

Secondary prevention of stroke

Jonathan Birns is Clinical Lecturer in Stroke Medicine and Maria Fitzpatrick is Clinical Nurse Specialist in Stroke, Department of Stroke Medicine, King's College Hospital, Denmark Hill London SE5 9RS, UK

ABSTRACT

Patients who have already suffered a stroke or transient ischaemic attack (TIA) are 10–15 times more likely than the general population to have another episode in the following year. The risk is greatest soon after the first event. This article describes approaches to secondary prevention of stroke, outlining specific lifestyle changes and treatment options that can lower a patient's risk. The specialist stroke nurse plays a central role in the successful implementation of these strategies, particularly with regard to patient education, monitoring and compliance.

Stroke has been defined as a rapid onset of focal neurological deficit lasting more than 24 hours, with no apparent cause other than disruption of the blood supply to the brain (World Health Organization, 1989). A transient ischaemic attack (TIA) refers to a similar presentation that resolves within 24 hours (Hankey and Warlow, 1994). Approximately 15% of strokes are haemorrhagic, with the rest being ischaemic.

Stroke is common, affecting approximately 150 000 people every year in the UK. It is the third leading cause of death and the single largest cause of adult physical disability in the world (Bath and Lees, 2000). At any given time there are about 2500 stroke patients in an average health district. Very few stroke survivors make a complete recovery; 12–18% are left with speech problems, 25% are unable to walk, 50% have residual weakness and 24–53% remain dependent on carers for day-to-day activity (Sacco, 1997). Although primary prevention remains the best method of reducing stroke, secondary prevention strategies have proven benefits (Straus et al, 2002).

Stroke recurrence

The risk of recurrent stroke is greatest early after the first stroke; about 2–3% of survivors of a first stroke have another stroke within the first 30 days, about 9% in the first 6 months and 10–16% within a year. This is about 15 times greater than the risk in the general population of the same age and sex. After the first year, the average annual risk of recurrent stroke for the next 4 years falls to about 5%. This risk is about nine times that of the general population of the same age and sex (Burn et al, 1994). These figures emphasize the importance of

preventing further strokes and the need to start preventive measures promptly.

Issues in secondary prevention

Of the 800 or so strokes that are potentially preventable each year, by treating TIA and stroke, considerably fewer are actually likely to be prevented (Hankey and Warlow, 1999). Not all patients suffering a stroke or TIA come to medical attention and certain treatments may not be appropriate for some patients. In addition, out of the patients who could benefit, some may not comply with treatment, some will have adverse effects, many do not respond and some do not want it.

Problems in implementing secondary preventive strategies have included poor communication, poor motivation, poor monitoring and the need for reinforcement over the longer term (Warlow et al, 2001). Stroke units, vascular risk clinics and specialist stroke physicians, nurses and therapists have helped by providing advice and education on risk factors and lifestyle modification, as well as initiating preventive measures, monitoring patients and providing specialist follow-up.

Clear evidence-based guidelines exist on stroke prevention for the different subtypes of stroke and it is important to find out the cause of a stroke before deciding on the best secondary preventive treatment (Wolf et al, 1999; Royal College of Physicians (RCP), 2004). Current national guidelines advise brain imaging in stroke patients within 24 hours of the onset of symptoms (RCP, 2004). This will show whether the stroke was haemorrhagic or ischaemic. Further cardiac and carotid artery investigations may be useful in determining the aetiology of ischaemic stroke.

Risk factor management

Major modifiable risk factors include: high blood pressure, diabetes mellitus, cigarette smoking, heavy alcohol use, physical inactivity and high cholesterol levels. In addition to risk-factor modification, three specific treatment strategies exist to prevent recurrence in patients with TIA or ischaemic stroke, namely antiplatelet therapy, anticoagulation and carotid endarterectomy (Wolf et al, 1999). Interventions are discussed below and summarized in *Table 1*.

