# Stroke information sheet

Detailed information for patients, families and staff

## What is a Stroke?

**The arteries:** The brain receives about 25% of the body's oxygen, but it cannot store it. Brain cells require a constant supply of oxygen to stay healthy and function properly. A reduction of, or disruption in, blood flow to the brain is the primary cause of a *stroke*. The two Stroke types include ***Ischaemic*** (caused by a blockage in an artery), and ***Haemorrhagic*** (caused by a tear in the artery that produces bleeding harmfully into the brain). Blockage for even a short period of time can be disastrous and cause brain damage or even death. The consequences of a stroke, the type of functions affected, and the severity, depend on where in the brain it has occurred and the extent of the damage. The cells die. Within minutes of a stroke, the zone of initial cell death is surrounded by additional damaged and dying brain cells. This process can continue for hours, leading to brain damage, perhaps irreversible.

Blood needs to be supplied to the brain continuously through two main arterial systems:

* The *carotid arteries* come up through either side of the front of the neck. (The pulse of a carotid artery can be felt by placing the fingertips gently against either side of the neck right under the jaw.)
* The *basilar artery* forms at the base of the skull from the vertebral arteries, which run up along the spine, join, and come up through the rear of the neck.

## Stroke Subtypes:

## Ischaemic:

Ischaemic strokes are by far the more common type, causing over 80% of all strokes. Ischaemia simply means the deficiency of oxygen in vital tissues.

### Thrombotic (or Large-Artery Stroke Atherosclerosis):

* About 60% of all strokes, it usually occurs when an artery to the brain is blocked by a *thrombus* (blood clot) that forms as the result of *atherosclerosis* (commonly known as hardening of the arteries). As the process continues, blood flow slows. In addition, the injured inner walls fail to produce enough nitric oxide, a substance critical for maintaining blood vessel elasticity. The arteries become calcified and lose elasticity, and susceptible to tearing. In this event, the *thrombus* (blood clot) forms, then blocks the already narrowed artery and shuts off oxygen to part of the brain.

### Embolic Strokes:

Usually caused by a dislodged blood clot that has travelled through the blood vessels (an *embolus*) until it becomes wedged in an artery. Embolic strokes account for about 25% of all strokes and may be due to various conditions:

* In about 15% of embolic strokes, the blood clots originally form as a result of a rhythm disorder known as ***atrial fibrillation***. This abnormal rhythm is a rapid quivering beat in the upper chambers of the heart (the atria). Because of the irregular pumping, some blood may remain in the heart chamber where it forms clots, which can then break off and travel to the brain as emboli.
* Emboli can originate from blood clots that form at the site of artificial heart valves or as a result of heart valve disorders.
* Emboli can also occur after a heart attack or in association with heart failure.
* Rarely, emboli are formed from fat particles, tumour cells, or air bubbles that travel through the blood stream.

### Lacunar Strokes:

* Very tiny, ischemic strokes, which cause clumsiness, weakness, numbness, movement disorders, or emotional variability. They are actually a subtype of thrombotic stroke and constitute about 38% of this major group. In some populations, such as among Japanese, they are the most common stroke subtypes. They can also sometimes serve as warning signs for a major stroke.

### Silent Brain Infarctions:

* Many elderly people have silent brain infarctions, which are small strokes that cause no apparent symptoms. They are detected in between 10% and 38% of elderly patients who undergo imaging tests for problems other than stroke. A 2002 study suggested that they double the risk for future stroke. They also may be major contributors to mental impairment in the elderly. Smokers and people with hypertension are at particular risk.

### Transient ischemic attacks (TIAs):

* These are mini-ischaemic strokes, usually caused by tiny emboli (often formed of pieces of calcium and fatty plaque) that lodge in an artery to the brain. They typically break up quickly and dissolve but they do temporarily block the supply of blood to the brain. The mental or physical disturbances resulting from TIAs generally clear up in less than a day, with nearly all symptoms resolving in less than an hour. A transient ischemic attack is often considered to be a warning signal of an ischemic stroke, just as *angina* (chest pain caused by coronary artery disease) is the red flag for a heart attack. Some experts believe TIAs should actually be thought of as part of the continuum of stroke. Because blood supply is quickly restored to the brain, there is usually no residual damage as there is in a full-blown stroke, although some people experience some persistent problems. About 5-17% of those who experience TIAs go on to suffer a full stroke within a month, and without preventive treatment, a third will have strokes within five years.

## Stroke Subtypes:

## Hemorrhagic:

Over 15% of strokes occur from haemorrhage (sudden bleeding) in the brain. In a healthy brain, brain cells called neurons are protected from exposure to blood by the *blood-brain barrier*, a wall of tiny vessels and structural cells. In a hemorrhagic stroke, however, this barrier is broken. Hemorrhagic strokes may be categorized by how and where they occur.

### Intracerebral haemorrhage:

* These strokes occur within the brain and account for about 10% of all strokes. They are most often the result of hypertension exerting excessive pressure on arterial walls already damaged by atherosclerosis. Heart attack patients who have been given drugs to break up blood clots or blood-thinning drugs have a slightly elevated risk of this type of stroke. These bleeds can also be associated with amyloid protein changes in the arteries that weaken the artery walls.

### Subarachnoid haemorrhage strokes:

* This other major hemorrhagic stroke accounts for about 5% of all strokes. They occur when a blood vessel on the surface of the brain bursts, and blood leaks into the *subarachnoid space*, an area between the brain and the skull. They are usually caused by the rupture of an *aneurysm*, a weakening in the blood vessel wall, which is often an inherited trait.

### Other underlying lesions causing bleeds:

* E.g. arteriovenous malformation is an abnormal connection between arteries and veins. If it occurs in the brain and ruptures, it can also cause a hemorrhagic stroke. Tumours, cavernous angioma, venous sinus thrombosis are other possible causes.

## What are the symptoms of a stroke?

People at risk and partners or caretakers of people at risk for stroke should be aware of the general symptoms, and the stroke victim should get to the hospital as soon as possible after these warning signs appear.

It is particularly important for people with migraines or frequent severe headaches to understand how to distinguish between their usual headaches and symptoms of stroke.

The speed of symptom onset of a major ischaemic stroke may indicate its source.

If the stroke is caused by a large embolus (a clot that has travelled to an artery in the brain), the onset is sudden.

When thrombosis (a blood clot that has formed within the brain) causes the stroke, the onset usually occurs more gradually, over minutes to hours. On rare occasions it progresses over days to weeks.

### Symptoms from Blockage in the Carotid Arteries*.*

Symptoms may occur in either the retina of the eye, where people describe the visual effect as a shade being pulled down. People may develop poor night vision. About 35% of TIAs are associated with temporary lost vision in one eye. Although such events are risk factors for future stroke, they pose a lower risk for a stroke and its complications than more widespread TIA symptoms. When the brain itself is affected, a person can experience problems with speech and partial and temporary paralysis, drooping eyelid, tingling, and numbness, usually on one side of the body. The stroke victim may be unable to express thoughts verbally or to understand spoken words. If the stroke injuries are on the right side of the brain, the symptoms will develop on the left side of the body and vice versa. Uncommonly, patients may experience seizures.

