Bedside Clinical Methods Useful as Screening Test for Aspiration in Elderly Patients with Recent and Previous Strokes. *Annals of the Academy of Medicine Singapore*. 2003;32(6):790-4.
- 233 Wu MC, Chang YC, Wang TG, Lin LC. Evaluating Swallowing Dysfunction Using a 100-ml Water Swallowing Test. *Dysphagia*. 2004;19(1):43-7.
- 234 Langmore SE, Schatz K, Olson N. Endoscopic and videofluoroscopic evaluations of swallowing and aspiration. *Ann Otol Rhinol Laryngol*. 1991;100(8):678-81.

- 235 Martineau J, Bauer JD, Isenring E, Cohen S. Malnutrition determined by the patient-generated subjective global assessment is associated with poor outcomes in acute stroke patients. *Clinical Nutrition*. 2005;24(6):1073-7.
- 236 Davis JP, Wong AA, Schluter PJ, Henderson RD, O'Sullivan JD, Read SJ. Impact of premorbid undernutrition on outcome in stroke patients. *Stroke*. 2004;35(8):1930-4.
- 237 Dennis M. Poor nutritional status on admission predicts poor outcomes after stroke observational data from the food trial. *Stroke*. 2003;34(6):1450-5.
- 238 Ferguson M, Capra S, Bauer J, Banks M. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. *Nutrition*. 1999;15(6):458-64.
- 239 Jukkola K, MacLennan P. Improving the efficacy of nutritional supplementation in the hospitalised elderly. *Australas J Ageing*. 2005;24(2):119-24.
- 240 Lazarus C, Hamlyn J. Prevalence and documentation of malnutrition in hospitals: a case study in a large private hospital setting. *Nutr Diet*. 2005;62(1):41-7.
- 241 Stratton RJ, Hackston A, Longmore D, Dixon D, Price S, Stroud M, et al. Malnutrition in hospital outpatients and inpatients: Prevalence, concurrent validity and ease of use of the 'malnutrition universal screening tool' ('MUST') for adults. *British Journal of Nutrition*. 2004;92(5):799-808.
- 242 Kelly J, Hunt BJ, Lewis RR, Swaminathan R, Moody A, Seed PT, et al. Dehydration and venous thromboembolism after acute stroke. *Qjm*. 2004 Jun;97(5):293-6.
- 243 Bhalla A, Sankaralingam S, Dundas R, Swaminathan R, Wolfe CD, Rudd AG. Influence of raised plasma osmolality on clinical outcome after acute stroke. *Stroke*. 2000 Oct;31(9):2043-8.
- 244 Finestone HM, Foley NC, Woodbury MG, Greene-Finestone L. Quantifying fluid intake in dysphagic stroke patients: a preliminary comparison of oral and nonoral strategies. *Archives of Physical Medicine and Rehabilitation*. 2001;82(12):1744-6.
- 245 Whelan K. Inadequate fluid intakes in dysphagic acute stroke. *Clinical nutrition (Edinburgh, Scotland)*. 2001;20(5):423-8.
- 246 Challiner YC, Jarrett D, Hayward MJ, al-Jubouri MA, Julious SA. A comparison of intravenous and subcutaneous hydration in elderly acute stroke patients. *Postgrad Med J*. 1994 Apr;70(821):195-7.
- 247 Perry L. Eating and dietary intake in communication-impaired stroke survivors: A cohort study from acute-stage hospital admission to 6 months post-stroke. *Clinical Nutrition*. 2004;23(6):1333-43.
- 248 Foley N, Finestone H, Woodbury MG, Teasell R, Greene-Finestone L. Energy and protein intakes of acute stroke patients. *Journal of Nutrition, Health and Aging*. 2006;10(3):171-5.
- 249 Esper DH, Coplin WM, Carhuapoma JR. Energy expenditure in patients with nontraumatic intracranial hemorrhage. *Journal of Parenteral and Enteral Nutrition*. 2006;30(2):71-5.
- 250 Hodgkinson B, Evans D, Wood J. Maintaining oral hydration in older adults: a systematic review. *Int J Nurs Pract*. 2003 Jul;9(3):S19-28.
- 251 Simmons SF, Alessi C, Schnelle JF. An intervention to increase fluid intake in nursing home residents: prompting and preference compliance. *J Am Geriatr Soc*. 2001 Aug;49(7):926-33.
- 252 Milne AC, Avenell A, Potter J. Meta-analysis: protein and energy supplementation in older people. *Annals of Internal Medicine*. 2006 Jan 3;144(1):37-48.
- 253 Gariballa S, Forster S, Walters S, Powers H. A Randomized, Double-Blind, Placebo-Controlled Trial of Nutritional Supplementation During Acute Illness. *American Journal of Medicine*. 2006;119(8):693-9.
- 254 James R, Gines D, Menlove A, Horn SD, Gassaway J, Smout RJ. Nutrition support (tube feeding) as a rehabilitation intervention. *Archives of Physical Medicine and Rehabilitation*. 2005;86(12 SUPPL.):S82-S92.
- 255 Horn SD, DeJong G, Smout RJ, Gassaway J, James R, Conroy B. Stroke rehabilitation patients, practice, and outcomes: Is earlier and more aggressive therapy better? *Archives of Physical Medicine and Rehabilitation*. 2005;86(12 SUPPL.):S101-S14.
- 256 FOOD Trial Collaboration. Does the timing and method of enteral tube feeding for dysphagic hospitalised stroke patients influence their outcomes? Results of the FOOD Trial: A multicentre international randomised controlled trial. *Lancet*. 2005;365:764-72.
- 257 Norton B, Homer-Ward M, Donnelly MT, et al. A randomised prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding after acute dysphagic stroke. *British Medical Journal*. 1996;312:13-6.
- 258 Kostadima E, Kaditis AG, Alexopoulos EI, Zakynthinos E, Sfyras D. Early gastrostomy reduces the rate of ventilator-associated pneumonia in stroke or head injury patients. *European Respiratory Journal*. 2005 Jul;26(1):106-11.
- 259 Hamidon BB, Abdullah SA, Zawawi MF, Sukumar N, Aminuddin A, Raymond AA. A prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with acute dysphagic stroke. *Medical Journal of Malaysia*. 2006 Mar;61(1):59-66.
- 260 FOOD Trial Collaboration. Does routine oral nutritional supplementation for hospitalised stroke patients improve their outcomes? Results of the FOOD Trial: A multicentre international randomised controlled trial. *Lancet*. 2005;365:755-63.
- 261 Bernhart J. Inactive and alone: physical activity within the first 14 days of acute stroke unit care. *Stroke*. 2004 Apr;35(4):1005-9.

- 262 Bamford J, Dennis M, Sandercock P, Burn J, Warlow C. The frequency, causes and timing of death within 30 days of a first stroke: The Oxfordshire Community Stroke Project. *Journal of Neurology Neurosurgery and Psychiatry*. 1990;53(10):824-9.
- 263 Allen C, Glasziou P, Del Mar C. Bed rest: A potentially harmful treatment needing more careful evaluation. *Lancet*. 1999;354(9186):1229-33.
- 264 Indredavik B, Bakke F, Slordahl SA, Rokseth R, Haheim LL. Treatment in a combined acute and rehabilitation stroke unit: Which aspects are most important? *Stroke*. 1999;30(5):917-23.
- 265 Kwakkel G, van Peppen R, Wagenaar RC, Wood Dauphinee S, Richards C, Ashburn A, et al. Effects of augmented exercise therapy time after stroke: a meta-analysis. *Stroke*. 2004;35(11):2529-39.
- 266 Bernhardt J, Collier JM, Legg L. Very early versus delayed mobilisation after stroke. (Protocol) *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD006187. DOI: 10.1002/14651858.CD006187.
- 267 Bernhardt J, Dewey H, Collier J, Thrift A, Lindley R, Moodie M, et al. A Very Early Rehabilitation Trial (AVERT). *International Journal of Stroke*. 2006;1(3):169-71.