Lifestyle modification

Being overweight, leading a sedentary lifestyle, excessive alcohol intake and poor diet all contribute to increased risk of vascular disease. Observational and epidemiological

Key words

- Stroke
- Secondary prevention
- Risk factor management
- Specialist stroke nurse

studies show, with reasonable consistency, that a diet rich in fresh fruit and vegetables is associated with a lower risk of stroke (Ness and Powles, 1999). In addition, a significant decrease in the risk of ischaemic stroke, after adjustment for other vascular risk factors, has been observed in individuals who include plenty of fish in their diet (Skerrett and Hennekens, 2003). By losing weight, increasing physical activity, and reducing sodium and alcohol intake, people have been able to reduce their systolic blood pressure by 4mmHg (McGuire et al, 2004). The National Service Framework for Older People recommends that people who have had a stroke are given access to a specialist stroke service and participate in a multidisciplinary programme of secondary prevention (Department of Health (DH), 2001). A multidisciplinary approach, using appropriately trained nurses, dietitians and allied health professionals, is essential to promote successful secondary preventive strategies.

There is a growing appreciation that the factors involved in persuading people to take up and sustain health-promoting behaviours, such as exercise and dietary change, are complex (Summerton, 2004). A systematic review of the effect of giving advice on physical activity in routine primary care consultations found mixed results (Lawlor and Hanratty, 2001). A later study suggested that to increase physical activity patients should be given an individualized exercise

plan combined with counselling (Little et al, 2004). A patient's compliance with lifestyle changes is vital and requires advice, reinforcement, monitoring and encouragement.

Cigarette smoking and alcohol use

Although no randomized controlled trials exist, observational studies suggest that cigarette smoking increases the risk of TIA and stroke by at least one and a half times (Hankey, 1999). All patients with cerebrovascular disease should be given advice on how to stop smoking and aids, such as nicotine replacement therapy, as appropriate. The number needed to treat is 43 to avoid one stroke per year (Hankey and Warlow, 1999).

All patients with cerebrovascular disease should be advised to keep their alcohol intake to less than two units per day. An intake greater than this predisposes to hypertension (Williams et al, 2004). Patients who are prescribed anticoagulant medication need to be particularly aware of the potential hazards of excessive alcohol intake and anticoagulant control.

High blood pressure

High blood pressure is the most important treatable and causal risk factor for stroke. One meta-analysis looked at 17 trials in individuals with elevated blood pressure ($n=734$) and 11 trials in individuals with normal blood

Table 1. Secondary prevention interventions

Intervention	Which patients?	Rationale
Lifestyle advice	All patients	Potential to reduce vascular risk by: stopping smoking improved diet weight loss increased exercise avoiding excess alcohol
Treatment of hypertension	Hypertensive patients in post-acute phase	Systematic reviews of randomized controlled trials show strong evidence of risk reduction
Optimization of diabetic control	All patients with diabetes mellitus	Tight glucose control reduces risk of stroke
Lipid-lowering therapy	All patients with non-haemorrhagic stroke and TIA with serum cholesterol >5mmol/l Patients with established or high risk for ischaemic heart disease, carotid atheroma or diabetes mellitus	Benefit shown in epidemiological studies Benefit shown in epidemiological studies and randomized controlled trials
Antiplatelet agents	All patients with non-haemorrhagic stroke or TIA with no contraindications, not on warfarin	Systematic reviews of randomized controlled trials show strong evidence of risk reduction
Anticoagulant treatment (warfarin)	Cardioembolic stroke or TIA with no contraindications	Systematic reviews of randomized controlled trials show strong evidence of risk reduction
Carotid endarterectomy	Patients with 70-99% stenosis of their symptomatic internal carotid artery	Randomized controlled trials show strong evidence of risk reduction

pressure ($n=2220$). It demonstrated that long-term reduction in salt intake had a significant and, from a population viewpoint, important effect on blood pressure in both those with normal and elevated blood pressure. Furthermore, a correlation was found between the magnitude of salt reduction and the magnitude of blood pressure reduction. Within the daily intake range of 3–12g/day, the lower the salt intake achieved, the lower the blood pressure (He and MacGregor, 2004).

