NATIONAL CLINICAL GUIDELINE FOR STROKE

for the United Kingdom and Ireland

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Chapter 5

Long-term management and secondary prevention

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5.0 Introduction

From the moment a person has a stroke or TIA they are at substantial increased risk of further events; 26% within 5 years of a first stroke and 39% by 10 years (Mohan et al, 2011). There are additional risks of about the same magnitude for other vascular events such as acute coronary syndrome. Stroke is not a single disease entity and in some cases (e.g. arterial dissection) the underlying pathology is associated with a relatively low risk of recurrence. Clinicians should seek to identify and reduce the risks that are specific to each individual. **[2016]**

The greatest risk of a vascular event is early after stroke or TIA and may be as high as 25% within three months, half of which is within the first four days (Johnston et al, 2000). Secondary prevention should therefore be commenced as soon as possible, and recent registry evidence suggests these measures can substantially reduce the risk of recurrent events (Amarenco & Steering Committee Investigators of the TIAregistry.org, 2016). Some of the recommendations for management in the acute phase, such as starting aspirin immediately after ischaemic stroke, are part of secondary prevention. This chapter assumes that all the recommendations made in Chapter 3 have been implemented, and the recommendations concerning early risk reduction are not repeated here. However, it is important that attention to secondary prevention is continued throughout the rehabilitation and recovery phase, as persistence with treatment is vital to long-term risk reduction. **[2016]**

Diet and lifestyle issues such as smoking, exercise and alcohol intake contribute significantly to cardiovascular risk, including the risk of first and recurrent stroke; their modification provides an important mechanism for influencing recurrent events. Much of the evidence here comes from primary prevention studies or from patients with coronary artery disease, with the presumption that the evidence translates to the secondary prevention of stroke based on the two conditions often sharing the same underlying pathology. Given the different causes of stroke, this will not always be the case. **[2016]**

People with stroke and their family/carers often face substantial challenges returning to life in the home, community and workplace. The huge variety of individual circumstances and the complex nature of the outcomes concerned complicate the design, conduct and interpretation of research into living with the long-term effects of stroke. As a consequence, the evidence to guide recommendations here is more difficult to interpret; this does not diminish the importance of the topics under consideration nor the need for expert guidance on best practice. **[2016]**

5.1 A comprehensive and personalised approach

Ensuring the identification and modification of all risk factors, including lifestyle issues, should lead to more effective secondary prevention of stroke and other vascular events. This section covers advice and general principles of management – specific interventions are covered in subsequent sections. The clinician's approach to the modification of risk factors through lifestyle changes or medication should observe the principles of shared decision making recommended in NICE guidance (NICE, 2021d) and these principles apply to all the following sections. **[2023]**

5.1 Recommendations

A People with stroke or TIA should receive a comprehensive and personalised strategy for

vascular prevention including medication and lifestyle factors, which should be implemented as soon as possible and should continue long-term. **[2016]**

B People with stroke or TIA should receive information, advice and treatment for stroke, TIA and vascular risk factors which is:
- given first in the hospital or clinic setting;
- reinforced by all health professionals involved in their care;
- provided in an appropriate format. **[2016]**

C People with stroke or TIA should have their risk factors and secondary prevention reviewed and monitored at least once a year in primary care. **[2016]**

D People with stroke or TIA who are receiving medication for secondary prevention should:
- receive information about the reason for the medication, how and when to take it and common side effects;
- receive verbal and written information about their medicines in an appropriate format;
- be offered compliance aids such as large-print labels, non-childproof tops and dosette boxes according to their level of manual dexterity, cognitive impairment, personal preference and compatibility with safety in the home;
- be aware of how to obtain further supplies of medication;
- have their medication regularly reviewed;
- have their capacity to take full responsibility for self-medication assessed (including cognition, manual dexterity and ability to swallow) by the multidisciplinary team as part of their rehabilitation prior to the transfer of their care out of hospital. **[2016]**

5.1 Sources

A Working Party consensus

B Ovbiagele et al, 2004; Maasland et al, 2007; Sit et al, 2007

C, D Working Party consensus

5.2 Identifying risk factors

The risk of recurrent vascular events may vary significantly between individuals according to underlying pathology, co-morbidities and lifestyle factors. This guideline applies to the vast majority of people with TIA and stroke, including those not admitted to hospital; some of the recommendations may not be appropriate for the small minority of people with unusual stroke pathologies. **[2016]**

5.2 Recommendations

A People with stroke or TIA for whom secondary prevention is appropriate should be investigated for risk factors as soon as possible within 1 week of onset. **[2016]**

B Provided they are eligible for any resultant intervention, people with stroke or TIA should be investigated for the following risk factors:
- ipsilateral carotid artery stenosis;
- atrial fibrillation;
- structural cardiac disease. **[2016]**

C People with evidence of non-symptomatic cerebral infarction on brain imaging (silent cerebral ischaemia) should have an individualised assessment of their vascular risk and secondary prevention. **[2016]**

5.2 Source

A-C Working Party consensus

5.2 Implications

The identification of risk factors for stroke and TIA should be part of the assessment during the acute phase. Regular review of risk factors and secondary prevention in primary care may require additional resources. **[2016]**

5.3 Carotid artery stenosis

Atheroma and stenosis of the carotid arteries is commonly associated with stroke and TIA, and surgical or radiological interventions (endarterectomy or stenting) have been used to reduce the risk of recurrent ipsilateral stroke. **[2016]**

5.3 Recommendations

A Following stroke or TIA, the degree of carotid artery stenosis should be reported using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. **[2016]**

B People with non-disabling carotid artery territory stroke or TIA should be considered for carotid revascularisation, and if they agree with intervention:

- they should have carotid imaging (duplex ultrasound, MR or CT angiography) performed urgently to assess the degree of stenosis;
- if the initial test identifies a relevant severe stenosis (greater than or equal to 50%), a second or repeat non-invasive imaging investigation should be performed to confirm the degree of stenosis. This confirmatory test should be carried out urgently to avoid delaying any intervention. **[2016]**

C People with non-disabling carotid artery territory stroke or TIA should be considered for carotid revascularisation if the symptomatic internal carotid artery has a stenosis of greater than or equal to 50%. The decision to offer carotid revascularisation should be:

- based on individualised risk estimates taking account of factors such as the time from the event, gender, age and the type of qualifying event;
- supported by risk tables or web-based risk calculators (e.g. the Oxford University Stroke Prevention Research Unit calculator, https://www.ndcn.ox.ac.uk/divisions/cpsd/carotid-stenosis-tool-1). **[2016]**

D People with non-disabling carotid artery territory stroke or TIA and a carotid stenosis of less than 50% should not be offered revascularisation of the carotid artery. **[2016]**

E Carotid endarterectomy for people with symptomatic carotid stenosis should be:

- the treatment of choice, particularly for people who are 70 years of age and over or for whom the intervention is planned within seven days of stroke or TIA;
- performed in people who are neurologically stable and who are fit for surgery using either local or general anaesthetic according to the person's preference;
- performed as soon as possible and within 1 week of first presentation;
- deferred for 72 hours in people treated with intravenous thrombolysis;
- only undertaken by a specialist surgeon in a vascular centre where the outcomes of carotid surgery are routinely audited. **[2016]**

F Carotid angioplasty and stenting should be considered for people with symptomatic

carotid stenosis who are:

- unsuitable for open surgery (e.g. high carotid bifurcation, symptomatic re-stenosis following endarterectomy, radiotherapy-associated carotid stenosis);

or

- less than 70 years of age and who have a preference for carotid artery stenting.

The procedure should only be undertaken by an experienced operator in a vascular centre where the outcomes of carotid stenting are routinely audited. **[2016]**

G People who have undergone carotid revascularisation should be reviewed post-operatively by a stroke physician to optimise medical aspects of vascular secondary prevention. **[2016]**

H Patients with atrial fibrillation and symptomatic internal carotid artery stenosis should be managed for both conditions unless there are contraindications. **[2016]**

5.3 Sources

A Working Party consensus

B Wardlaw et al, 2006

C, D Rothwell et al, 2004, 2005; Rerkasem and Rothwell, 2011

E Rerkasem and Rothwell, 2011; Bonati et al, 2012; Vaniyapong et al, 2013; Rantner et al, 2013; Working Party consensus

F Economopoulos et al, 2011; Bonati et al, 2015; Working Party consensus

G, H Working Party consensus

5.3 Evidence to recommendations

The principal evidence for carotid endarterectomy for people with recent symptoms is from the European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (Rothwell et al, 2003b). Only people with non-disabling stroke or TIA were included in these trials and the benefits of surgery cannot be assumed to apply to those with more disabling strokes. People with possible cardioembolism were also excluded. When allowance is made for the different methods used to measure stenosis from angiograms, the two trials report consistent findings. To avoid confusion regarding the degree of stenosis the technique used in NASCET should be used (the ratio of the diameter of the residual lumen at the point of maximum narrowing to that of the more distal internal carotid artery, expressed as a percentage). In a pooled analysis of the individual data from 6,092 patients, carotid endarterectomy reduced the 5-year absolute risk of ipsilateral ischaemic stroke by 16.0% in patients with 70–99% stenosis, and by 4.6% in patients with 50–69%. There was no benefit for patients with 30–49% stenosis and surgery increased the risk in patients with less than 30% stenosis. There was no evidence of benefit for patients with a near-occlusion. In these trials conducted in the 1980s the operative risk of stroke (ocular or cerebral) and death within 30 days of endarterectomy was 7%. **[2016]**

There is evidence of considerable heterogeneity in individual risk according to age, gender, degree of stenosis, presenting symptom, time from presenting symptom and presence of plaque ulceration (Rothwell et al, 2004). Prognostic models based on these characteristics have been derived which may be useful in the decision making process (Rothwell et al, 2005). These models are based on trial data which are now over 20 years old and with improvements in other treatments these models are likely to overestimate the absolute risk of stroke. Modified prognostic models incorporating corrections to allow for improvements in 'best medical therapy' have been developed (e.g. the Carotid Artery Risk score - www.ecst2.com/), but await validation. **[2016]**

In a systematic review of operative risks in relation to timing of surgery, no statistically significant difference for early versus late surgery was identified for patients with stable stroke (Rerkasem & Rothwell, 2009). In patients undergoing emergency surgery the pooled absolute risk of stroke and death was 20.2% for those with 'stroke-in-evolution' (fluctuating or progressive deficit) and 11.4% for those with crescendo TIA (more than 2 episodes in a week), significantly higher than for those undergoing non-emergency surgery (odds ratio [OR] 4.6). Such patients are likely to be at increased risk if surgery is not performed, but given these risks and the effectiveness of medical management it cannot be assumed that emergency surgery is beneficial in neurologically unstable patients. The outcome from carotid endarterectomy is not significantly influenced by whether the procedure is carried out under local or general anaesthesia (Vaniyapong et al, 2013), and if the person has a particular preference, this should be taken into account. **[2016]**

Compared to surgical endarterectomy, endovascular therapy involving carotid angioplasty and stenting is associated with an increased risk of stroke of any severity or death (Bonati et al, 2012). This increased risk is modified by age, with no difference in stroke or death when the comparison is confined to those below 70 years of age (International Carotid Stenting Study investigators, 2010). Long-term follow-up identifies an excess of procedure-related and non-disabling strokes with endovascular therapy (Bonati et al, 2015). By contrast, carotid endarterectomy is associated with an excess of cranial nerve palsy and myocardial infarction (Bonati et al, 2012). For endovascular procedures undertaken within the first few days after symptom onset there is an excess of disabling and fatal, as well as non-disabling strokes in comparison to carotid endarterectomy (Rantner et al, 2013). (Rantner et al, 2013). **[2016]**

There is no high quality evidence to guide decision making regarding the timing and indications for carotid revascularisation in patients presenting with ischaemic stroke who have been treated with intravenous thrombolysis. A number of case series have been reported with small numbers and few outcome events (Naylor, 2015). Activation of the coagulation system and fibrin formation occurs following alteplase therapy with changes peaking at 1 to 3 hours but detectable for up to 72 hours (Fassbender et al, 1999). It is not clear what impact if any these changes in the coagulation system may have on the balance of risks and benefits, but in the absence of high quality data it would seem reasonable to advise caution if considering surgery within 72 hours of intravenous thrombolysis. **[2016]**

5.3 Implications

Vascular surgery services should offer the option to perform carotid endarterectomy surgery under local or general anaesthetic. Multidisciplinary teams should include a carotid interventionist able to advise on and deliver carotid artery angioplasty and stenting. **[2016]**

5.4 Blood pressure

Blood pressure (BP) is the pre-eminent treatable risk factor for first and recurrent stroke. It is estimated to cause about 50% of ischaemic strokes and is the principal risk factor for intracerebral haemorrhage. The relationship to cerebral perfusion pressure means that changes in BP in people with hyperacute stroke may influence the extent of brain damage. Treatment recommendations therefore differ when comparing hyperacute management (Section 3.5 *Management of ischaemic stroke* and Section 3.6 *Management of intracerebral haemorrhage*) with long-term secondary prevention, with this section concentrating on the latter. **[2016]**

5.4 Recommendations

A People with stroke or TIA should have their blood pressure checked, and treatment should be initiated or increased as tolerated to consistently achieve a clinic systolic blood pressure below 130 mmHg, equivalent to a home systolic blood pressure below 125 mmHg. The exception is for people with severe bilateral carotid artery stenosis, for whom

a systolic blood pressure target of 140–150 mmHg is appropriate. Concern about potential adverse effects should not impede the initiation of treatment that prevents stroke, major cardiovascular events or mortality. **[2023]**

B For people with stroke or TIA aged 55 or over, or of African or Caribbean origin at any age, antihypertensive treatment should be initiated with a long-acting dihydropyridine calcium-channel blocker or a thiazide-like diuretic. If target blood pressure is not achieved, an angiotensin converting enzyme inhibitor or angiotensin II receptor blocker should be added. **[2016]**

C For people with stroke or TIA not of African or Caribbean origin and younger than 55 years, antihypertensive treatment should be initiated with an angiotensin converting enzyme inhibitor or an angiotensin II receptor blocker. **[2016]**

D People with stroke or TIA should have blood pressure-lowering treatment initiated prior to the transfer of care out of hospital or at 2 weeks, whichever is the soonest, or at the first clinic visit for people not admitted. **[2016]**

E People with stroke or TIA should have their blood pressure-lowering treatment monitored frequently in primary care and increased to achieve target blood pressure as quickly and safely as tolerated. People whose blood pressure remains above target despite treatment should be checked for medication adherence at each visit before escalation of treatment, and people who do not achieve their target blood pressure despite escalated treatment should be referred for a specialist opinion. Once blood pressure is controlled to target, people taking antihypertensive treatment should be reviewed at least annually. **[2023]**

F In people with stroke being treated with antihypertensive agents to reduce recurrent stroke risk, management guided by home or ambulatory BP monitoring should be considered, in order to improve treatment compliance and BP control. **[2023]**

G People with stroke using home BP monitoring should use a validated device with an appropriate measurement cuff and a standardised method. They (or where appropriate, their family/carer) should receive education on how to use the device, the implications of readings for management, and be provided with ongoing support, particularly if they have anxiety or cognitive and physical disability after stroke. **[2023]**

5.4 Sources

A Rothwell et al, 2003a; Ettehad et al, 2016

B PROGRESS Collaborative Group, 2001; NICE, 2022a

C NICE, 2022a

D Rothwell et al, 2007; NICE, 2022a; Working Party consensus

E Rothwell et al, 2007; NICE, 2022a; Guideline Development Group consensus

F Ovaisi et al, 2011; Kerry et al, 2013; Hanley et al, 2015; Guideline Development Group consensus

G Kerry et al, 2013; Breaux-Shropshire et al, 2015

5.4 Evidence to recommendations

There is high quality evidence that BP reduction after stroke or TIA prevents further vascular events including recurrent ischaemic and haemorrhagic stroke (PROGRESS Collaborative Group, 2001). In PROGRESS, giving two more BP-lowering medicines to people after stroke or TIA, 52% of whom were classified as normotensive, reduced BP by 12/5 mmHg and resulted in a 42% reduction in recurrent stroke and 35% fewer major coronary events. A net benefit was seen for those with baseline BP levels as low as 115/75 with the lowest risk of recurrent stroke seen in those achieving the lowest follow-up BP

levels. There was no evidence of increased stroke risk at lower BP (Arima et al, 2006). A meta-analysis of 123 studies and 613,815 participants found BP-lowering treatment significantly reduced cardiovascular events and death in proportion to the magnitude of BP reduction achieved, with no differences in the proportional benefits between trials with lower (below 130 mmHg) or higher systolic BP at baseline (Ettehad et al, 2016). There was also no difference in the proportional risk reductions for major cardiovascular events by baseline medical conditions, but calcium-channel blockers were found to be superior to other medication classes in the prevention of stroke. Overall, a 10 mmHg reduction in systolic BP reduced the risk of cardiovascular disease by 20% and stroke by 27%. **[2016]**