- 268 Legg L, Drummond AE, Langhorne P. Occupational therapy for patients with problems in activities of daily living after stroke. *The Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD003585. DOI: 10.1002/14651858.CD003585.pub2.
- 269 Leys D, Henon H, Mackowiak-Cordoliani MA, Pasquier F. Poststroke dementia. *Lancet Neurology*. 2005;4(11):752-9.
- 270 Tang WK, Chan SSM, Chiu HFK, Ungvari GS, Wong KS, Kwok TCY, et al. Frequency and clinical determinants of poststroke cognitive impairment in nondemented stroke patients. *Journal of Geriatric Psychiatry and Neurology*. 2006;19(2):65-71.
- 271 Ukraintseva S, Sloan F, Arbeev K, Yashin A. Increasing rates of dementia at time of declining mortality from stroke. *Stroke*. 2006;37(5):1155-9.
- 272 Srikanth VK, Thrift AG, Saling MM, Anderson JF, Dewey HM, Macdonell RA, et al. Increased risk of cognitive impairment 3 months after mild to moderate first-ever stroke: a Community-Based Prospective Study of Nonaphasic English-Speaking Survivors. *Stroke*. 2003 Jun;34(5):1136-43.
- 273 Srikanth V, Thrift AG, Fryer JL, Saling MM, Dewey HM, Sturm JW, et al. The validity of brief screening cognitive instruments in the diagnosis of cognitive impairment and dementia after first-ever stroke. *International Psychogeriatrics*. 2006;18(2):295-305.
- 274 Blake H, McKinney M, Treece K, Lee E, Lincoln NB. An evaluation of screening measures for cognitive impairment after stroke. *Age and ageing*. 2002;31(6):451-6.
- 275 Bowen A, McKenna K, Tallis RC. Reasons for variability in the reported rate of occurrence of unilateral spatial neglect after stroke. *Stroke*. 1999;30(6):1196-202.
- 276 Appelros P, Karlsson GM, Seiger A, Nydevik I. Neglect and anosognosia after first-ever stroke: Incidence and relationship to disability. *Journal of Rehabilitation Medicine*. 2002;34(5):215-20.
- 277 Ringman JM, Saver JL, Woolson RF, Clarke WR, Adams HP. Frequency, risk factors, anatomy, and course of unilateral neglect in an acute stroke cohort. *Neurology*. 2004;63(3):468-74.
- 278 Azouvi P, Bartolomeo P, Beis JM, Perennou D, Pradat-Diehl P, Rousseaux M. A battery of tests for the quantitative assessment of unilateral neglect. *Restorative Neurology and Neuroscience*. 2006;24(4-6):273-85.
- 279 Menon A, Korner-Bitensky N. Evaluating unilateral spatial neglect post stroke: Working your way through the maze of assessment choices. *Topics in Stroke Rehabilitation*. 2004;11(3):41-66.
- 280 Menon-Nair A, Korner-Bitensky N, Wood-Dauphinee S, Robertson E. Assessment of unilateral spatial neglect post stroke in Canadian acute care hospitals: Are we neglecting neglect? *Clinical Rehabilitation*. 2006;20(7):623-34.
- 281 Butler JA. How comparable are tests of apraxia? *Clin Rehabil*. 2002;16(4):389-98.
- 282 van Heugten CM, Dekker J, Deelman BG, Stehmann-Saris FC, Kinebanian A. A diagnostic test for apraxia in stroke patients: internal consistency and diagnostic value. *Clin Neuropsychol*. 1999;13(2):182-92.
- 283 Donkervoort M, Dekker J, Stehmann-Saris FC, Deelman BG. Efficacy of strategy training in left hemisphere stroke patients with apraxia: A randomised clinical trial. *Neuropsychological rehabilitation*. 2001;11(5):549.
- 284 Smania N, Girardi F, Domenicali C, Lora E, Aglioti S. The rehabilitation of limb apraxia: a study in left-brain-damaged patients. *Archives of Physical Medicine and Rehabilitation*. 2000 Apr;81(4):379-88.
- 285 Donkervoort M, Dekker J, Deelman B. The course of apraxia and ADL functioning in left hemisphere stroke patients treated in rehabilitation centres and nursing homes. *Clin Rehabil*. 2006;20(12):1085-93.
- 286 Geusgens C, van Heugten C, Donkervoort M, van den Ende E, Jolles J, van den Heuvel W. Transfer of training effects in stroke patients with apraxia: an exploratory study. *Neuropsychol Rehabil*. 2006;16(2):213-29.
- 287 Lincoln N, Drummond AER, Berman P. Perceptual impairment and its impact on rehabilitation outcome. *Disability & Rehabilitation: An International Multidisciplinary Journal*. 1997(6):231-4.
- 288 Engelter ST, Gostynski M, Papa S, Frei M, Born C, Ajdacic-Gross V, et al. Epidemiology of aphasia attributable to first ischemic stroke: Incidence, severity, fluency, etiology, and thrombolysis. *Stroke*. 2006;37(6):1379-84.

- 289 Berthier ML. Poststroke aphasia: Epidemiology, pathophysiology and treatment. *Drugs and Aging*. 2005;22(2):163-82.
- 290 Ferro JM, Mariano G, Madureira S. Recovery from aphasia and neglect. *Cerebrovascular Diseases*. 1999;9(SUPPL. 5):6-22.
- 291 Pedersen PM, Vinter K, Olsen TS. Aphasia after stroke: Type, severity and prognosis: The Copenhagen aphasia study. *Cerebrovascular Diseases*. 2004;17(1):35-43.
- 292 Yueh B, Shapiro N, MacLean CH, Shekelle PG. Screening and management of adult hearing loss in primary care: scientific review. *JAMA*. 2003;289(15):1976-85.
- 293 Salter K, Jutai J, Foley N, Hellings C, Teasell R. Identification of aphasia post stroke: A review of screening assessment tools. *Brain Injury*. 2006;20(6):559-68.
- 294 Greener J, Enderby P, Whurr R. Speech and language therapy for aphasia following stroke. *The Cochrane Database of Systematic Reviews* 1999, Issue 4 Art No: CD000425 DOI: 101002/14651858CD000425 1999.
- 295 Robey RR. A meta-analysis of clinical outcomes in the treatment of aphasia. *J Speech Lang Hear Res*. 1998 Feb;41(1):172-87.
- 296 Bhogal SK, Teasell R, Speechley M. Intensity of aphasia therapy, impact on recovery. *Stroke*. 2003 Apr;34(4):987-93.
- 297 Brennan AD, Worrall LE, McKenna KT. The relationship between specific features of aphasia-friendly written material and comprehension of written material for people with aphasia: An exploratory study. *Aphasiology*. 2005;19(8):693-711.
- 298 Rose TA, Worrall LE, McKenna KT. The effectiveness of aphasia-friendly principles for printed health education materials for people with aphasia following stroke. *Aphasiology*. 2003;17(10):947-63.
- 299 Kagan A, Black SE, Duchan FJ, Simmons-Mackie N, Square P. Training volunteers as conversation partners using "Supported Conversation for Adults with Aphasia" (SCA): a controlled trial. *J Speech Lang Hear Res*. 2001 Jun;44(3):624-38.
- 300 Wertz RT, Weiss DG, Aten JL, et al. Comparison of clinic, home and deferred language treatment for aphasia. *Archives of Neurology*. 1986;43:653-8.
- 301 Thomas LH, Barrett J, Cross S, French B, Leathley M, Sutton C, et al. Prevention and treatment of urinary incontinence after stroke in adults. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD004462. DOI: 10.1002/14651858.CD004462.pub2.
- 302 Martin JL, Williams KS, Abrams KR, Turner DA, Sutton AJ, Chapple C, et al. Systematic review and evaluation of methods of assessing urinary incontinence. *Health Technology Assessment*. 2006;10(6):iii-87.