A meta-analysis of data from nine randomized controlled trials on the effects blood pressure lowering drugs in 6752 survivors of stroke estimated a reduction in the relative risk of recurrent stroke of 29% (95% confidence interval: 5–47%) (Gueyffier et al, 1997). The British Hypertension Society guidelines for optimal blood pressure targets are: <140/85mmHg in people without diabetes and <130/80mmHg in those with diabetes (Williams et al, 2004). The Society's recommendations for the pharmacological management of hypertension are shown in *Figure 1*. Trials have shown that modest lowering of blood pressure in both hypertensive and non-hypertensive individuals reduces the risk of recurrent stroke (PROGRESS Collaborative Group, 2001). Lowering blood pressure by 9/4mmHg has been shown to produce a 28% relative risk reduction in subsequent stroke over 4 years of follow-up and lowering of blood pressure by 12/5mmHg has been shown to produce a 43% relative risk reduction in subsequent stroke over a similar time period (PROGRESS Collaborative Group, 2001). However, care should be taken with aggressive blood pressure reduction in certain patient groups, such those with severe carotid artery stenosis (Rothwell et al, 2003).

There is considerable controversy on how soon after stroke a patient's blood pressure should be lowered and it is the subject of ongoing research (Straus et al, 2002; Robinson and Potter, 2004). This is because cerebral

autoregulation may be impaired in acute stroke patients and adequate perfusion of the brain, especially in the infarcted region, may depend upon blood pressure (Dawson et al, 2000; Hacke et al, 2000). It is estimated that 7–10 days may be required to restore cerebral autoregulation. Common practice is that new antihypertensive treatment should be delayed until 1 week after stroke (RCP, 2004). These guidelines may be modified in the light of new evidence from ongoing studies (Robinson and Potter, 2004). There are circumstances, however, when treatment may be offered earlier under specialist supervision. Research by Schrader et al (2003) supports early antihypertensive therapy when the mean of at least two blood pressure measurements is 200mmHg systolic and/or 110mmHg diastolic at 6–24 hours after admission or 180mmHg systolic and/or 105mmHg diastolic at 24–36 hours after admission (Schrader et al, 2003).

Diabetes mellitus

Diabetes mellitus is an independent risk factor for stroke, and the mortality and disability of people with diabetes affected by stroke is significantly worse than that of non-diabetics (Mankovsky et al, 2004). All stroke patients should have their blood glucose levels checked. If blood glucose levels are raised at the time of, or soon after, a stroke, then fasting blood glucose levels and/or glucose tolerance tests should be undertaken. Targets for metabolic control and the control of vascular risk factors in people with diabetes are shown in *Table 2*.