In the Secondary Prevention of Small Subcortical Strokes (SPS3) trial targeting a systolic BP of below 130 mmHg in patients with recent lacunar stroke, reductions in the rate of all stroke, disabling or fatal stroke and the composite outcome of myocardial infarction or vascular death were not significant, but the rate of cerebral haemorrhage was reduced and the lower target was well tolerated (SPS Study Group, 2013). In addition to the PROGRESS trial (2001), further evidence to support the benefit of a SBP target of below 130/80 mmHg in reducing recurrent stroke was observed in a clinical trial and as a secondary outcome in another study (Mant et al, 2016; Kitagawa et al, 2019). Accompanying meta-analyses (Thomopoulos et al, 2015, 2016), have shown that lowering BP to below 130/80 mmHg, if tolerated, is beneficial in preventing stroke and major cardiovascular events. Two analyses with greater statistical power that included the Systolic Blood pressure Intervention trial (SPRINT research group, 2015) have shown that intensive treatment even to below 120 mmHg may be beneficial (Bangalore et al, 2017; Bundy et al, 2017). However, in SPRINT, patients with a history of stroke were excluded and the trial was not powered to assess a difference in stroke incidence (a secondary outcome). A U-shaped BP-cardiovascular risk relationship was observed both in the intensive and standard treatment groups in SPRINT, but randomised comparisons found a significant cardiovascular and mortality benefit for more versus less intensive treatment at each level of baseline BP (Beddhu et al, 2018). **[2023]**

There is uncertainty regarding the best time to start antihypertensive therapy following ischaemic stroke. Whilst BP can be successfully and safely reduced in the acute phase, there is no evidence that such early intervention results in long-term benefits (Bath & Krishnan, 2014). For patients admitted with stroke who are already taking antihypertensive medication, treatment can be safely withheld until patients are medically and neurologically stable and have suitable oral or enteral access (Bath et al, 2015). Unless there is severe hypertension or treatment is required for acute intracerebral haemorrhage (Section 3.6 *Management of intracerebral haemorrhage*) or to facilitate intravenous thrombolysis treatment (Section 3.5 *Management of ischaemic stroke*) antihypertensive medication should generally be initiated prior to the transfer of care out of hospital or at 2 weeks, whichever is the soonest, or at the first clinic visit for people not admitted. **[2016]**

Home BP monitoring may usefully contribute to hypertension management, but there are few trials of home BP monitoring in stroke. Kerry et al (2013) conducted a randomised trial of home BP monitoring with nurse-led support versus standard care in people with hypertension and a history of stroke. More changes to antihypertensive treatment were made in the intervention group than controls (60% v. 47%; p=0.02), but the fall in systolic BP from baseline did not differ significantly between the two groups. A post-hoc analysis showed a reduction of 6 mm Hg in systolic BP at 12 months in the intervention group (Kerry et al, 2013). A prospective cohort study found that half of people with stroke offered a BP monitor without nurse support continued monthly use for up to 18 months, but around a quarter of participants reported a disability that made it difficult to measure their BP unaided (Ovaisi et al, 2011). **[2023]**

Studies suggest that treatment based on home BP monitoring may reduce vascular risk, principally through improving long term compliance (Ovaisi et al, 2011; Kerry et al, 2013; Hanley et al, 2015). Further evidence is required to determine which people with stroke benefit, and the type of equipment (semi-automated v. automated), timing of measurement, ideal target and duration. Systematic reviews

emphasise that attention should be given to correct measurement and a clear management strategy for the patient (and carer as appropriate). It is also recommended that the pulse rhythm is recorded at each clinical contact to detect non-symptomatic atrial fibrillation (Cappuccio et al, 2004; Bray et al, 2010; Glynn et al, 2010; NICE, 2021c). **[2023]**

5.4 Implications

There should be a move away from the concept of treating hypertension and towards the concept of modifying BP as a risk factor. It is appropriate to lower BP in patients who previously would have been considered normotensive. **[2016]**

5.5 Lipid modification

Raised lipid levels, especially hypercholesterolaemia, are an important modifiable risk factor for cardiovascular events, especially myocardial infarction. Lipid-lowering treatment is an effective intervention for primary and secondary prevention of vascular events, including stroke. **[2016]**

5.5 Recommendations

A People with ischaemic stroke or TIA should be offered personalised advice and support on lifestyle factors to reduce cardiovascular risk, including diet, physical activity, weight reduction, alcohol moderation and smoking cessation. **[2023]**

B People with ischaemic stroke or TIA should be offered treatment with a statin unless contraindicated or investigation of their stroke or TIA confirms no evidence of atherosclerosis. Treatment should:
- begin with a high-intensity statin such as atorvastatin 80 mg daily. A lower dose should be used if there is the potential for medication interactions or a high risk of adverse effects;
- be with an alternative statin at the maximum tolerated dose if a high-intensity statin is unsuitable or not tolerated. **[2023]**

C Lipid-lowering treatment for people with ischaemic stroke or TIA and evidence of atherosclerosis should aim to reduce fasting LDL-cholesterol to below 1.8 mmol/L (equivalent to a non-HDL-cholesterol of below 2.5 mmol/L in a non-fasting sample). If this is not achieved at first review at 4-6 weeks, the prescriber should:
- discuss adherence and tolerability;
- optimise dietary and lifestyle measures through personalised advice and support;
- consider increasing to a higher dose of statin if this was not prescribed from the outset;
- consider adding ezetimibe 10 mg daily;
- consider the use of additional agents such as injectables (inclisiran or monoclonal antibodies to PCSK9) or bempedoic acid (for statin-intolerant people taking ezetimibe monotherapy);
- continue to escalate lipid-lowering therapy (in combination if necessary) at regular intervals in order to reduce LDL-cholesterol to below 1.8 mmol/L. **[2023]**

D People with ischaemic stroke or TIA in whom investigation confirms no evidence of atherosclerosis should be assessed for lipid-lowering therapy on the basis of their overall cardiovascular risk. **[2023]**

E People with intracerebral haemorrhage should be assessed for lipid-lowering therapy on the basis of their overall cardiovascular risk and the underlying cause of the haemorrhage. **[2023]**

F In people with ischaemic stroke or TIA below 60 years of age with very high cholesterol (below 30 years with total cholesterol above 7.5 mmol/L or 30 years or older with total cholesterol concentration above 9.0 mmol/L) consider a diagnosis of familial hypercholesterolaemia. **[2023]**

G In people with ischaemic stroke or TIA of presumed atherosclerotic cause below 60 years of age, consider the measurement of lipoprotein(a) and specialist referral if raised above 200 nmol/L. **[2023]**

5.5 Sources

A-D NICE, 2016a, b; 2021b, d; 2023a; Amarenco et al, 2020; NHS England Accelerated Access Collaborative, 2021; Lee et al, 2022

E Vergouwen et al, 2008; Guideline Development Group consensus

F NICE, 2023b

G HEART UK Medical Scientific and Research Committee, 2019

5.5 Evidence to recommendations

The benefit of lipid-lowering therapy with statins in reducing cardiovascular events and mortality has been confirmed in RCTs and meta-analyses both for individuals with cardiovascular disease and specifically those with cerebrovascular disease. The Cholesterol Treatment Trialists' Collaboration (Baigent et al, 2005) showed that for each 1.0 mmol/L reduction in LDL-cholesterol with statin therapy there was a relative risk reduction of 12% in all-cause mortality and a 21% reduction in major cardiovascular events, including a 17% reduction in fatal or non-fatal stroke (Baigent et al, 2005). The SPARCL trial investigated the effect of atorvastatin 80 mg daily in patients with TIA or stroke in the preceding 6 months and demonstrated a relative risk reduction of 15% in stroke and 35% in major coronary events with treatment (Amarenco et al, 2006). More recently, the Treat Stroke to Target Trial (TSTT) demonstrated that patients with ischaemic stroke or TIA in whom investigation confirmed evidence of atherosclerosis had a lower risk of subsequent cardiovascular events with a target LDL-cholesterol of below 1.8 mmol/L than those with a higher target of 2.3-2.8 mmol/L (Amarenco et al, 2020). 'Evidence of atherosclerosis' in TSTT included intracranial or extracranial artery stenosis, aortic atheroma or known coronary artery disease. A meta-analysis (11 RCTs of 20,163 people with stroke, including TSTT) compared intensive versus less intensive LDL-cholesterol lowering for secondary prevention (Lee et al, 2022). Intensive lowering over 4 years reduced the absolute risk of stroke (of any type) by 1.2%, and major cardiovascular events by 2.8%, but increased haemorrhagic stroke by 0.4%. Although small numerical increases were seen in both intracranial haemorrhage and newly diagnosed diabetes in the lower-target group in TSTT, these were not statistically significant and were more than outweighed by the benefits in prevention of major cardiovascular events. **[2023]**

In primary and secondary prevention studies, lowering LDL-cholesterol by 1.0 mmol/L leads to a relative risk reduction of 21% in major cardiovascular events, 9% in total mortality, and 15% in stroke (of any type) irrespective of baseline cholesterol and gender (Fulcher et al, 2015). Thus the decision to initiate treatment should be determined by a person's absolute cardiovascular risk rather than their cholesterol level. NICE clinical guideline CG181 for lipid modification (2021a) provides recommendations consistent with the findings from SPARCL and TSTT, and recommends high-intensity statin therapy with atorvastatin 80 mg daily with a lower starting dose for people at high risk of adverse events or medication interactions, with subsequent guidance identifying the role of newer agents (NICE, 2016b, a; NHS England Accelerated Access Collaborative, 2021; NICE, 2021b, a, 2022b). The Guideline Development Group emphasizes the importance of characterising the finding of atherosclerosis in communications to primary care about long-term risk factor management so the correct treatment strategy can be followed. The recommendations also reiterate NICE and specialist society guidance on

when to suspect familial hypercholesterolaemia, or lipoprotein abnormalities requiring specialist lipid clinic referral. **[2023]**

One randomised trial of icosapent ethyl in people with elevated triglycerides on optimal statin therapy (Bhatt et al, 2019) showed a significant reduction in major cardiovascular events that was greater than accounted for by the observed reduction in triglycerides (NICE, 2022b). For cardiovascular prevention after ischaemic stroke the emphasis remains on achieving LDL-cholesterol reduction to target, but people with raised triglycerides should be reviewed for lifestyle interventions such as alcohol reduction, weight reduction and diabetes control, and those with persistent severe hypertriglyceridaemia (greater than 10 mmol/L) should be referred to a lipid clinic to consider treatment to reduce the risk of pancreatitis. **[2023]**

5.6 Antiplatelet treatment

Antiplatelet treatment is one of the most important interventions for reducing the risk of recurrent vascular events including stroke. Most long-term evidence relates to aspirin, although combination antiplatelet therapy may offer the prospect of greater efficacy, tempered by an increased risk of bleeding. **[2016]**

5.6 Recommendations

A For long-term prevention of vascular events in people with ischaemic stroke or TIA without paroxysmal or permanent atrial fibrillation:
- clopidogrel 75 mg daily should be the standard antithrombotic treatment;
- aspirin 75 mg daily should be used for those who are unable to tolerate clopidogrel;

if a patient has a recurrent cardiovascular event on clopidogrel, clopidogrel resistance may be considered.

The combination of aspirin and clopidogrel is not recommended for long-term prevention of vascular events unless there is another indication e.g. acute coronary syndrome, recent coronary stent. **[2023]**

B People with ischaemic stroke with acute haemorrhagic transformation should be treated with long-term antiplatelet or anticoagulant therapy unless the prescriber considers that the risks outweigh the benefits. **[2023]**

C Patients who have a spontaneous (non-traumatic) intracerebral haemorrhage (ICH) whilst taking an antithrombotic (antiplatelet or anticoagulant) medication for the prevention of occlusive vascular events may be considered for restarting antiplatelet treatment beyond 24 hours after ICH symptom onset. **[2023]**

D Clinicians should consider the baseline risks of recurrent ICH and occlusive vascular events when making a decision about antiplatelet use after ICH outside randomised controlled trials. **[2023]**

E Wherever possible, patients with spontaneous (non-traumatic) ICH and a co-existent indication for antithrombotic medication treatment should be encouraged to participate in randomised controlled trials of antithrombotic therapy. **[2023]**

5.6 Sources

A NICE, 2010a; Guideline Development Group consensus

B Guideline Development Group consensus

C Al-Shahi Salman et al, 2019, 2021; Guideline Development Group consensus

D Charidimou et al, 2017; Li et al, 2021

E Guideline Development Group consensus

5.6 Evidence to recommendations

The Antithrombotic Trialists' Collaboration (2002) demonstrated a 22% reduction in the odds of a vascular event (myocardial infarction, stroke or vascular death) in patients with a previous stroke or TIA treated with antiplatelet medication. Comparative trials such as CAPRIE (CAPRIE Steering Committee, 1996), ESPRIT (ESPIRIT Study Group, 2006) and PRoFESS (Sacco et al, 2008) show that aspirin plus modified-release dipyridamole and clopidogrel monotherapy are equally effective, with both options superior to aspirin monotherapy. **[2016]**

The combination of aspirin and clopidogrel has been compared to clopidogrel monotherapy in patients with recent TIA or stroke (Diener et al, 2004). The combination was not superior to clopidogrel alone, with evidence of increased adverse effects particularly bleeding. There is evidence that even in short-term use the combination carries an increased risk of bleeding, particularly in aspirin-naive individuals (Geraghty et al, 2010). The use of combination antiplatelet treatment within the first few weeks after stroke or TIA is addressed in Section 3.3 *Management of TIA and minor stroke – treatment and vascular prevention* and Section 3.5 *Management of ischaemic stroke*. **[2016]**

RESTART was a UK multicentre open label pilot phase RCT (RESTART Collaboration, 2019) that included 537 participants in the UK with spontaneous (non-traumatic) intracerebral haemorrhage (ICH) who were taking an antithrombotic medication (antiplatelet or anticoagulant) for the prevention of occlusive vascular events. Participants were allocated at random to either start or avoid antiplatelet treatment, with a median time from ICH symptom onset to randomisation of 76 days (IQR 29-146). The primary outcome was recurrent ICH. Over a median follow-up period of two years, 4% of those allocated to antiplatelet therapy had recurrent ICH compared with 9% of those allocated to avoid antiplatelet therapy [adjusted hazard ratio 0.51, 95% CI 0.25 to 1.03; p=0.06]. There was no difference in major occlusive vascular events, but a reduction in all serious vascular events, as defined by the Antithrombotic Trialists' Collaboration, was reported. The results were consistent across subgroups including ICH location, time since symptom onset, type of antiplatelet medication, participant age, and history of atrial fibrillation, although the Guideline Development Group noted the lack of statistical power to test for these interactions. **[2023]**

After extended follow-up to five years (Al-Shahi Salman et al, 2021), ICH affected 22 of 268 participants (8.2%) allocated to antiplatelet therapy compared with 25 of 268 participants (9.3%) allocated to avoid antiplatelet therapy (adjusted hazard ratio, 0.87; 95%CI 0.49 to 1.55; p=0.64). A major vascular event affected 72 participants (26.8%) allocated to antiplatelet therapy compared with 87 participants (32.5%) allocated to avoid antiplatelet therapy (hazard ratio, 0.79; 95%CI 0.58 to 1.08; p=0.14). A brain imaging substudy of the RESTART trial (n=254 with MRI; Al-Shahi Salman et al, 2019) found no evidence of more frequent recurrent ICH in patients with two or more cerebral microbleeds compared to one or no cerebral microbleeds (adjusted hazard ratio 0.30 [95% CI 0.08 to 1.13] v. 0.77 [0.13 to 4.61]; p-interaction=0.41), nor in subgroups according to cerebral microbleed burden or strictly lobar location (that might indicate cerebral amyloid angiopathy [CAA]). **[2023]**

The Guideline Development Group considered the RESTART trial to be well conducted and of high quality although the small sample size limited statistical power and precision. There were also concerns regarding possible selection bias (average ICH volume of 4 mL smaller than most ICH seen in clinical practice) which might limit generalisability. There were few participants with probable CAA, a subgroup which appears to be at highest risk of ICH (Charidimou et al, 2017). The group also noted that the evidence from RESTART cannot be applied to patients very soon after ICH symptom onset (only 21 participants (4%) were randomised in the first week after ICH while most (74%) were randomised at or beyond 30 days), although RESTART appears to give some reassurance that restarting antiplatelet therapy after ICH may be safe with regard to recurrent ICH, the consensus was that the evidence was

insufficient to provide a strong recommendation. The group also identified some observational cohort studies, but due to methodological limitations (including risks of selection bias and confounding by indication) none was judged to provide sufficiently strong evidence to inform a recommendation about antiplatelet therapy after ICH. Further randomised trials are ongoing or planned and clinicians and patients are strongly encouraged to participate in these wherever possible. **[2023]**

In practice clinicians will continue to make case-by-case decisions based on their understanding of the baseline risk of future events including recurrent ICH and vaso-occlusive events. For example, in observational studies the recurrence risk for lobar ICH is consistently higher than for deep ICH (Li et al, 2021) while the risk of ICH recurrence in patients with probable CAA is substantially higher than in those without probable CAA (Charidimou et al, 2017). Haemorrhagic MRI biomarkers of CAA, including cerebral microbleeds and cortical superficial siderosis, are also associated with an increased risk of ICH recurrence. Clinicians are recommended to take these prognostic factors into account when deciding whether to recommend antiplatelet medication after ICH. **[2023]**

