National Clinical Guidelines for Stroke

Update 2002

Prepared by

The Intercollegiate Working Party for Stroke

Clinical Effectiveness
& Evaluation Unit

ROYAL COLLEGE OF PHYSICIANS

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Contents

The section numbers and headings accord with those used in the original guidelines.

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What's new

This supplement contains the 2002 updates to the *National Clinical Guidelines for Stroke* (first published by the Royal College of Physicians of London in 2000), as they appear on the College website: **www.rcplondon.ac.uk/pubs/books/stroke /index.htm**.

For those readers who are unfamiliar with the *National Clinical Guidelines for Stroke*, they cover the management of stroke from the acute illness, through to transfer of care from hospital to the community, to longer-term problems including carer support and secondary prevention. They are designed to be read by all health and social service professionals, including those working in primary care. The patient and carer information booklet based on the Guidelines is still available from the Stroke Association (**www.stroke.org.uk**) and can be purchased in bulk from the Royal College of Physicians Publications Department.

Since the Guidelines were originally published there have been some major developments in stroke research that are reflected in these updates which also include the management of Transient Ischaemic Attack (TIA). The new updates include:

- The recommendation that specialist stroke services include a neurovascular clinic to enable patients with TIA and minor stroke (where the patient has not been admitted to hospital) to be investigated and treated within a maximum of two weeks.
- Changes in the recommendations about the management of blood pressure after stroke following the publication of the HOPE and PROGRESS trials.
- Although advances in therapy research do not warrant radical alterations to practice, two changes have been made. These recommend (a) the use of resisted exercise to improve motor function in targeted muscles and (b) that patients should be given as much opportunity to practise tasks as possible.
- More precise recommendations on the management of depression.
- The withdrawal of some recommendations concerning the management of shoulder pain, deep venous thrombosis and biofeedback.

An updated version of the concise guidelines accompanies this publication. With the research evidence evolving at a rapid rate, the full Guidelines will be updated on a regular basis; a new edition will be published in 2004.

Dr Anthony Rudd
Chair of the Intercollegiate Working Party for Stroke

June 2002

1 Introduction

1.1 Scope of the guidelines

Addition of Transient Ischaemic Attack (TIA)

This update to the *National Clinical Guidelines for Stroke* includes the management of patients with transient ischaemic attack (TIA), which is defined identically to stroke except that the symptoms and signs last less than 24 hours. Throughout the guidelines the term stroke should be understood to encompass TIA.

Licensing of drugs

Recommendations about the use of specific drugs do not take into account whether the drug is licensed by the Medicines Control Agency for that particular use. It is up to individual physicians and their trusts to decide whether to permit the unlicensed use of drugs. There are many situations where it is entirely appropriate to use medication which has not been licensed for specific situations, eg aspirin in acute ischaemic stroke.

3 Service organisation

UPDATE NOTE – This section has been amended to take account of the reorganisation of health services in the last two years, the increasing evidence to support the various elements of an organised stroke service, together with the benefits to be achieved by early assessment and timely secondary prevention following TIA and stroke. The section is therefore shown in its entirety for convenience.

Each stroke patient leads clinicians down a unique pathway, identifying and resolving a host of different combinations of problems in each case. It is therefore difficult to give many guidelines that will apply to every patient. Efficient and effective management of patients depends upon a well organised, expert service that can respond to the particular needs of each individual patient. Consequently, the organisation of stroke services must be considered at every level: health district or primary care trust; general practice group; individual hospital; hospital ward; and patients in their own homes or in residential care.

3.1 Specialist stroke services

Guidelines

a Every organisation involved in the care of stroke patients over the first 6 months should ensure that all stroke patients are the responsibility of, and are seen by services specialising in stroke and rehabilitation (**A**). Any patient with moderate or severe symptoms should be referred to hospital with the expectation of admission to a stroke unit. Exceptions may include those relatively few patients for whom the diagnosis will make no difference to management.

   The stroke service should comprise:

   i a geographically identified unit acting as a base, and as part of the inpatient service (**A**)
   ii a co-ordinated multidisciplinary team (**A**)
   iii staff with specialist expertise in stroke and rehabilitation (**A**)
   iv educational programmes for staff, patients and carers (**A**)
   v agreed protocols for common problems (**A**)
   vi a neurovascular clinic for the rapid assessment of transient ischaemic attack and minor stroke (**C**)
   vii access to brain and vascular imaging services (**C**).

b After the acute phase, specialist stroke services can be delivered to patients equally effectively in hospital or in the community, provided that the patient can transfer from bed to chair before going home and provided that the patient continues to be seen by a specialised multidisciplinary stroke team (**A**).

c Specialist day hospital rehabilitation or specialist domiciliary rehabilitation can be offered to outpatients with equal effect (**A**).

d Each district should conduct a needs assessment exercise to determine the level of service so that all stroke patients in the area have access to the same standards of care (**C**).

e Patients with persisting impairments, not admitted to hospital, should be seen by a specialist rehabilitation team that includes a specialist occupational therapist (**A**).

Evidence *(Tables 3.1–3.7)*

Most of the evidence comes from meta-analyses or multiple randomised controlled trials (RCTs), but some is secondarily derived from those studies. The main references for each guideline are:

a Stroke Unit Trialists' Collaboration 1998. The evidence in support of this guideline is overwhelming, and achieving this guideline should be the highest priority of all clinicians and managers (**Ia**). Tables 3.1–3.7 contain most of the supporting evidence: for (i)–(iii) see Stroke Unit Trialists' Collaboration 1998; Kalra 2000 (**Ia**); (iv) Jones et al 1998 (**Ib**); (v) Naylor et al 1994 (**Ib**); (vi) Michaels et al 2000 (Health Technology Assessment); Blight et al 2000 (**IV**); (vii) Consensus of working party.

b Table 3.3: Rudd et al 1997; Early Supported Discharge Trialists 1999 (**Ia**).

c Table 3.4: Gladman et al 1993 (but see Dekker et al 1998); Forster et al 1999b. There are several studies investigating this; the cost-benefit equation is not yet fully investigated (**Ib**).

d Consensus of working party; Clinical Standards Advisory Group report 1998 (**IV**)

e Walker et al 1999; Gilbertson 2000 (**Ib**).

Local guidelines

All purchasers (primary health care trusts, health authorities) and all providers (hospital services, community services etc) in a health district will need to discuss and agree:

1 which local providers are to be involved in a co-ordinated, specialised stroke management service;

2 who will be the lead clinician, to be responsible for all local stroke services in general, and the multidisciplinary team in particular;

3 if more than one provider, how they allocate responsibilities and who leads;

4 who will undertake a local needs assessment, and how;

5 where the service is to have its central base (ie where the 'stroke unit' is sited);

6 the balance between hospital services, day hospitals, and domiciliary services;

7 how services will work together effectively;

8 how training and education is to be provided;

9 the numbers of specialist staff needed;

10 evidence-based protocols for common problems.