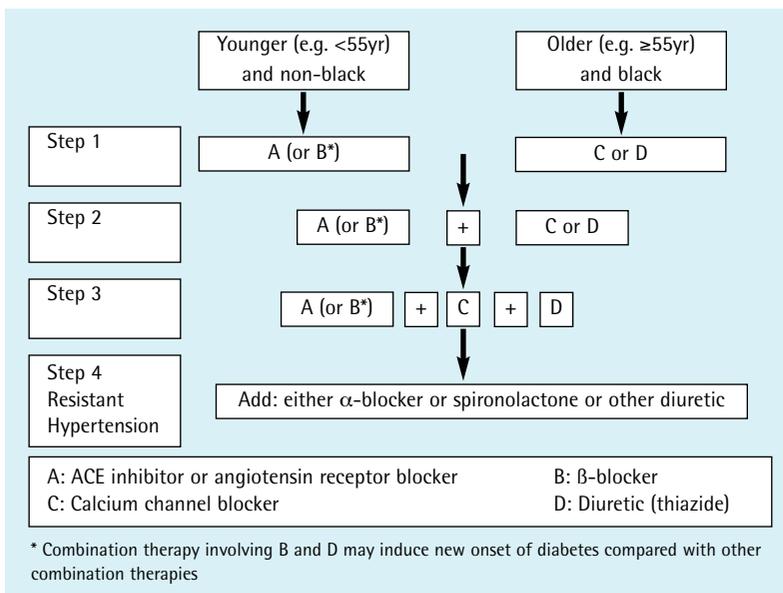
Lipid management

Epidemiological and observational studies have not shown a clear association between cholesterol concentrations and all causes of stroke (Thrift, 2004). However, large, long-term trials have shown that when patients with established, or at high risk for, coronary heart disease are given cholesterol-lowering therapy with statins, the incidence of stroke decreases. These statin trials in a combined total of 70 020 patients indicate relative and absolute risk reductions for stroke of 21% and 0.9%, respectively (Amarenco et al, 2004). Current guidelines advocate treatment with a statin in patients with ischaemic stroke or TIA when cholesterol concentration is >3.5 mmol/l (RCP, 2004). When the patient has carotid atherosclerosis, or pre-existing diabetes mellitus evidence supports empirical statin use (Oliver, 2000; Collins et al, 2003; Voelker, 2004). Future practice is likely to be guided by the results of the Stroke Prevention with Aggressive Reduction of Cholesterol Levels (SPARCL) trial, which is investigating the efficacy of statin therapy in the secondary prevention of stroke or TIA in patients without a past history of coronary events.

Antiplatelet agents

Large randomized controlled trials involving tens of thousands of patients worldwide have demonstrated the beneficial effect of aspirin treatment in the secondary

Figure 1. The British Hypertension Society recommendations for combining blood pressure lowering drugs (Williams et al, 2004)



prevention of ischaemic stroke (Chen et al, 2000). Giving aspirin to patients who have had an ischaemic stroke in daily doses above 75mg reduces the risk of stroke overall by about 13% and the stroke risk per year from 7% to 6%. This equates to one stroke being prevented for every 100 patients who are prescribed aspirin (DoH, 1997). Where patients are intolerant of aspirin, an alternative antiplatelet agent such as clopidogrel or dipyridamole may be used.

In patients with previous ischaemic stroke, myocardial infarction, or symptomatic atherosclerotic peripheral arterial disease, the CAPRIE trial showed clopidogrel to reduce significantly the annual risk of ischaemic stroke, myocardial infarction, or vascular death to 5.32% compared with 5.83% with aspirin ($P=0.04$) (CAPRIE Steering Committee, 1996). Although the CAPRIE study was not designed specifically to address secondary prevention of stroke, post hoc analyses showed that the benefit of clopidogrel was amplified in patients with diabetes and those receiving lipid-lowering therapy (Bhatt et al, 2000). The effectiveness of clopidogrel in combination with aspirin remains controversial. Studies in patients with significant carotid artery disease have experienced a reduction in the number of embolizations from the unstable plaque (Markus HS, personal communication, 2004). However, a large clinical study has shown that adding aspirin to clopidogrel in high-risk patients with recent ischaemic stroke or TIA had no significant effect in terms of reducing major vascular events, but increased the risk of major bleeding (Diener et al, 2004).

Another common combination for stroke prevention is the use of aspirin with dipyridamole. Although early trials of aspirin plus dipyridamole were unable to detect a significant benefit for combination therapy over aspirin alone, the large European Stroke Prevention Study 2 (ESPS-2) trial and meta-analysis of individual patient data from randomized controlled trials suggested that the combination reduces the risk of subsequent TIA and stroke by 19% compared with aspirin alone (Diener et al, 1996; Diener, 1998; Bath, 2004). A number of clinical trials of combinations of various antiplatelet agents (aspirin, dipyridamole, clopidogrel) in the acute and long-term management of stroke patients are currently in progress or being planned, and their results will provide additional evidence on their use (Hankey, 2004).

Anticoagulation

One in five ischaemic strokes is caused by cardiogenic embolism (Palacio and Hart, 2002). Anticoagulation should be considered for all patients who have ischaemic stroke associated with atrial fibrillation, valvular heart disease, prosthetic heart valves, or within 3 months of myocardial infarction (RCP, 2004). Anticoagulation should also be used after TIAs when cardiac embolism is suspected. Anticoagulants reduce the relative risk of stroke by 62%, corresponding to a reduction in the absolute risk of stroke of 8.4% per year for secondary prevention (Gubitz and Sandercock, 2000).