5.7 Anticoagulation

Treatment with anticoagulation after TIA or ischaemic stroke is now usually restricted to long-term secondary prevention of cardioembolic stroke due to atrial fibrillation (AF), intracardiac thrombus, valvular heart disease or mechanical heart valve replacement. **[2023]**

For over 50 years, the oral anticoagulant of choice has been a vitamin K antagonist (VKA) such as warfarin. Direct oral anticoagulants (DOACs; also known as non-vitamin K oral anticoagulants [NOACs]) which directly inhibit thrombin or factor Xa offer a number of practical advantages for both patient and prescriber and their use has been recommended as first-line treatment for stroke prevention in various European guidelines for the management of AF and stroke prevention (Klijn et al, 2019; Hindricks et al, 2021; Steffel et al, 2021). **[2023]**

5.7 Recommendations

A For people with ischaemic stroke or TIA and paroxysmal, persistent or permanent atrial fibrillation (AF: valvular or non-valvular) or atrial flutter, oral anticoagulation should be the standard long-term treatment for stroke prevention. Anticoagulant treatment:

- should not be given if brain imaging has identified significant haemorrhage;
- should not be commenced in people with severe hypertension (clinic blood pressure of 180/120 or higher), which should be treated first;
- may be considered for patients with moderate-to-severe stroke from 5-14 days after onset. Wherever possible these patients should be offered participation in a trial of the timing of initiation of anticoagulation after stroke. Aspirin 300 mg daily should be used in the meantime;
- should be considered for patients with mild stroke earlier than 5 days if the prescriber considers the benefits to outweigh the risk of early intracranial haemorrhage. Aspirin 300 mg daily should be used in the meantime;
- should be initiated within 14 days of onset of stroke in all those considered appropriate for secondary prevention;
- should be initiated immediately after a TIA once brain imaging has excluded haemorrhage, using an agent with a rapid onset (e.g. DOAC in non-valvular AF or subcutaneous low molecular weight heparin while initiating a VKA for those with valvular AF);

- should include measures to reduce bleeding risk, using a validated tool to identify modifiable risk factors. **[2023]**

B First-line treatment for people with ischaemic stroke or TIA due to non valvular AF should be anticoagulation with a DOAC. **[2023]**

C People with ischaemic stroke or TIA in sinus rhythm should not receive anticoagulation unless there is another indication. **[2023]**

D People with ischaemic stroke or TIA due to valvular/rheumatic AF or with mechanical heart valve replacement, and those with contraindications or intolerance to DOAC treatment, should receive anticoagulation with adjusted-dose warfarin (target INR 2.5, range 2.0 to 3.0) with a target time in the therapeutic range of greater than 72%. **[2023]**

E For people with cardioembolic TIA or stroke for whom treatment with anticoagulation is considered inappropriate because of a high risk of bleeding:

- antiplatelet treatment should not be used as an alternative when there are absolute contraindications to anticoagulation (e.g. undiagnosed bleeding);
- measures should be taken to reduce bleeding risk, using a validated tool to identify modifiable risk factors. If after intervention for relevant risk factors the bleeding risk is considered too high for anticoagulation, antiplatelet treatment should not be routinely used as an alternative;
- a left atrial appendage occlusion device may be considered as an alternative, provided the short-term peri-procedural use of antiplatelet therapy is an acceptable risk. **[2023]**

F People with cardioembolic TIA or stroke for whom treatment with anticoagulation is considered inappropriate for reasons other than the risk of bleeding may be considered for antiplatelet treatment to reduce the risk of recurrent vaso-occlusive disease. **[2023]**

G People who initially present with recurrent TIA or stroke should receive the same antithrombotic treatment as those who have had a single event. More intensive antiplatelet therapy or anticoagulation treatment should only be given as part of a clinical trial or in exceptional clinical circumstances. **[2023]**

5.7 Sources

A EAFT Study Group, 1993; Miller et al, 2012; Paciaroni et al, 2015; Gioia et al, 2016; Klijn et al, 2019; Hindricks et al, 2020; Labovitz et al, 2021; Steffel et al, 2021; De Marchis et al, 2022; Guideline Development Group consensus

B Guideline Development Group consensus

C De Schryver et al, 2012; Guideline Development Group consensus

D EAFT Study Group, 1993; Miller et al, 2012; Eikelboom et al, 2013; Ruff et al, 2014; Graham et al, 2015; Makam et al, 2018; Hirschl and Kundi, 2019; Hindricks et al, 2020; Shen et al, 2020; Steffel et al, 2021; Xu et al, 2021; Connolly et al, 2022

E Reddy et al, 2013; NICE, 2021a; Guideline Development Group consensus

F Benz et al, 2022

G Guideline Development Group consensus

5.7 Evidence to recommendations

Anticoagulant treatment is not more effective than antiplatelet therapy in people with non-cardioembolic ischaemic stroke or TIA and carries a greater risk of bleeding (Mohr et al, 2001; Sandercock et al, 2009). Neither is there evidence of greater efficacy for anticoagulation in embolic stroke of uncertain source (ESUS; Hart et al, 2018; Diener et al, 2019). A Cochrane review found no

evidence that early initiation of anticoagulation (within 2 weeks) in unselected patients with (all cause) ischaemic stroke reduced death or disability at or beyond 1 month. There was moderate grade evidence of large reductions in recurrent ischaemic stroke and pulmonary embolism with moderate increased rates of intracranial and extracranial bleeding (Wang et al, 2021b). **[2023]**

Intracranial haemorrhage (including haemorrhagic transformation of the acute infarct) should be assessed by brain imaging and taken into account when deciding whether and when to commence anticoagulation. Less severe degrees of haemorrhagic transformation may not necessarily be a contraindication to anticoagulation, an issue that will be clarified by ongoing randomised trials. In the case of patients with moderate-large volume infarction such as occurs often with cardioembolic stroke, there is concern that anticoagulation may increase the risk of haemorrhagic transformation of the infarct, and a delay of an arbitrary 2-week period has been recommended in previous editions of this guideline. Observational data have suggested a lower rate of the composite outcome of recurrent stroke, bleeding or symptomatic ICH when anticoagulation is started between days 4 and 14 compared to within 4 days of AF-associated stroke (Paciaroni et al, 2015). Cohort studies suggest that commencing anticoagulation with a DOAC may be safe between days 4 and 14 in patients with small- or medium-sized infarcts, at least (Gioia et al, 2016; Labovitz et al, 2021). Pooled data analysis of over 2,500 patients in European and Japanese prospective cohort studies showed no increase in ICH when a DOAC was started earlier (within 5 days) rather than later in people with AF-associated stroke (De Marchis et al, 2022). Such observational studies are vulnerable to selection bias and confounding by indication, but they suggest that for patients with minor stroke (e.g. NIHSS 0-3) and a lower risk of haemorrhagic transformation it may be appropriate to commence treatment sooner, at the discretion of the treating clinician. Recent evidence from the TIMING randomised trial showed early initiation of anticoagulation with a DOAC in people with AF-related stroke was non-inferior to delayed initiation, with no ICH in either group (Oldgren et al, 2022), although the majority of strokes in both groups were mild (median NIHSS of 4 in both groups). Definitive guidance, particularly in relation to moderate-severe stroke, must await the findings from RCTs addressing the issue of early versus late initiation in people with AF-related stroke that have either recently completed (e.g. ELAN: NCT03148457) or are ongoing (e.g. OPTIMAS: NCT03759938), and a planned individual participant data meta-analysis. **[2023]**

There is strong evidence for the use of anticoagulation for long-term secondary prevention of stroke in people with permanent AF (Saxena & Koudstaal, 2004), and the 12% risk of recurrent stroke per year (EAFT Study Group, 1993) substantially alters the balance of risk and benefit in favour of anticoagulation in almost every instance. In people with relative contraindications to anticoagulation identified through the use of a validated tool (e.g. HAS-BLED; (Pisters et al, 2010) or MICON-ICH; Best et al., 2021) it may be possible to intervene to reduce the bleeding risk through control of blood pressure, medication review, treatment of other conditions and multidisciplinary input to reduce risk of falls and improve medication adherence. Falls are associated with higher risk of injury and bleeding but the risk is very unlikely to outweigh the benefits of anticoagulation for stroke prevention (Man-Son-Hing et al, 1999) The safety and benefit of DOACs over VKA is maintained in people with a history of falls in the available RCT evidence (Steffel et al, 2016; Rao et al, 2018). Single-centre data also suggest a reduced risk of traumatic brain injury in people with a history of falls on DOACs compared with VKA (Scotti et al. 2019). Other imaging biomarkers that may influence the balance of risk and benefit from anticoagulation in individual patients are considered in Section 5.21 *Cerebral microbleeds*. **[2023]**

DOACs are rapidly replacing VKAs for secondary stroke prevention in people with non-valvular AF. These medications have a rapid onset of action, have fewer interactions with other medications and foodstuffs, do not require coagulation monitoring and are more patient-friendly. Meta-analysis of the four primary DOAC trials, RE-LY (Connolly et al, 2009), ROCKET AF (Patel et al, 2011), ARISTOTLE (Granger et al, 2011) and ENGAGE AF-TIMI 48 (Giugliano et al, 2013) involving over 70,000 patients, has shown significantly greater stroke and thromboembolic prevention (RR 0.81, 95% CI 0.73 to 0.91; p<0.0001), with a substantially reduced risk of intracranial bleeding compared to warfarin (Ruff et al, 2014). No age interaction was observed for efficacy or safety with any DOAC with the exception of

standard dose dabigatran and excess GI bleeding (Eikelboom et al, 2011; Graham et al, 2015). Subsequent meta-analyses with almost three million patient-years of observation have shown consistently better safety with DOACs compared to VKA (Hirschl & Kundi, 2019; Xu et al, 2021) and possibly better efficacy overall (Makam et al, 2018; Shen et al, 2020). **[2023]**

Given the high attributable risk of recurrent stroke in people with AF, unmodifiable relative contraindications (e.g. age, history of stroke) should not dissuade prescribers from the use of anticoagulation, as these patients are also at greatest of recurrent stroke (Olesen et al, 2011). Older people (aged 65 years or older) with AF have a reduced risk of stroke and thromboembolism on anticoagulant treatment compared to no treatment (relative risk 0.59, 95% CI 0.51 to 0.76, I^2 = 12.3%), and with a DOAC rather than a VKA (Bai et al, 2018). If, despite addressing modifiable risk factors for bleeding, the bleeding risk is still considered to be too high to use an anticoagulant safely, then aspirin cannot be regarded as a safer alternative, particularly among older patients (Mant et al, 2007). A current NICE guideline does not recommend the routine use of aspirin in these circumstances aside from when there are other indications unrelated to AF (NICE, 2021c). However, a recent systematic review and meta-analysis of antiplatelet use in patients with AF not treated with anticoagulation (Benz et al, 2022) identified an increased risk of major bleeding and intracerebral haemorrhage, and a reduced risk of myocardial infarction compared to no treatment, suggesting that in selected patients with a low or normal risk of bleeding and a higher risk of vaso-occlusive disease (such as in secondary vascular prevention), antiplatelet treatment may still be appropriate. There may be an emerging role for very low dose edoxaban in achieving an acceptable balance of overall benefit and risk in such patients (Okumura et al, 2020). **[2023]**

Bearing in mind that participants in all the original comparative trials of DOACs with warfarin had to be eligible for both treatments, the trials do not provide evidence regarding the safety or efficacy of DOACs in people for whom the bleeding risk is considered to be too high to safely use warfarin. However, such patients were included in the AVERROES trial comparing apixaban with aspirin (Connolly et al, 2011), and very low dose edoxaban (15 mg OD) in a high-risk elderly Japanese population appears to be effective and relatively safe (Okumura et al, 2020). **[2023]**

For selected patients with AF who cannot be treated with anticoagulation, it may be appropriate to consider a left atrial appendage occlusion device if the short-term use of antiplatelets/anticoagulation required following the procedure can be tolerated. In the PROTECT AF trial percutaneous left atrial appendage occlusion with a filter device (Watchman) was non-inferior to warfarin for stroke prevention in people with non-valvular AF (Holmes et al, 2009; Reddy et al, 2013). Device implantation was accompanied by warfarin anticoagulation for the first 45 days. No trials have compared left atrial appendage occlusion with DOAC treatment. **[2023]**

For people with mechanical heart valves or rheumatic heart disease-associated AF, VKA remains the anticoagulant of choice as DOACs have been shown to be inferior in these situations (Eikelboom et al, 2013; Connolly et al, 2022). There is evidence that combining antiplatelet medication with warfarin reduces the risk of thromboembolic complications, but with an increased risk of bleeding (Little & Massel, 2003; Dentali et al, 2007). Apart from some high-risk patients with mechanical heart valves and patients in AF requiring antiplatelet therapy after coronary stenting, there is no evidence that combining antiplatelet medication with warfarin is beneficial, but there is clear evidence of harm (Hart et al, 2005). **[2023]**

5.7 Implications

This guideline is likely to lead to an increase in the prescribing of DOACs, which are expensive but considered cost-effective by NICE and SMC, particularly when used for secondary prevention where the attributable risk of stroke is several times higher than in primary prevention. Management of patients with TIA or ischaemic stroke in association with AF requires an interdisciplinary team approach to stroke

prevention with close collaboration between stroke physicians/neurologists, cardiologists, general practitioners, pharmacists, specialist nurses. **[2023]**

5.8 Other risk factors

In about a quarter of people with stroke, and more commonly in younger age groups, no cause is evident on initial investigation. Other causes that should be considered include paroxysmal or occult atrial fibrillation (PAF), intracranial arterial disease, cervical artery dissection, antiphospholipid syndrome and other prothrombotic conditions, and patent foramen ovale (PFO). In younger people in whom no cause is identified with a history of venous or arterial thrombosis or early miscarriage, a thrombophilia screen should be performed. **[2016]**

5.9 Paroxysmal atrial fibrillation

All forms of atrial fibrillation (AF) represent a potentially significant risk for stroke. AF may be intermittent and not immediately evident. It can be classified as paroxysmal (PAF) if self-limiting, or persistent if not terminating spontaneously or lasting more than a week. There is no consensus concerning the shortest duration of PAF that constitutes a risk of cardioembolism. Secondary prevention with anticoagulation is the recommended intervention after ischaemic stroke or TIA in patients with AF or PAF. **[2023]**

5.9 Recommendations

A Patients with ischaemic stroke or TIA not already diagnosed with atrial fibrillation or flutter should undergo an initial period of cardiac monitoring for a minimum of 24 hours if they are appropriate for anticoagulation. **[2023]**

B Patients with ischaemic stroke or TIA, in whom no other cause of stroke has been found after comprehensive neurovascular investigation (stroke of undetermined aetiology or 'cryptogenic' stroke) and in whom a cardioembolic cause is suspected, should be considered for more prolonged sequential or continuous cardiac rhythm monitoring with an external patch, wearable recorder or implantable loop recorder if they are appropriate for anticoagulation. **[2023]**

5.9 Sources

A Kishore et al, 2014; Guideline Development Group consensus

B Kang et al, 2003; Grond et al, 2013, Higgins et al, 2013; Gladstone et al, 2014; Sanna et al, 2014; Sposato et al, 2015; Edwards et al, 2020; Buck et al, 2021; Noubiap et al, 2021; Rubiera et al, 2022; Guideline Development Group consensus

5.9 Evidence to recommendations

AF may not be detected by a standard 12-lead ECG and may require more prolonged monitoring. In a systematic review involving 5038 participants with recent stroke or TIA who had at least 12 hours of monitoring, the detection rate for new AF was 11.5% (Kishore et al, 2014). Rates of detection were higher in selected patients (e.g. by age, stroke pattern, pre-screening risk scores). In general, the more prolonged the period of ECG monitoring the greater the likelihood of detection (Grond et al, 2013; Higgins et al, 2013; Gladstone et al, 2014; Sanna et al, 2014). A sequential approach to investigation, involving four incrementally more prolonged phases of monitoring, provided detection rates of AF ranging from 7.7% to 16.9%; the overall AF detection rate was 23.7% after all phases (Sposato et al, 2015). **[2023]**

Implantable loop recorders (ILRs) have been shown to be superior to short-term external monitoring in detecting AF and could lead to better stroke reduction through the greater uptake of anticoagulation following a stroke or TIA. The use of ILRs seems superior to external monitoring strategies to detect AF in stroke of unknown aetiology or 'cryptogenic' stroke - 15.3 vs 4.7% at 12 months (Buck et al, 2021), with AF detected in 22.8% at 12 months with ILRs in another study (Noubiap et al, 2021). In a meta-analysis of three trials using ILRs compared to conventional monitoring, the 12-month detection rate for AF was 13% v. 2.4% and stroke or TIA occurred in 7% of participants with an ILR-based strategy v. 9% with usual care (odds ratio 0.8, 95% CI 0.5 to 1.2; Ko et al, 2022). ILR-monitored patients were also observed to have a reduced relative risk of stroke or TIA (0.49, 95% CI, 0.30 to0.81) in one meta-analysis (Tsivgoulis et al, 2019), but a subsequent larger meta-analysis of eight studies (five RCTs, three observational; 2,994 participants) by the same group showed that while patients with an ILR were more likely to receive anticoagulation, a reduction in stroke was not seen in the RCTs (Tsivgoulis et al, 2022). It therefore remains uncertain whether an ILR-based investigation strategy reduces stroke in an unselected population of patients after stroke or TIA. **[2023]**