Additions to tables of evidence

Table 3.1 Organisation of stroke care: specialised services

Source (references)	Design & Sample	Intervention(s)	Conclusions
Indredavik et al, 1999	RCT; n = 220 acute stroke patients; n = 41 survivors at 10 years	Stroke unit care or general medical care	Benefits of stroke unit persist for 10 years
Stegmayr et al, 1999	Obs; n = 14,308 acute stroke patients	Stroke unit care or general medical ward care	Benefits observed in trial also found, though less great
Rudd et al, 1999; 2001	Obs (audit); n = 6,894 and 5,375 acute strokes	Place of care	Benefits of stroke units found in practice
Kalra et al, 2000	RCT, n = 457 acute stroke patients	Stroke unit v mobile stroke team on general medical ward v Domiciliary management	Decreased mortality and morbidity seen only in stroke unit. Mobile stroke teams not effective. Need geographically located unit and team
Claesson et al, 2000	RCT; n = 249 acute stroke patients	Stroke unit and geriatric ward; or general medical ward	Costs similar in two groups; costs determined by severity
Blight et al, 2000	Obs; n = 211 patients referred to neurovascular clinic	One-stop clinic	90% managed with single consultation with potential cost savings

Obs Observational
RCT Randomised controlled trial

Table 3.3 Organisation of care: early discharge to community services

Source (references)	Design & Sample	Intervention(s)	Conclusions
Von Koch et al, 2000	RCT; n = 83 one week after stroke	Early supported discharge vs routine rehabiltation	No significant differences between early supported discharge and routine rehabilitation
Mayo et al, 2000	RCT; n = 114 medically stable acute stroke patients	4 week tailor-made home programme of rehab and nursing vs usual care	Intervention group had higher levels of instrumental ADL and social reintegration. Intervention group received less additional services than the usual care group
Anderson et al, 2000	RCT; n = 86 discharged patients after acute stroke	Early hospital discharge and home based rehabilitation vs conventional rehab	Early hospital discharge reduces the use of hospital beds without compromising clinical outcomes
Gilbertson et al, 2000	RCT; n = 138 stroke patients	Domiciliary OT after discharge or routine follow-up	Functional outcome and patient satisfaction improved with OT

ADL Activities of daily living
OT Occupational therapy
RCT Randomised controlled trial

Additional references

Specialised services and discharge to community services

Anderson C, Rubenbach S, Mhurchu CN *et al* (2000). Home or hospital for Stroke Rehabilitation? Results of a randomized controlled trial: I: Health outcomes at 6 months. *Stroke* **31**: 1024–31.

Blight A, Pereira AC, Brown MM (2000). A single consultation cerebrovascular disease clinic is cost effective in the management of transient ischaemic attack and minor stroke. *Journal of the Royal College of Physicians London* **34**(5): 452–5.

Claesson L, Gosman-Hedström G, Johannesson M *et al* (2000). Resource utilisation and costs of stroke unit care integrated in a care continuum: a 1-year controlled, prospective, randomised study in elderly patients. The Göteberg 70+ stroke study. *Stroke* **31**: 2569–2577.

Gilbertson L, Langhorne P, Walker A, Allen A (2000). Domiciliary occupational therapy for patients with stroke discharged from hospital: randomised controlled trial. *British Medical Journal* **320**: 603–6.

Indredavik B, Bakke F, Slordahl SA *et al* (1999). Stroke unit treatment 10 year follow-up. *Stroke* **30**: 1524–1527.

Kalra L, Evans A, Perez I, Knapp M *et al* (2000). Alternative strategies for stroke care: a prospective randomised controlled trial. *Lancet* **356**: 894–9.

Michaels J, Brazier J, Palfreyman S *et al* (2000). Cost and outcome implications of the organisation of vascular services. *Health Technology Assessment* **4**(11).

Mayo NE, Wood-Dauphinee S, Cote R *et al* (2000). There's no place like home: an evaluation of Early Supported Discharge for Stroke. *Stroke* **31**: 1016–23.

Rudd AG, Irwin P, Rutledge Z *et al* (1999). The national sentinel audit for stroke: a tool for raising standards of care. *Journal of Royal College of Physicians* 1999; **33**: 460–4.

Rudd AG, Lowe D, Irwin P *et al* (2001). National Stroke Audit: a tool for change? *Quality in Health Care* **10**: 141–51.

Stegmayr B, Asplund K, Hulter-Asberg K *et al* (1999). Stroke units in their natural habitat. Can results of randomised trial be reproduced in routine clinical practice? *Stroke* **30**: 709–14.

Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke (Cochrane Review). In: *The Cochrane Library,* Issue 4, 2001. Oxford: Update Software.

Von Koch, Holmquist LW, Kostulas V, Amazan J, de Pedro-Cuesta J (2000). A randomized controlled trial of rehabilitation at home after stroke in South West Stockholme: outcome at six months. *Scandinavian Journal of Rehabilitation Medicine* **32**: 80–6.

Walker MF, Gladman JF, Lincoln NB *et al* (1999). Occupational therapy for stroke patients not admitted to hospital: a randomised controlled trial. *Lancet* **354**: 278–80.

3.3 Acute care arrangements (hospital or home)

UPDATE NOTE – This section now incorporates the management of transient ischaemic attack (TIA) and stroke.

The evidence suggests that all patients benefit from being managed in specialised stroke units in hospital and that those managed at home do less well. There is evidence that neurovascular clinics are cost effective.

Guidelines

a Patients should be admitted to hospital for initial care and treatment (**A**).

b Patients should be managed at home **only if**:

  i the guidelines in *section 6* can be adhered to (**C**)

  ii care services can provide adequate and flexible support within 24 hours (**C**)

  iii the services delivered at home are part of a specialist stroke service (**A**).

c Patients first seen in the community with TIA, or with a stroke but having made a good recovery when seen, should be assessed and investigated in a specialist neurovascular clinic within 14 days of onset. They do not need admission to hospital **unless**:

  i The patient cannot be seen in a specialist neurovascular clinic within two weeks (**C**)

  ii An underlying cause requiring urgent treatment is suspected (**C**)

  iii The patient has had more than one TIA within a short period (crescendo TIA) (**C**).

d In hospital, care should be delivered in a ward or ward area where all staff have specialist expertise in stroke management (ie a stroke unit) (**A**).

e Stroke services and neurovascular clinics should have access to facilities for urgent investigation including brain and vascular imaging (including CT and MRI), carotid ultrasound and echocardiography (**C**).

Evidence *(Tables 3.1–3.6)*

The evidence is largely derivative. Evidence (see Section 3.1) shows that patients benefit from access to a specialist stroke service.

a Table 3.1: Stroke Unit Trialists' Collaboration 1998; Langhorne et al 1999. The evidence in support of this guideline is overwhelming (**Ia**).

b (i)(ii) Consensus of working party (**IV**)
(iii) Wade et al 1985a,b; Langhorne et al 1999 (**Ia**).

c Consensus of working party (**IV**).

d Table 3.1: Stroke Unit Trialists' Collaboration 1998.

e Blight et al 2000. One-stop clinics shown to be cost effective (**IV**). Consensus of working party (**IV**).

Local guidelines

These should specify

1 For patients managed at **home**:
   - i how specialist acute medical diagnostic services and specialist rehabilitation services are accessed quickly and easily for patients not admitted;
   - ii what emergency home care services are available;
   - iii their procedures (contact arrangements, etc).