Table 2. Targets for metabolic control and the control of vascular risk factors in people with diabetes mellitus (Diabetes UK, 2000)

	Good	Borderline	Poor
Plasma glucose - fasting (mmol/l)	4.4–6.1	6.2–7.8	>7.8
- postprandial (mmol/l)	4.4–8.0	8.1–10.0	>10.0
HbA _{1c} (%)	<6.5	6.5–7.5	>7.5
Urine glucose (%)	0	0–0.5	>0.5
Total cholesterol (mmol/l)	<5.2	5.2–6.5	>6.5
HDL-cholesterol (mmol/l)	>1.1	0.9–1.1	<0.9
Fasting triglycerides (mmol/l)	<1.7	1.7–2.2	>2.2
Body mass index : - males (kg/m ²)	20–25	26–27	>27
- females (kg/m ²)	19–24	25–26	>26
Blood pressure (mmHg)	<140/80	140/80–160/95	>160/95
Smoking	Non-smoker	Pipe	Cigarettes

There is uncertainty over how long after a cardioembolic ischaemic stroke clinicians should wait before starting secondary prevention with anti-coagulants. Current guidelines advise that anti-coagulation should not be started until 14 days after the onset of an ischaemic stroke to reduce the risk of intracranial haemorrhage (RCP, 2004). In some circumstances, however, such as in the case of minor stroke with small infarct size (seen on brain imaging) and a high-risk of cardioembolism, acute anti-coagulation under specialist supervision may provide benefit (Ferro, 2003).

Atrial fibrillation is the most common form of arrhythmia encountered in clinical practice, affecting about 1 in 20 people aged 65 years and over in the UK (Sudlow et al, 1998). For patients with atrial fibrillation, dose-adjusted warfarin is administered (international normalized ratio in the 2 to 3 range; target 2.5) unless there is a specific contraindication for that medication (European Atrial Fibrillation Trial Study Group, 1993; Atrial Fibrillation Investigators, 1994). The same target international normalized ratio is recommended for patients with other causes of cardioembolic stroke except for those with prosthetic heart valves who need higher intensity of anticoagulation. In patients for whom anticoagulation is contraindicated, aspirin should be used (Wolf et al, 1999).

Carotid surgery

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) Collaborators and European Carotid Surgery Trial (ECST) established that carotid endarterectomy (CEA) reduces the risk of recurrent stroke in patients with 70–99% stenosis of their symptomatic internal carotid artery (NASCET Collaborators, 1991; European Carotid Surgery Trialists' Collaborative Group, 1991). In the NASCET, patients

who underwent CEA had an absolute reduction of 17% in the risk of ipsilateral stroke at 2 years. In the ECST, surgery-allocated patients had an absolute risk reduction of 6.5% and a relative risk reduction of 39%. Further analysis of these trials (Rothwell et al, 2004) revealed benefit from surgery to be greatest in those who underwent CEA within 2 weeks of their last ischaemic event, with the benefit falling with increasing delay. Age per se is not a contraindication to surgery and particular benefit has been demonstrated in patients over 75 years (Rothwell et al, 2004). However, many older patients have comorbidities that may increase surgical risk and careful pre-operative assessment is essential. Carotid angioplasty or stenting have been developed as alternatives to surgery but they have been shown to have comparative procedural risks to CEA with no improvement in outcomes (Brown and Hacke, 2004).

Role of the specialist stroke nurse

There are many aspects of secondary prevention of stroke where the specialist stroke nurse can play a key role. These include providing the patient with advice and education concerning risk factors and lifestyle management. The stroke nurse can do this on the stroke unit both in the acute and post-acute phase of rehabilitation and by telephone, internet and face-to-face follow-up of patients when they have been discharged from the hospital setting (Pierce et al, 2004). Follow-up appointments also allow the nurse to monitor patients for adequate control of physiological risk factors and any adverse effects of treatment, as well as ensuring compliance with medication and health advice. Issues identified in the literature include the need for family assessment, education, advocacy and counselling to foster treatment compliance after stroke (Evans et al, 1992; Kalra et al, 2004).