The rate of detection of AF with ILRs at 12 months varies widely in reported studies (range 12-25%) and compared to conventional strategies it may be more cost-effective in patients with cryptogenic stroke with no AF detected after 24 hours of external monitoring (Edwards et al, 2020). Monitoring using smart digital technologies such as wearables and smartphone recording may be superior to traditional 'holter' monitoring and may be an alternative method where an ILR is not feasible or desired by patients (Koh et al, 2021). **[2023]**

In selecting patients for prolonged cardiac monitoring and/or ILR insertion those with stroke of undetermined aetiology ('cryptogenic') are more likely to have PAF (Kishore et al, 2014). Likewise, certain patterns of ischaemic change seen on brain imaging increase the likelihood of an underlying cardioembolic source such as cortical/subcortical infarcts or multiple lesions in anterior and posterior circulations and/or both cerebral hemispheres (Kang et al, 2003). **[2016]**

5.9 Implications

These recommendations are likely to increase the number of patients requiring prolonged cardiac rhythm monitoring and ILR insertion with implications for cardiac procedural and monitoring resources. Paroxysmal AF after stroke or TIA warrants treatment with anticoagulation or consideration for left atrial appendage occlusion where anticoagulation is contraindicated. Close collaboration between stroke physicians/neurologists and cardiologists, through a cardiology-stroke multidisciplinary meeting, can facilitate decision making in challenging cases, and agreement on local protocols for ILR implantation and explantation, and monitoring and alert-response procedures. **[2023]**

5.10 Patent foramen ovale

A patent foramen ovale (PFO) may predispose people to a TIA or stroke by acting as a conduit for paradoxical embolism of thrombus, fat or air from the venous into the arterial circulation, or by clot formation in the PFO channel itself. A PFO may be found in at least a quarter of the general population, but can be identified on contrast echocardiography in 40-56% of patients under 55 years old with ischaemic stroke of otherwise undetermined aetiology (Mesa et al, 2003; McCabe & Rakhit, 2007). A PFO is probably more relevant to the aetiology of stroke in younger patients (under 55 years), especially if there is a clear history of the symptoms occurring during or shortly after a Valsalva manoeuvre, in the setting of a deep venous thrombosis, or where there are recurrent strokes in different arterial territories of otherwise undetermined aetiology. However, a PFO may also be relevant to the aetiology of ischaemic stroke in older patients, with a higher prevalence of PFO observed in patients older than 55 years of age with ischaemic stroke of undetermined aetiology (28.3%) than in patients with stroke of known aetiology (12%; Handke et al, 2007). **[2023]**

5.10 Recommendations

A People with ischaemic stroke or TIA and a PFO should receive optimal secondary prevention treatment, including antiplatelet therapy, treatment for high blood pressure, lipid-lowering therapy and lifestyle modification. Anticoagulation is not recommended unless there is another recognised indication. **[2023]**

B Selected people below the age of 60 with ischaemic stroke or TIA of otherwise undetermined aetiology, in association with a PFO and a right-to-left shunt or an atrial septal aneurysm, should be considered for endovascular PFO device closure within six months of the index event to prevent recurrent stroke. This decision should be made after careful consideration of the benefits and risks by a multidisciplinary team including the patient's physician and the cardiologist performing the procedure. The balance of risk and benefit from the procedure, including the risk of atrial fibrillation and other recognised peri-procedural complications should be fully considered and explained to the person with stroke. **[2023]**

C People older than 60 years with ischaemic stroke or TIA of otherwise undetermined aetiology and a PFO should preferably be offered closure in the context of a clinical trial or prospective registry. **[2023]**

5.10 Sources

A Homma et al, 2002; Guideline Development Group consensus

B, C Furlan et al, 2012; Meier at al, 2013; Søndergaard et al, 2017; Saver et al, 2017; Mas et al, 2017; Lee at al, 2018; Guideline Development Group consensus

5.10 Evidence to recommendations

In some people with stroke or TIA, a PFO will be an incidental finding and optimal medical therapy and secondary prevention strategies alone should be used. There is no evidence that anticoagulation is superior to antiplatelet therapy in patients with stroke of undetermined aetiology in association with a PFO (Homma et al, 2002). Three multicentre RCTs did not show a significant benefit of PFO closure over medical therapy alone, based on an intention-to-treat analysis (Furlan et al, 2012; Carroll et al, 2013; Meier et al, 2013). However, three subsequent RCTs (Mas et al, 2017; Søndergaard et al, 2017; Lee et al, 2018), and extended follow-up data from the RESPECT trial (Saver et al, 2017) showed a significant reduction in recurrent stroke risk in patients allocated to endovascular PFO closure compared with medical therapy alone, most of whom were older than 60 years of age. It is important to note that these more recent trials which showed a benefit of PFO closure over medical therapy alone only included patients with a PFO and a large right-to-left shunt or an atrial septal aneurysm (Mas et al, 2017) or a PFO with a right-to-left shunt (Søndergaard et al, 2017; Lee et al, 2018). **[2023]**

Most of the RCTs described above excluded patients over the age of 60 years, so it is not known whether the observed benefit from PFO closure is applicable to older patients with ischaemic stroke of otherwise undetermined aetiology. Furthermore, there is insufficient evidence to address whether oral anticoagulation alone (either with a VKA or DOAC) is inferior, equivalent or superior to PFO closure, and more research is needed in this area. **[2023]**

PFO closure is associated with an approximately five-fold increase in the risk of developing AF (5-6.6% following closure), although the duration and nature of the resultant AF is not fully understood. Implantation is also associated with other peri-procedural risks, including inadequate PFO closure, implantation failure, pericardial effusion, and pseudoaneurysm formation. **[2023]**

5.10 Implications

These recommendations are likely to increase the number of patients referred for further investigation and treatment, and stroke services should establish regular multidisciplinary meetings with their colleagues in cardiology to consider and appropriately select patients for further investigation and consideration of endovascular device closure. Further research is needed to clarify optimal secondary preventative strategies in patients with a PFO and a co-existent thrombophilia as such patients were excluded from the definitive trials of PFO closure. **[2023]**

5.11 Other cardioembolism

Between 20-30% of ischaemic strokes can be attributed to cardioembolism (Sandercock et al, 1989; Kolominsky-Rabas et al, 2001), with the majority of these accounted for by AF. A variety of other cardiac pathologies have been implicated, often categorised as high risk (myocardial infarction, mitral stenosis, left ventricular aneurysm or thrombus, mechanical valve prosthesis) and low/uncertain risk (atrial septal aneurysm, mitral annular calcification, aortic stenosis). The value of echocardiography in people with TIA and stroke depends upon the assumption that the risk of recurrent stroke can be modified by treatment which would otherwise not have been considered, should one of these pathologies be detected. Identifying a putative cardioembolic source does not prove a cardioembolic mechanism, particularly in individuals with competing risk factors. With the notable exception of AF, it is unclear for the majority of potential cardioembolic pathologies what risk of stroke recurrence they pose, whether or not intervention genuinely lessens this risk and if so, whether the benefit outweighs the risk associated with intervention. **[2023]**

5.11 Recommendation

A People with stroke or TIA should be investigated with transthoracic echocardiography if the detection of a structural cardiac abnormality would prompt a change of management and if they have:

- clinical or ECG findings suggestive of structural cardiac disease that would require assessment in its own right, or
- unexplained stroke or TIA, especially if other brain imaging features suggestive of cardioembolism are present. **[2016]**

5.11 Sources

A Holmes et al, 2014; Working Party consensus

5.11 Evidence to recommendations

A systematic review and economic evaluation sought to evaluate the cost-effectiveness of routine echocardiography in the assessment of individuals presenting with first-ever ischaemic stroke or TIA (Holmes et al, 2014). Clinically identifiable cardiac pathologies were excluded. Across a range of cardiac pathologies, transthoracic echocardiography (TTE) was found to be less sensitive compared with transoesophageal (TOE), with both demonstrating high specificity. In consultation with an expert panel it was determined that only the identification of left atrial and left ventricular thrombus by echocardiography would alter patient management. A median prevalence of 0.8% was reported for left ventricular thrombus and of 1.4% for left atrial thrombus. Considerable variability was found for the reported prevalence of atrial septal aneurysm (median 9.3%, range 0.4-28%) and PFO (median 17%, range 0.25-73%). Economic analysis in the UK concluded that TTE is a cost-effective use of healthcare resources compared with TOE, when clinicians deem it the most appropriate test, and might be applied primarily to people with stroke of undetermined aetiology if they are also candidates for oral anticoagulation. Certain patterns of ischaemic change seen on brain imaging increase the suspicion of a

cardioembolic source such as cortico-subcortical infarcts or multiple lesions in anterior and posterior circulations and/or both cerebral hemispheres (Kang et al, 2003). **[2016]**

5.12 Vertebral artery disease

Stroke in the vertebrobasilar territory accounts for 20% of all strokes and is more often associated with corresponding large artery stenosis than is the case for carotid territory stroke (Marquardt et al, 2009). Pooled individual patient data from two prospective studies found a 90-day risk of stroke after vertebrobasilar stroke or TIA of 9.6% in those with vertebrobasilar stenosis and 2.8% in those without, with the highest risk (13.9%) if the stenosis was intracranial (Gulli et al, 2013). **[2016]**

5.12 Recommendation

A People with ischaemic stroke or TIA and symptomatic vertebral artery stenosis should receive optimal secondary prevention including antithrombotic therapy, blood pressure treatment, lipid-lowering therapy and lifestyle modification. Angioplasty and stenting of the vertebral artery should only be offered in the context of a clinical trial. **[2016]**

5.12 Sources

A Compter et al, 2015; Working Party consensus

5.12 Evidence to recommendations

The open randomised phase 2 study VAST compared stenting with medical management in patients with recently symptomatic vertebral artery stenosis of more than 50% (Compter et al, 2015). The study was terminated early, after enrolment of 115 patients. There were no significant differences between the two groups, and based on the low stroke recurrence rate seen in the trial, a conclusive phase 3 trial would need to include 9,500 patients. A subsequent pre-planned individual participant data meta-analysis of three randomised trials including 354 patients did not show a significant benefit from extracranial or intracranial vertebral artery stenting (Markus et al, 2019). There is therefore no evidence to suggest that revascularisation for people with vertebral artery stenosis (stenting, endarterectomy or reconstruction/transposition) is superior to best medical therapy. **[2016]**

5.13 Intracranial artery stenosis

In Western populations, atherosclerotic stenosis of the large intracranial arteries is found in about 40% of patients with ischaemic stroke and is likely to be causative in about 7% (Sacco et al, 1995; Mazighi et al, 2008). Significantly higher rates are seen in African-Americans, and in Asian populations it is the dominant pathology. **[2016]**

5.13 Recommendation

A People with ischaemic stroke or TIA due to severe symptomatic intracranial stenosis should be offered dual antiplatelet therapy with aspirin and clopidogrel for the first three months in addition to optimal secondary prevention including blood pressure treatment, lipid-lowering therapy and lifestyle modification. Endovascular or surgical intervention should only be offered in the context of a clinical trial. **[2016]**

5.13 Sources

A Chimowitz et al 2005, 2011; Working Party consensus

5.13 Evidence to recommendations

The recurrent stroke rate in people with intracranial artery stenosis is high; in the WASID RCT comparing aspirin with warfarin in people with greater than 50% stenosis of intracranial arteries, those on aspirin had a 22% risk of stroke or death during a mean follow-up of 1.8 years (Chimowitz et al, 2005). This trial confirmed an association between increasing degree of intracranial stenosis and stroke risk and showed that the development of an effective collateral circulation is protective (Liebeskind et al, 2011). Warfarin anticoagulation was no more effective than aspirin for stroke prevention in WASID, including for the subgroup enrolled with stroke whilst on antithrombotic therapy, but was associated with significantly more adverse events. **[2016]**

The SAMMPRIS trial (Chimowitz et al, 2011) compared angioplasty and stenting of intracranial stenosis of greater than 70% with medical management, including an initial 90 days of dual antiplatelet therapy with clopidogrel plus aspirin. The 30-day rate of stroke or death in the SAMMPRIS control group was lower than in WASID (5.8% v. 10.7%) suggesting dual antiplatelet therapy may be superior to aspirin alone. Targeted risk factor modification, particularly BP and LDL-cholesterol reduction, was also more frequently achieved in SAMMPRIS, and the trial found that medical management was superior to angioplasty and stenting with the difference maintained over a median follow-up of 32 months (Derdeyn et al, 2014). The VISSIT trial exploring the effect of balloon-expandable stents in people with symptomatic intracranial stenosis was halted following the results of SAMMPRIS, with analysis also demonstrating an increased risk of recurrent stroke with endovascular intervention (Zaidat et al, 2015). No comparison of dual antiplatelet therapy with clopidogrel monotherapy in this setting has yet been conducted. **[2016]**

5.14 Oral contraception and hormone replacement therapy

The observation that stroke tends to affect women at a later age than men raises the possibility that female sex hormones, and specifically oestrogens, might protect against vascular disease. This was initially supported by observational studies suggesting hormone replacement therapy (HRT) might reduce the risk of stroke in postmenopausal women. There is now evidence that oestrogen actually increases the risk of cardiovascular events including ischaemic stroke both when used by younger women as the combined oral contraceptive (COC) and by postmenopausal women as HRT. **[2016]**

5.14.1 Oral contraception

5.14.1 Recommendation

A Premenopausal women with stroke and TIA should not be offered the combined oral contraceptive pill. Alternative hormonal (progestogen-only) and non-hormonal contraceptive methods should be considered instead. **[2016]**

5.14.1 Source

A Working Party consensus

5.14.1 Evidence to recommendations

No studies have assessed how the COC modifies the risk of recurrent stroke or TIA. Studies in women with no history of stroke or TIA indicate that there may be an approximate doubling of the relative risk of ischaemic stroke associated with use of combined (low-dose) oestrogen oral contraception. A Cochrane review of one cohort study and 23 case-control studies compared the risk of myocardial infarction or ischaemic stroke in users and non-users of COC (Roach et al, 2015). The relative risk of ischaemic stroke was 1.7 for COC users and the risk increased according to the dose of oestrogen. The

risk was not influenced by the progestogen used. It has been estimated that for 10,000 women using a 20 µg oestrogen COC for 1 year, 2 will have an arterial thrombosis (Lidegaard et al, 2012). Pregnancy is associated with a risk of stroke of about 3 per 10,000 deliveries (James et al, 2005). **[2016]**

A meta-analysis of six case-control studies comprising 3,091 cases and 11,385 controls found no association between progestogen-only contraceptive (POC) use and stroke risk (Chakhtoura et al, 2009). The analysis provides limited support for use of the POC in situations where hormonal contraception is necessary, but the full range of contraceptive methods (hormonal and non-hormonal) should be considered. **[2016]**

5.14.2 Hormone replacement therapy

5.14.2 Recommendations

A Post-menopausal women with ischaemic stroke or TIA who wish to start or continue hormone replacement therapy should receive advice based on the overall balance of risk and benefit, taking account of the woman's preferences. **[2016]**

B Post-menopausal women with ischaemic stroke or TIA should not be offered hormone replacement therapy for secondary vascular prevention. **[2016]**

5.14.2 Sources

A Working Party consensus

B Boardman et al, 2015

5.14.2 Evidence to recommendations

Treatment decisions concerning HRT must balance clinical need (treatment of premature menopause or relief of menopausal symptoms) against a number of different risks. A Cochrane review of 19 RCTs (40,410 participants) comparing hormonal therapy with placebo or no treatment found no benefit in all-cause mortality, cardiovascular death, non-fatal myocardial infarction, angina or revascularisation (Boardman et al, 2015). An increased risk of stroke was found in primary prevention studies, but the effect was not significant in secondary prevention studies (5,172 participants in five studies). For the subgroup of women starting HRT within a mean of 10 years after the menopause or who were less than 60 years of age, treatment was associated with a significant all cause mortality benefit and coronary heart disease benefit compared with placebo, although with a persisting risk of venous thromboembolism and a trend towards increased risk of stroke (9,838 participants in three studies). In a nested case-control study of 15,710 cases of stroke matched to 59,958 controls from the UK General Practice Research Database, the risk of stroke was not increased with use of low-dose oestrogen patches (alone or with progestogen) when compared with no use in post-menopausal women (Renoux et al, 2010). The stroke rate was increased with use of high-dose patches. **[2016]**

5.15 Obstructive sleep apnoea

There is a prevalence of obstructive sleep apnoea (OSA) of between 30 and 70% in people with ischaemic or haemorrhagic stroke, depending upon the diagnostic criteria used (Johnson & Johnson, 2010). Not only are typical cardiovascular risk factors such as hypertension, hyperlipidaemia, diabetes, smoking, AF and obesity more prevalent in people with OSA, but OSA itself is an independent risk factor for stroke (Loke et al, 2012). **[2016]**