2 For patients admitted to **hospital**:
   - i which wards have the necessary expertise and organisation.

4 Approaches to rehabilitation

4.4 Underlying approach to therapy

UPDATE NOTE – Emerging evidence is showing advantages of a task-specific training or practice approach over impairment focused approaches. Giving patients the opportunity to practise tasks is a major element in improved outcomes. The recommendations have been changed accordingly.

All approaches focus on the modification of impairment and improvement in function within everyday activities. Differences in approaches centre around the type of stimuli used and/or the emphasis on task-specific practice and/or the principles of learning followed.

Guidelines

a Any of the current therapeutic approaches to movement re-education should be used to improve function (**A**).

b For the specific objectives of i) improving reaching for objects, ii) increasing walking speed, a task-specific approach should be used rather than an impairment focused approach (**B**).

c Patients should be given as much opportunity as possible to practise tasks (**B**).

Evidence *(Tables 4.3, 4.4 and 9.13)*

Research is accumulating to suggest that patients derive benefit from therapy focused on the management of disability.

a Basmajian et al 1987; Jongbloed et al 1989; Richards et al 1993; Nelson et al 1996; Dean & Shepherd 1997; Dean et al 2000; Edmans et al 2000; Langehammer and Stangehelle 2000 (**Ib**).

b i) Van Vliet et al 1995; Nelson et al 1996; Trombly and Wu 1999; Wu et al 2000 ii)Hesse et al 1994; Richards et al 1993; Dean et al 2000; Gelber et al 1995; Patel et al 1998; Langhammer and Stanghelle 2000 (**II**).

c Smith et al 1981a; Langhorne et al 1996; Kwakkel et al 1999 (**Ia**).

Local guidelines

Local discussions should:

1 agree the approach to be used by all members of the team.

Additional tables of evidence

Table 4.3 Therapeutic approaches

Source (references)	Design & Sample	Intervention(s)	Conclusions
Gelber et al, 1995	RCT; n = 27 inpatients 1.3–13.8 days post stroke	Bobath vs functional approach	No differences in LOS, gait, arm skills or FIM
Edmans et al, 2000	RCT; n = 80 acute stroke patients with perceptual problems	Transfer of training approach or functional training approach	Both approaches gave equivalent results
Langhammer & Stanghelle, 2000	RCT; n = 61 acute stroke inpatients	Bobath physiotherapy or Motor Relearning Programme (MRP)	MRP associated with much shorter inpatient stay and better recovery in some areas
Dean et al, 2000	RCT; n = 12 patients 6+ months after stroke, walking	Task-related training to leg or arm (control)	Specific locomotor training improved function and reduced impairment
Trombly & Wu, 1999	RCT; n = 13 patients more than 5 months post-stroke, some arm function	Reaching for an object, or to a point; and reaching within a context, or outside a context	Goal-directed movement more normal; contextual appropriateness had no influence
Wu et al, 2000	RCT; n = 14 patients 5+ months after stroke	Reaching for coins, or to 'empty' space	Quality of performance better if task is embedded

FIM Functional Independence Measure
LOS Length of stay
RCT Randomised controlled trial

Table 4.4 Intensity of therapy input

Source (references)	Design & Sample	Intervention(s)	Conclusions
Ruff et al, 1999	CCT; n = 113 acute stroke patients. (quasi random, but 7 day group younger)	Therapy six or seven days/week	Patients preferred 6 days; no significant differences in length of stay or recovery rate
Partridge et al, 2000	RCT; n = 114 acute stroke patients	30 min regular rehabilitation v 60 min regular rehab	No significant differences at 6 weeks, although there was a positive trend noted for the more intensive rehabilitation group

Additional references

Therapeutic approaches and intensity of therapy input

Dean CM, Richards CL, Malouin F (2000). Task-related circuit training improves performance of locomotor tasks in chronic stroke: a randomised, controlled pilot trial. *Archives of Physical Medicine and Rehabilitation* **81**: 409–17.

Edmans JA, Webster J, Lincoln NB (2000). A comparison of two approaches in the treatment of perceptual problems after stroke. *Clinical Rehabilitation* **14**: 230–43.

Gelber DA, Josfcyle PB, Herrman D (1995). Comparison of two therapy approaches in the rehabilitation of the pure motor hemiparetic stroke patient. *Journal of Neurological Rehabilitation* **9**: 191–6.

Langhammer B, Stanghelle JK (2000). Bobath or Motor Relearning Programme? A comparison of two different approaches of physiotherapy in stroke rehabilitation: a randomised controlled study. *Clinical Rehabilitation* **14**: 361–9.

Partridge C, Mackenzie M, Edwards S *et al* (2000). Is dosage of physiotherapy a critical factor in deciding patterns of recovery from stroke: a pragmatic randomised controlled trial. *Physiotherapy Research International* **5**: 230–40.

Ruff RM, Yarnell S, Marinos JM (1999). Are stroke patients discharged sooner if inpatient rehabilitation services are provided seven v six days per week? *American Journal of Physical Medicine and Rehabilitation* **78**: 143–6.

Trombly CA, Wu CY (1999). Effect of rehabilitation tasks on organisation of movement after stroke. *American Journal of Occupational Therapy* **53**: 333–44.

Wu C, Trombly CA, Lin K, Tickle-Degnen L (2000). A kinematic study of contextual effects on reaching performance in persons with and without stroke: influences of object availability. *Archives of Physical Medicine and Rehabilitation* **81**: 95–101.

6 Acute (specific, medical) diagnosis

UPDATE NOTE – Brain imaging is an essential investigation in stroke. Computerised tomography (CT) is adequate in most cases. Magnetic resonance imaging (MRI) has advantages of better anatomical resolution and increased sensitivity. New techniques of MRI including diffusion and perfusion imaging have advantages in the rapid diagnosis of stroke and may be useful for the selection of patients for treatment such as thrombolysis. MRI is also useful for detecting changes in old haemorrhage.

Guidelines

a It should be recognised that 'stroke' is primarily a clinical diagnosis, and that the clinical diagnosis can be relied upon in most cases. Care is needed in the young, if the history is uncertain, or if there are other unusual clinical features such as gradual progression over days, unexplained fever, severe headache or symptoms and signs of raised intracranial pressure (**B**).

b The initial neurological assessment should document the localisation of the likely cerebral area affected (**C**).

c Brain imaging should be undertaken in all patients to detect intracerebral or subarachnoid haemorrhage and exclude other causes of the stroke syndrome, within 48 hours of onset, unless there are good clinical reasons for not doing so (**C**).

d Brain imaging should be undertaken as a matter of urgency if the patient has: (**B**)

- i a depressed level of consciousness;
- ii unexplained progressive or fluctuating symptoms;
- iii papilloedema, neck stiffness or fever;
- iv severe headache at onset;
- v a history of trauma prior to onset;
- vi indications for thrombolysis or early anticoagulation;
- vii a history of anticoagulant treatment, or has a known bleeding tendency.

e Brain imaging should always be undertaken before anticoagulant treatment is started (**C**).

f The diagnosis should always be reviewed by an experienced clinician with expertise in stroke (**B**).

g The patient's cardiovascular status must be reviewed (**C**).

h Chest X-ray should not be undertaken as a routine investigation at admission unless symptoms specifically indicate it (**B**).

i MRI should be considered if CT scan is normal and the diagnosis of stroke is in doubt, especially in patients with brain stem or cerebellar symptoms, or to exclude old haemorrhage (**C**).

j Patients with hemispheric TIA should have brain imaging to exclude arterio-venous malformation, subdural haematoma and tumours (**C**).