Nurses contribute to the promotion of healthy eating and national guidelines include the need for nurses to ensure the information they give patients about issues, such as healthy eating, is as up to date as possible (Strachan-Bennett and Hainsworth, 2004). Nurse-led diabetes, hypertension and vascular risk factor management and education services have all been shown to be effective (Terry, 2000; Ko et al, 2004, Rudd et al, 2004).

The education of nursing colleagues and allied health professionals is as important as the education of patients and their carers. Similarly, the introduction of patients and their carers to patient support groups can facilitate health promotion and improved compliance with secondary prevention strategies and minimize stroke recurrence (Richardson et al, 1996).

Conclusions

Considerable evidence in the literature supports an active approach towards secondary prevention of stroke. Much of this evidence comes from randomized controlled trials and systematic reviews that have considered risk factors and identified treatments to be both clinically and cost effective. Stroke prevention is complex and multifaceted and its benefit depends on successful implementation and monitoring. The specialist stroke nurse has a pivotal role to play in ensuring that patients understand the rationale for their treatment, are motivated, comply with advice and are monitored for maximum benefit. Equally important, is the initiation of a change in health behaviour so that patients themselves are responsible for positive health.

BJNN

- Atrial Fibrillation Investigators (1994) Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation: analysis of pooled data from five randomized controlled trials. *Arch Intern Med* **154**: 1449–57
- Amarenco P, Lavallee P, Touboul PJ (2004) Stroke prevention, blood cholesterol, and statins. *Lancet Neurol* **3**: 271–8
- Bath P (2004) Dipyridamole for preventing recurrent stroke: a metaanalysis of individual patient data from randomized controlled trials. British Association of Stroke Physicians Annual Scientific Meeting January 2004 Cambridge Abstracts
- Bath PMW, Lees KR (2000) ABC of arterial and venous disease. Acute stroke. *BMJ* **320**: 920–3
- Bhatt D, Foody J, Hirsch A, Ringleb P, Hacke W, Topol E (2000) Complementary, additive benefit of clopidogrel and lipid-lowering therapy in patients with atherosclerosis. *J Am Coll Cardiol* **35** (Suppl A): 326
- Brown MM, Hacke W (2004) Carotid artery stenting: the need for randomised trials. *Cerebrovasc Dis* **18**: 57–61
- Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C (1994) Long-term risk of recurrent stroke after a first-ever stroke. The Oxfordshire Community Stroke Project. *Stroke* **25**: 333–7
- CAPRIE Steering Committee (1996) A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* **348**: 1329–39
- Chen ZM, Sandercock P, Pan HC et al (2000) Indications for early aspirin use in acute ischemic stroke: A combined analysis of 40 000

KEY POINTS

- Patients who have suffered a stroke or transient ischaemic attack have an increased risk of further stroke
- Evidence based guidelines exist for prevention of further stroke
- Key areas include:
 - Lifestyle modification
 - Management of high blood pressure, diabetes mellitus, lipids
 - Antithrombotic drug therapy
 - Carotid surgery for symptomatic carotid stenosis
- The specialist stroke nurse plays a major role in directing stroke prevention strategies including the management of behavioural and physiological risk factors