Symptoms from Blockage in the Basilar Artery. Symptoms may include

* Temporarily dim, gray, blurry, or lost vision.
* Tingling or numbness in the mouth, cheeks, or gums.
* Headache, usually in the back of the head.
* Dizziness.
* Nausea and vomiting.
* Difficulty swallowing.
* Weakness in the arms and legs, sometimes causing a sudden fall.

Such strokes usually occur in the brain stem, which can have profound affects on breathing, blood pressure, heart rate and other vital functions, but does not affect thinking or language.

Cerebral Haemorrhage Symptomstypically begin very suddenly and evolve over several hours and include:

* Headache.
* Nausea and vomiting.
* Altered mental states.
* Seizures.

Subarachnoid Haemorrhage*.* Warning signs may occur from the leaky blood vessel a few days to a month before the aneurysm fully develops and ruptures. Warning signs may include:

* Abrupt headaches.
* Nausea and vomiting.
* Sensitivity to light.
* Various neurologic abnormalities.
* Seizures, for example, occur in about 8% of patients.

When the aneurysm ruptures, the stroke victim may experience the following:

* A terrible headache.
* Neck stiffness.
* Vomiting.
* Altered states of consciousness.
* The eyes may become fixed in one direction or lose vision.
* Stupor, rigidity, and coma.

## HOW SERIOUS ARE STROKES?

A stroke is always serious. Stroke is the third leading cause of death in the western world. The mortality rates are declining, however. Over 75% of patients survive a first stroke during the first year and over half survive beyond five years. People who suffer *ischaemic* strokes have a much better chance for survival than those who experience *hemorrhagic* strokes. Among the ischaemic stroke categories, the greatest dangers are posed by embolic strokes, followed by large-artery (thrombotic) and lacunar strokes. Hemorrhagic stroke not only destroys brain cells, but it poses other complications as well, including increased pressure on the brain or spasms in the blood vessels, both of which can be very dangerous. Studies suggest, however, that survivors of hemorrhagic stroke had a greater chance for recovering function than those who suffered ischemic stroke, and that that recovery may start a little later after bleeds.

Between 50% and 70% of people recover functional independence after a stroke. However, between 15% and 30% of those who survive either an ischaemic or haemorrhage stroke suffer some permanent disability. On the encouraging side, one 1998 study reported that people who survived for many years after a stroke had a chance for independent living that was about the same as for their peers who had not suffered strokes. The stroke patients even appeared to be less depressed than the comparison group. The National Institutes of Health scoring system (NIHSS) helps predict the severity and outcome of the stroke. Up to 70% of patients with ischaemic strokes who score less than ten have a favourable outlook after a year, while only 4% to 16% of patients do well if their score is more than 20.

The risk for recurring stroke is highest within the first few weeks and months. The risk is about 14% in the first year and about 5% thereafter, so preventive measures should be instituted as soon as possible. Some specific risk factors for early recurrence include being older, having other blocked arteries (past history of coronary, peripheral, or cerebral artery disease), having a symptomatic internal carotid artery stenosis, having stroke (rather than just TIA), diabetes, alcoholism, valvular heart disease, or atrial fibrillation.

## WHICH LIFESTYLE AND DEMOGRAPHIC FACTORS REDUCE STROKE RISK?

New or recurrent strokes affect about 7,600 New Zealanders every year (5640 first ever, 1960 recurrences). Although incidence of stroke increased over the last 1-2 decades, more people are surviving stroke, and the death rate from this condition fell by about 15% during that period. While **age** is the major risk factor, in general, people with stroke are likely to have more than one risk factor. Differing stroke types are associated with differing risks of recurrence. For example a tight carotid artery narrowing in the neck from “hardening of the arteries” carries a 30% 2 year risk, whereas a torn artery (dissection) in the same location carries a much lower risk if medically managed. Atrial Fibrillation carries 12-17% risk over 1 year, whereas other cardiac sources of clot the risk is much lower. Lacunar strokes have a low recurrence rate. A stroke victim’s individual characteristics may play a role in the development of the first stroke, but also in recurrence. Some such as age, past medical history, ethnicity, sex and to some degree socio-economic status are not modifiable, but others are able to be changed.

***Mediterranean diet:*** (fruit veges,seeds,nuts, olive oil, exercise, avoid processed or packaged foods) has been shown in a recent large excellent scientific trial to reduce risk of stroke+heart attack+death by 1/3 and when a half-handful of walnuts and other nuts per day was added the stroke rate was reduced by 1/2. This is the single best evidence available in 2013 that we can change our risk by changing our lifestyle. The control group in the trial was on a careful low-fat diet which clearly was not effective by comparison.

***Smoking:*** People who smoke a pack a day have almost two and a half times the risk for stroke as non-smokers. Smoking increases both hemorrhagic and ischaemic stroke risk. The risk for stroke may remain elevated for as long as 14 years after quitting (although a sizeable reduction in risk occurs over 2 years), so the earlier one quits the better. All people should stop smoking and avoid passive smoking.

***Exercise.*** The benefits of exercise on stroke are less established than on heart disease, but a number of studies, including the following, suggest positive benefits: According to one analysis of a group of 11,000 men, those who burned between 2,000 and 3,000 calories a week (about an hour of brisk walking five days a week) cut their risk of stroke in half. Groups who burned between 1,000 and 2,000 calories or more than 3,000 calories per week also gained some protection against stroke but to a lesser degree. In the same study, exercise that involved recreation was more protective than exercise routines consisting simply of walking or climbing. A 2000 study of women also found substantial protection from brisk walking or striding (rather than casual walking). Everyone in normal health should engage in at least moderate physical activity for a minimum of 30 minutes on most days of the week for people whose careers involve mobility (e.g. hairdressers, teachers). Sedentary careers should target 60 minutes puffing and sweating per day, 5-6 days per week; vigorous careers probably provide adequate exercise. Progressive loss of excess weight should be used as an indicator that enough exercise is being done at a high enough intensity in any one individual.

***Healthy Diet.*** Everyone should aim for a diet that contains a healthy balance of fruits, vegetables, grains, fish, nuts, legumes, poultry, lean meat, and low-fat dairy items. Avoid saturated fats and trans-fatty acids. There is good evidence that 6-9 servings of fruit and vegetables per day is associated with much lower risks of vascular events like stroke. Vegetarian diets, regular fish eaters, and “occasional meat eaters” all have 25-30% less vascular risk when compared to regular meat eaters. A target might be to have meat 2x/week, fish 2-3x/week and vegetarian meals the remainder. Artificial sugars are an unknown quantity and whilst well tolerated for some, they marry carry unwanted effects. They may be particularly useful for those with diabetes or impaired glucose tolerance.

