

# Secondary stroke prevention

## Key concepts

- People who have had a stroke or a TIA are at increased risk of a future stroke
- Secondary stroke prevention includes lifestyle interventions, blood pressure management, antithrombotic treatment, lipid lowering and maintaining good control of diabetes
- Carotid surgery (usually endarterectomy) may be considered after a TIA or a non-disabling stroke involving the carotid artery territory



## People who have had a stroke are at increased risk of having another

People who have had a stroke or a TIA are at increased risk of future stroke, especially in the following few months.<sup>1</sup> About 10% of those who survive their initial stroke have another stroke within one week, 14% by one month and 18% by three months.<sup>2</sup> Thereafter the risk falls to approximately 5% per year. There is also an increased risk of a MI (2–3% per year) and death from cardiovascular causes (approximately 7% per year).<sup>3,4</sup>


Secondary stroke prevention includes:

- Lifestyle interventions, especially smoking cessation
- Blood pressure management
- Antithrombotic treatment
- Lipid lowering agents
- Good control of diabetes
- Carotid surgery

## Lifestyle interventions

Patients should be supported to identify, prioritise and manage their individual risk factors:

- Stopping smoking
- Eating a healthy diet and achieving a satisfactory weight
- Avoiding excess alcohol
- Regular exercise

 For further information see “The science behind lifestyle risk factors for cardiovascular disease” BPJ 18, Dec 2008.

## Encourage all smokers to stop

Smoking is a major cause of strokes with smokers four times more likely to have a stroke compared with non-smokers.<sup>5</sup> Stopping smoking halves the risk of mortality from ischaemic heart disease within one year and the risk of stroke declines significantly after two to five years. By 10 to 15 years after quitting the risk of stroke is the same as that of a non-smoker.<sup>6</sup>

## Dietary modification

All patients should receive general advice about a healthy diet with plenty of fish, fibre, fruit and vegetables and low in saturated fat and salt.

Dietary improvements have been shown to reduce vascular risk factors.<sup>7</sup> Reducing salt intake to less than approximately one teaspoon per day may achieve a reduction in blood pressure equivalent to a single antihypertensive agent (~2–8 mmHg systolic).<sup>8</sup>

Dietary supplements such as folate or antioxidants have not been shown to improve stroke risk.<sup>9,10</sup>

## Alcohol in moderation is acceptable, but dangerous in excess

Alcohol consumption in moderation is acceptable and some studies have demonstrated a protective effect on the risk of stroke.<sup>11</sup> However excessive alcohol consumption increases the risk of haemorrhagic stroke.<sup>12</sup>

- Advise men to consume no more than three units of alcohol per day
- Advise women to consume no more than two units of alcohol per day
- Advise everyone to avoid binge drinking

## Regular exercise is part of a healthy lifestyle

There is good evidence for improved cardiovascular health with exercise although no direct evidence that exercise reduces the risk of stroke directly. However inactivity is associated with an increased risk of stroke.<sup>13</sup>

After a stroke exercise should be tailored to the level of disability, but in general:

- Advise people to undertake 30 minutes of at least moderate intensity exercise per day, which can be in bouts of 10 minutes or more throughout the day, at least five days per week
- Encourage people, who cannot manage this, to exercise at their maximum safe capacity
- Recommend exercise that can be incorporated into everyday life, such as brisk walking or using stairs

## Reducing blood pressure, reduces the risk of recurrent stroke

Reducing blood pressure is beneficial irrespective of the type of stroke, baseline blood pressure (even if normotensive) or age.<sup>14</sup> An average reduction of 8 mmHg systolic and 4 mmHg diastolic pressure reduces the relative risk of recurrent stroke by about one-quarter and reduces the risk of a MI or vascular death by about one-fifth.<sup>15</sup>

It is advisable to wait two weeks after a disabling stroke before reducing blood pressure. It is recommended to start, or use additional, antihypertensive medication as required to achieve a blood pressure of 130/80 mmHg or below depending on the individual patient.<sup>16</sup> One exception is patients with severe carotid stenosis who require a systolic blood pressure in the range 140–150 mmHg.<sup>16, 17</sup>

Thiazide diuretics or a combination of thiazides plus ACE-inhibitor have the greatest evidence of benefit for secondary prevention of stroke.<sup>15</sup> Although the benefit is believed to be mainly from the reduction in blood pressure rather than the specific antihypertensive, it seems reasonable to start with a thiazide and to add in an ACE-inhibitor as required.

## Antithrombotic treatment benefits most patients who have had ischaemic stroke

Antithrombotics reduce the risk of recurrent ischaemic stroke, however there is a risk of adverse effects, mainly intracranial and gastrointestinal haemorrhage.


### Antiplatelet therapy reduces the risk of ischaemic stroke

For the majority of patients the overall benefits of antiplatelet treatment outweigh the risks.<sup>18</sup> Antiplatelet therapy should be prescribed routinely unless there are clear contraindications or anticoagulants are more appropriate. Contraindications include:

- Recent gastrointestinal or other bleeding
- Symptoms of active peptic ulcer disease
- Allergy to aspirin or other antiplatelet drugs
- Intracranial haemorrhage

### Aspirin plus dipyridamole is the best antiplatelet therapy to reduce the risk of ischaemic stroke (Table 1).<sup>19</sup>

In most cases it is appropriate to start antiplatelet therapy as soon as intracranial haemorrhage has been excluded via brain imaging.