- randomized patients from the Chinese acute stroke trial and the international stroke trial. On behalf of the CAST and IST collaborative groups. *Stroke* **31**: 12
- Collins R, Armitage J, Parish S, Sleight P, Peto R; Heart Protection Study Collaborative Group (2003) MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* **361**: 2005–16
- Dawson SL, Blake MJ, Panerai RB, Potter J (2000) Dynamic but not static cerebral autoregulation is impaired in acute ischaemic stroke. *Cerebrovasc Dis* **10**: 126–32
- Department of Health (1997) *Our Healthier Nation: a Contract for Health*. DH, London
- DH (2001) *National Service Framework for Older People*. DH, London
- Diabetes UK (2000) *Recommendations for the Management of Diabetes in Primary Care*. Diabetes UK, London
- Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A (1996) European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. *J Neurol Sci* **143**: 1–13
- Diener HC (1998) Dipyridamole trials in stroke prevention. *Neurology* **51**: S17–9
- Diener HC, Bogousslavsky J, Brass LM et al; MATCH investigators (2004) 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* **364**: 331–7
- European Atrial Fibrillation Trial Study Group (1993) Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. *Lancet* **342**: 1255–62
- European Carotid Surgery Trialists' Collaborative Group (1991) MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis. *Lancet* **337**: 1235–43
- Evans RL, Hendricks RD, Haselkorn JK, Bishop DS, Baldwin D (1992) The family's role in stroke rehabilitation. A review of the literature. *Am J Phys Med Rehabil* **71**: 135–9
- Ferro JM (2003) Cardioembolic stroke: an update. *Lancet Neurol* **2**: 177–88
- Gubitz G, Sandercock P (2000) Prevention of ischemic stroke. *BMJ* **321**: 1455–9
- Gueyffier F, Boissel JP, Boutitie F et al (1997) Effect of antihypertensive treatment in patients having already suffered from stroke. Gathering the evidence. The INDANA (INdividual Data ANalysis of Antihypertensive intervention trials) Project Collaborators. *Stroke* **28**: 2557–62
- Hacke W, Kaste M, Olsen TS, Orgogozo J-M, Bogousslavsky J (2000) European Stroke Initiative Recommendations for Stroke Management. *Cerebrovasc Dis* **10**: 335–351
- Hankey G (1999) Smoking and risk of stroke. *J Cardiovasc Risk* **5**: 207–11
- Hankey G, Warlow C (1994) *Transient Ischaemic Attacks of the Brain and Eye*. WB Saunders, London
- Hankey GJ, Warlow CP (1999) Treatment and secondary prevention of stroke: evidence, costs, and effects on individuals and populations. *Lancet* **354**: 1457–63
- Hankey GJ (2004) Ongoing and planned trials of antiplatelet therapy in the acute and long-term management of patients with ischaemic brain syndromes: setting a new standard of care. *Cerebrovasc Dis* **17**(Suppl 3): 11–6
- He FJ, MacGregor GA (2004) Effect of longer-term modest salt reduction on blood pressure. *Cochrane Database Syst Rev* **3**: CD004937
- Kalra L, Evans A, Perez I et al (2004) Training carers of stroke patients: randomised controlled trial. *BMJ* **328**: 1099–104
- Ko GT, Li JK, Kan EC, Lo MK (2004) Effects of a structured health education programme by a diabetic education nurse on cardiovascular risk factors in Chinese Type 2 diabetic patients: a 1-year prospective randomized study. *Diabet Med* **21**: 1274–9
- Lawlor D, Hanratty B (2001) The effect of physical activity advice given in routine primary care consultations: a systematic review. *J Public Health Med* **23**: 219–26
- Little P, Dorward M, Grafton S et al (2004) A randomized controlled trial of three pragmatic approaches to initiate increased physical activity in sedentary patients with risk factors for cardiovascular disease. *Br J Gen Pract* **54**: 189–95
- Mankovsky BN, Ziegler D (2004) Stroke in patients with diabetes mellitus. *Diabetes Metab Res Rev* **20**: 268–87