***Fruits and Vegetables****.* Studies now suggest that individuals can protect their heart and circulation by eating plenty of fruits and vegetables. Eating such foods, according to a 2002 study, reduces blood pressure and protects against both heart attack and stroke. Important foods include most fruits (especially potassium-rich fruits including bananas, oranges, prunes, and melons) and vegetables (especially carrots, spinach, celery, alfalfa, mushrooms, lima beans, potatoes, avocados, broccoli). Vegetables, such as broccoli and kale may be specifically protective against a first ischemic and possibly hemorrhagic stroke. Foods such as apples and tea, which are high in food chemicals called flavonoids, may also be very beneficial. A 2000 study reported a lower incidence in stroke in women who had a high intake of whole-grain foods (e.g. muesli). Nuts may also be protective.

***Ground flaxseed (=linseed).*** A small pilot study showed marked improvements in blood pressure (the single greatest risk factor for stroke) in patients with peripheral artery disease who added this to their diet (~3 Tablespoons per day).

***Potassium***  is important in controlling blood pressure and may also have protective effects against stroke: Some evidence suggests that diets rich in potassium (fruit, veges, seeds, nuts, chocolate) may protect against stroke by 22% to 40%, mostly by reducing blood pressure but also possibly because of other mechanisms. Low potassium levels may also increase the risk for stroke in certain people. In a 2000 study, potassium-poor diets were associated with a higher risk for stroke only in men with hypertension. A major 1999 study reported that calcium intake is associated with a lower risk for stroke in women, which supports an earlier study reporting a lower risk for stroke in men who drank more milk. Magnesium deficiencies may increase the risk for atrial fibrillation. No evidence yet exists, however, that taking magnesium supplements is protective.

***Salt restriction****.* Although the effects of salt restriction are not entirely clear, a 2002 study indicated that even a modest reduction in salt intake for more than month might reduce the risk of deaths from stroke by 14% in people with high blood pressure and 6% in people with normal blood pressure.

***Fats and Oils, Meat and Fish****.* The effects of fats and oils on stroke are complex. One study indicated that middle-aged men without heart disease who had the highest intake of monounsaturated or saturated fat (but not polyunsaturated oils) also had the lowest risk for stroke. Monounsaturated oils, obtained in olive and canola oils may have protective benefits against both heart disease and stroke. Saturated fats, found in animal products, are known risk factors for heart disease. Some studies suggest, however, that low intake of animal protein and saturated fats increases the risk of hemorrhagic stroke. Other fat compounds that may be stroke protective are omega-3 fatty acids: One form called alpha-linolenic acid is found in canola oil, soybeans, and walnuts. It has particular benefits against stroke by helping to prevent the formation of blood clots. Omega-3 fatty acids are further categorized as docosahexaenoic (DHA) and eicosapentaneoic acids (EPA). They are found in oily fish and may be obtained in supplements. These compounds have anti-inflammatory and anti-blood clotting effects and may be significantly beneficial to the heart and reduce the risk for stroke.

Consuming fish two or three times a week, in any case, helps the heart and one study suggested that eating fish only one to three times a month protected against ischaemic stroke. It should be noted that some studies have suggested that very high amounts (five or six servings weekly) of these fish can be harmful. A very high intake, for example, can increase the risk for a hemorrhagic stroke.

***Antioxidant Vitamins****.* The effects of antioxidant vitamins and carotenoids on stroke, dementia, or both have been studied. Studies are conflicting, however. A very important 2001 study reported no protection from stroke with vitamins A (more death), E (more bleeds) or beta carotene.

***Coffee****.* In healthy people with normal blood pressure, drinking a couple of cups of coffee a day is unlikely to do any harm. In fact, caffeine may have nerve-protecting properties that may help stroke survivors. Caffeine drinkers, however, might do better to choose tea, which may have beneficial nutrients, and people with existing hypertension should avoid caffeine altogether (since caffeine may increase the risk for stroke in this group).

***Alcohol.*** Mild to moderate alcohol use (one to seven drinks a week) is associated with a significantly *lower* risk for ischaemic stroke, although not hemorrhagic stroke. Heavy alcohol use, particularly a recent history of drinking, is associated with a higher risk of both ischaemic and hemorrhagic stroke.

***Obesity:*** may increase the risk for both ischaemic and hemorrhagic stroke independently of other risk factors that often co-exist with excess weight, including insulin resistance and diabetes, high blood pressure, and unhealthy cholesterol level. Weight that is centred around the abdomen (the so-called apple shape) has a particularly high association with stroke, as it does for heart disease, in comparison to weight distributed around hips (pear-shape). People should aim for a BMI index of 18.5 to 24.9. In people who are obese, reducing weight to this level can reduce the risk for stroke by 15% in men and 22% in women.

***Stress:*** One survey revealed that men who had a more intense response to stressful situations, such as waiting in line or problems at work, were more likely to have strokes than those who did not report such distress. In some people, prolonged or frequent mental stress causes an exaggerated increase in blood pressure. In fact, a 2001 study has linked for the first time a higher risk for stroke and elevated blood pressure during times of stress in adult Caucasian men (particularly those in lower socioeconomic groups). Depression has also been linked to a higher risk for having a stroke and lower survival rates after one. In one 2000 study, for example, patients with severe depression had a 73% higher risk for stroke, and those with moderate depression had a 25% higher risk than average.

***Migraine:*** Studies have found that migraine or severe headache is a risk factor for stroke in both men and women, especially before age 50. Interestingly there is some evidence that patients with raised Homocysteine (above the median of 9.2) have less troublesome Migraine when on the high dose B vitamins described in the previous section of this paper. Overall, between 1.8% and 3% of ischaemic strokes occur in people with a history of migraine. However, in patients under age 45, about 15% of all strokes (and 30% to 60% of strokes in young women) are associated with a history of migraines, particularly migraine with aura. Some evidence suggests that some strokes in these cases may actually be due to excessive activation of the nervous system and dehydration (e.g. from vomiting) that occurs during a severe migraine with aura. There is some weak evidence to suggest that stroke patients with a history of migraines tend to have a better outlook than other stroke patients. Interestingly, a 2001 study reported that in people who experienced migraine-related stroke, the frequency of migraines declined afterward. The actual stroke risk for migraineurs is low, however. In one study, women with migraines had a 2.7% risk of stroke, with the time of greatest risk between the ages of 45 and 65. Men with migraines had a 4.6% risk and their greatest time of risk was before age 45. In both genders, the risk then diminished with age. Studies suggest specific risk factors for younger women with migraines, particularly those with auras, include taking high-oestrogen oral contraceptives (OCs). (Whether progesterone-alone contraceptives carry any risk is unknown.) In migraineurs who take OCs, the risk increases with high blood pressure, smoking, or both.

***Sleep apnoea:*** may contribute to the narrowing of the carotid artery, appears to increase the risk for stroke three- to six-fold, but the success of treatment for stroke prevention is unknown.

***Pregnancy:*** carries a very small risk for stroke, mostly in women with pregnancy related high blood pressure and in those with caesarean delivery. The risk appears to be higher in the postpartum (post-delivery) period, perhaps because of the sudden change in circulation and hormone levels. Strokes are often from venous but can also be from arterial blockages.