5.15 Recommendation

A People with stroke or TIA should be screened for obstructive sleep apnoea with a valid clinical screening tool. People who screen positive who are suspected of having sleep

apnoea should be referred for specialist respiratory/sleep medicine assessment. **[2016]**

5.15 Source

A Working Party consensus

5.15 Evidence to recommendations

People with stroke and OSA have been shown to have worse functional outcomes, longer hospitalisation and an increased risk of stroke recurrence (Kaneko et al, 2003; Rola et al, 2008). Treatment with continuous positive airways pressure (CPAP) has been shown to favourably modify cardiovascular risk factors such as hypertension (Marin et al, 2012) and in a prospective observational study to reduce the risk of recurrent cardiovascular events (Martinez-Garcia et al, 2012). Several small RCTs have failed to confirm a reduction in cardiovascular events with CPAP (Sandberg et al, 2001; Hsu et al, 2006; Bravata et al, 2011; Parra et al, 2011; Ryan et al, 2011; Parra et al, 2015). Whilst uncertainty remains concerning stroke recurrence, there are other benefits from recognising and treating OSA and given the high reported prevalence, presentation with stroke provides an opportunity to screen patients for OSA. As in the general population, patients with stroke and OSA may not declare a classical history of severe snoring and subjective daytime sleepiness. The use of a simple clinical screening tool (such as the 'STOP-BANG' questionnaire) in people with stroke or TIA will identify those who are likely to benefit from further specialist assessment (Silva et al, 2011). **[2016]**

5.15 Implications

There will be resource implications for sleep services from an increased awareness of OSA among people with stroke or TIA. **[2016]**

5.16 Antiphospholipid syndrome

Antiphospholipid syndrome (APS) is an autoimmune disorder which may occur with or without associated rheumatic disease, particularly systemic lupus erythematosus. Patients with APS are at increased risk of venous and arterial thrombotic events, including ischaemic stroke. Pregnancies in women with APS have an increased risk of miscarriage, intrauterine growth retardation and premature birth (Cervera et al, 2015). The condition is diagnosed in individuals with a history of venous or arterial thrombosis and/or pregnancy-related morbidity in the presence of persistent antiphospholipid antibodies. A finding of antiphospholipid antibodies is more likely to be of relevance in people younger than 50 years in whom other risk factors for stroke have been excluded. **[2016]**

5.16 Recommendations

A People with ischaemic stroke or TIA in whom other conditions such as atrial fibrillation and large or small vessel atherosclerotic disease have been excluded should be investigated for antiphospholipid syndrome (with IgG and IgM anticardiolipin ELISA and lupus anticoagulant), particularly if the person:

- is under 50 years of age;
- has any autoimmune rheumatic disease, particularly systemic lupus erythematosus;
- has a history of one or more venous thromboses;
- has a history of recurrent first trimester pregnancy loss or at least one late pregnancy loss (second or third trimester). **[2016]**

B People with antiphospholipid syndrome who have an ischaemic stroke or TIA:

- should be managed acutely in the same way as people without antiphospholipid syndrome;
- should have decisions on long-term secondary prevention made on an individual basis

in conjunction with appropriate specialists including haematology and/or rheumatology. **[2016]**

5.16 Source

A, B Working Party consensus

5.16 Evidence to recommendations

There is uncertainty concerning the most effective strategy to prevent arterial thrombotic events in people with APS. Recommendations include long-term low-dose aspirin, low-, medium- and high-intensity warfarin and the combination of aspirin and warfarin. There is little RCT evidence and those RCTs that are available have either not shown an advantage for any particular strategy (Crowther et al, 2003; Levine et al, 2004; Finazzi et al, 2005) or have included only very small numbers (Okuma et al, 2010). Until better evidence becomes available, the Working Party recommends that treatment decisions should be made on an individual basis, ideally involving multispecialty input. **[2016]**

5.17 Insulin resistance

Insulin resistance is a component of the metabolic syndrome in which a diminished target cell response to insulin results in a compensatory increase in insulin secretion to maintain normoglycaemia. The resulting hyperinsulinaemia leads to complex metabolic changes and the development of hypertension, central obesity, glucose intolerance, elevated triglyceride levels and reduced HDL-cholesterol. Genetic predisposition, ageing, oversupply of dietary lipid, sedentary lifestyle and central obesity are associated with the development of insulin resistance. It is estimated that about half of non-diabetic people with stroke or TIA have insulin resistance (Kernan et al, 2003), an independent risk factor for ischaemic stroke (Rundek et al, 2010; Thacker et al, 2011). Insulin resistance may be a modifiable target for secondary stroke prevention. Insulin-sensitising thiazolidinedione ('glitazone') medication have been developed to treat diabetes, with pioglitazone the only medicine in this class currently licensed in the UK and Ireland. **[2016]**

5.17 Recommendation

A People with stroke or TIA should not receive pioglitazone for secondary vascular prevention. **[2016]**

5.17 Source

A Kernan et al, 2016

5.17 Evidence to recommendations

The PROactive study (Dormandy et al, 2005) assessed secondary prevention with pioglitazone in people with diabetes and prior vascular disease and was neutral in terms of the primary outcome of major vascular events, but did show a reduction in a secondary outcome that included stroke. A subsequent Cochrane review (Liu & Wang, 2015) found that glitazones might reduce recurrent stroke in people with stroke or TIA. The IRIS trial (Kernan et al, 2016) compared pioglitazone with placebo in 3876 non-diabetic participants with insulin resistance and a history of stroke or TIA, excluding those with diabetes, structural heart disease or congestive cardiac failure. The primary outcome (first fatal/non-fatal stroke or non-fatal MI) occurred in 9% with pioglitazone and 11.8% with control over 4.8 years of follow-up. Progression to diabetes was also reduced, but weight gain, oedema and bone fractures were all significantly increased with pioglitazone. Based on these results, for every 100 patients treated with pioglitazone for about 5 years, 3 fewer would suffer stroke or MI; 4 fewer would develop diabetes mellitus; 2 more would suffer bone fracture requiring hospitalisation; 18 more would gain >4.5 kg in weight, and 11 more would have new or worsening peripheral oedema. The study did not report quality

of life outcomes and more evidence would be required before glitazone treatment can be recommended routinely for patients with insulin resistance. Targeting lifestyle modification, particularly exercise and diet, appears to be a safe and effective approach for reducing insulin resistance and progression to diabetes (Knowler et al, 2002; Lindstrom et al, 2006; Ivey et al, 2007). **[2016]**

5.18 Fabry disease

Fabry disease is a multi-system disorder in which reduced activity of the enzyme α-galactosidase leads to the accumulation of glycolipid in various organs damaging tissues, particularly the skin, eye, kidney, heart, brain, and peripheral nervous system. The disorder is X-linked, affecting 1 in 40,000-60,000 males; females can also be affected. Onset is usually in childhood or adolescence, typical symptoms and signs including episodes of severe pain in the extremities (acroparesthesias), cutaneous vascular lesions typically more pronounced in the bathing-trunk distribution (angiokeratomas), decreased sweating, corneal opacities, tinnitus, hearing loss and proteinuria. Premature cardiovascular disease occurs as well as progressive deterioration in renal function leading to end-stage renal disease. Cerebrovascular manifestations primarily relate to small vessel disease and may be ischaemic or haemorrhagic. **[2016]**

5.18 Recommendations

A Young people with stroke or TIA should be investigated for Fabry disease if they have suggestive clinical features such as acroparesthesias, angiokeratomas, sweating abnormalities, corneal opacities, unexplained renal insufficiency or a family history suggesting the condition. **[2016]**

B People with stroke or TIA and a diagnosis of Fabry disease should receive optimal secondary prevention and be referred to specialist genetic and metabolic services for advice on other aspects of care including the provision of enzyme replacement therapy. **[2016]**

5.18 Source

A, B Working Party consensus

5.18 Evidence to recommendations

Early diagnosis allows timely screening for secondary complications, treatment to delay renal and cardiovascular effects, lifestyle advice particularly in relation to smoking cessation, and genetic counselling. The diagnosis should be considered in people with any of the clinical features above, and can be confirmed by tests measuring α-galactosidase activity and/or with molecular genetic testing for mutations of the GLA gene. Treatment with α-galactosidase A enzyme replacement therapy has been available for some years, but long-term effectiveness in preventing cerebrovascular complications has not so far been demonstrated (Rombach et al, 2013; Anderson et al, 2014; Germain et al, 2015). **[2016]**

5.19 Cerebral amyloid angiopathy

Sporadic cerebral amyloid angiopathy (CAA), a common age-related cerebral small vessel disease, is an important cause of lobar intracerebral haemorrhage (ICH), particularly in older people. It is caused by the deposition of amyloid-beta peptide in small cortical and leptomeningeal vessels. CAA can be diagnosed as a probable cause of lobar ICH with good accuracy using brain imaging as described in the MRI-based Boston criteria (Linn et al, 2010); more recently CT-based Edinburgh criteria have also been proposed (Rodrigues et al, 2018). The risk of recurrent ICH in patients with CAA is approximately 7% per year (Charidimou et al, 2017) in comparison to about 1% for ICH associated with arteriolosclerosis. However, patients with ICH are also at risk of vaso-occlusive cardiovascular diseases including ischaemic stroke, which is associated with AF in people with ICH (Li et al, 2021). **[2023]**

5.19 Recommendations

A Patients with lobar ICH associated with probable CAA should be considered for blood pressure lowering to below a long-term target of 130/80 mmHg. Wherever possible patients should be offered participation in a randomised trial of blood pressure-lowering treatment. **[2023]**

B Patients with lobar ICH associated with probable CAA may be considered for antiplatelet therapy for the secondary prevention of vaso-occlusive events, but wherever possible patients should be offered participation in a randomised trial. If participation in a randomised trial is not possible then clinicians should make an individualised decision based on estimates of the future risks of recurrent ICH and vaso-occlusive events. **[2023]**

C Patients with lobar ICH associated with probable CAA and AF may be considered for oral anticoagulation for stroke prevention, but wherever possible patients should be offered participation in a randomised trial. If participation in a randomised trial is not possible then clinicians should make an individualised decision based on estimates of the future risks of recurrent ICH and vaso-occlusive events. **[2023]**

D Patients with lobar ICH associated with probable CAA and AF may be considered for a left atrial appendage occlusion (LAAO) device, but wherever possible patients should be offered participation in a randomised trial. If participation in a randomised trial is not possible then LAAO may be considered based on an estimation of the future risks of recurrent ICH and vaso-occlusive events. **[2023]**

5.19 Sources

A Rodrigues et al, 2018; Charidimou et al, 2017

B Arima et al, 2010; Linn et al, 2010

C Linn et al, 2010; SoSTART Collaboration, 2021; Schreuder et al, 2021

D Linn et al, 2010; Biffi et al, 2015

5.19 Evidence to recommendations

There are few directly relevant randomised trials relating to secondary prevention of recurrent ICH, and none specifically in people with CAA. In the PROGRESS trial (2001) which included 6,105 people with ischaemic stroke or ICH, treatment with 2-4 mg perindopril for all participants (plus 2-2.5 mg indapamide for those with neither an indication for nor a contraindication to a diuretic) reduced blood pressure (BP) by an average of 12 mmHg systolic and 5 mmHg diastolic, lowering the risks of first and recurrent ICH (adjusted HR 0.44 [95% CI 0.28 to0.69] and 0.37 [95% CI 0.10 to 1.38] respectively; PROGRESS Collaborative Group, 2001). Patients with prior ICH derived the greatest benefit, and the risk of stroke decreased with lower follow-up BP without evidence of a lower threshold for hazard. In a PROGRESS subgroup analysis, intensive BP treatment reduced the relative risk of probable CAA-related ICH by 77% (95% CI 19 to 93%), that of probable hypertension-related ICH by 46% (95% CI 4 to 69%), and that of unclassified ICH by 43% (95% CI -5 to 69%) There are few directly relevant randomised trials relating to secondary prevention of recurrent ICH, and none specifically in people with CAA. In the PROGRESS trial (2001) which included 6,105 people with ischaemic stroke or ICH, treatment with 2-4 mg perindopril for all participants (plus 2-2.5 mg indapamide for those with neither an indication for nor a contraindication to a diuretic) reduced blood pressure (BP) by an average of 12 mmHg systolic and 5 mmHg diastolic, lowering the risks of first and recurrent ICH (adjusted HR 0.44 [95% CI 0.28 to0.69] and 0.37 [95% CI 0.10 to 1.38] respectively; PROGRESS Collaborative Group, 2001). Patients with prior ICH derived the greatest benefit, and the risk of stroke decreased with lower follow-up BP without evidence of a lower threshold for hazard. In a PROGRESS subgroup analysis, intensive BP treatment reduced the relative risk of probable CAA-related ICH by 77% (95% CI 19 to 93%), that of probable hypertension-related ICH by 46% (95% CI 4 to 69%), and that of unclassified ICH by 43% (95% CI -5 to 69%) (Arima et

al, 2010). An observational cohort study in 1,145 people after ICH found that higher BP during follow-up was associated with increased risk of lobar ICH recurrence (HR 1.33 per 10 mmHg increase [95% CI 1.02 to 1.76]) and that the risk of recurrent ICH increased with systolic BP above 120 mmHg and diastolic above 80 mmHg (Biffi et al, 2015). However, such observational studies are subject to selection and severity bias and confounding by indication. Further RCTs of intensive BP reduction after lobar ICH probably or possibly due to CAA are required. **[2023]**

The RESTART trial in people after ICH associated with antithrombotic medication use did not find evidence for hazard of antiplatelet treatment in the small subgroup of participants with lobar ICH probably due to CAA, defined by the Edinburgh CT-based or Boston MRI-based criteria (Rodrigues et al, 2018; Al-Shahi Salman et al, 2019), but estimates in this subgroup were imprecise due to the limited sample size. In an observational study, resumption of oral anticoagulation (OAC) after lobar ICH attributed to CAA was associated with decreased mortality and a more favourable functional outcome, but such observational studies are subject to selection and severity bias and confounding by indication (Biffi et al, 2017). Two pilot-phase randomised trials (APACHE-AF and SoSTART) of OAC for AF after ICH (Schreuder et al, 2021; SoSTART Collaboration, 2021) did not find evidence of benefit or harm from OAC, but their sample sizes were insufficient to investigate the effect of OAC in the subgroup of patients with lobar ICH probably due to CAA, so further RCTs are ongoing (e.g. ENRICH-AF NCT03950076 and PRESTIGE-AF NCT03996772). Left atrial appendage occlusion with short duration antithrombotic therapy might be an alternative to OAC in ICH associated with CAA, and this is being investigated in an RCT (e.g. STROKECLOSE NCT02830152). **[2023]**

There are no proven disease modifying therapies for CAA. In a small RCT the monoclonal antibody ponezumab did not show benefit on vascular reactivity in patients with probable CAA (Leurent et al, 2019). **[2023]**

5.20 CADASIL

CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy) is caused by mutations in the *NOTCH3* gene, and is the most common single gene disorder causing stroke. Since it was first clinically and genetically characterised in the early 1990s, increasing numbers of cases are being recognised and diagnosed. It should be considered in younger patients with lacunar stroke or TIA, particularly in the presence of one or more of the following features: a family history of stroke or dementia, characteristic MRI changes particularly MRI white matter hyperintensities in the anterior temporal pole, and other features such as mood disorders or migraine with aura (Mancuso et al, 2020). **[2023]**

5.20 Recommendations

A People with clinical and radiological features that are suggestive of CADASIL should only be offered genetic testing after appropriate counselling and discussion. Predictive testing in other family members should be performed by a specialist clinical genetics service after appropriate counselling. **[2023]**

B People with CADASIL should be considered for intensive cardiovascular risk factor management, particularly with respect to blood pressure management (target to below 130/80 mmHg) and smoking cessation advice. They should also be considered for active management of other risk factors including lipid lowering treatment (including with statins), and diabetes mellitus, and offered lifestyle advice (including regarding obesity and exercise). **[2023]**

C People with CADASIL and ischaemic stroke or TIA may be considered for antiplatelet therapy; cerebral microbleeds are not a contraindication. **[2023]**

5.20 Sources

A Mancuso et al, 2020; Guideline Development Group consensus

B Peters et al, 2006; Adib-Samii et al, 2010; Mancuso et al, 2020

C Puy et al, 2017

5.20 Evidence to recommendations

There are no RCTs examining secondary prevention approaches in people with CADASIL. Observational studies have shown that both smoking and hypertension are associated with an increased risk of stroke in this group (Peters et al, 2006; Adib-Samii et al, 2010). For this reason most clinicians, and the European Academy of Neurology (EAN) guidelines (Mancuso et al, 2020) recommend tight control of cardiovascular risk factors, particularly BP reduction and smoking cessation. Evidence is not available on other risk factors including exercise, obesity, and cholesterol, but most clinicians also actively treat these risk factors. These should be treated from the time of diagnosis, rather than waiting until the person has had a stroke. **[2023]**

