

THEME

Stroke





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Acute stroke patients

Early hospital management

BACKGROUND

Patients with acute stroke have improved outcomes when managed in a stroke unit providing multidisciplinary care, including early rehabilitation.

OBJECTIVE

This article provides an overview of early hospital management and rehabilitation for stroke patients.

DISCUSSION

Stroke and transient ischaemic attack are medical emergencies. Both have time dependent therapy and the risk of a recurrent event is highest in the hours to days after the initial event. Important aspects of early hospital management include: rapid confirmation of the stroke diagnosis with computerised tomography or magnetic resonance imaging, urgent investigations for the cause of stroke, acute therapy, early institution of specific secondary prevention strategies, comprehensive risk factor management including antihypertensive therapy, early rehabilitation, and discharge planning. Investigation and management needs to be tailored to the individual patient, taking into account presentation and comorbidities.

There is compelling evidence that stroke unit care (organised care provided by dedicated staff within a defined geographic area) is not only cost effective, but highly effective in preventing death and long term disability in stroke patients compared to care provided on general medical wards alone.^{1–3} Important aspects of effective stroke unit care include:

- accurate and rapid confirmation of the stroke diagnosis, likely causation and associated risk factors
- evidence based treatment
- close monitoring of neurological status and physiological parameters
- prevention of the complications of stroke and recurrent stroke, and
- early institution of multidisciplinary rehabilitation focused on achieving functional goals and early development of an individualised discharge plan.

Confirming a diagnosis of stroke

Key clinical features of stroke are sudden onset and the presence of focal neurological symptoms and signs. Typically, the patient has been well before the event.⁴ Loss of consciousness without focal neurological signs and isolated vertigo are rarely due to stroke. The Oxfordshire

Community Stroke Project (OCSP) classification⁵ (*Table 1*) is a useful schema for assessment of stroke subtype at the bedside and, together with brain imaging, can assist with prognostication and planning of further investigations.

The distinction between ischaemic and haemorrhagic stroke cannot be made on clinical grounds, and other pathology (eg. subdural haematoma) may mimic stroke, so it is essential to urgently confirm the diagnosis of stroke with computerised tomography (CT) or magnetic resonance imaging (MRI). Immediate brain imaging is also required to confirm eligibility for intravenous alteplase.⁶ Early CT imaging is frequently normal in ischaemic stroke, or changes may be subtle. Multimodal CT imaging adds useful diagnostic and prognostic information and is discussed in more detail in an accompanying article.

If initial CT is normal and there is any doubt about the diagnosis, CT imaging should be repeated in 3–7 days or MRI performed. Topographic information is a guide to likely causation and appropriate further investigations (*Table 1*). Acute MRI has greater overall sensitivity for acute stroke than noncontrast CT scanning (83 vs. 26%);⁷ however access to urgent MRI is limited. Additional imaging may be appropriate when the aetiology of stroke remains uncertain or there are recurrent events.

Table 1. The Oxfordshire Community Stroke Project stroke classification (modified)

Subtype	Defining features	Usual cause and prognosis
TACI (total anterior circulation infarct)	Contralateral motor and/or sensory deficit, and higher cortical dysfunction (eg. dysphasia, neglect), and homonymous hemianopia	Large middle cerebral artery infarct due to embolism from the heart or proximal arterial source; high likelihood of death or long term dependency
PACI (partial anterior circulation infarct)	Two of three deficits necessary for TACI, or higher cortical dysfunction alone, or restricted motor/sensory deficit (eg. confined to one limb or face and hand)	Smaller infarct but same arterial causes as TACI; better prognosis for recovery but high risk of early recurrence
LACI (lacunar infarct)	Pure motor hemiparesis, pure sensory stroke, sensory motor stroke, ataxic hemiparesis	Small deep infarct due to small vessel disease; relatively good prognosis
POCI (posterior circulation infarct)	Brain stem signs Cerebellar dysfunction without ipsilateral long tract signs (ie. not ataxic hemiparesis), or isolated homonymous hemianopia	Infarct in the posterior cerebral hemisphere, brain stem or cerebellum due to large or small vessel disease or cardiac embolism; variable prognosis
ICH (intracerebral haemorrhage)	Signs depend on site and size of haemorrhage	Multiple causes, worse prognosis than ischaemic stroke
		Deep location: usually due to rupture of small, deep perforating artery, often associated with hypertension
		Superficial/lobar location: cerebral amyloid angiopathy often the cause, older patient
		Other common causes: arteriovenous malformation/ cavernoma, ruptured saccular aneurysm, coagulopathy