- 303 Dumoulin C, Korner-Bitensky N, Tannenbaum C. Urinary incontinence after stroke: Does rehabilitation make a difference? A systematic review of the effectiveness of behavioral therapy. *Topics in Stroke Rehabilitation*. 2005;12(3):66-76.
- 304 Harari D, Coshall C, Rudd AG, Wolfe CD. New-onset fecal incontinence after stroke: prevalence, natural history, risk factors, and impact. *Stroke*. 2003;34:144-50.
- 305 Hackett ML, Yapa C, Parag V, Anderson CS. Frequency of depression after stroke: A systematic review of observational studies. *Stroke*. 2005;36(6):1330-40.
- 306 Hackett ML, Anderson CS. Predictors of depression after stroke: A systematic review of observational studies. *Stroke*. 2005;36(10):2296-301.
- 307 Aben I, Verhey F, Lousberg R, Lodder J, Honig A. Validity of the Beck Depression Inventory, Hospital Anxiety and Depression Scale, SCL-90, and Hamilton Depression Rating Scale as screening instruments for depression in stroke patients. *Psychosomatics*. 2002;43(5):386-93.
- 308 Johnson G, Burvill PW, Anderson CS, Jamrozik K, Stewart-Wynne EG, Chakera TMH. Screening instruments for depression and anxiety following stroke: Experience in the Perth community stroke study. *Acta Psychiatrica Scandinavica*. 1995;91(4):252-7.
- 309 Lincoln NB, Nicholl CR, Flannaghan T, Leonard M, Van der Gucht E. The validity of questionnaire measures for assessing depression after stroke. *Clinical Rehabilitation*. 2003;17(8):840-6.
- 310 Watkins C, Daniels L, Jack C, Dickinson H, Van den Broek M. Accuracy of a single question in screening for depression in a cohort of patients after stroke: Comparative study. *British Medical Journal*. 2001;323(7322):1159.
- 311 Williams LS, Brizendine EJ, Plue L, Bakas T, Tu W, Hendrie H, et al. Performance of the PHQ-9 as a screening tool for depression after stroke. *Stroke*. 2005;36(3):635-8.
- 312 Bennett HE, Thomas SA, Austen R, Morris AM, Lincoln NB. Validation of screening measures for assessing mood in stroke patients. *Br J Clin Psychol*. 2006;45(3):367-76. Erratum in: *Br J Clin Psychol*. 2007 Jun;46(Pt 2):following 251.
- 313 House A, Dennis M, Mogridge L, Warlow C, Hawton K, Jones L. Mood disorders in the year after first stroke. *British Journal of Psychiatry*. 1991;158(JAN.):83-92.
- 314 Benaim C, Cailly B, Perennou D, Pelissier J. Validation of the aphasic depression rating scale. *Stroke*. 2004 Jul;35(7):1692-6.
- 315 House AO, Hackett ML, Anderson CS, Horrocks JA. Pharmaceutical interventions for emotionalism after stroke. *The Cochrane Database of Systematic Reviews* 2004, Issue 1 Art No: CD003690pub2 DOI: 101002/14651858CD003690pub2.
- 316 Hackett ML, Anderson CS, House AO. Interventions for treating depression after stroke. *The Cochrane Database of Systematic Reviews* 2004, Issue 2 Art No: CD003437pub2 DOI: 101002/14651858CD003437pub2.

- 317 Anderson CS, Hackett ML, House AO. Interventions for preventing depression after stroke. The Cochrane Database of Systematic Reviews 2004, Issue 1 Art No: CD003689pub2 DOI: 10.1002/14651858CD003689pub2.
- 318 Almeida OP, Waterreus A, Hankey GJ. Preventing depression after stroke: Results from a randomized placebo-controlled trial. *Journal of Clinical Psychiatry*. 2006 Jul;67(7):1104-9.
- 319 Niedermaier N, Bohrer E, Schulte K, Schlattmann P, Heuser I. Prevention and treatment of poststroke depression with mirtazapine in patients with acute stroke. *Journal of Clinical Psychiatry*. 2004 Dec;65(12):1619-23.
- 320 Davis MC. Life review therapy as an intervention to manage depression and enhance life satisfaction in individuals with right hemisphere cerebral vascular accidents. *Issues in Mental Health Nursing*. 2004;25(5):503-15.
- 321 Watkins CL, Auton MF, Deans CF, Dickinson HA, Jack CIA, Lightbody CE, et al. Motivational interviewing early after acute stroke: A randomized, controlled trial. *Stroke*. 2007;38(3):1004-9.
- 322 Choi-Kwon S, Han SW, Kwon SU, Kang DW, Choi JM, Kim JS. Fluoxetine treatment in poststroke depression, emotional incontinence, and anger proneness a double-blind, placebo-controlled study. *Stroke*. 2006;37(1):156-61.
- 323 Rampello L, Alvano A, Chiechio S, Raffaele R, Vecchio I, Malaguarnera M. An evaluation of efficacy and safety of reboxetine in elderly patients affected by "retarded" post-stroke depression. A random, placebo-controlled study. *Archives of gerontology and geriatrics*. 2005;40(3):275-85.
- 324 Murray V, von Arbin M, Bartfai A, Berggren AL, Landtblom AM, Lundmark J, et al. Double-blind comparison of sertraline and placebo in stroke patients with minor depression and less severe major depression. *The Journal of clinical psychiatry*. 2005;66(6):708-16.
- 325 Williams LS, Kroenke K, Bakas T, Plue LD, Brizendine E, Tu W, et al. Care management of poststroke depression: A randomized, controlled trial. *Stroke*. 2007;38(3):998-1003.
- 326 Van der Wurff FB, Stek ML, Hoogendijk WL, Beekman ATF. Electroconvulsive therapy for the depressed elderly. The Cochrane Database of Systematic Reviews 2003, Issue 2 Art No: CD003593 DOI: 10.1002/14651858CD003593.
- 327 Morley NCD, Berge E, Cruz Flores S, Whittle IR. Surgical decompression for cerebral oedema in acute ischaemic stroke. Cochrane Database of Systematic Reviews 2002, Issue 3 CD003435. DOI: 10.1002/14651858.CD003435.
- 328 Qizilbash N, Lewington SL, Lopez-Arrieta JM. Corticosteroids for acute ischaemic stroke. The Cochrane Database of Systematic Reviews 2001, Issue 4 Art No: CD000064 DOI: 10.1002/14651858CD000064 2001.
- 329 Hofmeijer J, Van Der Worp HB, Kappelle LJ. Treatment of space-occupying cerebral infarction. *Critical Care Medicine*. 2003;31(2):617-25.
- 330 Sherman DG. Prevention of Venous Thromboembolism, Recurrent Stroke, and Other Vascular Events After Acute Ischemic Stroke: The Role of Low-Molecular-Weight Heparin and Antiplatelet Therapy. *Journal of Stroke and Cerebrovascular Diseases*. 2006;15(6):250-9.
- 331 Andre C, De Freitas GR, Fukujima MM. Prevention of deep venous thrombosis and pulmonary embolism following stroke: A systematic review of published articles. *European Journal of Neurology*. 2007;14(1):21-32.
- 332 Goodacre S, Sampson F, Stevenson M, Wailoo A, Sutton A, Thomas S, et al. Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis. *Health Technology Assessment*. 2006;10(15):iii-99.
- 333 Linkins LA, Choi PT, Douketis JD. Clinical impact of bleeding in patients taking oral anticoagulant therapy for venous thromboembolism: a meta-analysis. *Annals of Internal Medicine*. 2003 Dec 2;139(11):893-900.
- 334 Sandercock P, Counsell C, Stobbs SL. Low-molecular-weight heparins or heparinoids versus standard unfractionated heparin for acute ischaemic stroke. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD000119. DOI: 10.1002/14651858.CD000119.pub2.