There is no research to guide clinicians on whether antiplatelet agents should be given to patients with CADASIL. Most practitioners, and the EAN guidelines (Mancuso et al, 2020) recommend avoiding antiplatelet agents prior to the onset of clinical stroke, but treating with a single antiplatelet agent (aspirin or clopidogrel) rather than dual antiplatelet agents after a stroke or TIA. The presence of cerebral microbleeds is associated with an increased risk of ischaemic stroke and should not prevent administration of antiplatelets after a stroke or TIA (Puy et al, 2017). **[2023]**

5.21 Cerebral microbleeds

Cerebral microbleeds are small haemosiderin deposits detected by blood-sensitive MRI scans including T2-weighted gradient recalled echo and susceptibility-weighted imaging (SWI), Their identification has generated clinical concern as a potential marker of increased intracranial bleeding risk in people treated with antithrombotic medication, leading some clinicians to avoid giving antithrombotic medication if they are present (Wilson & Werring, 2017). **[2023]**

5.21 Recommendations

A In patients with ischaemic stroke or TIA requiring antiplatelet or anticoagulant treatment, the presence of cerebral microbleeds (regardless of number or distribution) need not preclude antithrombotic medication use. **[2023]**

B In patients with recent ischaemic stroke or TIA treated with antithrombotic (i.e. antiplatelet or anticoagulant) medication, the use of a validated risk score (such as the MICON-ICH score) may be considered for predicting the risk of symptomatic intracranial haemorrhage to allow the mitigation of bleeding risk, including assertive management of modifiable factors (e.g. hypertension, alcohol intake and review of concurrent medication). **[2023]**

5.21 Source

A, B Guideline Development Group consensus

5.21 Evidence to recommendations

In patients prescribed oral anticoagulants after cardioembolic stroke or TIA in the CROMIS-2 (Wilson et al, 2018) and HERO (Martí-Fàbregas et al, 2019) prospective multicentre cohort studies the presence of cerebral microbleeds was independently associated with an approximate three-fold increase in the risk of symptomatic ICH, but the absolute risk of ischaemic stroke was consistently higher than that of

symptomatic ICH independent of the presence of cerebral microbleeds. The Microbleeds International Collaborative Network [MICON]) included 20,322 patients taking any antithrombotic medication(s) (Wilson et al, 2019) and found that the absolute risk of ischaemic stroke exceeded that of ICH even in patients with 10 or more microbleeds (annual rates: ICH: 2.7%; ischaemic stroke: 6.4%), or microbleeds in a strictly lobar distribution suggesting CAA (annual rates: ICH: 1.3%; ischaemic stroke: 4.8%). The MICON-ICH collaborative group also demonstrated that a cerebral microbleed-based risk score (MICON-ICH) improves the prediction of intracranial haemorrhage during follow-up for patients with ischaemic stroke or TIA taking antiplatelets, anticoagulants, or both compared to widely used clinical prediction instruments like HAS-BLED, ATRIA, or ORBIT (Best et al, 2021). A high predicted risk of ICH might lead clinicians to pursue assertive management of modifiable bleeding risk factors such as BP and alcohol intake, and review concurrent medication. A secondary analysis of the NAVIGATE-ESUS trial (Shoamanesh et al, 2021) did not find evidence that microbleeds modify the net benefit or harm of anticoagulant versus antiplatelet therapy. However, in the PICASSO trial, which enrolled Asian participants with previous ischaemic stroke and previous intracranial bleeding (symptomatic or radiological intracerebral bleeding or at least two cerebral microbleeds), in those with microbleeds only at baseline, cilostazol was associated with a lower risk of intracranial bleeding than aspirin (Park et al, 2021). More data are needed regarding the prognostic significance of cerebral microbleeds in patients taking direct oral anticoagulants (DOACs); moreover, the balance of risk and benefit is uncertain for patients with cerebral microbleeds taking combined antiplatelet and anticoagulant therapy and for patients with a large number of cerebral microbleeds beyond five years. **[2023]**

5.22 Lifestyle measures

The evidence for lifestyle interventions relates mainly to the primary prevention of vascular events; little high quality research has studied the secondary prevention of stroke or TIA. It would seem that changes in lifestyle are as important in secondary prevention as they are in primary prevention. Effective lifestyle interventions require changes in behaviour such as smoking, exercise, diet and alcohol consumption. Although it is the responsibility of the individual to change his or her own behaviour, healthcare practitioners have a responsibility to give accurate information, advice and support to help people to make and maintain lifestyle changes. In theory, the combination of lifestyle changes and other secondary prevention measures could deliver a greater than 80% risk reduction in vascular events for people with stroke or TIA (Hackam & Spence, 2007). In practice, the paucity of data makes it difficult to confirm the expected benefits (Lennon et al, 2014). **[2016]**

5.23 Physical activity

People who have sustained a stroke often become physically deconditioned, with low cardiorespiratory fitness, muscle strength and muscle power (Smith et al, 2012; Saunders et al, 2013). This low physical fitness is associated with functional limitation and disability (Saunders et al, 2013). Physical activity programmes to improve fitness and muscle strength have been implemented without adverse effects in people with stroke screened for contraindications (Billinger et al, 2014). A systematic review (Ammann et al, 2014) identified the need for better reporting of exercise prescription to improve the delivery of physical activity programmes, and the importance of peer support. **[2016]**

5.23 Recommendations

A People with stroke or TIA should participate in physical activity for fitness unless there are contraindications. Exercise prescription should be individualised, and reflect treatment goals and activity recommendations. **[2016]**

B People with stroke or TIA should aim to be active every day and minimise the amount of time spent sitting for long periods. **[2016]**

C People with stroke should be offered cardiorespiratory training or mixed training regardless of age, time since having the stroke, and severity of impairment.
- Facilities and equipment to support high-intensity (greater than 70% peak heart rate) cardiorespiratory fitness training (such as bodyweight support treadmills, or static or recumbent cycles) should be available;
- The dose of training should be at least 30-40 minutes, 3 to 5 times a week for 10-20 weeks;
- Programmes of mixed training (medium intensity cardiorespiratory [40%-60% of heart rate reserve] and strength training [50-70% of one-repetition maximum]) such as circuit training classes should also be available at least 3 days per week for 20 weeks;
- The choice of programme should be guided by patients' goals and preferences and delivery of the programme individualised to their level of impairment and goals. **[2023]**

D People with stroke or TIA who are at risk of falls should engage in additional physical activity which incorporates balance and co-ordination, at least twice per week. **[2016]**

E Physical activity programmes for people with stroke or TIA should be tailored to the individual after appropriate assessment, starting with low-intensity physical activity and gradually increasing to moderate levels. **[2016]**

F Physical activity programmes for people with stroke or TIA may be delivered by therapists, fitness instructors or other appropriately trained people, supported by interagency working where possible. When delivered outside statutory health services, physical fitness training should be delivered by professionals with appropriate education and training in stroke and exercise (e.g. Chartered Institute for the Management of Sport and Physical Activity [CIMSPA]-endorsed exercise professionals or clinical exercise physiologists). **[2023]**

G Stroke rehabilitation services should build links with community-based exercise facilities (such as support groups, gyms, leisure centres or exercise referral schemes) to support people with stroke to transition to ongoing physical activity on completion of an exercise programme. **[2023]**

H Stroke services should consider working with other established rehabilitation services, such cardiac or pulmonary rehabilitation, to develop exercise-based programmes and ensure access to equipment and screening protocols. **[2023]**

5.23 Sources

A Ada et al, 2006; English and Hillier, 2010; Marsden et al, 2013; Saunders et al, 2013; Kendall and Gothe, 2015

B Department of Health (UK), 2019

C English and Hillier, 2010; Marsden et al, 2013; Saunders et al,et al, 2013; Kendall and Gothe, 2015; MacKay-Lyons et al, 2020

D, E Department of Health (UK), 2019; Working Party consensus

F-H Guideline Development Group consensus

5.23 Evidence to recommendations

There are Cochrane reviews (English & Hillier, 2010; Saunders et al, 2013), other systematic reviews (Ada et al, 2006; van de Port et al, 2007; Veerbeek et al, 2014) and one high quality, moderate-sized RCT , other systematic reviews (Ada et al, 2006; van de Port et al, 2007; Veerbeek et al, 2014) and one high quality, moderate-sized RCT (English et al, 2015) on physical activity after stroke. Overall, the evidence

shows that activity programmes have a positive effect on global disability, albeit in the predominantly ambulant stroke population (Saunders et al, 2013). Treatment benefits physical function and supports the use of aerobic exercise and mixed training programmes to improve gait (English & Hillier, 2010; Marsden et al, 2013; Saunders et al, 2013; Kendall & Gothe, 2015). Other studies also suggest positive effects on outcomes such as vascular function (Moore et al, 2015) and psychosocial benefits (Faulkner et al, 2015). **[2016]**

Cardiorespiratory training, especially when involving walking, appears to be the most effective for cardiorespiratory fitness (with a moderate effect size) but also for walking and balance. Mixed training has a slightly lesser effect. Resistance training is most effective to improve muscle strength and endurance (Saunders et al, 2020). Thus the type of exercise prescribed depends on the patient's own goals and preferences. However, cardio-respiratory training involving walking has the greatest overall benefit which can persist into the long-term (Saunders et al, 2020). **[2023]**

5.24 Smoking cessation

About 1 in 5 adults in the UK and Ireland are smokers (Department of Health (Ireland), 2021; Office of National Statistics, 2022). Each year, an estimated 454,700 hospital admissions in England can be attributed to smoking including around 1 in 4 strokes. Smokers have up to three times the risk of stroke and double the risk of recurrent stroke compared to non-smokers, but if they are able to stop, the risk decreases significantly and is at the level of non-smokers after about five years. The health benefits of reducing rather than stopping smoking are not clear. About two-thirds of smokers express the desire to stop but long-term success rates are low at 2-3%. **[2016]**

5.24 Recommendation

A People with stroke or TIA who smoke should be advised to stop immediately. Smoking cessation should be promoted in an individualised prevention plan using interventions which may include pharmacotherapy, psychosocial support and referral to statutory stop smoking services. **[2016]**

5.24 Sources

A NICE, 2023a; Working Party consensus

5.24 Evidence to recommendations

There have been a large number of Cochrane reviews assessing a variety of interventions to promote smoking cessation in the general population (for the individual reviews, see https://www.cochranelibrary.com/). A beneficial effect has been demonstrated for nicotine replacement therapy, nicotinic receptor partial agonists (varenicline, cytisine), antidepressant medication (bupropion, nortriptyline), combined pharmacotherapy and behavioural interventions, financial incentives, motivational interviewing, e-cigarettes, exercise, print-based self-help, telephone counselling and brief physician and nurse interventions. The evidence for interventions to increase smoking cessation in people with stroke is limited. A systematic review identified only four studies involving a total of 354 patients (Edjoc et al, 2012). Meta-analysis was not possible and a simple summed cessation rate of 24% for those receiving an intervention compared with 21% for controls was reported. **[2016]**

NICE public health guidelines (NICE guideline [NG209] Tobacco: preventing uptake, promoting quitting and treating dependence; NICE, 2023) provide guidance on smoking cessation services for all smokers. Stopping in one step is recommended as the approach must be likely to provide lasting success. Recommended interventions include behavioural counselling, group therapy, pharmacotherapy

(licensed nicotine containing products, varenicline or bupropion) and referral to statutory stop smoking services, alone or in combination. **[2016]**

5.25 Nutrition (secondary prevention)

Long-term adherence to cardioprotective diets, when combined with other lifestyle modifications, may reduce stroke recurrence (Appel et al, 1997; Appel et al, 2003; Fung et al, 2008). While there is evidence that tailored dietary modifications can favourably modify cardiovascular risk factors, there is limited evidence that this translates into a reduction in stroke recurrence and mortality (Rees et al, 2013; Adler et al, 2014). **[2016]**

5.25 Recommendations

A People with stroke or TIA should be advised to eat an optimum diet that includes:
- five or more portions of fruit and vegetables per day from a variety of sources;
- two portions of oily fish per week (salmon, trout, herring, pilchards, sardines, fresh tuna). **[2016]**

B People with stroke or TIA should be advised to reduce and replace saturated fats in their diet with polyunsaturated or monounsaturated fats by:
- using low-fat dairy products;
- replacing butter, ghee and lard with products based on vegetable and plant oils;
- limiting red meat intake, especially fatty cuts and processed meat. **[2016]**

C People with stroke or TIA who are overweight or obese should be offered advice and support to aid weight loss including adopting a healthy diet, limiting alcohol intake to 2 units a day or less and taking regular exercise. Targeting weight reduction in isolation is not recommended. **[2016]**

D People with stroke or TIA should be advised to reduce their salt intake by:
- not adding salt to food at the table;
- using little or no salt in cooking;
- avoiding high-salt foods, e.g. processed meat such as ham and salami, cheese, stock cubes, pre-prepared soups and savoury snacks such as crisps and salted nuts. **[2016]**

E People with stroke or TIA who drink alcohol should be advised to limit their intake to 14 units a week, spread over at least three days. **[2016]**

F Unless advised to do so for other medical conditions, people with stroke or TIA should not routinely supplement their diet with:
- B vitamins or folate;
- vitamins A, C, E or selenium;
- calcium with or without vitamin D. **[2016]**

5.25 Sources

A He et al, 2006; NICE, 2007; Chowdhury et al, 2012; Rees et al, 2003

B Marik and Varon, 2009; Galan et al, 2010; Hooper et al, 2011

C NICE, 2007c; Working Party consensus

D Adler et al, 2014

E Zhang et al, 2014; Department of Health (UK), 2016

F Bazzano et al, 2006; Galan et al, 2010; Bin et al, 2011; Bolland et al, 2010, 2014; Marti-Carvajal et al, 2015

5.25 Evidence to recommendations

Cardioprotective diet

A Cochrane review of the Mediterranean diet for the primary prevention of cardiovascular disease found very small reductions in total and LDL-cholesterol (Rees et al, 2013). Three of five RCTs showed a positive effect on BP, with reductions of 0.7-7.8 mmHg in systolic and 0.7-3.7 mmHg in diastolic BP. The Dietary Approaches to Stop Hypertension (DASH) diet lowered systolic and diastolic BP when followed for 8 weeks (Appel et al, 1997). Long-term follow-up for up to 24 years (Fung et al., 2008) demonstrated that adherence to a DASH-style diet is associated with a lower risk of coronary heart disease and stroke among middle-aged women. Effects on stroke recurrence and mortality are not known. A Cochrane review (Adler et al, 2014) of dietary salt reduction for the prevention of cardiovascular disease confirms that small reductions in BP can be achieved in normotensive individuals, and greater reductions in hypertensive individuals. Many of the component trials lacked sufficient detail to assess bias; any benefits in terms of cardiovascular mortality and morbidity were modest or non-significant and confined to hypertensive groups. **[2016]**

Weight-reducing diet

Overweight and obesity is a significant risk factor for the development of cardiovascular disease and is associated with an increase in all-cause mortality (Adams et al, 2006; Bazzano et al, 2006). Both overweight (body mass index [BMI] greater than 25 kg/m^2) and obesity (BMI greater than 30 kg/m^2) are associated with an increased risk of ischaemic stroke (Strazzullo et al, 2010). Customary advice has targeted a healthy BMI to reduce risk of stroke but high quality intervention studies to support this approach are lacking. Some observational studies have reported a paradoxical inverse relationship between BMI and mortality following stroke (Kim et al, 2011; Vemmos et al, 2011) with overweight and obese people having reduced mortality, but how this observation might translate into an intervention to reduce recurrent stroke is unclear. **[2016]**

Alcohol

A meta-analysis of 27 prospective studies with 1,425,513 participants reviewed the dose-response relation between alcohol and risk of stroke (Zhang et al, 2014). In the majority of the component studies, alcohol intake was self-reported. Low alcohol intake (below 15 g/day) was associated with a reduced risk of total stroke, ischaemic stroke and stroke mortality with no significant effect on haemorrhagic stroke (one UK unit = 8 g of alcohol). Moderate alcohol intake (15-30 g/day) had little or no effect on risk of total stroke, haemorrhagic stroke, ischaemic stroke or stroke mortality. Heavy alcohol intake (above 30 g/day) was associated with an increased risk of total stroke. It is not known if a similar relationship would apply to people who have already experienced stroke. **[2016]**

Micronutrient supplementation

A Cochrane review (Marti-Carvajal et al, 2015) examined the use of B-vitamin supplementation to prevent cardiac events. No benefit was found for homocysteine-lowering interventions in the form of supplements of vitamins B6, B9 or B12 given alone or in combination, at any dosage. Two meta-analyses (Alkhenizan & Al-Omran, 2004; Bin et al, 2011) and one systematic review (Eidelman et al, 2004) examined the effects of vitamin E supplementation on stroke recurrence and mortality, with no benefit seen. Dietary calcium and/or vitamin D supplementation has not been shown to reduce cardiovascular risk (Elamin et al, 2011; Bolland et al, 2014) and in one systematic review it was associated with a modest increased risk (Bolland et al, 2010). Confining the analysis to people with vitamin D deficiency likewise showed no benefit. The impact of other nutrients, including plant stanols/sterols, antioxidants such as vitamins A and C or selenium in stroke prevention is unknown (Hookway et al, 2015). **[2016]**