Investigations for the cause of stroke

Stroke and transient ischaemic attack (TIA) are both medical emergencies, as there is time dependent effective treatment. Importantly, the risk of a recurrent event is highest in the hours to days after the initial event.⁸ Therefore, effective secondary prevention strategies should be initiated as soon as possible. All patients with acute stroke should have:

- baseline electrocardiogram (to exclude atrial fibrillation, acute coronary syndrome and evidence of structural or ischaemic heart disease)
- electrolytes and renal function
- blood sugar level
- full blood examination, and
- erythrocyte sedimentation rate.

Further investigations need to be tailored to the individual and their stroke syndrome (*Table 1*) and take into account stroke severity and concomitant disease. Severe stroke (eg. total anterior circulation infarct, large intracerebral haemorrhage [ICH]) is associated with a poor prognosis and a palliative care approach will be appropriate for some patients.

Carotid imaging should be performed urgently in all patients considered to be candidates for carotid revascularisation to exclude a high grade (>70%) internal carotid artery stenosis.⁹ In the Australian setting, carotid duplex ultrasound is usually the most appropriate and accessible first line investigation. The benefits from carotid endarterectomy are greatest when performed early after first symptoms,¹⁰ therefore, patients with symptomatic high grade (>70%) carotid stenosis should be referred urgently to a vascular surgeon. Carotid endarterectomy is generally safe within 2 weeks after ischaemic stroke and should be performed as soon as possible after TIA.

Echocardiography may be indicated in some patients to search for a cardiac or aortic source of embolism.¹³ Transoesophageal echocardiography is more sensitive than transthoracic echo to cardiac sources of emboli and allows visualisation of the aortic arch. Thick (>4mm) and/or mobile aortic arch atheroma is now recognised as an important risk factor for stroke.¹¹

General management within a stroke unit

Specific acute therapy for stroke

Aspirin 160–300 mg/day should be commenced within 48 hours of onset of acute ischaemic stroke.¹²

Intravenous alteplase, a tissue plasminogen activator, is a highly effective treatment for patients presenting within 3 hours of stroke.¹³ Currently, the most common reason for exclusion from treatment is delay in presentation to hospital. Intravenous heparin is NOT recommended standard treatment for acute stroke as its use is associated with an increased risk of ICH.¹⁴

Large hemispheric infarcts may be complicated by major brain swelling. Hemicraniectomy within 48 hours

has been shown to substantially improve outcomes from this complication.¹⁵

Specific acute therapy for ICH

Intracerebral haemorrhage due to anticoagulation should be urgently reversed. Surgical evacuation is not routinely recommended for ICH but may be considered in some patients (eg. cerebellar hemisphere haemorrhage >3 cm).

General care

Patients with stroke should be maintained in a euvolaemic state. Hyper- and hypo-glycaemia should be avoided. Oxygen supplementation should be provided if the patient is hypoxic.

Blood pressure management

It remains uncertain whether elevated blood pressure (BP) should be lowered acutely after stroke. Current international guidelines recommend tolerating BP up to 220/120 without treatment in the first hours to days after stroke unless there is serious concomitant disease mandating BP reduction (eg. aortic dissection).^{6,9} In patients receiving intravenous alteplase, BP is more tightly controlled to $\leq 185/110$ as higher BP is associated with an increased risk of ICH.^{6,9} It is generally accepted that BP lowering in ICH patients is indicated to keep mean arterial BP (MAP) below 130 mmHg (MAP = diastolic BP + 1/3 systolic-diastolic BP).⁹

Specialised nursing care

Expert nursing care is a key aspect of effective stroke unit care. Management of the impairments associated with stroke must be individualised (*Table 2*). However, stroke nursing will include attention to bladder and bowel function, skin care, mouth and eye care, nutrition and fluid support.