Evidence *(Tables 6.1,6.2)*

Little directed research has been undertaken on the process of diagnosis, and most data come incidentally from other studies. No research has evaluated critically the role of brain imaging.

a Twomey 1978; von Arbin et al 1981; Sandercock et al 1985; Ferro et al 1998 (**III**).

b Consensus of working party; Royal College of Physicians of Edinburgh 1998 (**IV**).

c This is primarily a consensus guideline, drawing upon several published consensus statements, (eg Edinburgh statement (Royal College of Physicians of Edinburgh 1998) and Royal College of Radiologists (1998), and agreed by the working party (**IV**).

d Sandercock et al 1985 (**III**).

e Consensus of working party (**IV**).

f Ricci et al 1991; Kothari et al 1995a,b; Martin et al 1997 (**III**).

g Consensus of working party (**IV**).

h Sagar et al 1996 (**IIa**).

i Consensus of working party (**IV**).

j Consensus of working party (**IV**).

Local guidelines

There is no evidence to guide doctors investigating patients after stroke, but the approach discussed by Warlow et al (2000) on page 266 seems appropriate.

It is likely that local services will wish to develop local guidelines for:

1 CT scanning (given the resource implications);

2 which physicians or neurologists should formally review the diagnosis;

3 cardiovascular assessment;

4 use of MRI scanning, if available;

5 investigation of the underlying cause of stroke;

6 the 'routine' investigations to be used in every patient;

7 the secondary investigations to be used and when they should be used.

Additional reference

Warlow CP, Dennis MS, van Gijn J *et al* (2001). *Stroke: a Practical Guide to Management.* 2nd edition. Blackwell Science. Oxford.

7 Acute (medical/surgical) interventions

UPDATE NOTE – The emphasis in this section has been altered to reflect the importance of thrombolysis, so the recommendations for local guidelines now include services being clear as to the circumstances in which aspirin is given by ambulance crews. The role of surgery for intracerebral haemorrhage remains unclear and is the subject of a current randomised controlled trial (RCT).

Guidelines

a Aspirin (160-300 mg) should be given as soon as possible after the onset of stroke symptoms if a diagnosis of haemorrhage is considered unlikely (**A**).

b Thrombolytic treatment with tissue plasminogen activator (tPA) should only be given provided that it is administered within 3 hours of onset of stroke symptoms, that haemorrhage has been definitively excluded, and that the patient is in a specialist centre with appropriate experience and expertise (**A**).

c No other drug treatment aimed at treatment of the stroke should be given unless as part of an RCT (**A**).

d Neurosurgical opinion should be sought for cases of secondary hydrocephalus (**B**) (For involvement in the RCT of spontaneous intracerebral haemorrhage, e-mail: stich@ncl.ac.uk).

e Anticoagulation should be considered for all patients in atrial fibrillation, but not started until intracerebral haemorrhage has been excluded by brain imaging, and usually only after 14 days (**A**).

f Centrally acting drugs should be avoided if possible (**B**).

g In each hospital the neurologist or physician with special responsibility for stroke should review the Cochrane Collaboration regularly, and should be responsible for being aware of new developments in acute treatment (**C**).

h Local policies should be agreed in relation to the early management of hypertension, hyperglycaemia, hydration and pyrexia (**C**).

Evidence *(Tables 7.1, 7.2)*

Meta-analyses have been undertaken for many drug interventions. For most drugs the evidence is simply too weak to recommend use at this point. Surgical interventions are not well researched, but there is no evidence to support **routine** surgical evacuation of intracerebral haemorrhage. The tables show the Cochrane Collaboration reviews and other studies. There are over 100 individual trials, not all of which are referred to here.

a International Stroke Trial Collaborative Group 1997. This is strongly supported by large trials, though the effect is relatively limited; Chinese Acute Stroke Trial 1997; Gubitz et al 2000 (**Ia**).

b Wardlaw et al 2000; Liu & Wardlaw 1998. The European license for tPA is expected shortly (**Ia**).

c See Table 7.1: Cochrane reviews. There is insufficient evidence to warrant the use of most drugs, and some can be considered detrimental (**Ia**).

d Mathew et al 1995; Prasad & Shrivastava 1998; (**III**). Zuccarello et al 1999 (**1b**).

e Stroke Prevention in Atrial Fibrillation Investigators 1996; Gubitz et al 1999. Few patients with atrial fibrillation (AF) have been included in trials of early anticoagulation after stroke. The benefits of early anticoagulation may be offset by the risks of haemorrhage, though these may be less for small strokes (**Ia**). Saxena et al 2001 proved there was no advantage to the use of heparin in patients with AF in the acute phase of ischaemic stroke (**Ia**).

f Goldstein, 1995. This study supports animal work (**IIa**).

g Consensus of working party (**IV**).

h Consensus of working party (**IV**).

Local guidelines

Local guidelines should specify details on:

1 who is the physician responsible for keeping up-to-date on acute stroke treatment;

2 how the Cochrane database is accessed by anyone freely;

3 aspirin use, whether or when brain imaging should be undertaken; whether ambulance crews withhold administration of aspirin until haemorrhage has been formally excluded in hospital;

4 anticoagulation (eg who will be responsible for monitoring);

5 neurosurgical referrals for intracerebral haemorrhage;

6 involvement in RCTs of new drugs;

7 acute management of common areas of clinical concern. Four are given below, with suggested guidance, but there is currently no evidence, so local clinicians should discuss their own guidelines on whether:

   i blood pressure should not be lowered in the first week unless there is accelerated hypertension or dissection, but existing antihypertensive medication should be continued;

   ii blood glucose should be controlled within normal limits;

   iii hydration should be maintained within normal plasma osmolality;

   iv pyrexia should be controlled with paracetamol, fan and treatment for the underlying cause.

Additions to tables of evidence

Table 7.1 Specific treatment (drugs and surgery) of acute stroke: Cochrane reviews

Source (references)	Design & Sample	Intervention(s)	Conclusions
Gubitz et al, 2000	MA; n = 8 trials, 41,325 patients	Anti-platelet drugs within 14 days of acute stroke	Aspirin 160-300 mg within 48 hours of stroke reduces mortality and morbidity
Asplund et al, 2000	MA; n = 16 trials, 2,956 patients	Haemodilution treatment within 72 hours of stroke	No evidence of benefit
Wardlaw et al, 2000	MA; n = 17 trials, 5,126 patients	Any thrombolytic treatment	Thrombolysis increases mortality but may reduce disability in survivors

Table 7.2 Specific treatment (drugs and surgery) of acute stroke: other studies

Source (references)	Design & Sample	Intervention(s)	Conclusions
Zuccarello et al, 1999	RCT; 20 acute intra-cerebral haemorrhages	Evacuation, or best medical management	Trend only towards better outcome after early surgery
Scott et al, 2000	RCT; 52 acute stroke patients with glucose 7.0-17.0 mmol/L	Glucose potassium insulin infusion (GKI) or saline infusion	Administration of GKI safe; no significant effect on glucose; outcomes similar
Saxena et al, 2001	RCT; 3169 patients with AF	UFH 12,500 v 5000 iu BID subcutaneous unfractionated heparin v no heparin. Within groups patients assigned to aspirin 300mg daily	In patients with AF the absolute risk of early stroke recurrent stroke is low, and there was no net advantage to treatment with heparin

AF Atrial fibrillation
BID Twice daily
MA Meta-analysis
RCT Randomised controlled trials
UFH Unfractionated heparin

Additional references

Drugs and surgery

Asplund K, Israelsson K, Schampi I (2000). Haemodilution for acute ischaemic stroke (Cochrane Review). In: *The Cochrane Library, Issue 3, 2000.* Oxford: Update Software.