***Infections and Inflammation:*** Inflammation that occurs with various infections has been associated with stroke. A 1998 study found that patients hospitalized for stroke were three times more likely than patients without strokes to have recently been exposed to infections, usually mild ones in the respiratory tract. Varicella zoster virus (the virus that causes chicken pox and shingles) has been associated with cerebral vasculitis, a condition in which blood vessels in the brain become inflamed. It is a very rare cause of stroke in children. The virus has also been associated with some cases of stroke in young adults. Some investigators suspect that some infections may produce inflammation in the arteries that can lead to stroke over time. (Similar work is underway in heart disease.) Researchers are particularly interested in *Chlamydia pneumoniae,* a non-bacterial organism that causes mild pneumonia in adults. Chronic infection has been linked with a higher risk for stroke and evidence of the organism has been observed in thickened inner vessel walls of the carotid arteries in some studies. *Chlamydia* has also been linked to heart disease. *Periodontal Disease.* A number of studies now strongly support an association between periodontal disease and cardiovascular disorders. According to a major 2003 analysis, periodontal (gum) disease is associated with a 20% higher risk for ischemic stroke and heart disease. (The added risk may be even greater in adults under 65.) Recent evidence is pointing to the inflammatory response as the common element.

***Anti-phospholipid antibodies:*** Nearly 40% of young people with strokes and 10% of all stroke patients have components of the immune system known as anti-phospholipid antibodies that increase the chance for blood clots.

***Sickle-cell anaemia:*** People with sickle-cell anaemia are at risk for stroke at a young age.

***Drug abuse***, particularly with cocaine and increasingly methamphetamine (an amphetamine), is a major factor in the incidence of stroke in young adults.

***Neck manipulation****.* Some studies have reported a higher risk for stroke from injury to the carotid artery after neck manipulation by a chiropractor.

***Anabolic Steroids:*** Steroids used for body-building increase the stroke risk.

***Older adults.*** People most at risk for stroke are older adults, particularly those with high blood pressure, who are sedentary, overweight, smoke, or have diabetes. Older age is also linked with higher rates of post-stroke dementia. In the older age groups, studies are mixed on the effects of stroke by gender. Younger people are not immune, however; about 28% of stroke victims are under 65. Strokes in younger people affect men and women equally.

***Gender:*** In most age groups except older adults, stroke is more common in men than in women. However, it kills more women than men, regardless of ethnic groups. Women may have a higher risk for hemorrhagic strokes than men (although this risk is not consistent in all countries). It is not clear why women have a higher mortality rate from stroke. In one study comparing men and women with atherosclerosis (hardening of the arteries), the risk for stroke in women appeared to be higher with less blockage in the blood vessels. Another study also reported that women had a higher risk for fatal strokes after heart surgery, and also after carotid endarterectomy surgery used to prevent strokes. The arteries that lead to the brain may be more vulnerable to the effects of plaque build-up in women than in men.

***Ethnicity:*** Maori and Pacific peoples face a significantly higher risk for stroke and stroke death than Pakeha. The risk is also higher in Asians, although some evidence reports a marked decline in incidence in this group over the past decades. The greatest disparity in risk occurs in young adults. These high-risk groups have a higher prevalence of diabetes and hypertension than other groups, and studies suggest socioeconomic factors are important in these differences. Poorer diets, higher stress levels, and lack of access to health care certainly play a role in the higher rates. Socioeconomic disparities may play a large role in the differences in mortality between ethnic groups.

***Past history of Heart disease:*** often have risk factors for stroke, such as high blood pressure, atherosclerosis (hardening of the arteries), and diabetes. The risk of stroke is also increased during surgical procedures involving the coronary arteries, including coronary bypass operations and angioplasty. Coronary bypass poses the greater risk--about 2% to 5%. Anti-clotting drugs used for treatment of heart disease and heart attacks slightly increase the risk for hemorrhagic stroke. A heart attack itself poses a high risk for stroke, which, according to a major 2002 study, is 5% per year. The highest risk group (4% within six months) in an American study tended to be older (over age 75), African American, or to have a history of a previous stroke, atrial fibrillation, hypertension, diabetes, or peripheral artery disease. Most people at high risk have more than one of these problems.

***Peripheral artery disease (PAD):*** is atherosclerosis of the extremities, particularly the feet and legs is associated as a similar pathology to large artery stroke types.

***Genetics:*** may be responsible for many of the causes of stroke. Studies indicate that a family history of stroke, particularly in one's father, is a strong risk factor for stroke.

***Subarachnoid Haemorrhage*** *(SAH):* genetics account for between 7% and 20% of SAH, and genetic ruptured aneurysms happen younger, are smaller, are more apt to recur, and first-degree relatives have a high lifetime risk of 2 - 5%. Some experts recommend screening for aneurysms in people with more than one close relative who suffered a hemorrhagic stroke.

***Stroke:*** Some cases of atrial fibrillation may be inherited. Genetic disorders that cause connective tissue disorders are also associated with stroke from haemorrhage; they include polycystic kidney disease, Ehlers-Danlos syndrome type IV, neurofibromatosis type 1, Marfan's syndrome, and moyamoya disease. Factors causing blood clots (and hence stroke) include protein C and S deficiencies in the young (2 factors which inhibit blood clotting), factor V Leiden, a prothrombin mutation, homocysteine metabolism deficits. People who have inherited a gene called apolipoprotein (Apo) E-4 may be at increased risk of stroke but more studies are needed. In addition factors such as cholesterol, diabetes, blood pressure have both genetic and environmental contributions.

**WHAT ARE THE MEDICAL AND SURGICAL MEASURES FOR PREVENTING A STROKE?**

## Summary: Every person with Stroke should be assessed and informed of their risk factors for a further Stroke and possible strategies to modify identified risk factors. The role of antiplatelets or anticoagulants, blood pressure lowering, statins and lipid lowering, and carotid surgery should be considered in all patients.

1. Optimal BP (SBP intensive targets ~135/80mmHg if tolerated (but for bleeding strokes and lacunar strokes and for diabetics with stroke aim is lower < 130/80)
2. Cholesterol lowering, especially in large artery disease: LDL (<1.8 on Atorvastatin), HDL(>1.0 men, >1.2 women), TG (<2). Not used for bleeding strokes, and minimally effective in lacunar strokes.
3. Antiplatelet medications (clopidogrel or aspirin+dipyridamole) control achieves 75% RRR for stroke.
4. In TIAs and minor strokes, at high risk aspirin+clopidogrel but only x 3-4 weeks then monotherapy with clopidogrel (CHANCE trial)
5. Dabigatran for stroke/TIA patients 150mg bd for AF and PAF gives a RRR for stroke of 75%, (and about 25% less strokes than when on warfarin in our stroke/TIA cohort)
6. Endarterectomy (ASAP for TIA, and milder strokes) for high grade stenosis achieves **absolute** RR of 25% (90-99% stenosis), 20% (80-90% stenosis), 12.5% (70-80% stenosis), and 6.25% (males 50-75% stenosis, or possibly very high risk females=hemispheric infarct, DM, >70yo, multiple, BP, prior MI) when performed out to 6 months from event (meta-analysis), but with most events occurring first 6/52. Early CEA is desirable except for major infarcts, then delay 2 weeks.