 For further information see “The role of antiplatelet agents” BPJ 19, Feb 2009.

### Anticoagulants are more appropriate for patients with atrial fibrillation and ischaemic stroke


People with atrial fibrillation and prior ischaemic stroke or TIA are at substantial risk of stroke (approximately 12% per year). Adjusted-dose warfarin treatment with a target INR of 2.5 results in a relative risk reduction of about two-thirds.<sup>20</sup> Benefit is shown in people of all ages including those who are very elderly.<sup>21</sup>

There are however many contraindications to anticoagulant therapy and up to 50% of people in this high risk group may

**Table 1:** Antiplatelet therapy for reducing recurrent ischaemic stroke or arterial origin.

Antiplatelet therapy	Recommendations
<b>Aspirin plus dipyridamole</b>	Best combination to reduce further stroke. Dipyridamole is now fully funded without restriction (since July 2009). Patients should be warned of the risk of dipyridamole-related headache that occurs in one-third of patients but usually settles in one to two weeks. Treat aspirin-related dyspepsia symptoms with PPI rather than swap to clopidogrel
<b>Aspirin</b>	Use alone only if intolerant to dipyridamole
<b>Clopidogrel</b>	Second line alternative to aspirin (or aspirin + dipyridamole) in those with true allergy or intolerance. Special Authority required.
<b>Dipyridamole</b>	Not recommended as single agent
<b>Aspirin plus clopidogrel</b>	Not recommended for routine prevention as increased risk of haemorrhage but benefit in severe carotid stenosis under specialist advice

not be able to take anticoagulants. Warfarin should not be started within 14 days of a disabling ischaemic stroke. For those unable, or unwilling, to take anticoagulants aspirin is a less effective but reasonable alternative.

 For further information see “Warfarin vs aspirin” BPJ 19, Feb 2009.

Some contraindications to anticoagulant therapy include:

- Haemorrhagic stroke
- Uncontrolled hypertension
- Recent gastrointestinal or other bleeding (previous six months)
- Severe liver disease
- Poor compliance with medication and monitoring (cognitive impairment, confusion, chaotic lifestyle, difficulty accessing anticoagulation services)
- Tendency to falls
- Planned surgery
- Pregnancy

Rarely patients may be treated with both anticoagulants and antiplatelets if they are at particularly high risk of thromboembolic disease e.g. mechanical heart valve. Generally the risks of a major bleed with this combination far outweigh the benefits.

### **Reducing cholesterol with statins reduces risk of ischaemic stroke**

Reducing total cholesterol blood levels with a statin reduces the risk of ischaemic stroke as well as other vascular events. The reduction in risk is directly proportional to the reduction of LDL cholesterol and is significant with changes as small as 1.0 mmol/L, regardless of the statin used.<sup>22</sup> Cholesterol reduction with a statin is recommended in all patients with a prior ischaemic stroke or TIA with baseline total cholesterol >3.5 mmol/L or LDL >2.6 mmol/L.<sup>23,24</sup>

In contrast the effect of statin treatment on the risk of haemorrhagic stroke is uncertain and may be detrimental. Current recommendations are to avoid statins in the majority of patients with haemorrhagic stroke.

Statins are usually well tolerated. Sometimes a patient who cannot tolerate one statin may tolerate another. Simvastatin 40 mg is recommended in New Zealand, although a lower starting dose of 20 mg may be appropriate in frail elderly people.<sup>13</sup> Atorvastatin is funded under special authority when high risk patients are intolerant of simvastatin or, despite compliance at maximum doses, have poor reduction of LDL.

For patients who cannot tolerate a statin, alternative lipid-lowering interventions (e.g. fibrates, diet) to try to reduce the LDL concentration could be considered. However the evidence of beneficial effect on stroke risk reduction appears to be limited to statins alone.

### **Management of diabetes**

Good glycaemic control has not been shown to directly improve the risk of macrovascular disease such as stroke.<sup>25</sup> However the prevention of microvascular complications, such as nephropathy, is likely to be beneficial.

### **Carotid surgery is beneficial for some carotid artery territory strokes**

Carotid surgery (usually endarterectomy) may be considered for some people after a TIA or a non-disabling stroke involving the carotid artery territory. It is not recommended for those with disabling stroke. Approximately 20% of all ischaemic strokes are associated with carotid artery disease (carotid stenosis). Endarterectomy is of clear benefit for patients with greater than 70% stenosis, but may be considered in those with 50–69% stenosis. It is of less benefit in near-occlusions or stenoses of less than 50%. Other factors that are taken into account are age, gender, time since last symptomatic event, type of symptomatic event(s) and plaque surface morphology.

Because any delay in surgery may result in what could have been a preventable stroke it is recommended that, if fit for possible surgery, patients with recent carotid artery territory symptoms should be referred urgently for carotid imaging and specialist review.<sup>26</sup>

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