Gubitz G, Sandercock P, Counsell C. (2000). Antiplatelet therapy for acute ischaemic stroke (Cochrane Review) In: *The Cochrane Library, Issue 3, 2000.* Oxford: Update Software. (**Replaces Counsell & Sandercock 1998**).

Saxena R, Lewis S, Berge E *et al* (2001). (For the International Stroke Trial Collaborative Group). Risk of early death and recurrent stroke and effect of Heparin in 3,169 patients with acute ischaemic stroke and atrial fibrillation in the International Stroke Trial. *Stroke* **32**: 2333–7.

Scott JF, Robinson GM, French JM *et al* (1999). Glucose potassium insulin infusions in the treatment of acute stroke patients with mild to moderate hyperglycaemia. The glucose insulin in stroke trial (GIST). *Stroke* **30**; 793–9.

Wardlaw JM, del Zoppo G, Yamaguchi T (2000). Thrombolysis for acute ischaemic stroke (Cochrane Review) In: *The Cochrane Library, Issue 3, 2000.* Oxford: Update Software. (**Replaces Wardlaw et al 1996**).

Zuccarello M, Brott T, Derex L *et al* (1999). Early surgical treatment for supratentorial intracerebral haemorrhage. A randomised feasibility study. *Stroke* **30**: 1833–9.

8 Early disability assessment and management

8.3.2 Venous thromboembolism

UPDATE NOTE – Recommendation 8.3.2c on length of compression stockings has been withdrawn until the Clots in Legs or TEDS after Stroke (CLOTS) trial on prevention of deep vein thrombosis in people with stroke has reported.

Those wishing to enrol in the multi-centre CLOTS trial may do so through the website http://www.dcn.ed.ac.uk/clots

9 Rehabilitation interventions

9.1 Psychological impairment

9.1.1 Mood disturbance: depression, emotionalism and anxiety

UPDATE NOTE – Recommendations for management of depression are further strengthened with changes to 9.1.1g and an additional one (h) on length of treatment.

Guidelines

g Patients with persistently depressed mood (duration at least one month) should be considered for a trial of antidepressant medication (**A**).

h Antidepressants should be continued for at least 6 months, if a good response has been achieved (**C**).

Evidence *(Tables 9.1, 9.2)*

There is much evidence on the prevalence of depressive symptoms after stroke, but it is difficult to use the available evidence to guide specific treatment. The primary difficulty is in deciding whether a specific intervention is needed to improve the mood state and, if so, what intervention.

g Lipsey et al 1984; Andersen et al 1994; Kimura et al 2000 (**Ib**).

h Consensus of working party (**IV**).

Additions to table of evidence

Table 9.1 Epidemiology and treatment of depression after stroke

Source (references)	Design & Sample	Intervention(s)	Conclusions
Kimura et al, 2000	RCT; n = 47 depressed stroke patients, 4+ months after stroke	Nortriptyline or placebo	a) intervention patients who took drug reduced depression faster b) reduction of depression associated with improved cognition

RCT Randomised controlled trial

Additional reference

Epidemiology and treatment of depression

Kimura M, Robinson RG, Kosier JT (2000). Treatment of cognitive impairment after post-stroke depression. A double-blind treatment trial. *Stroke* **31**: 1482–6.

9.3.2 Improving motor control: biofeedback

UPDATE NOTE – The research in the last two years has produced no evidence of advantage of biofeedback over traditional therapy in standing balance. The recommendation 9.3.2b on using biofeedback as an addition to traditional therapy when retraining in standing balance has therefore been withdrawn. More research is required in this area.

Evidence *(Table 9.5 and additions to evidence table below)*

Dursun et al 1996; Sackley & Lincoln 1997; Walker et al 2000; Geiger et al 2001 (**Ib**).

Additions to tables of evidence

Table 9.5 Technologically assisted feedback including biofeedback.

Source (references)	Design and Sample	Intervention(s)	Conclusions
Geiger et al, 2001	RCT; n = 13 outpatients between 15–538 days post stroke	PT v PT +balance master training for 4 weeks	No differences between groups. Both groups improved on Berg balance and TUG test
Walker et al, 2000	RCT; n = 46 within 80 days post stroke	Visual feedback + regular PT v balance ex. + regular PT v regular PT	All groups improved; no between group differences in TUG, Berg score or 10m walk

RCT Randomised controlled trials
PT Physiotherapy
TUG Timed Up-and-Go test

Additional references

Technologically assisted feedback

Geiger RA, Allen JB, O'Keefe J, Hick RR. (2001). Balance and mobility following stroke: effects of physical therapy interventions with and without biofeedback/forceplate training. *Physical Therapy.* **81**: 995–1005.

Walker C, Brouwer BJ, Culham EG. (2000). Use of visual feedback in retraining balance following acute stroke. *Physical Therapy.* **80**: 886–95.

9.3.6 Strength training – (new section)

As the evidence is growing for the use of resisted exercise training to improve motor function even in the longer term after stroke, a new recommendation has been added. The evidence table is a summary of the key evidence, with more detailed tables for those with a particular interest in this area.

Guidelines

a Resisted exercise should be considered to improve motor function in targeted muscles (B).

Evidence (Table see below)

- Bütefisch et al 1995; Engardt et al 1995; Brown and Kautz 1998; Smith et al 1999; Teixeira-Salmela et al 1999.

Summary new evidence table

Strength training

Source (references)	Design & Sample	Intervention(s)	Conclusions
Bütefisch et al,1995	CCT; n = 27, 3-19 weeks post-stroke	Multiple repetitive hand exercises against resistance	↑ grip strength, peak force and acceleration
Engardt et al,1995	CCT; n = 20, 27–28 months post-stroke	Eccentric knee v concentric knee exercise against resistance	↑ knee strength and symmetry of weight distribution in sit-to-stand for eccentric training. ↑ Strength in both types of training but advantage for eccentric work
Brown and Kautz, 1998	CCT, n = 27, 15 patients > 6 months post-stroke	Pedal ergometer 12 randomly ordered Workload & Cadence combinations	No ↑ in spasticity in paretic limb as workload increased
Teixeira-Salmela et al, 1999	RCT; n = 13 patients 9+ months after stroke	Aerobic exercises and muscle strengthening, or nil (control)	Exercise regime improved gait and strength, and activity and mood
Smith et al, 1999	CCT; n = 14, >6 months post stroke	3 months of low intensity aerobic exercise using a treadmill	↑ in hamstring torque, decrease in reflexive torque (spasticity)

CCT Clinically controlled trial
NDT Neurodevelopmental technique
PRE Progressive resisted exercises
RCT Randomised controlled trial
↑ – Increase

Additional references

Strength training

Brown DA, Kautz SA (1998). Increased workload enhances force output during pedalling exercise in persons with post-stroke hemiplegia. *Stroke* **29**: 598–606.