Management of stroke related impairments

Stroke patients commonly experience difficulties with swallowing, communication, independent movement and personal care, continence, perception and mood (Table 2). Well trained multidisciplinary teams are best placed to manage these impairments and are an important part of good early stroke care. To date, research that helps guide acute management of these difficulties is limited. Notable exceptions include the growing body of research into early swallowing screening,7 and the FOOD trial, which aimed to identify best early nutritional practices.¹⁶ The large, multicentre early mobilisation trial (AVERT) is currently underway in Australia,¹⁷ as is the United Kingdom based ACTNoW trial of acute aphasia therapy.¹⁸ Both trials will help inform early rehabilitation interventions, however, neither will be completed for some years. Nevertheless, early commencement of rehabilitation is believed to contribute to the positive outcomes achieved by patients receiving stroke unit care.¹⁹ Comprehensive recommendations for postacute rehabilitative care can be found elsewhere.^{20,21}

Management of complications

Frequent monitoring of neurological status and vital signs is important and allows early detection and prompt treatment of complications (*Table 3*). Conscious level, neurological status and physiological parameters (BP, pulse, oxygenation, respiratory pattern, temperature, fluid status, blood sugar) should be monitored frequently (at least hourly) early after stroke. Later, the frequency of observations should be tailored to the individual.

Complications after stroke are common, with 62–85% of patients experiencing at least one complication within the first few months after stroke.^{22,23} Neurological worsening is common early after stroke, with stroke progression reported in up to 40% of cases.²⁴ Secondary complications such as urinary tract and chest infections, pressure sores, falls, deep vein thrombosis, pulmonary embolism and musculoskeletal pain occur more frequently. Disorders of mood, such as depression and anxiety, are thought to be under-reported.²⁵

Intrinsic factors (eg. comorbidities, stroke severity) are associated with increased complication risk poststroke. Although studies included in the systematic review of stroke unit care lack detailed complication data,¹ there is consensus that improved outcomes are likely to be related to reduced complication rates as a result of the provision of earlier and more coordinated care.

Common complications and recommended management are summarised in *Table 3* (a strong recommendation against an approach is highlighted).

Risk factor assessment and management

Hypertension

Hypertension is the most important modifiable risk factor for recurrent stroke. Most patients with stroke or TIA should be commenced on antihypertensive medication, regardless of baseline BP.⁹ Patients with both 'normal' and 'high' BP benefit from antihypertensive treatment to prevent recurrent stroke. The most direct evidence is for the use of an angiotensin converting enzyme inhibitor (ACEI) or the combination of an ACEI + diuretic.²⁶ However, the choice of antihypertensive medication is less important than effective BP lowering. The best timing for commencement of antihypertensive medication is uncertain. Blood pressure lowering medication appears safe if commenced 2–4 days poststroke. Commencement of secondary prevention strategies during inpatient stay has been associated with greater adherence at 3 months poststroke.²⁷

lable 2. Common early poststroke impairments and recommended management (consensus opinion guides these recommendations unless level of evidence is included: Level I [meta-analysis of RCTs]; Level II [RCTs]) ⁹				
Consequence	Recommended management	Not recommended		
Dysphagia	Early screening (<24 hours) by a trained professional is strongly recommended before patients are given food or drink. No single screening tool can be recommended to date, however the 50 mL water swallow test in combination with monitoring oxygen saturation is well regarded ³⁹ Patients who fail screening should be referred to a speech pathologist	The gag reflex is not a valid screen for dysphagia ⁹		
	is complete			
Malnutrition/ dehydration	Close monitoring of hydration status and supplementation of fluids should be considered. Glucose containing fluids are generally avoided as hyperglycaemia is associated with poor outcome after stroke All patients should be screened for malnutrition using a validated nutritional assessment tool and/or nutritional markers and supplementation offered to those with poor or deteriorating nutritional status. A dietician should be consulted where there is a risk of malnutrition (including patients with dysphagia). Nasogastric feeding is preferred in the first month poststroke for patients without a functional swallow	Percutaneous endoscopic gastrostomy (PEG) is not recommended within the first month poststroke		
Communication deficits	Patients identified as having a probable communication deficit after screening should undergo detailed assessment by a speech pathologist. There is some indication that early and intensive language therapy is helpful. Training of carers in supportive communication techniques and providing information to patients in an aphasia friendly format are both recommended			
Reduced mobility	Early mobilisation (getting out of bed, sitting, standing, walking) may help recovery and no harm has been identified. ⁴⁰ The phase II AVERT trial established that commencing mobilisation within 24 hours of stroke onset was feasible and no safety issues were identified ⁴¹ Based on available data, it is recommended that patients be mobilised as early and frequently as possible			
Reduced activities of daily living	Early formulation of a management plan targeting specific difficulties is recommended. An occupational therapist should advise staff and carers on techniques and equipment to optimise performance			
Incontinence	Functional assessments by trained personnel and development of a management plan for patients with confirmed difficulties is recommended. A portable bladder ultrasound scan can aid diagnosis and management A postdischarge continence management plan should be developed with the patient and carer before discharge and should include how continence resources can be accessed in the community	Indwelling catheters should be avoided as an initial management strategy		
Cognition/perception difficulties	Screening is recommended, with full assessment of those with identified problems. Postacute intervention strategies are included in guidelines ²¹			
Mood disorders: depression and anxiety	lood disorders: epression and anxiety Patients with suspected altered mood (eg. depression, anxiety, emotional lability) should be assessed using a standardised tool (Level II) After discharge, use of a case management model focusing on education, screening and management, linked with the primary care physician, may reduce poststroke depression (Level II) Antidepresent to use the word focus of a case with the primary care physician, may reduce poststroke depression (Level II)			
	Antidepressants and/or psychological interventions may be used for patients with depression or anxiety (Level I)			
Sleep apnoea	Although it is unclear whether sleep apnoea is a risk factor for stroke or a consequence of stroke (or both), continuous positive airways pressure (CPAP) should be considered a first line treatment (Level I)			