5.26 Life after stroke

Stroke research has tended to concentrate on the acute and early phases of recovery yet for about half of those who survive, life after stroke involves some permanent impairment and restriction of their activities. As well as coping with the physical consequences, many people with stroke and their family/carers have long-term psychological and emotional needs. Defining these needs is challenging, and researchers and healthcare professionals may not prioritise the same outcomes as people with stroke. In a UK survey of patients between 1 and 5 years after stroke, about half reported having one or more (median three) unmet needs (McKevitt et al, 2011). Communication problems, worsening disability and ethnicity were associated with a greater number of reported unmet needs, as was living in a more deprived area. Self-reported outcomes after stroke included 52% with a negative change in work activity, 67% a change for the worse in relation to leisure activities or interests, 18% a loss of income, 31% an increase in expenses, and 42% a negative impact on the relationship with their partner. Over half of respondents reported needing more information about stroke, including diet, applying for benefits, aids and adaptations to the home and driving. Of those who reported emotional problems (over a third), the great majority felt they did not receive the support they needed. No relationship between unmet need and time since stroke was identified, indicating that these needs are persistent and long-term. **[2016]**

5.27 Further rehabilitation

Following discharge from rehabilitation, many people with stroke experience a discontinuity in their care (Hartford et al, 2019) whilst still adjusting to life after stroke. In addition to ongoing needs, the discharge process is likely to give rise to new needs because of changes in physical, psychological, social and environmental circumstances (Pringle et al, 2013; Hodson et al, 2016) for which people with stroke and their families often feel inadequately prepared, leaving them feeling unsupported (Tholin & Forsberg, 2014) or even abandoned (Pindus et al, 2018). The needs of people with stroke and their families are likely to change over time, as adjusting to life after stroke is an evolving, long-term challenge for many (Pallesen, 2014; Hall et al, 2022). **[2023]**

A systematic review of unmet needs after stroke identified that, on average, each person with stroke experiences between two and five unmet needs (Chen et al, 2019). Common unmet needs related to body function include fatigue, cognitive problems, neuropsychological and emotional needs and pain; those related to activity and participation include secondary prevention, mobility, work, leisure and hobbies, while those related to the environment include information, transport, therapy and home support or personal care. **[2023]**

In order to address these needs, many people with stroke seek to continue rehabilitation in the longer term, either continuously or on an intermittent basis. As well as facilitating recovery, rehabilitation (including exercise) delivered later after stroke may prevent regression of physical or cognitive gains achieved in the earlier stages of recovery, and prevent deconditioning. Furthermore, people affected by stroke often seek sources of support outside of the health and social care system (Forster et al, 2021). These may include advice lines and patient advocacy organisations, communication support groups, exercise groups and other informal gatherings to provide social, emotional and psychological support. **[2023]**

The provision of appropriate, person-centred follow-up rehabilitation and long-term support after stroke is advocated by several key organisations, including the British Society of Rehabilitation Medicine in their Specialist Standards for Community Rehabilitation (British Society of Rehabilitation Medicine, 2021), the Community Rehabilitation Alliance in their Manifesto (Community Rehabilitation Alliance, 2021), NHS England in their National Stroke Service Model for England (NHS England, 2021), the Scottish Government in their Programme for Government (Scottish Government, 2022), and the National Stroke

Strategy (Ireland) (Health Service Executive, 2022). Inter-agency partnership working is highlighted in particular to ensure people are able to access the right service at the right time, preventing gaps in service transitions. **[2023]**

Healthcare professionals should facilitate timely access to services that are necessary to enable people with stroke and their families to address their evolving needs over time. Follow-up health and social care may be warranted, but a wide range of other support services may also be sought from the third sector (e.g. the Stroke Association, Chest Heart & Stroke Scotland, Different Strokes, the Irish Heart Foundation). Furthermore, healthcare professionals play a pivotal role in supporting people with stroke and their families in designing self-management plans and reviewing these (see also Section 4.4 *Self-management*). **[2023]**

As this guideline does not include a section dedicated to support services outside of health or social care, recommendations in this section include signposting to such services, to ensure that people affected by stroke are referred to the appropriate services to address their needs. **[2023]**

5.27 Recommendations

A People with stroke, including those living in a care home, should be offered a structured, holistic review of their individual needs by a healthcare professional with appropriate knowledge and skills, using an appropriate mode of communication (e.g. face-to-face, by telephone or online).
- This review should cover physical, neuropsychological and social needs, seek to identify what matters most to the person, and be undertaken at 6 months after stroke, or earlier if requested by the person with stroke.
- At this 6-month review, the reviewer should discuss with the person with stroke who would be best placed to undertake the next review at 1 year post-stroke (or at another point in time, depending on the person's needs), as well as the agreed mode of communication.
- This review should be offered annually thereafter (or at another point in time, if requested by the person with stroke), for as long as a need for ongoing review continues and on request thereafter. **[2023]**

B People with stroke who have further needs identified at a 6-month or subsequent review should be considered for intervention or referral for health or social care assessment if:
- new health or social care needs are identified;
- existing health or social care needs have escalated;
- further rehabilitation goals related to specific physical, psychological, vocational, family or social needs can be identified and agreed;
- risk factors or co-morbidities are identified that would lead to deterioration if no action were taken. **[2023]**

C People with stroke who have further needs identified at a 6-month or subsequent review that do not require health or social care input should be provided with information about or referred to other appropriate services to address their needs (e.g. community-based support groups provided by voluntary or statutory services). Healthcare professionals should discuss with the person if they could facilitate the transition with their agreement (e.g. by providing relevant information to the service, or by a scheduling a joint session). **[2023]**

D Healthcare professionals providing 6-month or subsequent reviews of people with stroke should maintain an up-to-date overview of appropriate health and social care services, and other service providers (e.g. community support groups and local councils) to facilitate

transitions to other services as required. **[2023]**

E People with stroke should be provided with the contact details of a named healthcare professional (e.g. a stroke co-ordinator or key worker) who can provide further information, support and advice, as and when needed. **[2023]**

F People with stroke should be supported to develop their own self-management plan, based on their individual needs, goals, preferences and circumstances. **[2023]**

G People with stroke who are unable to undertake their own self-management should be referred in a timely manner to appropriate health, social care, or other voluntary or statutory services depending on their needs. **[2023]**

5.27 Sources

A Guideline Development Group consensus

B Rodgers et al, 2019b; Shaw et al, 2020

C-G Guideline Development Group consensus

5.27 Evidence to recommendations

The literature related to follow-up after the end of formal rehabilitation is diverse; it includes specific rehabilitation interventions already described in Chapter 4 and overlaps with other areas, including secondary stroke prevention (Chapter 5), Vocational rehabilitation (Section 4.15 *Return to work*), and Supported self-management (Section 4.4 *Self-management*). **[2023]**

An intervention aimed at maintaining motor function using individual coaching was compared with usual care in a Norwegian RCT of moderate quality (Askim et al, 2018; Døhl et al, 2020). This intervention was provided once a month for 18 months, initially delivered mostly face-face, gradually introducing telephone contact. Individual goals were set and monthly schedules were agreed, which comprised 45 to 60 minutes of exercise (including 2 to 3 periods of vigorous activity) once a week plus physical activity for 30 minutes daily. Participants were given various options to join groups in different settings to match their requirements. Findings showed that this coaching intervention was safe but it had no additional effect on any aspect of motor function, ADL, fatigue, mood, quality of life, or caregiver strain. The cost analysis (Døhl et al, 2020) indicated that the intervention added costs to usual care. **[2023]**

An extended stroke rehabilitation service (Rodgers et al, 2019; Shaw et al, 2020), which aimed to maximise recovery and adjustment to residual disability in the context of everyday activities, was compared with usual care in a high quality, UK-wide RCT. It comprised five extra telephone reviews (including goal setting and action planning) with senior therapists over 18 months after the end of early supported discharge. Compared with usual care, this intervention did not improve extended ADL but it did improve health-related quality of life, anxiety and depression, and patient satisfaction (including whether needs had been met, and whether sufficient treatment had been received to improve mobility). The intervention may also be cost-effective due to the quality of life advantages and a tendency towards lower overall costs in primary care. Participants with stroke felt that the reviews were reassuring, thorough and comprehensive, and that the goal setting had motivated them, but they were unclear if actual outcomes had been improved. Therapists thought that the intervention addressed the unmet need for ongoing support for people living with stroke and that reviews were comprehensive, but they disapproved of having to deliver the intervention by telephone only. They also thought that the reviews were useful, primarily around emotional and social issues, and they valued being able to connect people with stroke to services, although they felt uncomfortable if they were unable to provide the necessary support or onward referral for an identified rehabilitation need. **[2023]**

An intervention which aimed to identify physical, cognitive and emotional problems in daily life, provide support and psycho-education and refer to further specialised healthcare as required, was compared with usual care in a Dutch study (Verberne et al, 2021; Verberne et al, 2022). It comprised face-to-face sessions of up to 45 minutes each in a primary care centre at 6 months after hospital discharge, with the number of sessions depending on the nurse's judgement. This intervention did not result in any improvements in mood or social participation compared to usual care, whilst other outcomes were not reported. The authors concluded that the intervention was cost-effective (Verberne et al, 2021), but due to the low quality of the study design and differences in healthcare systems, no conclusions can be drawn to support a recommendation. **[2023]**

The Improving Longer Term Stroke Care (LoTS2Care) programme (Forster et al, 2021) was designed to develop and test a longer-term integrated stroke care intervention to improve quality of life for people with stroke and their family/carers by addressing unmet needs and enhancing participation in life situations. Based on service user experiences, systematic literature reviews, and an evaluation of existing service models, a novel intervention (New Start) was designed, refined and tested in a feasibility cluster RCT involving 10 stroke services across England and Wales, recruiting 269 participants. Further development work will be undertaken before a full trial evaluation, and findings will inform subsequent editions of this guideline. **[2023]**

Some people start or continue to improve many months or years after the event, and these people may benefit from further rehabilitation or other support at a later stage. Whilst limited, there is evidence to suggest that for some people improvements in communication, arm function, walking, physical fitness and ADL can be achieved with interventions more than 6 months after stroke (Palmer & Enderby, 2007; Duncan et al, 2011; Ferrarello et al, 2011; Lohse et al, 2014; Veerbeek et al, 2014; Ward et al, 2019). To provide personalised care to this group and to identify other unmet needs, the consensus of the Guideline Development Group is that a comprehensive, structured needs reassessment should be undertaken at 6 months – or earlier, depending on the individual's needs. Structured, planned follow-up may reduce some of the health inequalities between those with higher and lower levels of education (Irewall et al, 2019). **[2023]**

This review should consider physical, psychological and social needs (including relationships and work, where applicable) related to adjusting to life after stroke. The review should identify what matters most to the person with stroke, ensuring that any referrals are appropriately targeted. The role of the professional is to support the person with stroke to identify and prioritise their needs and goals and act as a facilitator, initiating timely referrals or providing guidance to appropriate service providers within health and social care or beyond, as and when required. Referrers should consider health and social care services, and services offered by other organisations, including stroke support groups (e.g. communication support provided by the Stroke Association, Chest Heart and Stroke Scotland, the Irish Heart Foundation or Different Strokes) and local councils (e.g. exercise referral schemes). **[2023]**

There is no 'one size fits all' with regard to onward referral; instead, given the diversity in recovery profiles, needs and timing, as well as the cultural contexts in which people with stroke lead their lives, a personalised approach is required. This is to ensure that the aims, content, mode of delivery (e.g. face-face, online) and timing of any services are aligned with the priorities, needs, goals and circumstances of the person with stroke and their family/carers where appropriate. **[2023]**

5.27 Implications

Primary care teams, in collaboration with hospital-based or community stroke teams, specialist community neurorehabilitation or brain injury rehabilitation teams, will need to consider the resource implications of implementing follow-up and annual review for people with stroke living in the community and make appropriate provision. **[2023]**

5.28 Social integration and participation

Helping people with stroke to integrate back into the community in the way that they want is a key goal of healthcare; engagement in community activity is associated with improved quality of life. Most healthcare focuses on improving a person's capacity to undertake activities. The wider task of achieving social and community integration depends upon factors such as the person with stroke and their family/carers having information about local opportunities and being aware of the physical and mental health benefits of activity and engagement, the availability of accessible social settings and transport and the appropriate training of community providers of leisure and social activities. Stroke voluntary sector services and peer support groups can play an important role in helping community integration. Lack of accessible transport is often a significant barrier to participation for disabled people. **[2016]**

Other aspects of stroke and stroke recovery of relevance to integration and participation are covered in other parts of this guideline and include Section 2.7 *Transfers of care – general principles*, Section 2.11 *Psychological care – organisation and delivery*, Section 4.8 *Extended activities of daily living*, Section 4.14 *Driving*, Section 4.15 *Return to work*, Section 4.25 *Fatigue*, Section 4.38 *Mood and well-being*, Section 4.13 *Sex*. **[2016]**

5.28 Recommendations

A As part of their self-management plan, people with stroke should be supported to identify social and leisure activities that they wish to participate in, taking into account their cognitive and practical skills. Healthcare professionals should:
- advise the person with stroke and their family/carers about the benefits of participating in social and leisure activities;
- identify and help them to overcome any barriers to participation (e.g. low self-confidence or lack of transport). **[2016]**

B People with stroke should be provided with information and referral to statutory and voluntary community organisations that can support the person in social participation. **[2016]**

C People with stroke whose social behaviour is causing distress to themselves or others should be assessed by an appropriately trained healthcare professional to determine the underlying cause and advise on management. Following the assessment:
- the nature of the problem and its cause should be explained to family/carers, other people in social contact and the rehabilitation team;
- the person should be helped to learn the best way to interact without causing distress;
- those involved in social interactions should be trained in how to respond to inappropriate or distressing behaviour;
- psychosocial management approaches should be considered;
- antipsychotic medicines may be indicated if other causes have been excluded and the person is at risk of harm to themselves or others. The balance of risk and benefit from antipsychotic medication should be carefully considered. Treatment should be started with a low dose and increased slowly according to symptoms, and should be short-term (e.g. one week) or intermittent and withdrawn slowly. **[2016]**

5.28 Sources

A Langstaff et al, 2014; Dorstyn et al, 2014; Obembe and Eng, 2015

B Working Party consensus

C NICE, 2010b, 2019a; Obembe and Eng, 2015; Working Party consensus

5.28 Evidence to recommendations

A metasynthesis of qualitative research identified several themes which, from the perspective of people with stroke, acted as barriers or facilitators to community reintegration (Walsh et al, 2015). As well as the primary effects of the stroke (impairments and fatigue), these comprised personal factors (perseverance, adaptability, emotional challenges, relevance of activities), social factors (sense of belonging versus stigmatisation, levels of support, environmental limitations) and interactions with professionals (levels of support, joint decision-making, relevance of rehabilitation to real world requirements). Anger, frustration and more challenging behavioural problems may present barriers to social and community integration but other than generic principles, there is limited evidence to guide management for people or families/carers with these problems. **[2016]**

A systematic review of leisure therapy including eight studies and 615 participants identified methodological shortcomings but nonetheless some evidence of short-term improvements in quality of life and mood as well as increased participation and satisfaction with leisure activities (Dorstyn et al, 2014). In a review of 24 studies (including 2042 people with stroke) that included measures of social participation as an outcome, a small beneficial effect was identified for interventions utilising exercise (Obembe & Eng, 2015). A community walking training programme in which people with stroke undertook walking therapy in a real-world environment resulted in greater improvements in walking function and social participation (Kim et al, 2014), but a Cochrane review found the available evidence insufficient to establish effectiveness (Barclay-Goddard et al, 2015). **[2016]**

Glossary

Activities of daily living	Refers to activities that people normally undertake (e.g. bathing, dressing, feeding themselves).
Acupuncture	A complementary medicine that involves inserting thin needles into the skin.
Acute stroke service	Consists of: a) a comprehensive stroke centre (CSC) providing hyperacute, acute and inpatient rehabilitation including thrombectomy (thrombectomy centre) and neurosurgery; or b) an acute stroke centre (ASC) providing hyperacute, acute and inpatient rehabilitation. All components of a specialist acute stroke service should be based in a hospital that can investigate and manage people with acute stroke and their medical and neurological complications.
Aerobic exercise	Low- to moderate-intensity exercise that can be sustained for long periods of time (e.g. cycling, swimming or walking).
Agnosia	The inability for a patient to recognise or make proper sense of sensory information.
Alteplase	A drug used for thrombolysis.
Aneurysm	A bulge in the wall of a blood vessel that is filled with blood. This can burst and cause a haemorrhage.
Angiography	A technique that uses X-ray technology to image blood vessels.
Anticoagulants	A group of drugs used to reduce the risk of clots by thinning the blood.
Antiphospholipid syndrome	Sometimes called 'sticky blood syndrome' because blood clots form too quickly; this is due to antibodies against the body's phospholipid part of every cell in the body.
Antiplatelets	A group of drugs used to prevent the formation of clots by stopping platelets in the blood sticking together.
Antithrombotics	The generic name for all drugs that prevent the formation of blood clots. This includes antiplatelets and anticoagulants.
Aphasia	Communication difficulties after a stroke which can affect a person's speech, processing, reading and writing.
Arterial dissection	This is caused as a result of a small tear forming in the lining of the arterial wall.
Atherosclerosis	Fatty deposits that harden on the inner wall of the arteries (atheroma) and roughen its surface; this makes the artery susceptible to blockage either by narrowing or by formation of a blood clot.
Atrial fibrillation	A heart condition that causes an irregular heartbeat, often faster than the normal heart rate.
Audit (clinical)	A method of evaluating the performance of a clinical service against a set of standards/criteria.
Bobath therapy	Treatment which aims to use facilitative handling which prioritises normal movement and muscle tone or inhibition of reflex activity rather than maximising practice and patient activity. Also known as neurophysiological or neurodevelopmental treatment.
Body mass index (BMI)	An index of body weight corrected for height.
Botulinum toxin	A toxin which when injected can relax muscles to reduce spasticity.