- McGuire HL, Svetkey LP, Harsha DW, Elmer PJ, Appel LJ, Ard JD (2004) Comprehensive lifestyle modification and blood pressure control: a review of the PREMIER trial. *J Clin Hypertens (Greenwich)* **6**: 383–90
- Ness A, Powles J (1999) The role of diet, fruit and vegetables and anti-oxidants in the aetiology of stroke. *J Cardiovasc Risk* **6**: 229–34
- North American Symptomatic Carotid Endarterectomy Trial Collaborators (1991) Beneficial effect of carotid endarterectomy in patients with high-grade carotid stenosis. *N Engl J Med* **325**: 445–53
- Oliver MF (2000) Cholesterol and strokes. Cholesterol lowering is indicated for strokes due to carotid atheroma. *BMJ* **320**: 459–60
- Palacio S, Hart RG (2002) Neurologic manifestations of cardiogenic embolism: an update. *Neurol Clin* **20**: 179–93
- Pierce LL, Steiner V, Govoni AL, Hicks B, Cervantez Thompson TL, Friedemann ML (2004) Internet-based support for rural caregivers of persons with stroke shows promise. *Rehabil Nurs* **29**: 95–9, 103
- PROGRESS Collaborative Group (2001) Randomised trial of a perindopril-based blood-pressure-lowering regime among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* **358**: 1033–41
- Richardson E, Warburton F, Wolfe CD, Rudd AG (1996) Family support services for stroke patients. *Prof Nurse* **12**: 92–6, 99
- Robinson TG, Potter JF (2004) Blood pressure in acute stroke. *Age Ageing* **33**: 6–12
- Rothwell PM, Howard SC, Spence JD; Carotid Endarterectomy Trialists' Collaboration (2003) Relationship between blood pressure and stroke risk in patients with symptomatic carotid occlusive disease. *Stroke* **34**: 2583–90
- Rothwell PM, Eliasziw M, Gutnikow SA, Warlow CP, Barnett HJM for the Carotid Endarterectomy Trialist Collaboration (2004) Endarterectomy for symptomatic carotid artery stenosis in relation to clinical subgroups and timing of surgery. *Lancet* **364**: 915–25
- Royal College of Physicians (2004) *National Clinical Guidelines for Stroke*. RCP, London
- Rudd P, Miller NH, Kaufman J et al (2004) Nurse management for hypertension. A systems approach. *Am J Hypertens* **17**: 921–7
- Sacco RL (1997) Risk factors, outcomes, and stroke subtypes for ischaemic stroke. *Neurology* **49**(5 Suppl 4): S39–44
- Schrader J, Luders S, Kulschewski A et al (2003) The ACCESS study: evaluation of acute candesartan cilexetil therapy in stroke survivors. *Stroke* **34**: 1699–703
- Skerrett PJ, Hennekens CH (2003) Consumption of fish and fish oils and decreased risk of stroke. *Prev Cardiol* **6**: 38–41
- Strachan-Bennett S, Hainsworth T (2004) New Essence of Care benchmark to focus all nurses on health promotion. *Nurs Times* **100**: 48: 3
- Straus SE, Majumdar SR, McAlister FA (2002) New evidence for stroke prevention. *JAMA* **288**: 1388–95
- Sudlow M, Thomson R, Thwaites B, Rodgers H, Kenny RA (1998) Prevalence of atrial fibrillation and eligibility for anticoagulants in the community. *Lancet* **352**: 1167–71
- Summerton N (2004) Risk factors. *Geriatr Med* **34**(7): 15–7
- Terry J (2000) A nurse-led initiative to screen and treat hypertension. *Community Nurse* **6**: 23–4
- Thrift AG (2004) Cholesterol is associated with stroke, but is not a risk factor. *Stroke* **35**: 1524–5
- Voelker R (2004) Widespread statin use recommended for patients with type 2 diabetes. *JAMA* **291**: 2419–20
- Warlow CP, Dennis MS, van Gijn J et al (2001) *Stroke. A Practical Guide to Management*. 2nd edn. Blackwell Press
- Williams B, Poulter NR, Brown MJ et al; British Hypertension Society (2004) Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS IV. *J Hum Hypertens* **18**: 139–85
- Wolf PA, Clagett GP, Easton JD et al (1999) Preventing ischemic stroke in patients with prior stroke and transient ischemic attack: a statement for healthcare professionals from the Stroke Council of the American Heart Association. *Stroke* **30**: 1991–4
- World Health Organisation Special Report. (1989) Stroke - 1989: recommendations on stroke prevention, diagnosis and therapy. *Stroke* **20**: 1407–31