Atrial fibrillation

Warfarin (INR 2–3) is appropriate secondary prevention in patients with stroke/TIA and atrial fibrillation, valvular disease or recent myocardial infarction unless there is a clear contraindication. For this subset of patients, the benefits for stroke prevention clearly outweigh the risks of serious haemorrhage.²⁸ The most appropriate timing for commencement of warfarin for secondary prevention poststroke remains uncertain and stroke physicians vary in their practice. There is consensus that warfarin should be commenced as soon as possible after TIA, once CT scanning has excluded ICH.⁹ For patients with stroke, a delay of 1–2 weeks is reasonable.⁹ Commencement of warfarin before discharge as part of secondary prevention has been associated with greater adherence at 3 months poststroke.²⁷ Before commencement of warfarin, aspirin should be used.⁹

Diabetes

Elevated blood sugar level is common in patients presenting with stroke or TIA.⁶ Good glycaemic control is essential for prevention of the long term micro- and non-vascular complications of this disease.

Smoking

Cigarette smoking is a potent risk factor for stroke. A range of effective behavioural and pharmacological approaches to cessation are available and need to be individually tailored.

Table 3. Common poststroke complications and recommended management (where recommendations are supported by evidence, the level of evidence is included: Level I [meta-analysis of RCTs], Level II [RCTs])⁹

Complication	Recommended management	Not recommended
Seizure	Anticonvulsant medication may be used for people with recurrent seizures (Level I)	
Cerebral oedema	Urgent referral to a neurosurgeon for hemicraniectomy should be considered for selected patients with significant middle cerebral artery infarction (Level I)	Corticosteriods have no benefit and may cause harm (Level I)
	Osmotherapy and hyperventilation may help while awaiting neurosurgical consultation	
Infections: chest, urinary tract, other	Antipyretic therapy comprising regular paracetamol and/or physical cooling should be routinely used where fever occurs (Level II)	
Deep vein thrombosis, pulmonary embolus	Antiplatelet therapy should be used to prevent DVT/PE in those with ischaemic stroke (Level I)	
	In selected patients with ischaemic stroke, low molecular weight heparin or heparin in prophylactic doses may be used with caution (Level I). Treatment with heparin is associated with increased risk of cerebral haemorrhage when used early poststroke, so risk/benefit needs to be considered	
	Thigh length antithrombotic stockings (Level II) may also be used with caution, as the benefits are inconclusive and risk of acute limb ischaemia and peripheral neuropathy need to be considered	
	Early mobilisation and adequate hydration should be encouraged (consensus opinion)	
Pressure ulcers	Immobile patients should have a pressure care risk assessment completed (consensus opinion) and those at high risk of ulcers (older, more severe stroke, immobile, incontinent, diabetic and with poor nutritional status) should be provided with a pressure relieving mattress (Level I)	
Pain	Musculoskeletal pain should be managed according to pain management guidelines (www.nhmrc.gov.au/publications/synopses/ cp104syn.htm). In patients exhibiting central poststroke pain, amitriptyline should be preferred over carbamazepine (Level II)	
Falls	There are no stroke specific studies to guide fall prevention in acute stroke. However, general falls prevention guidelines should be followed for this population (www.health.gov.au/internet/safety/ publishing.nsf/Content/falls)	

Hypercholesterolaemia

Epidemiology studies have shown that higher cholesterol is associated with a higher risk of stroke but a lower risk of haemorrhagic stroke.²⁹ Two large randomised controlled trials have provided evidence for the benefits of lipid lowering with statin therapy in patients with stroke or TIA, with no significant increase in haemorrhagic stroke.^{30,31} Therefore statin therapy should be commenced in all patients with stroke or TIA.