- 335 van Dongen CJJ, van den Belt AGM, Prins MH, Lensing AWA. Fixed dose subcutaneous low molecular weight heparins versus adjusted dose unfractionated heparin for venous thromboembolism. The Cochrane Database of Systematic Reviews 2004, Issue 4. Art. No.: CD001100.pub2. DOI: 10.1002/14651858.CD001100.pub2.
- 336 Sherman DG, Albers GW, Bladin C, Fieschi C, Gabbai AA, Kase CS, et al. The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischaemic stroke (PREVAIL Study): an open-label randomised comparison. *Lancet*. 2007;369(9570):1347-55.
- 337 Diener HC, Ringelstein EB, von Kummer R, Landgraf H, Koppenhagen K, Harenberg J, et al. Prophylaxis of thrombotic and embolic events in acute ischemic stroke with the low-molecular-weight heparin certoparin: Results of the PROTECT trial. *Stroke*. 2006;37(1):139-44.
- 338 Mazzone C, Chiodo GF, Sandercock P, Miccio M, Salvi R. Physical methods for preventing deep vein thrombosis in stroke. Cochrane Database of Systematic Reviews 2004, Issue 4. Art. No.: CD001922. DOI: 10.1002/14651858.CD001922.pub2.
- 339 Lacut K, Bressollette L, Le Gal G, Etienne E, De Tinteniac A, Renault A, et al. Prevention of venous thrombosis in patients with acute intracerebral hemorrhage. *Neurology*. 2005;65(6):865-9.

- 340 Roderick P, Ferris G, Wilson K, Halls H, Jackson D, Collins R, et al. Towards evidence-based guidelines for the prevention of venous thromboembolism: Systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis. *Health Technology Assessment*. 2005;9(49):iii-76.
- 341 Amaragiri SV, Lees TA. Elastic compression stockings for prevention of deep vein thrombosis. *The Cochrane Database of Systematic Reviews* 2000, Issue 1 Art No: CD001484 DOI: 10.1002/14651858CD001484.
- 342 Hajat C, Hajat S, Sharma P. Effects of post-stroke pyrexia on stroke outcome: a meta-analysis of studies in patients. *Stroke*. 2000;31(2):410-4.
- 343 Langhorne P, Tong BL, Stott DJ. Association between physiological homeostasis and early recovery after stroke. *Stroke*. 2000;31(10):2518-9.
- 344 Mayer SA, Kowalski RG, Presciutti M, Osiapkovich ND, McGann E, Fitzsimmons BF, et al. Clinical trial of a novel surface cooling system for fever control in neurocritical care patients. *Critical Care Medicine*. 2004;32(12):2508-15.
- 345 Cullum N, McInnes E, Bell-Syer SE, Legood R. Support surfaces for pressure ulcer prevention. *Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No.: CD001735. DOI: 10.1002/14651858.CD001735.pub2.
- 346 Pancorbo-Hidalgo PL, Garcia-Fernandez FP, Lopez-Medina IM, Alvarez-Nieto C. Risk assessment scales for pressure ulcer prevention: A systematic review. *Journal of Advanced Nursing*. 2006;54(1):94-110.
- 347 Baba-Akbari Sari A, Flemming K, Cullum NA, Wollina U. Therapeutic ultrasound for pressure ulcers. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD001275. DOI: 10.1002/14651858.CD001275.pub2.
- 348 Royal College of Nursing, National Institute for Health and Clinical Excellence. The management of pressure ulcers in primary and secondary care: A clinical practice guideline. June 2005.
- 349 Langer G, Schloemer G, Knerr A, Kuss O, Behrens J. Nutritional interventions for preventing and treating pressure ulcers. *The Cochrane Database of Systematic Reviews* 2003, Issue 4 Art No: CD003216 DOI: 10.1002/14651858CD003216.
- 350 Australian Council for Safety and Quality in Health Care. Preventing falls and harm from falls in older Australians. Best practice guidelines for Australian hospitals and aged care facilities. Available from URL <http://www.safetyandquality.gov.au>. 2005.
- 351 Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year risk of first recurrent stroke and disability after first-ever stroke in the Perth Community Stroke Study. *Stroke*. 2004 Apr;35(3):731-5.
- 352 Rudd AG, Lowe D, Hoffman A, Irwin P, Pearson M. Secondary prevention for stroke in the United Kingdom: results from the National Sentinel Audit of Stroke. *Age & Ageing*. 2004 May;33(3):280-6.
- 353 Hamann GF, Weimar C, Glahn J, Busse O, Diener HC, German Stroke Data B. Adherence to secondary stroke prevention strategies--results from the German Stroke Data Bank. *Cerebrovascular Diseases*. 2003;15(4):282-8.
- 354 Kurth T, Kase CS, Berger K, Gaziano JM, Cook NR, Buring JE. Smoking and risk of hemorrhagic stroke in women. *Stroke*. 2003;34(12):2792-5.
- 355 Kurth T, Kase CS, Berger K, Schaeffner ES, Buring JE, Gaziano JM. Smoking and the risk of hemorrhagic stroke in men. *Stroke*. 2003 Jun;34(5):1151-5.
- 356 Shinton R, Beevers G. Meta-analysis of relation between cigarette smoking and stroke. *British Medical Journal*. 1989;298(6676):789-94.
- 357 Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation and decreased risk of stroke in women. *JAMA*. 1992;269(2):232-6.
- 358 Wannamethee SG, Shaper AG, Whincup PH, Walker M. Smoking cessation and the risk of stroke in middle-aged men. *JAMA*. 1995;274(2):155-60.
- 359 Silagy C, Lancaster T, Stead L, Mant D, Fowler G. Nicotine replacement therapy for smoking cessation. *The Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No.: CD000146.pub2. DOI: 10.1002/14651858.CD000146.pub2.
- 360 Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database of Systematic Reviews* 2007, Issue 1. Art. No.: CD000031. DOI: 10.1002/14651858.CD000031.pub3. 2007.
- 361 Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database of Systematic Reviews* 2007, Issue 1. Art. No.: CD006103. DOI: 10.1002/14651858.CD006103.pub2.
- 362 Stead LF, Lancaster T. Group behaviour therapy programmes for smoking cessation. *The Cochrane Database of Systematic Reviews* 2005, Issue 2 Art No: CD001007 DOI: 10.1002/14651858CD001007pub2.
- 363 Sinclair HK, Bond CM, Stead LF. Community pharmacy personnel interventions for smoking cessation. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD003698. DOI: 10.1002/14651858.CD003698.pub2.
- 364 Rice VH, Stead LF. Nursing interventions for smoking cessation. *The Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD001188.pub2. DOI: 10.1002/14651858.CD001188.pub2.
- 365 Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. *Cochrane Database of Systematic Reviews* 2005, Issue 2 Art No: CD001292 DOI: 10.1002/14651858CD001292pub2.
- 366 Stead LF, Perera R, Lancaster T. Telephone counselling for smoking cessation. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD002850. DOI: 10.1002/14651858.CD002850.pub2.

- 367 He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. *The Cochrane Database of Systematic Reviews* 2004, Issue 1 Art No: CD004937 DOI: 10.1002/14651858CD004937.
- 368 Hooper L, Bartlett C, Davey Smith G, Ebrahim S. Advice to reduce dietary salt for prevention of cardiovascular disease. *The Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD003656.pub2. DOI: 10.1002/14651858.CD003656.pub2.
- 369 Jurgens G, Graudal NA. Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD004022. DOI: 10.1002/14651858.CD004022.pub2.
- 370 Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *New England Journal of Medicine*. 2001 Feb 4;344(1):3-10.
- 371 Nagata C, Takatsuka N, Shimizu N, Shimizu H. Sodium intake and risk of death from stroke in Japanese men and women. *Stroke*. 2004;35(7):1543-7.
- 372 He FJ, Nowson CA, MacGregor GA. Fruit and vegetable consumption and stroke: Meta-analysis of cohort studies. *Lancet*. 2006;367(9507):320-6.
- 373 Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *New England Journal of Medicine*. 1997 May 17;336(16):1117-24.