Bütefisch C, Hummelsheim H, Denzler P, Mauritz KH (1995). Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. *Journal of Neurological Sciences* **130**: 59–68.

Engardt M, Knutsson E, Jonsson E, Sternhag M (1995). Dynamic muscle strength training in stroke patients; effects on knee extension torque, electromyographic activity and motor function. *Archives of Physical Medicine and Rehabilitation* **76**: 419–25.

Smith GY, Silver KHC, Goldberg AP, Macko RF (1999). 'Task-oriented' exercise improves hamstring strength and spastic reflexes in chronic stroke patients. *Stroke* **30**: 2112–8.

Teixeira-Salmela LF, Olney SJ, Nadeaus S, Brouwer B (1999). Muscle strengthening and physical conditioning to reduce impairment and disability in chronic stroke survivors. *Archives of Physical Medicine and Rehabilitation* **80**: 1211–8.

Detailed new evidence tables – Strength training

Table 1 Isokinetic studies

Source	Design & Sample	Intervention(s)	Outcome measures	Conclusions
Dean et al, 2000	RCT; n =12 post-stroke > 3 months	Lower limb training Kinetron Treadmill v upper limb training 3 x per week x 4 weeks	Gait speed 10m walk test 6 min. test Step test TUG	↑ gait speed ↑ endurance ↑ repetitions of step test
Lindsley et al, 1994	RCT; n = 20 chronic stroke	6-week PRE + Kinetron v Bobath	Gaitlab	↑ in stride length in PRE and Kinetron No ↑ in Bobath
Richards et al, 1993	RCT; n = 27 age 40–80 years 0–7 days onset	Kinetron + Treadmill v NDT (Bobath)	Gaitlab	↑ Gait velocity in experimental group Early intervention

NDT Neurodevelopmental technique RCT Randomised controlled trial ↑ – increase
PRE Progressive resisted exercises TUG Timed up-and-go test

Table 2 Progressive resistive exercise studies

Source	Design & Sample	Intervention(s)	Outcome measures	Conclusions
Dickstein et al, 1986	CCT; n = 131 acute stroke	Exercise v PNF v Bobath for 6 weeks	Barthel Index, 5 Point Ordinal Scale for Tone, ROM, Muscle strength Ambulation	All ↑ in Tone No difference between approaches
Duncan et al, 1998	RCT; n = 20 30–40 days since onset	Home based exercise programme 2x week x 8 weeks PNF, T-Band, bike v conventional treatment	Fugl – Meyer 10m walk 6 min. test Berg Balance Barthel index	↑ Gait velocity ↑ In all outcome measures Minimal changes in control group No change in Barthel scores

continued

Table 2 continued

Source	Design & Sample	Intervention(s)	Outcome measures	Conclusions
Inaba et al, 1973	RCT; n = 77 chronic stroke survivors	PRE, ADL, Active Exercise v ADL, Active Exercise v ADL training	Manual muscle Test 10 Repetitions ADL Barthel Index	↑ in strength in PRE, ADL and active exercise groups; minimal change in remaining 2 groups
Rimmer et al, 2000	RCT; n = 35 post-stroke	Exercise training programme x 12 weeks (Cardio-pulmonary exercise and strength)	Peak VO_2 (ml/min^{-1}), 10 repetitions on bench and leg press	↑ VO_2 (ml/min^{-1}) ↑ strength No change in control group
Teixeira-Salmela et al, 1999	RCT; n = 13 > 9 months onset	Aerobic and lower limb muscle strengthening exercise programme 3 x per week x 10 weeks	Peak torque Pendulum test Gait speed Stair climb Human Activity Profile Nottingham Health Profile	↑ strength; ↑ on all outcome measures No ↑ in spasticity strength training is appropriate

ADL Activities of daily living
CCT Clinically controlled trial
EMG Electromyography
NDT Neuro-developmental technique
PNF Proprioceptive neuromuscular function
PRE Progressive resisted exercises
RCT Randomised controlled trial
ROM Range of movement
$VO_2(ml/min^{-1})$ oxygen uptake
↑ increase ↓ decrease

Table 3 Aerobic exercise studies

Source	Design & Sample	Intervention(s)	Outcome measures	Conclusions
Brown & Kautz, 1998	CCT, n = 27; 15 Patients > 6 months post-stroke	Pedal ergometer 12 randomly ordered Workload and Cadence Combinations	EMG Pedal Force	No ↑ in spasticity in paretic limb as workload increased
Kwakkel et al, 1999	RCT, n = 101; post-stroke <14 days	Arm v Leg training v Control (5 x wk x 20 wk)	10m walk test Barthel index Action research arm test	↑ ADL; ↑ walking ability ↑ dexterity in lower limbs ↑dexterity in arms

ADL Activities of daily living
CCT Clinically controlled trial
EMG Electromyography
RCT Randomised controlled trial
↑ increase ↓ decrease

Additional references

Strength training and aerobic exercise studies

Brown DA, Kautz SA (1998). Increased workload enhances force output during pedalling exercise in persons with post-stroke hemiplegia. *Stroke* **29**: 598–606.

Dean CM, Richards CL, Malouin F (2000). Task-related circuit training improves performance of locomotor tasks in chronic stroke: a randomized, controlled pilot trial. *Archives of Physical Medicine and Rehabilitation* **81**: 409–17.

Dickstein R, Hockerman S, Pillar T, Shaham R (1986). Stroke rehabilitation. 3 exercise therapy approaches. *Physical Therapy* **66**(8): 1233–8.

Duncan P, Richards L, Wallace D *et al* (1998). A randomized, controlled pilot study of a home-based exercise program for individuals with mild and moderate stroke. *Stroke* **29**: 2055–60.

Inaba M, Edberg E, Montgomery J (1973). Effectiveness of functional training, active exercise, and resistive exercise for patients with hemiplegia. *Physical Therapy* **53**: 28–35.

Kwakkel G, Wagenaar RC, Twisk JWR *et al* (1999). Intensity of leg and arm training after primary middle-cerebral artery stroke: a randomised trial. *Lancet* **354**: 191–6.

Lindsley HG, Musser L, Stewart MR (1994). The effects of Kinetron training on gait patterns of patients with stroke. *Neurology Report* **19**: 29–34.

Richards CL, Malouin F, Wood-Dauphinee S *et al* (1993). Task-specific physical therapy for optimization of gait recovery in acute stroke patients. *Archives of Physical Medicine and Rehabilitation* **74**: 612–20.

Rimmer JH, Riley B, Creviston T, Nicola T (2000). Exercise training in a predominantly African-American group of stroke survivors. *Medicine and Science in Sports and Exercise* **32**: 1990–6.

Teixeira-Salmela LF, Olney SJ, Nadeaus S, Brouwer B (1999). Muscle strengthening and physical conditioning to reduce impairment and disability in chronic stroke survivors. *Archives of Physical Medicine and Rehabilitation* **80**: 1211–8.