Antiplatelet therapy

There is Level 1 evidence that in patients presenting with stroke or TIA, antiplatelet therapy reduces the risk of subsequent serious vascular events;29 and aspirin reduces subsequent serious vascular events by ~13% compared to placebo,33 and is effective in low (75-150 mg) and high (300-1300 mg) doses. Low doses are associated with less gastrointestinal side effects.³² Combination aspirin/extended release dipyridamole (Asasantin SR) has been shown to be more effective for secondary stroke prevention (18% RRR compared to aspirin alone), however about 20% of patients cannot tolerate this medication because of persistent headache.34 Commencement of Asasantin SR at lower dose (1 tablet per day for the first week) is better tolerated.³⁵ Clopidogrel 75 mg/day is modestly more effective than aspirin in the prevention of vascular events,³² but substantially more expensive. Clopidogrel is indicated when aspirin is not tolerated (eq. allergy or risk of gastrointestinal haemorrhage). The combination of low dose aspirin and clopidogrel has not been found to be more effective than clopidogrel alone, but is associated with more bleeding.36

A coordinated approach to discharge

Good discharge planning is crucial for successful reintegration into the community and relies on effective communication between team members, patients, carers and community service providers including the general practitioner. There is consensus that predischarge needs assessment helps to identify the postdischarge physical, emotional, social and financial needs of the patient. A home visit may be required to ensure safety and community access. Carers may need training before discharge; and carer training has been found to improve outcomes for both patients and carers and is cost effective over 12 months.^{37,38} The patient's GP, other primary health professional and community service providers should all be involved in, and informed about, discharge plans and agree on postdischarge management. Written care plans should outline community care after discharge, including the development of self management plans, provision of equipment and support services, and outpatient appointments. Despite consensus about what should be done to ease the transition from hospital to home, currently there is insufficient attention and resources provided for this process.

Conclusion

Hospitalised stroke patients are best managed in a stroke unit where evidence based care can be delivered by a skilled team in an organised, coordinated fashion. Better discharge planning could be achieved with improved systems and resources.

Summary of important points

- All stroke patients should be managed in a stroke unit if available.
- CT brain should be performed urgently in all patients with suspected stroke/TIA. Key additional investigations include ECG and carotid duplex ultrasound.
- All patients with stroke/TIA are at high risk of further vascular events. The risk of recurrent stroke is highest in the first hours to days after the initial event.
- Patients with ischaemic stroke should receive aspirin as soon as possible (within 48 hours) poststroke.
- In the acute setting, BP should not be routinely lowered. Patients with ICH should have MAP maintained below 130 mmHg.
- Antihypertensive medication will be indicated for secondary prevention in the majority of patients with stroke/TIA regardless of BP level.
- Secondary prevention poststroke/TIA will usually include antiplatelet medication (aspirin, clopidogrel or aspirin/ dipyridamole) and a statin.

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References

- StrokeUnitTrialists' Collaboration: organised inpatient (stroke unit) care for stroke (Cochrane Review). Oxford: Updated Software: Cochrane Library, 2001.
- Moodie M, Cadilhac D, Pearce D, et al. Economic evaluation of Australian stroke services. A prospective, multicentre study comparing dedicated stroke units with other care modalities. Stroke 2006;37:2790–5.
- Patel A, Knapp M, Perez I, Evans A, Kalra L. Alternative strategies for stroke care. Cost effectiveness and cost utility analyses from a prospective randomised controlled trial. Stroke 2004;35:196–204.
- Hand PJ. Kwan J. Lindley RI. Dennis MS. Wardlaw JM. Distinguishing between stroke and mimic at the bedside: the brain attack study. Stroke 2006;37:769–75.
- Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. Lancet 1991;337:1521–6.
- Adams HP Jr, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke. A guideline From the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care. Outcomes in research interdisciplinary working groups. Stroke 2007;38:1655–711.
- 7. Chalela JA, Kidwell CS, Nentwich LM, et al. Magnetic resonance imaging

and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison. Lancet 2007;369:293–8.