- 374 Barzi F, Woodward M, Marfisi RM, Tavazzi L, Valagussa F, Marchioli R. Mediterranean diet and all-causes mortality after myocardial infarction: results from the GISSI-Prevenzione trial. *Eur J Clin Nutr*. 2003 May;57(4):604-11.
- 375 de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation*. 1999 Mar 16;99(6):779-85.
- 376 Hooper L, Summerbell CD, Higgins JP, Thompson RL, Clements G, Capps N, et al. Reduced or modified dietary fat for preventing cardiovascular disease. *The Cochrane Database of Systematic Reviews* 2001, Issue 3 Art No: CD002137 DOI: 10.1002/14651858CD002137.
- 377 Jula A, Marniemi J, Huupponen R, Virtanen A, Rastas M, Ronnema T. Effects of diet and simvastatin on serum lipids, insulin, and antioxidants in hypercholesterolemic men: a randomized controlled trial. *JAMA*. 2002 Feb 6;287(5):598-605.
- 378 Sdringola S, Nakagawa K, Nakagawa Y, Yusuf SW, Boccacandro F, Mullani N, et al. Combined intense lifestyle and pharmacologic lipid treatment further reduce coronary events and myocardial perfusion abnormalities compared with usual-care cholesterol-lowering drugs in coronary artery disease. *J Am Coll Cardiol*. 2003 Jan 15;41(2):263-72.
- 379 Mulrow CD, Chiquette E, Angel L, Cornell J, Summerbell C, Anagnostis B, et al. Dieting to reduce body weight for controlling hypertension in adults. *The Cochrane Database of Systematic Reviews* 1998, Issue 4 Art No: CD000484 DOI: 10.1002/14651858CD000484.
- 380 Brown BG, Zhao XQ, Chait A, Fisher LD, Cheung MC, Morse JS, et al. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. *N Engl J Med*. 2001 Dec 29;345(22):1583-92.
- 381 Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ, et al. Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. *JAMA*. 2004 Mar 4;291(5):565-75.
- 382 Heart Protection Study Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20 536 people with cerebrovascular disease or other high-risk conditions. *Lancet*. 2004;363:757-67.
- 383 Howard BV, Van Horn L, Hsia J, Manson JE, Stefanick ML, Wassertheil-Smoller S, et al. Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA*. 2006;295(6):655-66.
- 384 National Health and Medical Research Council. *Dietary Guidelines for Australian Adults*. Canberra: Commonwealth of Australia. 2003.
- 385 National Heart Foundation of Australia. *Summary of evidence statement on the relationships between dietary electrolytes and cardiovascular disease*. 2006.
- 386 Lee CD, Folsom AR, Blair SN. Physical activity and stroke risk: a meta-analysis. *Stroke*. 2003 Nov;34(10):2475-81.
- 387 Wendel-Vos GCW, Schuit AJ, Feskens EJM, Boshuizen HC, Verschuren WMM, Saris WHM, et al. Physical activity and stroke. A meta-analysis of observational data. *International Journal of Epidemiology*. 2004;33(4):787-98.
- 388 Oguma Y, Shinoda-Tagawa T. Physical activity decreases cardiovascular disease risk in women: Review and meta-analysis. *American Journal of Preventive Medicine*. 2004;26(5):407-18.
- 389 Saunders DH, Greig CA, Young A, Mead GE. Physical fitness training for stroke patients. *The Cochrane Database of Systematic Reviews* 2004, Issue 1 Art No: CD003316pub2 DOI: 10.1002/14651858CD003316pub2.
- 390 Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: A meta-analysis of randomized, controlled trials. *Annals of Internal Medicine*. 2002;136(7):493-503.

- 391 Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews* 2006, Issue 3 Art No: CD002968 DOI: 101002/14651858CD002968pub2.
- 392 Reynolds K, Lewis B, Nolen JD, Kinney GL, Sathya B, He J, et al. Alcohol consumption and risk of stroke: a meta-analysis. *Jama*. 2003 Mar 5;289(5):579-88.
- 393 Ovbiagele B, Saver JL, Fredieu A, Suzuki S, McNair N, Dandekar A, et al. PROTECT: A coordinated stroke treatment program to prevent recurrent thromboembolic events. *Neurology*. 2004;63(7):1217-22.
- 394 Ovbiagele B, Saver JL, Fredieu A, Suzuki S, Selco S, Rajajee V, et al. In-hospital initiation of secondary stroke prevention therapies yields high rates of adherence at follow-up. *Stroke*. 2004;35(12):2879-83.
- 395 Rubak S, Sandbaek A, Lauritzen T, Christensen B. Motivational interviewing: a systematic review and meta-analysis. *Br J Gen Pract*. 2005;55(513):305-12.
- 396 Pignone M, Mulrow CD. Evidence based management of hypertension: Using cardiovascular risk profiles to individualise hypertensive treatment. *British Medical Journal*. 2001;322(7295):1164-6.
- 397 National Heart Foundation of Australia. Hypertension management Guide for Doctors 2004 [Available from: http://www.heartfoundation.com.au/downloads/hypertension_management_guide_2004.pdf]
- 398 Rashid P, Leonardi-Bee J, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. *Stroke*. 2003 Nov;34(11):2741-8.
- 399 Schrader J, Luders S, Kulschewski A, Hammersen F, Plate K, Berger J, et al. Morbidity and mortality after stroke, eprosartan compared with nitrendipine for secondary prevention: Principal results of a prospective randomized controlled study (MOSES). *Stroke*. 2005;36(6):1218-24.
- 400 Nazir FS, Overell JR, Bolster A, Hilditch TE, Reid JL, Lees KR. The effect of losartan on global and focal cerebral perfusion and on renal function in hypertensives in mild early ischaemic stroke. *Journal of hypertension*. 2004;22(5):989-95.
- 401 Nazir FS, Overell JR, Bolster A, Hilditch TE, Lees KR. Effect of perindopril on cerebral and renal perfusion on normotensives in mild early ischaemic stroke: a randomized controlled trial. *Cerebrovascular Diseases*. 2005;19(2):77-83.
- 402 Antithrombotic Trialists Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of patients death, myocardial infarction, and stroke in high risk patients. *British Medical Journal*. 2002;324:71-86.
- 403 Serebruany VL, Malinin AI, Eisert RM, Sane DC. Risk of bleeding complications with antiplatelet agents: meta-analysis of 338,191 patients enrolled in 50 randomized controlled trials. *American Journal of Hematology*. 2004 Feb;75(1):40-7.
- 404 Volpato S, Maraldi C, Blè A, Ranzini M, Rita Atti A, Dominguez LJ, et al. Prescription of antithrombotic therapy in older patients hospitalized for transient ischemic attack and ischemic stroke: the GIFA study. *Stroke*. 2004;35(4):913-7.
- 405 Algra A, Van Gijn J. Aspirin at any dose above 30 mg offers only modest protection after cerebral ischaemia. *Journal of Neurology Neurosurgery and Psychiatry*. 1996;60(2):197-9.
- 406 ESPRIT Study Group; Halkes PH vGJ, Kappelle LJ, Koudstaal PJ, Algra A. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. *Lancet*. 2006;367(9523):1665-73.
- 407 De Schryver EL, Algra A, van Gijn J. Dipyridamole for preventing stroke and other vascular events in patients with vascular disease. *Cochrane Database of Systematic Reviews* 2006, Issue 2. Art. No.: CD001820. DOI: 10.1002/14651858.CD001820.pub2.
- 408 Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. *Lancet*. 2004 Aug 24;364(9431):331-7.
- 409 Bhatt DL, Fox KAA, Hacke W, Berger PB, Black HR, Boden WE, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *New England Journal of Medicine*. 2006;354(16):1706-17.
- 410 Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridine derivatives (ticlopidine, clopidogrel) versus aspirin for preventing stroke and other serious vascular events in high vascular risk patients. *Cochrane Database of Systematic Reviews* 2000, Issue 1. Art. No.: CD001246. DOI: 10.1002/14651858.CD001246.