**a) medical**

***Blood thinning antiplatelet drugs.*** People whose risk for heart disease within ten years is 10% or more should take a low-dose aspirin every day, unless they have medical reasons to avoid aspirin. It may also be helpful to prevent a second stroke, although it is unclear if it is helpful in preventing a first stroke, except possibly in patients with TIAs. Dipyridamole combined with aspirin doubles the protective effect of aspirin in patients presenting with TIAs or stroke. One third of patients cannot tolerate it for headache or gut side-effects, but those who can take this usually well tolerated drug will benefit. Together a ~40% reduction in further events was obtained, compared with ~20% with aspirin alone. This would take an average 5 year risk of 25% for having another stroke to 20% on Aspirin alone, and 15% on the combination.

**Aspirin is the acute Stroke choice**, reducing death/disability if given ASAP,

probably used alone for as long as the first 2 weeks for large infarctions (or until 1 week or until earlier discharge for mild-moderate strokes):

initially give 300mg dispersible orally for rapid effect. The ongoing dose is 100-300 mg. Dispersible formulations are recommended for lower doses (eg 25mg bd or 75mg od), especially in larger patients due to aspirin pharmacodynamics.

Gives a 20% relative risk reduction in events but monotherapy alone beyond the acute phase is now superceded by more effective options below.

Aspirin is still appropriate therapy after haemorrhagic transformation of ischaemic Stroke, unless there is massive bleeding when initiation of aspirin should be delayed.

**Aspirin+Dipyridamole** (150mg bd or tds) is effective in most ischaemic Strokes. Prefer in those needing Fluoxetine, or in those having an event on Clopidogrel. Dipyridamole can be problematic for migraine sufferes, worsening headaches.

ESPRIT and ESPS2 trials support a further 20% relative risk reduction in events over and above aspirin alone (RRR 40% vs Placebo).

EARLY trial was a small open label study with trends favouring initiation of Aspirin+Dipyridamole within 24hrs compared with > 1 week. Side effects were again problematic. Stroke/MI/Death at 90days was 10% <24hr vs 15% >7d, HR=0.73, p=0.20.

Combination therapy offers the advantage of making drug resistance less likely

5% cannot tolerate headache and GI side-effects if started slowly, but 25-33% if started quickly. Begin 75mg (1/2 a scored 150mg tablet) od then bd then 75/150mg then 150mg bd then possibly tds. Escalations as soon as tolerated. Swap to Clopidogrel if not tolerated.

**Clopidogrel** 300 load then 75mg daily. It will be preferred over Aspirin+Dipyridamole in most cases (as 1 tablet once daily is simpler), especially for those having an event on Aspirin. Avoid Omeprazole and Fluoxetine.

is as effective as Aspirin+Dipyridamole (PROFESS study), and is better than Aspirin alone (RRR 8% in one CAPRIE, but A+D is RRR 19% vs Aspirin, ESPS2). This is also true for early recruitment<1 week of onset

**Aspirin+Clopidogrel short term:**

**CHANCE** trial 2013 supports this combination for 3 weeks then clopidogrel alone, after stroke NIHSS<4 or TIA ABCD2>/=4. This was also supported by the EXPRESS and FASTER trials.

**SAMMPRIS** trial showed very impressive stroke rates in intracranial atheroma, stenosis>70% when treated for 3 months with this combination (10% at 1 year compared with WASID trial on Aspirin of 24% 10 years earlier)

MATCH trials combining aspirin and clopidogrel long term in Stroke was negative. Ischaemic stroke gains slightly outweighed by haemorrhagic problems.

CHARISMA trial PostHoc (Graham Hankey) subanalysis with transient ischaemic attack and ischaemic stroke for the primary efficacy outcome = stroke, and safety outcome severe bleeding, during the 2 yr follow-up period, for those randomised within 30 days (1334 highest risk patients)

Stroke; A+C 5.1% vs 6.9% A, HR=0.74, NSS

Severe bleeding A+C 1.4% vs 1.6% A, HR=0.83, NSS

Stroke/MI/Vascular death 14.3% vs 17.2%, HR= 0.82, p=0.15

**Antiplatelet resistance and laboratory testing**

Several different tests appear to confirm the notion that laboratory resistance has clinical relevance, however none of the tests correlate with each other, nor have any useful sensitivity nor specificity for clinical events. Most commentators say there is no role yet for platelet function testing (a paradox of great concern)

Omeprazole has a definite effect reducing clopidogrel platelet effects, but no clinical efficacy has been proven. Pantoprazole does not have this issue so use it.

Aspirin resistance is also well recognised but of uncertain clinical relevance. Aspirin doses < 100mg should be soluble rather than slow release. Large people should have aspirin >/=150mg daily. Do not test for platelet function as a routine.

Aspirin+Dipyridamole offers some protection against single drug resistence.

There are 2 effective options. Clinical resistance to one should lead to swapping to the other. If patients have noted significant bleeding/bruising tendencies, the regime is probably working. If an event has happened on one, then consider changing to the other option, or increasing the Dipyridamole from 150mg bd to tds.

Much of antiplatelet resistance is probably compliance failure

***Improve Cholesterol.*** Cholesterol and other lipids play a major role in heart disease, but their role in stroke is less clear. In Ischaemic stroke, one study suggested that the risk increases when total cholesterol is above 7.2 mmol/l. HDL (good cholesterol) may protect against ischaemic stroke (although statins have little effect on HDL). In Hemorrhagic stroke HDL may also reduce the risk, but cholesterol levels below 4.2 mmol/l may be at increased risk, especially if they also have high blood pressure. People with at least two risk factors and a 10-year risk for heart disease or stroke of more than 20% (Stroke patients almost always fulfil this) should aim for LDL levels of less than 2.56 mmol/l. Raising HDL levels is important for people at risk for stroke. HMG-CoA reductase inhibitors, commonly called statins are very effective at lowering cholesterol. According to a 2003 major analysis of over 200 studies, they reduce risk for heart events by 60% and stroke by 17%. Statins have nerve-protecting properties and some evidence suggests that taking statins may help stroke sufferers recover more quickly. More research is needed to confirm this. The cholesterol medication most readily available in New Zealand (Lipex 40mg/day fully funded) is known to assist all vascular case in preventing bad outcomes. Unfortunately whenever Stroke patients are analyzed alone (excluding heart attack patients from the data), trials consistently indicate that no benefit was obtained. Only one extremely aggressive treatment was actually proven to safely prevent stroke. Atorvastatin 80mg/day is funded in NZ for stroke patients but caution in the elderly/frail with lower doses used.

**Statins:** There is now data for Stroke reduction with statins from secondary Stroke prevention studies. Check fasting lipids on all ischaemic stroke/TIA patients, start statins early to achieve LDL targets, and recheck fasting lipids in 1 month before FU clinic. Do not use in ICH.