- Coull AJ, Lovett JK, Rothwell PM, on behalf of the Oxford Vascular Study. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. BMJ 2004;328:326.
- National Stroke Foundation. Clinical guidelines for acute stroke management. Melbourne: NSF, 2007.
- Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP. Barnett HJ. Carotid Endarterectomy Trialists Collaboration. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. Lancet 2004;363:915–24.
- Macleod MR, Amarenco P, Davis SM, Donnan GA. Atheroma of the aortic arch: an important and poorly recognised factor in the aetiology of stroke. Lancet Neurol 2004;3:408–14.
- 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.
- 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;363:768–74.
- Gubitz G, Sandercock P, Counsell C. Anticoagulants for acute ischaemic stroke. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD000024.
- Katayoun Vahedi, Jeannette Hofmeijer, Eric Juettler, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. Lancet Neurol 2007;6:215–22.
- Dennis M, Lewis S, Warlow CP, Collaboration FT. Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicentre randomised controlled trial. Lancet 2005;365:764–72.
- Bernhardt J, Dewey H, Collier J, et al. A Very Early Rehabilitation Trial (AVERT). Int J Stroke 2006;1:169–71.
- ACTNoW Trial Assessing Communication Therapy in the North West. Available at www.psych-sci.manchester.ac.uk/actnow/.
- Stroke Unit Trialists' Collaboration. How do stroke units improve patient outcomes? Stroke 1997;28:2139–44.
- Dewey H, Sherry L, Collier J. Stroke rehabilitation 2007: what should it be? Int J Stroke 2007;2:191–200.
- National Stroke Foundation. Clinical guidelines for stroke rehabilitation and recovery. Melbourne: NSF, 2005.
- Langhorne P, Stott D, Robertson L, et al. Medical complications after stroke: a multicenter study. Stroke 2000;31:1223–9.
- Roth E, Lovell L, Harvey RL, Heinemann AW, Semik P, Diaz S. Incidence of and risk factors for medical complications during stroke rehabilitation. Stroke 2001;32:523–9.
- Birschel P, Ellul J, Barer D. Progressing stroke: towards an internationally agreed definition. Cerebrovasc Dis 2004;17:242–52.
- Hackett M, Yapa C. Frequency of depression after stroke: a systematic review of observational studies. Stroke 2005;36:1330–40.
- Rashid P, Leonardi-Bee J, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. Stroke 2003;34:2741–8.
- Ovbiagele B, Saver JL, Fredieu A, et al. In-hospital initiation of secondary stroke prevention therapies yields high rates of adherence at follow-up. Stroke 2004;35:2879–83.
- 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.
- Hankey GJ. Role of lipid modifying therapy in the prevention of initial and recurrent stroke. Curr Opin Lipidol 2002;13:645–51.
- 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.
- Amarenco PJ, Bogousslavsky J, Callahan A 3rd, et al. High dose atorvastatin after stroke or transient ischemic attack. (SPARCL). N Engl J Med 2006;355:549–59.
- Antithrombotic Trialists Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ 2002;324:71–86.
- Algra A, van Gijn J. Cumulative meta-analysis of aspirin efficacy after cerebral ischaemia of arterial origin. J Neurol Neurosurg Psychiatry

1999;66:255.

- ESPRIT Study Group. Halkes PH, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006;367:1665–73.
- Chang YJ, Ryu SJ, Lee TH. Dose titration to reduce dipyridamole related headache. Cerebrovasc Dis 2006;22:258–62.
- Diener HC, Bogousslavsky J, Brass LM, 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;364:331–7.
- Kalra L, Evans A, Perez I, et al. Training carers of stroke patients: randomised controlled trial. BMJ 2004;726:1099.
- Patel A, Knapp M, Evans A, Perez I, Kalra L. Training care givers of stroke patients: economic evaluation. BMJ 2004;726:1102.
- Smith H, Lee S, O'Neil P, Connolly M. The combination of bedside swallowing assessment and oxygen saturation monitoring of swallowing in acute stroke: a safe and humane screening tool. Age Ageing 2000;29:495–9.
- Indredavik B, Bakke RPT, Slordahl SA, Rokseth R, Haheim LL. Treatment in a combined acute and rehabilitation stroke unit: which aspects are most important? Stroke 1999;30:917–23.
- Bernhardt J, Dewey HM, Thrift AG, Collier J, Donnan GA. Very Early Rehabilitation Trial for Stroke (AVERT): phase II safety and feasibility. Stroke 2007; in press.