- 411 Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A. European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. *J Neurol Sci*. 1996;143(1-2):1-13.
- 412 Algra A, De Schryver EL, van Gijn J, Kappelle LJ, Koudstaal PJ. Oral anticoagulants versus antiplatelet therapy for preventing further vascular events after transient ischaemic attack or minor stroke of presumed arterial origin. *Cochrane Database of Systematic Reviews* 2006, Issue 3 Art No: CD001342 DOI: 101002/14651858CD001342pub2.
- 413 ESPRIT Study Group, Algra A. Medium intensity oral anticoagulants versus aspirin after cerebral ischaemia of arterial origin (ESPRIT): a randomised controlled trial. *Lancet Neurol*. 2007;6(2):115-24.
- 414 Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, et al. Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. *New England Journal of Medicine*. 2005;352(13):1305-16+97.

- 415 Saxena R, Koudstaal P. Anticoagulants versus antiplatelet therapy for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischemic attack. *Cochrane Database of Systematic Reviews* 2004, Issue 4 Art No: CD000187 DOI: 10.1002/14651858CD000187pub2.
- 416 Hankey GJ. Role of lipid-modifying therapy in the prevention of initial and recurrent stroke. *Current Opinion in Lipidology*. 2002;13(6):645-51.
- 417 Amarenco P, Labreuche J, Lavalley P, Touboul PJ. Statins in stroke prevention and carotid atherosclerosis: Systematic review and up-to-date meta-analysis. *Stroke*. 2004;35(12):2902-9.
- 418 Amarenco P, Bogousslavsky J, Callahan A, 3rd, Goldstein LB, Hennerici M, Rudolph AE, et al. High-dose atorvastatin after stroke or transient ischemic attack (SPARCL). *New England Journal of Medicine*. 2006 Aug 10;355(6):549-59.
- 419 Cholesterol Treatment Trialists' Collaboration. Efficacy and safety of cholesterol-lowering treatment: Prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins. *Lancet*. 2005;366(9493):1267-78.
- 420 Law M, Rudnicka AR. Statin Safety: A Systematic Review. *American Journal of Cardiology*. 2006;97(8 SUPPL. 1):S52-S60.
- 421 De Denus S, Spinler SA, Miller K, Peterson AM. Statins and Liver Toxicity: A Meta-Analysis. *Pharmacotherapy*. 2004;24(5):584-91.
- 422 Sanossian N, Saver JL, Liebeskind DS, Kim D, Razinia T, Ovbiagele B. Achieving target cholesterol goals after stroke: Is in-hospital statin initiation the key? *Archives of Neurology*. 2006;63(8):1081-3.
- 423 Petty GW, Brown RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Survival and recurrence after first cerebral infarction: a population-based study in Rochester, Minnesota, 1975 through 1989. *Neurology*. 1998;50(1):208-16.
- 424 Hillen T, Coshall C, Tilling K, Rudd AG, McGovern R, Wolfe CD, et al. Cause of stroke recurrence is multifactorial: patterns, risk factors, and outcomes of stroke recurrence in the South London Stroke Register. *Stroke*. 2003;34(6):1457-63.
- 425 Diabetes Australia Guideline Development Consortium. National Evidence Based Guidelines for the Management of Type 2 Diabetes Mellitus. Part 3 - Evidence Based Guideline for Case Detection and Diagnosis of Type 2 Diabetes. 2004.
- 426 Diabetes Australia Guideline Development Consortium. National Evidence Based Guidelines for the Management of Type 2 Diabetes Mellitus. Part 4 - Guideline for Blood Pressure Control in Type 2 Diabetes. 2004.
- 427 Diabetes Australia Guideline Development Consortium. National Evidence Based Guidelines for the Management of Type 2 Diabetes Mellitus. Part 5 - Guideline for the Prevention and Detection of Macrovascular Disease in Type 2 Diabetes. 2004.
- 428 Diabetes Australia Guideline Development Consortium. National Evidence Based Guidelines for the Management of Type 2 Diabetes Mellitus. Part 7 - Evidence Based Guideline for Lipid Control in Type 2 Diabetes. 2004.
- 429 Cina CS, Clase CM, Haynes RB. Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database of Systematic Reviews* 1999, Issue 3. Art. No.: CD001081. DOI: 10.1002/14651858.CD001081.
- 430 Rothwell PM, Eliasziw M, Gutnikov SA, Fox AJ, Taylor DW, Mayberg MR, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet*. 2003 Jan 11;361(9352):107-16.
- 431 Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJM. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet*. 2004;363(9413):915-24.
- 432 Chambers BR, Donnan GA. Carotid endarterectomy for asymptomatic carotid stenosis. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD001923. DOI: 10.1002/14651858.CD001923.pub2.
- 433 Rothwell PM, Slattery J, Warlow CP. A systematic review of the risks of stroke and death due to endarterectomy for symptomatic carotid stenosis. *Stroke*. 1996;27(2):260-5.
- 434 Engelter S, Lyrer P. Antiplatelet therapy for preventing stroke and other vascular events after carotid endarterectomy. *Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD001458. DOI: 10.1002/14651858.CD001458.
- 435 Payne DA, Jones CI, Hayes PD, Thompson MM, London NJ, Bell PR, et al. Beneficial Effects of Clopidogrel Combined with Aspirin in Reducing Cerebral Emboli in Patients Undergoing Carotid Endarterectomy. *Circulation*. 2004;109(12):1476-81.
- 436 Markus HS, Droste DW, Kaps M, Larrue V, Lees KR, Siebler M, et al. Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using doppler embolic signal detection: The clopidogrel and aspirin for reduction of emboli in symptomatic carotid stenosis (CARESS) trial. *Circulation*. 2005;111(17):2233-40.
- 437 Coward LJ, Featherstone RL, Brown MM. Percutaneous transluminal angioplasty and stenting for carotid artery stenosis. *Cochrane Database of Systematic Reviews* 2004, Issue 2. Art. No.: CD000515. DOI: 10.1002/14651858.CD000515.pub2.
- 438 SPACE Trialists. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. *Lancet*. 2006;368(9543):1239-47.
- 439 Mas JL, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin JP, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. *New England Journal of Medicine*. 2006;355(16):1660-71.

- 440 Messe SR, Silverman IE, Kizer JR, Homma S, Zahn C, Gronseth G, et al. Practice Parameter: Recurrent stroke with patent foramen ovale and atrial septal aneurysm. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2004;62(7):1042-50.
- 441 Khairy P, O'Donnell CP, Landzberg MJ. Transcatheter Closure versus Medical Therapy of Patent Foramen Ovale and Presumed Paradoxical Thromboemboli: A Systematic Review. *Annals of Internal Medicine*. 2003;139(9):753-60.
- 442 Homma S, Sacco RL, Di Tullio MR, Sciacca RR, Mohr JP. Effect of medical treatment in stroke patients with patent foramen ovale: Patent foramen ovale in Cryptogenic Stroke Study. *Circulation*. 2002;105(22):2625-31.
- 443 Harrer JU, Wessels T, Franke A, Lucas S, Berlit P, Klotzsch C. Stroke recurrence and its prevention in patients with patent foramen ovale. *Canadian Journal of Neurological Sciences*. 2006 Feb;33(1):39-47.
- 444 Schuchlenz HW, Weihs W, Berghold A, Lechner A, Schmidt R. Secondary prevention after cryptogenic cerebrovascular events in patients with patent foramen ovale. *International Journal of Cardiology*. 2005;101(1):77-82.
- 445 Windecker S, Wahl A, Nedeltchev K, Arnold M, Schwerzmann M, Seiler C, et al. Comparison of medical treatment with percutaneous closure of patent foramen ovale in patients with cryptogenic stroke. *Journal of the American College of Cardiology*. 2004;44(4):750-8.