Statins may not be appropriate in the very elderly (begin gently, if at all), those with low cholesterol or in patients with cardioembolic events unless there is another indication for lipid therapy.

The **SPARCL** trial provides the best data for a benefit in Stroke patients with Atorvastatin 80mg daily. This drug is preferred. High dose Simvastatin is now considered potentially dangerous. Monitor muscle symptoms, CK, LFT. Target LDLs are <1.8mM, with markedly better outcomes when this was achieved, no excess of ICH

Note that patients who have had a TIA or Stroke are also at high risk of a cardiac event and there is probably a greater benefit from statins in the reduction in MI than in preventing Stroke

Ezetimibe is probably not clinically useful.

**Niacin (Vitamin B3)** may be helpful (begin low, build slow) if the HDL (bad cholesterol, optimal >1.0 men, >1.2mM women) is severely low (eg<0.85) but otherwise use Statins alone. AIM-HIGH had a placebo group with HDL average 0.99 and a small improvement in HDL on Niacin and this was not effective when added to Statin.

***Keep Blood Pressure Low.*** High Blood Pressure (Hypertension) contributes to 70% of all strokes. In fact, researchers have estimated that nearly 40% of strokes could be averted by controlling blood pressure. Two numbers are used to describe blood pressure phases and may affect stroke risk separately: *a) the systolic pressure* (the higher and first number) is measured as the heart contracts to pump out the blood. Evidence suggests that elevated systolic pressure poses a significant danger for heart events and stroke events when diastolic is normal, a condition called *isolated systolic hypertension*. The wider the spread between the systolic and diastolic measurements, the greater the danger. b) *The diastolic pressure* (the lower and second number) is measured as the heart relaxes to allow blood to refill the heart between beats. Abnormally higher *diastolic* pressure is a strong predictor of heart attack and stroke in most people with hypertension. Patients with certain health problems, such as stroke should aim for a low BP. There is evidence that at a young age “lower is better”, as long as side-effects do not results. An arbitrary target in younger years might be aggressively set at 120/70 mmHg. Lifestyle factors such as Mediterranean diet, ground flaxseed, smoking cessation, small amounts of dark chocolate, weight loss, exercise, low salt, low caffeine, managing obstructive sleep apnoea are all important. Medications might include diuretics, calcium channel blockers or Beta-blockers (the latter not good for lipids, diabetes, asthma or poor sleep). Over and above these drugs the use of Angiotensin Converting Enzyme inhibitors (ACEi) is highly effective. The combination of ACEi/diuretic reduced bad outcomes by 40% in ischaemic stroke, and by 75% in Haemorrhagic stroke. Either of those two treatments alone was minimally effective 5% reduction only).Two ACEi have been proven, Ramipril (Tritace or Altace) alone, and Perindopril in combination with Indapamide (Coversyl Plus). Neither of these are funded in NZ. Indapamide is funded. Several combination ACEI/diuretics are available funded in NZ. This includes Accuretic, Co-Renitec, Inhibace plus, and there is no strong reason to assume these will be less effective than Coversyl Plus, and they are much cheaper agents. Drug therapy is always recommended for people with hypertension where there is evidence that it is affecting the organs. An important study in 2003 suggested that using low-doses of three different agents to lower pressure may reduce the risk of stroke by 63% and heart disease by half. Using low doses also reduces the risk for side effects.

* Based on the PROGRESS trial the target BP should be 135/80 in the first 6 months after stroke, and based on the PROFESS trial one could aim a little lower (<130/80) from 6 months onwards. In addition target BP should be at least < 130 systolic in Diabetics after stroke, and in patients with lacunar stroke and those with bleeding stroke, especially amyloid angiopathy. However **caution is required with aggressive BP approaches**; vasculopaths have
  + Rigid vessels due to age, poor autoregulation
  + Rigid vessels due to atheroma or chronic BP, poor autoregulation
  + Occluded large arteries with compromised cerebral perfusion around the circle of willis making the brain vulnerable to hypotensive insults.

For this reason large artery imaging with Duplex, MRA or CTA is advised prior to zealous BP lowering (eg targets of <120/80), and aggressive approaches should not be used if critical large artery pathology is detected. A very gradual and incremental approach to achieving such intensive targets over many months might still be considered. Careful attention to BP and a 24 hr BP monitor should also be used to this end.

* Other medications for BP: Short-acting BP medications should be avoided. Preferred drugs also include Felodipine, Nifedipine ER, Angiotensin receptor antagonists, and in resistant cases K+-sparing diuretics may be required.
* Delay starting treatment for large artery strokes in view of altered cerebral autoregulation in the first 2 weeks. It is probably best to wait a 1 week for lacunar Strokes or other moderate strokes. After TIA start early (again cautions re vasculopaths above apply)

***Homocysteine and Vitamin B Deficiencies:***  this is a controversial area, and the final answers are not quite here. Studies show that Homocysteine-lowering is not an appropriate treatment for ischaemic heart disease (MI or angina patients possibly suffering worse symptoms). Metanalysis of all stroke-related data (2010) showed that it is likely that this treatment benefits small vessel injury in the brain but not large artery or cardioembolic proceses. A 2015 chinese study reveals that in that population folate replacement reduces stroke, but there is an interplay with a common genetic b-vitamin metabolism mutation (MTHFR). The study suggests that if you are folate deficient you’ll respond to Folate 0.8mg daily, but if you are genetically predisposed you won’t benefit from this level and may therefore need higher dose (eg 5mg 3 days per week = my interpretation)

* B-vitamins may reduce stroke in high risk vascular patients by 8% (p=0.05) but didn’t reduce MI, nor combined (Stroke MI or vascular death) endpoints.
* from the VITATOPS study; Those who benefit most in % reduction of the endpoint (ie stroke or heart attack or vascular cause of death) after an average of 3.4yrs followup were TIAs (14🡪10%), milder strokes (more often small vessel stroke types) (22🡪18%), small artery strokes (17🡪14%), intracerebral haemorrhage (ie another small vessel stroke type) (18🡪12%), and those with normal renal function (renal failure is often associated with large artery disease) (18🡪15%).
* The main factors to reduce Homocysteine are B-vitamins. Vitamin B12 is very difficult for some patients to absorb from the stomach, so treatment either under the tongue, or by injection may be needed, and blood levels should rise to the upper end of the normal range.

**Folate** 5mg tablet every 3 days (2mg daily was the researched dose) (prescribed or OTC)

**Pyridoxine (B6)** 100mg every 3 days (25-50mg/d = researched dose) (prescribed or OTC)

**Vitamin B12** at 1000mcg po or s/l every 3 days. (500-1000mcg daily was researched). Find a dose which pushes their B12 level to upper range and corrects homocysteine. Oral formulations Methylcobalamin are not funded (obtain from “health food stores”).