9.4.2 Shoulder pain

UPDATE NOTE – The following two recommendations have been withdrawn due to the results of recent trials shown below:

- *shoulder strapping (9.4.2aiii)*
- *intra-articular triamcinolone (9.4.2biii)*

Evidence

Previously cited evidence demonstrated the need for further study in this area. The results of recent trials are as follows:

Shoulder strapping (9.4.2aiii)

Hanger et al 2000, a larger study than that previously cited for shoulder strapping, demonstrated no benefit from shoulder strapping (**Ib**).

Intra-articular injections of triamcinolone (9.4.2biii)

Snels et al 2000 showed no benefit from intra-articular injections of triamcinolone (**Ib**).

Additions to table of evidence

Table 9.10 Shoulder pain after stroke

Source (references)	Design & Sample	Intervention(s)	Conclusions
Hanger et al, 2000	RCT; n = 98; acute stroke inpatients	Strapping of shoulder, or not	No benefit demonstrated; pain was common
Snels et al, 2000	RCT; n = 37 patients with hemiplegic shoulder pain for 2+ weeks, any time post-stroke	40 mg triamcinolone injections x3, or placebo	No strong evidence for benefit (trend only, low numbers)
Price & Pandyan, 2001	Systematic review	Review to determine efficacy of any form of surface electrical stimulation in the prevention and/or treatment of pain around the shoulder at any time after stroke	Evidence does not confirm or refute use of ES around the shoulder

ES

RCT Randomised controlled trial

Additional references

Shoulder pain

Hanger HC, Whitewood P, Brown G *et al* (2000). A randomised controlled trial of strapping to prevent post-stroke shoulder pain.*Clinical Rehabilitation* **14**: 370–80.

Price CIM, Pandyan AD. (2001). Electrical stimulation for preventing and treating post-stroke shoulder pain (Cochrane Review). In: *The Cochrane Library, Issue 3, 2001*. Oxford: Update Software.

Snels IAK, Beckerman H, Twisk JWR *et al* (2000). Effect of triamcinolone injections on hemiplegic shoulder pain. A randomised clinical trial. *Stroke* **31**: 2396–401.

11 Long-term patient management

11.3 Secondary prevention

UPDATE NOTE – This section has undergone major revision since the first edition and is therefore reproduced in its entirety. It covers prevention after both transient ischaemic attack (TIA) and stroke.

Patients who have suffered a stroke remain at an increased risk of a further stroke (about 7% per annum). Patients with TIA and Stroke also have an increased risk of myocardial infarction and other vascular events. The risk of further stroke is highest early after stroke or TIA. Therefore high priority should be given to secondary prevention.

Guidelines

These guidelines apply to **all patients** with TIA and stroke, even those not admitted to hospital. Therefore they refer to patients either **before discharge from hospital or before 2 weeks have passed from stroke onset**, whichever is the sooner.

a All patients should have their blood pressure checked, and hypertension persisting for over one month should be treated. The British Hypertension Society guidelines are: optimal blood pressure treatment targets are systolic blood pressure <140 mmHg and diastolic blood pressure <85 mmHg; the minimum accepted level of control recommended is <150/ <90 mmHg. For patients with diabetes the target level of control should be 140/85 (**A**).

b Further reduction of blood pressure should be considered using a combination of long-acting ACE inhibitor (eg perindopril or ramipril) and a thiazide diuretic (**eg** Indapamide) (**A**).

c All patients with ischaemic stroke who are not on anticoagulation, should be taking an antiplatelet agent, ie aspirin (75–325 mg) daily (**A**), or clopidogrel, or a combination of low-dose aspirin and dipyridamole modified release (MR). Where patients are aspirin intolerant an alternative antiplatelet agent (clopidogrel 75mg daily or dipyridamole MR 200mg twice daily) should be used (**A**).

d Anticoagulation:

   i should not be used after transient ischaemic attacks or minor strokes unless cardiac embolism is suspected (**A**).

   ii should not be started until brain imaging has excluded haemorrhage, and 14 days have passed from the onset of an ischaemic stroke (**A**).

   iii should be started in every patient in atrial fibrillation (valvular or non-valvular) unless contraindicated (**A**).

iv should be considered for all patients who have ischaemic stroke associated with mitral valve disease, prosthetic heart valves, or within 3 months of myocardial infarction (**C**).

e Any patient with a carotid artery area stroke, and minor or absent residual disability should be considered for carotid endarterectomy (**A**).

f Carotid ultrasound should be performed on all patients who would be considered for carotid endarterectomy. Magnetic Resonance Angiography (MRA) is a reasonable alternative in centres with the appropriate expertise. (**A**).

g Carotid endarterectomy:

i should be considered where carotid stenosis is measured at greater than 70% (**A**).

ii should only be undertaken by a specialist surgeon with a proven low complication rate (**A**).

h Carotid angioplasty or stenting is an alternative to surgery but should be carried out only in centres with a proven low complication rate (**A**).

i All patients should be assessed for other vascular risk factors and be treated or advised appropriately (**B**).

j All patients should be given appropriate advice on lifestyle factors (such as not smoking, regular exercise, diet, avoiding excess alcohol, achieving a satisfactory weight, reducing the use of added salt) (**C**).

k Therapy with a statin should be considered for all patients with a history of ischaemic heart disease and a cholesterol >5.0 mmol/l following stroke (**A**).

Evidence *(Tables 11.3, 11.4)*

Much of the evidence is derived from research into primary prevention, but there are now also studies investigating secondary prevention.

a Post Stroke Antihypertensive Treatment Study collaborative group 1995; Ramsay et al 1999 (British Hypertension Society guidelines) (**Ib**).

b Heart Outcomes Prevention Evaluation (HOPE) 2000a,b; PROGRESS 2001.

c AntithromboticTrialists Collaboration 2002 (**Ia**).

d i) Stroke Prevention in Reversible Ischaemia Trial 1997 (**Ib**). ii) European Atrial Fibrillation Trial (EAFT) study group 1993, 1995 (**Ib**). iii) European Atrial Fibrillation Trial (EAFT) study group, 1993, 1995 (**Ia**). iv) Consensus of working party (**IV**).

e European Carotid Surgery Trialists' Collaborative Group 1998; North American Symptomatic Carotid Endarterectomy Trial Collaborators 1998 (**Ib**).

f Young et al 1996a and b; Wardlaw et al 2001; Westwood et al 2002 (**Ia**).

g Cina et al 1999 (**Ib**).

h Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) 2001 (**Ib**). Both the endovascular and the surgical group had an equally bad complication rate of 10%. More research is required and any patients should be entered into CAVATAS 2.

i Hebert et al 1997 (**IIa**).

j Consensus of working party; Elliott et al 1996; Midgley et al 1996; Cutler et al 1997; Whelton et al 1998 (**IV**).

k Blauw et al 1997; Hebert et al 1997; Crouse et al 1997, 1998 (**Ia**).

Local guidelines

These will be need to specify local policies for:

1 antiplatelet treatments, taking into consideration the cost implications of implementing routine use of agents other than aspirin

2 referral to specialist vascular surgeons for carotid surgery

3 controlling anticoagulation

4 cholesterol lowering drugs

5 dietary advice and follow-up

6 smoking cessation therapy.