- 446 Schroeder K, Fahey T, Ebrahim S. Interventions for improving adherence to treatment in patients with high blood pressure in ambulatory settings. *The Cochrane Database of Systematic Reviews* 2004, Issue 3 Art No: CD004804 DOI: 101002/14651858CD004804.
- 447 Schedlbauer A, Schroeder K, Peters TJ, Fahey T. Interventions to improve adherence to lipid lowering medication. *The Cochrane Database of Systematic Reviews* 2004, Issue 2 Art No: CD004371pub2 DOI: 101002/14651858CD004371pub2.
- 448 Haynes RB, Yao X, Degani A, Kripalani S, Garg A, McDonald HP. Interventions to enhance medication adherence. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD000011. DOI: 10.1002/14651858.CD000011.pub2.
- 449 McGraw C. Multi-compartment medication devices and patient compliance. *British Journal of Community Nursing*. 2004;9(7):285-90.
- 450 Heneghan CJ, Glasziou P, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD005025. DOI: 10.1002/14651858.CD005025.pub2.
- 451 Royal Australian College of General Practitioners. Putting Prevention into Practice. Guidelines for the implementation of prevention in the general practice setting. 2nd ed. Melbourne: RACGP; 2006.
- 452 Winkler D, Farnworth L, Sloan S. People under 60 living in aged care facilities in Victoria. *Australian Health Review*. 2006;30(1):100-8.
- 453 Barras. A systematic and critical review of the literature: the effectiveness of occupational therapy home assessment on a range of outcome measures. *Australian Occupational Therapy Journal*. 2005;52(4):326-36.
- 454 Gillespie LD, Gillespie WJ, Robertson MC, Lamb SE, Cumming RG, Rowe BH. Interventions for preventing falls in elderly people. *The Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD000340. DOI: 10.1002/14651858.CD000340.
- 455 Steultjens EM, Dekker J, Bouter LM, Jellema S, Bakker EB, van den Ende CH. Occupational therapy for community dwelling elderly people: a systematic review. *Age and Ageing*. 2004;33(5):453-60.
- 456 Shepperd S, Parkes J, McClaren J, Phillips C. Discharge planning from hospital to home. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD000313. DOI: 10.1002/14651858.CD000313.pub2.
- 457 Dai YT, Chang Y, Hsieh CY, Tai TY. Effectiveness of a pilot project of discharge planning in Taiwan. *Research in nursing & health*. 2003;26(1):53-63.
- 458 Forster A, Young J, Langhorne P, for the Day Hospital Group. Medical day hospital care for the elderly versus alternative forms of care. *The Cochrane Database of Systematic Reviews* 1999, Issue 3. Art. No.: CD001730. DOI: 10.1002/14651858.CD001730.
- 459 Britton M, Andersson A. Home rehabilitation after stroke: reviewing the scientific evidence on effects and costs. *International Journal of Technology Assessment in Health Care*. 2000;16(3):842-8.
- 460 Tyson S, Turner G. Discharge and follow-up for people with stroke: what happens and why. *Clin Rehabil*. 2000 Aug;14(4):381-92.
- 461 Christie D, Weigall D. Social work effectiveness in two-year stroke survivors: a randomised controlled trial. *Community Health Stud*. 1984;8(1):26-32.
- 462 Towle D, Lincoln NB, Mayfield LM. Service provision and functional independence in depressed stroke patients and the effect of social work intervention on these. *J Neurol Neurosurg Psychiatry*. 1989 Apr;52(4):519-22.
- 463 Forster A, Young J. Specialist nurse support for patients with stroke in the community: a randomised controlled trial. *British Medical Journal*. 1996 Jun 29;312(7047):1642-6.
- 464 Goldberg G, Segal ME, Berk SN, Schall RR, Gershkoff AM. Stroke transition after inpatient rehabilitation. *Topics in Stroke Rehabilitation*. 1997(1):64-79.
- 465 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. *British Medical Journal*. 1997 Apr 12;314(7087):1071-6; discussion 6-7.

- 466 Glass TA, Berkman LF, Hiltunen EF, Furie K, Glymour MM, Fay ME, et al. The families in recovery from stroke trial (FIRST): Primary study results. *Psychosomatic Medicine*. 2004;66(6):889-97.
- 467 Andersen HE, Eriksen K, Brown A, Schultz-Larsen K, Forchhammer BH. Follow-up services for stroke survivors after hospital discharge--a randomized control study. *Clin Rehabil*. 2002 Sep;16(6):593-603.
- 468 Lincoln NB, Francis VM, Lilley SA, Sharma JC, Summerfield M. Evaluation of a stroke family support organiser: a randomized controlled trial. *Stroke*. 2003 Jan;34(1):116-21.
- 469 Mant J, Carter J, Wade DT, Winner S. Family support for stroke: a randomised controlled trial. *Lancet*. 2000 Sep 2;356(9232):808-13.
- 470 Tilling K, Coshall C, McKeivitt C, Daneski K, Wolfe C. A family support organiser for stroke patients and their carers: a randomised controlled trial. *Cerebrovascular Diseases*. 2005;20(2):85-91.
- 471 Mistiaen P, Poot E. Telephone follow-up, initiated by a hospital-based health professional, for postdischarge problems in patients discharged from hospital to home. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD004510. DOI: 10.1002/14651858.CD004510.pub3.
- 472 Austroads. *Assessing Fitness to Drive: Commercial and Private Vehicle Drivers*. 2006 (3rd ed).
- 473 Vos T, Corry J, Haby MM, Carter R, Andrews G. Cost-effectiveness of cognitive-behavioural therapy and drug interventions for major depression. *Australian and New Zealand Journal of Psychiatry*. 2005;39(8):683-92.
- 474 World Health Organisation. *The World Health Report 2002: Reducing Risks, Promoting Healthy Lifestyle*. Geneva: World Health Organisation.
- 475 Asplund PK. What MONICA told us about stroke. *Lancet Neurology*. 2005;4(1):64-8.
- 476 Brady BK, McGahan L, Skidmore B. Systematic review of economic evidence on stroke rehabilitation services. *International Journal of Technology Assessment in Health Care*. 2005;21(1):15-21.
- 477 Moodie M, Cadilhac D, Pearce D, Mihalopoulos C, Carter R, Davis S, et al. Economic evaluation of Australian stroke services: A prospective, multicenter study comparing dedicated stroke units with other care modalities. *Stroke*. 2006;37(11):2790-5.
- 478 Patel A, Knapp M, Perez I, Evans A, Kalra L. Alternative Strategies for Stroke Care: Cost-Effectiveness and Cost-Utility Analysis from a Prospective Randomized Controlled Trial. *Stroke*. 2004;35(1):196-203.
- 479 Moodie ML, Carter R, Mihalopoulos C, Thrift AG, Chambers BR, Donnan GA, et al. Trial application of a Model of Resource Utilization, Costs, and Outcomes for Stroke (MORUCOS) to assist priority setting in stroke. *Stroke*. 2004;35(5):1041-6.
- 480 Cadilhac DA, Lalor EE, Pearce DC, Levi CR, Donnan GA. Access to stroke care units in Australian public hospitals: Facts and temporal progress. *Internal Medicine Journal*. 2006;36(11):700-4.
- 481 Cadilhac DA, Carter RC, Thrift AG, Dewey HM. Why invest in a national public health program for stroke? An example using Australian data to estimate the potential benefits and cost implications. *Health Policy*, March 15. 2007;83(2-3):287-94.
- 482 Sulch D, Perez I, Melbourne A, Kalra L. Randomized controlled trial of integrated (managed) care pathway for stroke rehabilitation. *Stroke*. 2000;31(8):1929-34.
- 483 Read SJ, Levy J. Effects of care pathways on stroke care practices at regional hospitals. *Internal Medicine Journal*. 2006;36(10):638-42.
- 484 Wolff AM, Taylor SA, McCabe JF. Using checklists and reminders in clinical pathways to improve hospital inpatient care. *Medical Journal of Australia*. 2004;181(8):428-31.