***Control Diabetes and Insulin Resistance:*** Heart disease and stroke are the leading causes of death in people with diabetes. Diabetes is a strong risk factor for ischaemic stroke, perhaps because of accompanying risk factors, such as obesity and high blood pressure. Studies have also implicated the milder condition of “impaired glucose tolerance” (insulin resistance), which is an important disease mechanism in type 2 diabetes, as an independent factor in the development of atherosclerosis and stroke. With this condition, insulin levels are normal to high, but the body is unable to use the insulin normally to make use of blood sugar. It can be detected with a fasting blood sugar followed by a syrupy drink followed by a 2 hour repeat blood glucose test (oral glucose tolerance test). The body compensates by raising the level of insulin, which can, in turn, increase the risk for blood clots and reduce HDL-cholesterol levels (good cholesterol). Diabetes does not appear to increase the risk for hemorrhagic stroke. Some studies have also reported a worse outcome in patients whose blood sugar levels are high at the time of a stroke. People with diabetes should aim for fasting blood glucose levels of less than 6.28 mmol/l and haemoglobin A1C of less than 7%. Intensive approaches to diabetes with insulin have been proven to prevent some of the vascular diseases associated with Diabetes.

## Heart Abnormalities Causing Travelling Blood Clots (Embolisms):

***Atrial Fibrillation (AF).*** More than one in six strokes are due to AF. This is a heart rhythm disorder in which the atria (the upper chambers in the heart) beat very quickly and non-rhythmically. The blood pools instead of being pumped out, increasing the risk for formation of blood clots that break loose and travel toward the brain. AF, in fact, poses a six-fold increased risk for stroke and may also pose a higher risk for complications after a stroke. AF is uncommon in people under 60 years old, but about 6% of adults over 80 have this heart rhythm disorder. In this patient group, the risk for stroke may be higher or lower with the presence of other risk factors, including having heart failure, high blood pressure, diabetes, and a previous history of stroke, TIA, or rheumatic heart disease. More women than men have AF, but risk for stroke is higher in women with this condition than in men. The annual risk of stroke after a warning TIA or stroke with AF is 4-17%. Detection of paroxysmal atrial fibrillation in an evolving field, as implantable monitors (eg REVEAL) can detect any such events over 3 years of monitoring, but it is uncertain what to do about finding only minimal occasional atrial fibrillation, and the cost is high ($3000 per implant + monitoring)

***Anticoagulants****.* People with atrial fibrillation should use anticoagulants to reduce their risk of blood clots. Treatments to bring the rhythm back to normal used to be routine early on in the disorder, but this does not reduce stroke risk because of the tendency for recurrence. A cardiologist opinion should be sought if AF has not been of long-standing. Treatment for atrial fibrillation always includes the use of agents (especiallydabigatran and warfarin, 2 anti-coagulants) to prevent clots from forming. After a diagnosis of atrial fibrillation and stroke or TIA, options include Dabigatran high dose (~75% reduction in strokes) Warfarin (66% reduction), Dabigatran low dose (~50-60% reduction) Aspirin+Clopidogrel (40% reduction) or Aspirin alone (20% effect) is essential to prevent blood clots. When used correctly, these agents reduce the risk for stroke. Warfarin was the agent of choice in preventing first and second strokes in high-risk patients with atrial fibrillation.However in July 2011 PHARMAC funded Dabigatran, a new anticoagulant with fewer interaction, no monitoring and dramatically less intracranial bleeding. Except for specific high-risk individuals however, the protection from anticoagulants far outweighs any danger for bleeding. Those at particular risk for bleeding are patients with a history of alcohol abuse, chronic kidney disease, or previous gastrointestinal bleeding. Aspirin is less effective, but also has a lower risk for bleeding. It is highly protective, however, and the preferred treatment for younger people with atrial fibrillation and for people with no other risk factors for stroke, such as high blood pressure or diabetes. It may also be used by people at higher risk who cannot tolerate anticoagulation therapy.

**Warfarin is effective**, reducing risk from typically 12-18%/year to 4-6%/yr (RRR 66%).

Strict control of hypertension is associated with a 50% reduction in ICH bleeding

Drug, food and blood testing complications are complex

Some patients cannot achieve INR stability, but those who can do well, and generally shouldn’t be changed from warfarin for medical (risk-benefit) reasons. Centres with excellent INR control still showed benefit (less so than poor centres) of Dabigatran over Warfarin in Re-Ly study. Individual patient data shows that for patients with “better than the median INR success for the Re-Ly study”, that the 110mg dose looked less attractive, but the 150mg dose still looked to be best when compared with Warfarin (data not published, but referred to in Lancet FDA commentary).

Long term efficacy and rare side-effect profile is well known

Warfarin may be more effective where compliance is sporadic as Dabigatran has shorter half life, however compliance will lead to complications either way

Patients who had a contra-indication for warfarin were NOT STUDIED in Re-Ly

**Dabigatran 150 mg bd** **is more effective** than warfarin, but is not the preferred dose in stroke and TIA patients.

**Dabigatran 110mg bd** **is the optimal treatment in stroke and TIA patients who have Atrial Fibrillation** (an area of some international controversy; high vs low dose). This had by far the lowest rates of death and of bleeding strokes (the two feared risks) and did not have the elevated rates of bowel bleed and heart attack seen on the higher dose.

**Reversal in bleeding:**Concerns have been raised regarding reversal of Dabigatran effect in the presence of a major bleed. Pharmac has produced guidelines for NZ, and Dr J Bell, local haematologist has been involved. New Dabigatran reversal treatments are currently being investigated.

***Atrial******Fibrillation*** *(Restoring versus Controlling Heart Rhythm):* One of two other approaches are available in addition to anticoagulants, either of which are effective in managing this disorder:   
1) Restoring or maintaining normal heart rhythm. This is accomplished with anti-arrhythmic drug, cardioversion procedures, or surgery to remove the defective area. 2) Controlling heart rate. Important studies are reporting that controlling heart rate may be the preferable approach. In two 2002 studies, rhythm control offered no survival advantages and did not protect against ischaemic stroke. Therapies aimed at controlling heart rate, furthermore, had fewer complications. Drugs Used to control heart rate include beta-blockers (such as propranolol) or calcium channel blockers. Digitalis, an older drug, is not used as often but is proving to be very effective in combination with the other agents. These agents are used to reduce heart rate at the onset of atrial fibrillation.

To restore heart rhythm, anti-arrhythmic drugs may be used. If they fail to restore normal rhythm electrical shock cardioversion is often effective. Low-energy implanted cardioverters (e.g., Atrioverter, Jewel AF) are being investigated for maintenance. Studies are very promising. For maintaining a stable rhythm, for patients with no heart disease, the first choices include sotalol, flecainide, or if these fail, then amiodarone may be tried. Amiodarone is more effective than most others and has been thought to be safer than many other similar drugs. Even in low doses, however, there is a high incidence of side effects, including thyroid disorders, neurologic, skin, and eye problems, and abnormally slow heart beats. Many anti-arrhythmic drugs carry a small but significant increased risk, however, for a life-threatening arrhythmia called “torsades des pointes” and should be avoided by people with certain heart conditions. *Surgical Procedures for Complex AF.* In some difficult cases, surgery may be recommended.