Additional tables of evidence

Table 11.3 Secondary prevention after stroke

Source (references)	Design & Sample	Intervention(s)	Conclusions
Plehn et al, 1999 (CARE trial)	RCT; n = 4,159; patients post MI with average total and LDL serum cholesterol levels	Pravastatin 40mg/day or placebo with follow-up over 5 years	Pravastatin significantly reduced the incidence of stroke and TIA after MI in patients with average serum cholesterol
Man-Son-Hing et al, 1999	RCT; n = 287 patients in atrial fibrillation on aspirin, considered for warfarin	Audio-booklet (tape and booklet) explaining trial results and risks and benefits of warfarin	Audiobooklet increased knowledge and understanding but did not alter decision or compliance
Harker et al, 1999 (CAPRIE)	RCT; n = 19,185 patients with symptomatic atherosclerosis – ischaemic stroke, MI or peripheral arterial disease	Clopidogrel 75mg/day v aspirin 325mg/day for 1–3 years.	Clopidogrel reduced combined risk of ischaemic stroke, MI or vascular death by 8.7%. Bleeding and gastrointestinal side-effects were less in the clopidogrel group
Bhatt et al, 2000 (CAPRIE)	RCT; n = 19,185 patients with symptomatic atherosclerosis – ischaemic stroke, MI or peripheral arterial disease	Clopidogrel 75mg/day v aspirin 325mg/day for 1–3 years	Clopidogrel group had significantly fewer re-hospitalisations for ischaemic events or bleeding
Cao et al, 2000	RCT; n = 1,353; patients needing carotid endarterectomy	Standard endarterectomy or eversion	Eversion associated with less re-stenosis but equal stroke event rate

continued

Table 11.3 continued

Source (references)	Design & Sample	Intervention(s)	Conclusions
HOPE 2000a,b	RCT; n = 9,297 high risk patients with vascular disease or diabetes + one other cardiovascular risk factor (not heart failure)	ACE inhibitor (Ramipril 10mg daily) for mean of 5 yrs v placebo	Ramipril significantly reduces cardiovascular death (by 37%), MI (by 22%) and stroke (by 33%) in high risk patients. The cardio-vascular benefit was greater than that attributable to decrease in blood pressure
PROGRESS 2001	RCT; n = 6,105 patients with history of stroke or TIA	Perindopril (ACE inhibitor) 4mg daily v Perindopril 4mg + indapamide (thiazide diuretic) v placebo over 4 yrs	Combination therapy superior to single therapy: reduced BP by 12/5mmHg compared to 5/3mmHg. Stroke risk reduction 43% compared to none discernable; similar reductions achieved in both hypertensive and non-hypertensive patients
CAVATAS, 2001	RCT; n = 504 patients with carotid stenosis	Carotid endarterectomy v endovascular treatment (stents or balloon angioplasty)	No significant differences in outcome within 30 days. At 1 year post treatment severe carotid stenosis in 14% endovascular group compared to 4% of group treated surgically. No substantial differences in the rate of ipsilateral stroke up to 3 years
Wardlaw et al, 2001	Obs; n = 44 with recently symptomatic tight carotid stenosis (>70% on Doppler ultrasound)	Intra-arterial angiography and magnetic resonance angiograms during the same admission (before carotid endarterectomy)	Magnetic resonance angiograms consistently over-estimated the % stenosis according to intra-arterial angiography
Antithrombotic Trialists Collaboration, 2002	287 RCTs; 135,000 pts	Comparisons of antiplatelet therapy v control	Daily doses of 75–150mg aspirin seem to be as effective as higher doses for longer-term treatments
	77,000	Comparisons of different antiplatelet regimens	Clopidogrel is an appropriate alternative for patients with a contra-indication to aspirin
Westwood et al, 2002	MA 26 heterogenous RCTs	Comparison of MRA v intra-arterial digital subtraction or cut film angiography to screen for carotid stenosis	MRA is accurate for selecting patients for carotid endarterectomy, but the evidence is not robust due heterogeneity of the trials

ACE Angiotensin-converting-enzyme inhibitor
BP Blood pressure
LDL
MA Meta-analyses
MI Myocardial infarction
MRA Magnetic resonance angiography
TIA Transient ischaemic attack
RCT Randomised controlled trial
Obs Observational

Additional references

Secondary prevention

Antithrombotic Trialists Collaboration (2002). Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *British Medical Journal* **324**: 71–86.

Bhatt DL, Hirsch AT, Ringleb PA (2000). Reduction in the need for hospitalisation for recurrent ischaemic events and bleeding with Clopidogrel instead of aspirin. CAPRIE investigators. *American Heart Journal* **140**: 67–73.

Cao P, Giordano G, Rango PD *et al* and collaborators of the EVEREST study group (2000). Eversion versus conventional carotid endarterectomy: late results of a prospective multi-centre randomised trial. *Journal of Vascular Surgery* **31**:19–30.

CAVATAS Investigators (2001). Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. *Lancet* **357**: 1729–37.

Harker LA, Boissel JP, Pilgrim AJ, Gent M (1999). Comparative safety and tolerability of clopidogrel and aspirin: results from CAPRIE. CAPRIE Steering Committee and investigators. Clopidogrel versus aspirin in patients at high risk of ischaemic events. *Drug Safety* **21**: 325–35.

Heart Outcomes Prevention Evaluation Study Investigators (HOPE) (2000a). Effects of an angiotensin-converting-enzyme inhibitor, Ramipril, on cardiovascular events in high-risk patients. 2000; *New England Journal of Medicine* 342: 145–153.

Heart Outcomes Prevention Evaluation Study Investigators (HOPE) (2000b). Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. *Lancet* 355: 253–259.

Man-Son-Hing M, Laupacis A, O'Connor AM *et al* (for the Stroke Prevention in Atrial Fibrillation investigators) (1999). A patient decision aid regarding anti-thrombotic therapy for stroke prevention in atrial fibrillation. A randomised controlled trial. *JAMA* 282: 737–743.

Plehn JF, Davis BR, Sacks FM, *et al* (1999). Reduction of stroke incidence after myocardial infarction with pravastatin: the Cholesterol and Recurrent Events (CARE) study. The Care Investigators. *Circulation* **99**(2): 185–8.

PROGRESS Collaborative Group (2001). Randomized trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. *Lancet* 358: 1033–41.

Young GR, Humphrey PRD, Nixon TE, Smith ETS (1996). Variability in measurement of extracranial internal carotid artery stenosis as displayed by both digital subtraction and magnetic resonance angiography: an assessment of three caliper techniques and visual impression of stenosis. *Stroke* 27: 467–473.

Wardlaw JM, Lewis SC, Humphrey P (2001). How does the degree of carotid stenosis affect the accuracy and inter-observer variability of magnetic resonance angiography. *Journal of Neurology, Neurosurgery and Psychiatry* **71**: 155–60.

Westwood ME, Kelly S, Berry E (2002). Use of magnetic resonance angiography to select candidates with recently symptomatic carotid stenosis for surgery: systematic review. *British Medical Journal* **324**: 198–201.