- 485 Quaglini S, Cavallini A, Gerzeli S, Micieli G. Economic benefit from clinical practice guideline compliance in stroke patient management. *Health Policy*. 2004;69(3):305-15.
- 486 Fjaertoft H, Indredavik B, Magnussen J, Johnsen R. Early supported discharge for stroke patients improves clinical outcome. Does it also reduce use of health services and costs? One-year follow-up of a randomized controlled trial. *Cerebrovascular Diseases*. 2005;19(6):376-83.
- 487 Anderson C, Ni Mhurchu C, Brown PM, Carter K. Stroke Rehabilitation Services to Accelerate Hospital Discharge and Provide Home-Based Care: An Overview and Cost Analysis. *PharmacoEconomics*. 2002;20(8):537.
- 488 Tseng MC, Chang KC. Cost-effectiveness analysis of tissue plasminogen activator for acute ischemic stroke: a comparative review. *Acta Neurologica Taiwanica*. 2004 Sep;13(3):149-55.
- 489 Mar J, Begiristain JM, Arrazola A. Cost-effectiveness analysis of thrombolytic treatment for stroke. *Cerebrovascular Diseases*. 2005;20(3):193-200.
- 490 Mihalopoulos C, Cadilhac DA, Moodie ML, Dewey HM, Thrift AG, Donnan GA, et al. Development and application of Model of Resource Utilization, Costs, and Outcomes for Stroke (MORUCOS): An Australian economic model for stroke. *International Journal of Technology Assessment in Health Care*. 2005;21(4):499-505.
- 491 Murtagh J, Foerster V, Warburton RN, Lentle BC, Wood RJ, Mensinkai S, et al. Clinical and cost effectiveness of CT and MRI for selected clinical disorders: results of two systematic reviews. 2006 [Available from: <http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060857/frame.html>]

- 492 Buskens E, Nederkoorn PJ, Buijs-Van Der Woude T, Mali WP, Kappelle LJ, Eikelboom BC, et al. Imaging of carotid arteries in symptomatic patients: cost-effectiveness of diagnostic strategies. *Radiology*. 2004 Oct;233(1):101-12.
- 493 Patel A, Knapp M, Evans A, Perez I, Kalra L. Training care givers of stroke patients: economic evaluation. *British Medical Journal*. 2004;328(7448):1102.
- 494 Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, et al. Cost of stroke in Australia from a societal perspective: results from the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2001 Oct;32(10):2409-16.
- 495 Benade MM, Warlow CP. Costs and benefits of carotid endarterectomy and associated preoperative arterial imaging: a systematic review of health economic literature. *Stroke*. 2002;33(2):629-38.
- 496 Nussbaum ES, Heros RC, Erickson DL. Cost-effectiveness of carotid endarterectomy. *Neurosurgery*. 1996 Cited as structured abstract from NHS Economic Evaluation Database (NHSEED) 2007;38:237-44.
- 497 Holloway RG, Benesch CG, Rahilly CR, Courtright CE. A systematic review of cost-effectiveness research of stroke evaluation and treatment. *Stroke*. 1999;30(7):1340-9.
- 498 Smith MG, Neville AM, Middleton JC. Clinical and economic benefits of ramipril: An Australian analysis of the HOPE study. *Internal Medicine Journal*. 2003;33(9-10):414-9.
- 499 Marissal JP, Selke B, Amarenco P. Economic assessment of the secondary prevention of ischaemic stroke with dipyridamole plus aspirin (Aggrenox(registered trademark)/Asasantin(registered trademark)) in France. *PharmacoEconomics*. 2004;22(10):661-70.
- 500 Chambers M, Hutton J, Gladman J. Cost-effectiveness analysis of antiplatelet therapy in the prevention of recurrent stroke in the UK: Aspirin, dipyridamole and aspirin-dipyridamole. *PharmacoEconomics*. 1999;16(5 II):577-93.
- 501 Schleinitz MD, Weiss JP, Owens DK. Clopidogrel versus aspirin for secondary prophylaxis of vascular events: A cost-effectiveness analysis. *American Journal of Medicine*. 2004;116(12):797-806.
- 502 Shah H, Gondek K. Aspirin plus extended-release dipyridamole or clopidogrel compared with aspirin monotherapy for the prevention of recurrent ischemic stroke: A cost-effectiveness analysis. *Clinical Therapeutics*. 2000;22(3):362-70.
- 503 Jones L, Griffin S, Palmer S, Main C, Orton V, Sculpher M, et al. Clinical effectiveness and cost-effectiveness of clopidogrel and modified-release dipyridamole in the secondary prevention of occlusive vascular events: A systematic review and economic evaluation. *Health Technology Assessment*. 2004;8(38):iii-108.
- 504 Sarasin FP, Gaspoz JM, Bounameaux H. Cost-effectiveness of new antiplatelet regimens used as secondary prevention of stroke or transient ischemic attack. *Archives of Internal Medicine*. 2000;160(18):2773-8.
- 505 Heart Protection Study Collaborative Group. Lifetime cost effectiveness of simvastatin in a range of risk groups and age groups derived from a randomised trial of 20,536 people. *British Medical Journal*. 2006;333(7579):1145-50.
- 506 Ebrahim S. Cost-effectiveness of stroke prevention. *British Medical Bulletin*. 2000;56(2):557-70.
- 507 Shearer J, Shanahan M. Cost effectiveness analysis of smoking cessation interventions. *Australian and New Zealand Journal of Public Health*. 2006;30(5):428-34.
- 508 Tomson T, Helgason A, Gilljam H. Quitline in smoking cessation: a cost-effectiveness analysis. *Int J Technol Assess Health Care*. 2004;20(4):469-74.
- 509 Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health technology assessment (Winchester, England)*. 2004;8(21):iii-iv, 1-182.
- 510 Nicholl JPCPBJE. Health and healthcare costs and benefits of exercise. *Pharmacoeconomics*. 1994;5(2):109-22.
- 511 Sevick MA, Dunn AL, Morrow MS, Marcus BH, Chen GJ, Blair SN. Cost-effectiveness of lifestyle and structured exercise interventions in sedentary adults. Results of project ACTIVE. *American Journal of Preventive Medicine*. 2000;19(1):1-8.
- 512 Dalziel K, Segal L, Elley CR. Cost utility analysis of physical activity counselling in general practice. *Australian and New Zealand Journal of Public Health*. 2006;30(1):57-63.
- 513 Elley CR, Kerse N, Arroll B, Swinburn B, Ashton T, Robinson E. Cost-effectiveness of physical activity counselling in general practice. *New Zealand Medical Journal*. 2004;117(1207):15p.
- 514 Marshall T. Evaluating national guidelines for prevention of cardiovascular disease in primary care. *Journal of Evaluation in Clinical Practice*. 2005;11(5):452-61.
- 515 Murray CJL, Lauer JA, Hutubessy RCW, Niessen L, Tomijima N, Rodgers A, et al. Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: A global and regional analysis on reduction of cardiovascular-disease risk. *Lancet*. 2003;361(9359):717-25.
- 516 Pocock SJ, McCormack V, Gueyffier F, Boutitie F, Fagard RH, Boissel JP. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. *British Medical Journal*. 2001;323(7304):75-81.

- 517 Sesso HD, Chen RS, L'Italien GJ, Lapuerta P, Lee WC, Glynn RJ. Blood Pressure Lowering and Life Expectancy Based on a Markov Model of Cardiovascular Events. *Hypertension*. 2003;42(5):885-90.
- 518 Manuel DG, Lim J, Tanuseputro P, Anderson GM, Alter DA, Laupacis A. Revisiting Rose: strategies for reducing coronary heart disease. *British Medical Journal*. 2006;332(7542):659-62.
- 519 National Stroke Foundation. Walk in our shoes: Stroke survivors and carers report on support after stroke. Melbourne: National Stroke Foundation; 2007.



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