Cardiovascular disease	Disease of the heart and/or blood vessels.
Care pathway	A tool used by healthcare professionals to define the sequence and timings of a set of tasks or interventions that should be performed for a patient who enters a healthcare setting (e.g. a hospital) with a specific problem.
Carotid angioplasty	A surgical procedure that widens the internal diameter of the carotid artery, after it has been narrowed by atherosclerosis.
Carotid arteries	Main blood vessels in the neck, which supply oxygenated blood to the brain.
Carotid endarterectomy (CEA)	A surgical procedure used to clear the inside of the carotid artery of atheroma.
Carotid stenosis	The narrowing of the carotid arteries in the neck.
Carotid stenting	Insertion of a tube into the carotid artery in order to prop the artery open and reduce narrowing.
Caval filter	A device that is inserted into the veins to prevent a blood clot entering the lungs.
Cerebral venous thrombosis	A blood clot that forms within a vein inside the brain.
Clinician	A registered healthcare professional such as a doctor, nurse or therapist.
Cochrane review	A systematic review of research in health care and health policy that is published in the Cochrane Database of Systematic Reviews.
Commissioner (health services)	Person or organisation in some parts of the UK National Health Service (NHS) that decides how to allocate the health budget for a service.
Community stroke team, community stroke rehabilitation team	A stroke specialist multidisciplinary team that provides stroke rehabilitation for patients in their own home or other community setting (including care homes and nursing homes). This may be following hospital discharge, after a patient has been discharged from an early supported discharge team or at any point post stroke where rehabilitation needs are identified. The intensity and duration of this service should be determined by patient need.
Compensatory strategies	Learning an alternative way of completing a task.
Computed tomography (CT)	An X-ray technique used to examine the brain.
Confidence interval (CI)	When analysing a research study, this is the range (‘interval’) of possible results that statisticians are 95% confident the actual result lies between.
Constraint-induced movement therapy	Therapy that involves preventing the use of the unaffected side of the body thus forcing the use of the affected side.
Cost-effectiveness	The extent to which the benefits of a treatment outweigh the costs.
Decompressive hemicraniectomy	A surgical procedure for the treatment of raised pressure inside the brain from fluid, blood or swelling. A piece of skull is removed to allow the brain to swell.
Deep vein thrombosis (DVT)	A blood clot that develops in the large veins, usually in the legs.
Diabetes, diabetes mellitus	A metabolic disease in which a person has high blood sugar.
Diagnostic accuracy	The degree to which a diagnostic (or screening) tool or procedure is able to distinguish between cases and non-cases. See also ‘sensitivity’ or ‘specificity’.
Doppler ultrasound	An imaging technique that measures blood flow and velocity through blood vessels.

Dysarthria	Difficulty producing clear speech, caused by muscle weakness.
Dyspepsia	Indigestion.
Dysphagia	Difficulty in swallowing.
Early supported discharge	An intervention delivered by a co-ordinated, stroke specialist, multidisciplinary team that facilitates the earlier transfer of care from hospital into the community and provides responsive (within 24 hours) and intensive stroke rehabilitation in the patient's place of residence (usually over a time-limited period).
Endarterectomy	The surgical removal of plaque from a blocked artery to restore blood flow.
Face Arms Speech Time (FAST) test	A test used to screen for the possibility of a stroke or a TIA.
Fatigue	Physical or mental exhaustion that does not get better through normal periods of rest.
Foot-drop	A condition in which the foot hangs limply whilst walking.
Gastrointestinal bleeding	Bleeding anywhere between the throat and the rectum.
Gastrostomy	A surgical opening into the stomach to enable feeding.
Gastrostomy feeding (also tube feeding)	Provision of nutrition and fluids via a tube directly into the gastrointestinal tract.
Goal attainment	Rehabilitation goals for particular tasks are set by the patient and therapists together.
Haemorrhage	Bleeding caused by blood escaping into the tissues.
Haemorrhagic stroke	A stroke that happens when a blood vessel bursts, leading to bleeding in the brain (also called a 'brain haemorrhage').
Healthcare professional	A professional involved in stroke care, such as a doctor, nurse, therapist, or care staff.
HEART UK	A cholesterol charity.
Hemianopia	Blindness or some loss of vision in one part of the visual field.
Homeostasis	Regulation of internal environment (e.g. body temperature regulated at 37°C).
Hydrocephalus	A build up of fluid within the skull.
Hyperacute stroke unit/centre/service	A stroke unit, centre or service that treats patients in the first 72 hours of symptom onset.
Hyperlipidaemia	Raised levels of lipids (cholesterol, triglycerides or both) in the blood serum.
Hypertension	Raised blood pressure.
Hypertensive encephalopathy	Brain damage caused by raised blood pressure.
Hypoglycaemia	Blood sugar levels lower than the normal range.
Hypoxia	Blood oxygen levels outside the normal range, e.g. below 95% saturation.
Incontinence	Inability to control passing of urine and/or faeces.
Infarct	An area of cell death due to a deprived blood supply.
Integrated community stroke service	An integrated service that provides early supported discharge and community stroke rehabilitation.

International Classification of Functioning, Disability and Health (ICF)	A classification of health used as a framework by the World Health Organization (WHO) to measure health and disability.
Ischaemic stroke	A stroke that happens when a blood clot blocks an artery that is carrying blood to the brain.
Lumbar puncture	A diagnostic or therapeutic procedure that involves collection of fluid from the base of the spine.
Magnetic resonance imaging (MRI)	A non-invasive imaging technique that allows for detailed examination of the brain.
Malnutrition Universal Screening Tool (MUST)	A screening tool consisting of five steps to help identify which adults are malnourished or at risk of malnourishment.
Meta-analysis	A statistical technique for combining the results of a number of studies that address the same question and report on the same outcomes to produce a summary result.
Mouth care	Also referred to as oral health care. Refers to the promotion and maintenance of a clean oral cavity including the teeth, gums, cheeks, tongue and palate. A clean mouth requires the removal of traces of food and debris and dental plaque.
MRI with diffusion-weighted imaging	This type of scan shows areas of recent ischaemic brain damage.
Musculoskeletal pain	Pain of the muscles and/or joints.
National Institute for Health and Care Excellence (NICE)	A special health authority set up within the NHS to develop appropriate and consistent advice on healthcare technologies, and to commission evidence-based guidelines. Its remit extends in most cases to England, Wales and Northern Ireland.
National Institute of Health Stroke Scale (NIHSS)	A score to assess the severity of a stroke.
Neuropathic pain	Pain caused by damage to nerves.
Orthosis	An appliance used to support or align an area of the body to facilitate movement, or prevent or correct damage.
Palliative care	Care that relieves rather than treats symptoms.
Pneumonia	An inflammatory condition of the lungs usually caused by infection.
Pulmonary embolism	A blood clot in the lungs.
Quality of life	Refers to the level of comfort, enjoyment, and ability to pursue daily activities.
Quality standard	A standard set (e.g. by NICE) that is used to define whether the quality of care is of a high standard.
Randomised controlled trial (RCT) (often 'randomised trial')	A trial in which people are randomly assigned to two (or more) groups: one (the experimental group) receiving the treatment that is being tested, and the other (the comparison or control group) receiving an alternative treatment, a placebo (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. Such trial designs help minimise experimental bias.

Recognition of stroke in the emergency room (ROSIER)	A tool used to establish the diagnosis of stroke or TIA.
Rehabilitation	A set of treatments and activities to promote recovery and reduce disability. Rehabilitation treatments are provided by therapists and therapy assistants.
Saturated fat	A type of fat that is commonly found in meat and dairy products as opposed to fats found in plants and fish, which may be unsaturated.
Self-efficacy	A person's belief in their own competency.
Self-management	Actions and confidence of individuals to manage the medical and emotional aspects of their condition in order to maintain or create new life roles.
Sensitivity	The ability of a test to detect a problem.
Service planners	Those responsible for planning and sanctioning health services in Ireland.
Side effect	An adverse event that occurs because of a therapeutic intervention.
SIGN	Scottish Intercollegiate Guidelines Network, an organisation set up to develop evidence-based guidelines. It is part of Healthcare Improvement Scotland and its remit covers Scotland.
Spasticity	Increased stiffness of the muscles that occurs in the paralysed limbs after stroke.
Specialist	A healthcare professional with the necessary knowledge and skills in managing people with stroke and conditions that mimic stroke, usually by having a relevant further qualification and keeping up to date through continuing professional development. This does not require the healthcare professional exclusively to manage people with stroke, but does require them to have specific knowledge and practical experience of stroke.
Specialist team	A group of specialists who work together regularly managing people with stroke and conditions that mimic stroke, and who between them have the knowledge and skills to assess and resolve the majority of problems. At a minimum, any specialist unit, team or service must be able to deliver all the relevant recommendations made in this guideline. This does not require the team exclusively to manage people with stroke, but the team should have specific knowledge and practical experience of stroke.
Specificity	The ability of a test to detect the right problem.
Splint	A custom or ready-made external device to support a joint or limb in a certain position.
Stenosis	Abnormal narrowing of a blood vessel.
Stenting	A metal mesh tube is placed in an artery or blood vessel to increase blood flow to an area blocked by stenosis.
Stroke	A clinical syndrome, of presumed vascular origin, typified by rapidly developing signs of focal or global disturbance of cerebral functions lasting more than 24 hours or leading to death.
Subarachnoid haemorrhage (SAH)	A haemorrhage from a cerebral blood vessel, aneurysm or vascular malformation into the subarachnoid space (the space surrounding the brain where blood vessels lie between the arachnoid and pia mater).
Subluxation	An incomplete or partial dislocation of a joint.
Systematic review	A way of combining the findings from a variety of different research studies to better analyse whether the studies have provided a convincing answer to a research question.

Telemedicine	The use of telecommunication and information technologies in order to provide clinical healthcare at a distance.
Tenecteplase	A drug used for thrombolysis.
Therapist	In the context of the guideline this includes the allied health professionals (UK) and health and social care professionals (Ireland) involved in stroke care. The main ones are dietitians, occupational therapists, orthoptists, orthotists, physiotherapists, and speech and language therapists.
Thrombectomy	The excision of a blood clot from a blood vessel.
Thrombectomy centre	A centre providing thrombectomies without providing acute stroke care.
Thrombolysis	The use of drugs to break up a blood clot. An example of a thrombolysis drug is alteplase, also sometimes called tPA.
Thrombosis	A formation of a blood clot.
Transient ischaemic attack (TIA)	An acute loss of focal cerebral or ocular function with symptoms lasting less than 24 hours and which is thought to be due to inadequate cerebral or ocular blood supply as a result of low blood flow, thrombosis or embolism associated with diseases of the blood vessels, heart, or blood.
Tube feeding (also gastrostomy feeding)	Provision of nutrition and fluids via a tube directly into the gastrointestinal tract.
Venography	An X-ray test that provides an image of the leg veins after a contrast dye is injected into a vein in the patient's foot.
Videofluoroscopy	A test for assessing the integrity of the oral and pharyngeal stages of the swallowing process. It involves videotaping X-ray images as the patient swallows a bolus of barium.
Vocational rehabilitation	A co-ordinated plan to optimise a person's ability to participate in paid or voluntary work.
Work	Different forms of occupation, including paid employment, vocational training, sheltered, therapeutic or voluntary work, and adult education.
Xanthochromia	The yellowish appearance of cerebrospinal fluid that occurs after bleeding into the fluid, usually after subarachnoid haemorrhage.

Abbreviations and acronyms

ABCD2	Age, blood pressure, clinical features, duration of TIA, and presence of diabetes
ADL	Activities of daily living
AF	Atrial fibrillation
APS	Antiphospholipid syndrome
ASC	Acute stroke centre
ASPECTS	Alberta Stroke Program Early Computed Tomography Score
ASA	Atrial septal aneurysm
BADS	Behavioural Assessment of the Dysexecutive Syndrome
BMI	Body mass index
BOA	Behavioural Outcomes of Anxiety
BP	Blood pressure
BPPV	Benign paroxysmal positional vertigo
CAA	Cerebral amyloid angiopathy
CADASIL	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy
CI	Confidence interval
CIMT	Constraint-induced movement therapy
COC	Combined oral contraceptive
COVID-19	Coronavirus disease
CPAP	Continuous positive airways pressure
CPSP	Central post-stroke pain
CSC	Comprehensive stroke centre
CT	Computed tomography
CTA	Computed tomography angiography
CVT	Cerebral venous thrombosis
DISCs	Depression Intensity Scale Circles
DOAC	Direct oral anticoagulant
DVA	Driver and Vehicle Agency (Northern Ireland)
DVLA	Driver and Vehicle Licencing Agency (England, Scotland, Wales)
DVT	Deep vein thrombosis
DWI	Diffusion-weighted imaging
EADL	Extended activities of daily living
ECG	Electrocardiogram
ELISA	Enzyme-linked immunosorbent assay
EMA	European Medicines Agency
FAST test	Face Arm Speech Time test
FEES	Fibre-optic endoscopic evaluation of swallowing
FLAIR	Fluid attenuated inversion recovery
GDG	Guideline Development Group
GP	General practitioner
HAS-BLED	Hypertension, Abnormal score renal and liver function, Stroke, Bleeding, Labile INRs, Elderly, Drugs or alcohol score
HDL	High density lipoprotein
HIIT	High intensity interval training
HR	Hazard ratio
HRT	Hormone replacement therapy
HSE	Health Service Executive (Ireland)

IAPT	Improving Access to Psychological Therapies
ICF	International Classification of Functioning, Disability and Health
ICH	Intracerebral haemorrhage
ILR	Implantable loop recorder
INR	International normalised ratio (for blood clotting time)
IQR	Interquartile range
LDL	Low density lipoprotein
MCA	Middle cerebral artery
mCIMT	Modified constraint-induced movement therapy
MDT	Multidisciplinary team
MHRA	Medicines and Healthcare Products Regulatory Agency
MI	Myocardial infarction
MICON	Microbleeds International Collaborative Network
MR	Magnetic resonance
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
mRS	Modified Rankin Scale score
MSU	Mobile stroke unit
MUST	Malnutrition Universal Screening Tool
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NDLS	National Driver Licence Service (Ireland)
NHS	National Health Service (UK)
NICE	National Institute for Health and Care Excellence
NIHSS	National Institutes of Health Stroke Scale
NIMAST	Northern Ireland Multidisciplinary Association of Stroke Teams
NMES	Neuromuscular electrical stimulation
NNT	Number needed to treat
NOAC	Non-vitamin K anticoagulant
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
OSA	Obstructive sleep apnoea
PADL	Personal activities of daily living
PAF	Paroxysmal atrial fibrillation
PC-ASPECTS	Posterior circulation – Alberta Stroke Program Early Computed Tomography Score
PCC	Prothrombin complex concentrate
PE	Pulmonary embolism
PES	Pharyngeal electrical stimulation
PFO	Patent foramen ovale
POC	Progestin only contraceptive
RBMT	Rivermead Behavioural Memory Test
RCP	Royal College of Physicians of London
RCT	Randomised controlled trial
ROSIER	Recognition of Stroke in the Emergency Room
RR	Relative risk
SAH	Sub arachnoid haemorrhage
SARA	Scale for the Assessment and Rating of Ataxia
SBP	Systolic blood pressure
SIGN	Scottish Intercollegiate Guidelines Network
SLT	Speech and language therapy
SMC	Scottish Medicines Consortium
SRU	Stroke rehabilitation unit
SSNAP	Sentinel Stroke National Audit Programme

SSRI	Selective serotonin reuptake inhibitor
SWI	Susceptibility-weighted imaging
tDCS	Transcranial direct current stimulation
TENS	Transcutaneous electrical nerve stimulation
TIA	Transient ischaemic attack
TMS	Transcranial magnetic stimulation
TOE	Transoesophageal echocardiogram
TTE	Transthoracic echocardiogram
TULIA	Test of Upper Limb Apraxia
VA	Vertebral artery
VKA	Vitamin K antagonist
VNS	Vagus nerve stimulation
VOSP	Visual Object and Space Perception battery
VR	Vocational rehabilitation
VTE	Venous thromboembolism
WHO	World Health Organization
WTE	Whole time equivalent

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