Note: It had been commonly believed that mitral-valve prolapse is a major cause of stroke in young people, but the connection has not been well researched. A 1999 study found no evidence that this usually mild heart abnormality has any effect on stroke.

**b) Surgery for stroke**

***Carotid endarterectomy*** is a surgical procedure used to clean out and open up the narrowed carotid artery. It is sometimes used after a stroke in certain patients. In such cases, patients have reported improvements in vision, speech, swallowing, functioning of arms and legs, and general quality of life. The studies showing such high benefits of surgery versus drug therapy were done in institutions whose surgeons are experienced with such operations. Anyone undergoing this procedure should be sure their surgeon is experienced in recent techniques and that the medical center has complication rates of less than 3%. A 2000 study reported that older surgeons had a worse record than younger ones, possibly because they relied on residents or were less likely to adopt new procedures.

***Symptomatic cases****: Determining who should have surgery.* Evidence strongly suggests that most patients with severe and symptomatic stenosis (over 70% of the carotid artery is obstructed and a stroke or TIA has occurred (2 year non-surgery risk of stroke ~30%)) can benefit from endarterectomy. It is also clear that patients with mild stenosis (less than 50% obstruction) would do better with medications than surgery. The benefits of endarterectomy for people with stenosis between 50% to 70% are not so clear; however it appears to be favourable for older male patients, who have lower surgical risk. There is a risk of a heart attack or even stroke from the procedure. Studies have reported, in fact, that strokes occur during or immediately after the operation in up to 9% of these operations, but generally 2-5%. Women appear to have a significantly higher risk for postoperative stroke than men. The number of people needed to treat with surgery in order to prevent one stroke (NNT) depends on the severity of the artery narrowing. At 70-80% narrowing, 80-90%, and 90-99% the NNT respectively is 8, 5 and 4. These indicate a dramatic effect of surgery. In the 50-70% narrowing patients this NNT is 16 for men and 125 for women, although it may be possible to tease out a small group (<1/3) of high-risk woman (>7 points) whose NNT is 11. The latter evidence is not convincing, but emphasized several factors (“brain not retinal”, recurrence, diabetes (3 points each), and to a lesser degree “stroke-not TIA”, age>70 (2 points each), and less again a history of BP or prior MI (1 point each)) *(Stroke*. 2005;36:27-31)

. Age is a factor in the risk-benefit analysis regarding surgery over 2 years follow up. Patients over 75 years with a narrowing >70% reduced the risk of bad outcomes by 29%, those 65-75 by 15%, and those younger than 65 by 9% whereas the risk of surgery (surprisingly) was lower in the older groups than the younger groups. In the 50-70% narrowing age was also a factor, favouring those over 75 years getting surgery although the benefits were certainly not large (NNT 12 for a 5 year (not 2 year) improved stroke rate).

The best candidates for preventive carotid endarterectomy in such cases may be when

* They have symptoms that indicate artery blockage in the part of the brain supplied by the artery that is narrowed in the neck.
* They are male. The benefits of this procedure for women are less pronounced.
* They have a history of a stroke that occurred three months earlier or less.

The major complications rates after endarterectomy are less than 3%.

***Asymptomatic carotid endarterectomy****:* Significant controversy surrounds the treatment of patients who have severe stenosis but who do *not* have symptoms. A 1995 study estimated that endarterectomy in such patients would reduce the risk for stroke from 11% to 5%. However, these patients were treated in medical centres with highly skilled staff and less experienced centres have reported higher complications and lower success rates. A 2002 study suggested that, in any case, asymptomatic patients even with blockages of well over 50% actually have a low risk for a stroke. In this small study, such patients had only a 9.3% risk for a stroke at 10 years and a 15% risk at 15. Furthermore, an important 2000 study found that only 3.5% of the strokes that occurred in such patients were due to blockage in the carotid arteries (the only condition that is benefited by carotid endarterectomy). Over half of the strokes in that study were caused by embolisms (travelling clots) or lacunar infarcts (very tiny, ischemic strokes). Some experts still believe that many asymptomatic patients are good candidates for the procedure. However, to be beneficial, the procedures should be performed only in experienced medical centres.

***Carotid angioplast****y:* has been extensively investigated and such intra-arterial ballon expansions and stent/cage insertions are not as safe as Carotid endarterectomy surgery. However surgery is only available for one particular carotid segment in the neck. Unfortunately there has been only negative trials for these techniques at other sited when comparing intra-arterial treatments against “best medial therapy”. They are therefore only used if

1. Radiation induced carotid stenosis
2. A clear contraindication to endarterectomy
3. Other extracranial or appropriate intracranial stenosis refractory to medical therapy, and not at a location where small vessels will likely be occluded.

***Patent Foramen Ovale: (PFO)***is a flap-like opening between chambers of the heart. The foramen ovale is always open during foetal development to enhance blood flow to the foetus. It then typically closes after birth when the lungs take over. However, evidence suggests that it remains open in up to 30% of adults. In such cases, blood moves backward (right to left) through this opening when pressure in the right chamber exceeds the left, particularly with coughing or straining, and particularly dangerous in the presence of clots that have formed in the legs and are travelling through the heart of the lungs. Large PFOs in fact, are probably a major cause of stroke, particularly in younger adults. A 2001 study suggested that stroke patients with PFO have a higher risk for a recurring stroke only if they also have atrial septal aneurysm. The process leading to blood clots and stroke in such cases are complex and not entirely clear. Cardiac emboli tend to be large (not small vessel changes on brain imaging), and can affect any arterial territory. Hence multiple clinical stroke-like events affecting more than one territory point to the need to consider the heart or the aorta in the chest as the source of the event. “Multiple” can be defined as actual clinical events, or those seen on brain imaging but producing no symptoms. Particular features of concern include young strokes (PFOs get larger as people age, but other causes of stroke become by far the more likely than PFO after the age of about 40), whose event occurred whilst straining (e.g. weight lifting) when the clot can be pushed across the hole in the heart. Swollen injured legs and prolonged immobility which may point to a deep venous thrombosis (clot) will also make PFO a more likely source for the stroke. Treatments include anti-clotting agents (aspirin has been shown to be as effective as warfarin and carries lower risks) and procedures for closing the opening. Three recent trials have largely proven we should NOT close all PFOs eve.n if we have not found any other cause of stroke. Only those with

1. Unexplained recurrence on aspirin or warfarin or
2. high risk appearances on echocardiogram, or
3. brain imaging showing multiple territory large artery infarcts or
4. whose clinical presentation is very suggestive of the PFO being the cause

should be considered for closure

## WHAT ARE THE INITIAL STEPS IN MANAGING A STROKE?

Until recently, the treatment of stroke was restricted to basic life support at the time of the stroke and rehabilitation later. Now, however, treatments are being used that are proving to be very beneficial when administered as soon as possible after the onset of the stroke. It is critical then to get to the hospital and be diagnosed as soon as possible. There are number of steps in the initial assessment and management of person with stroke.

***Get to the Hospital Immediately:***If significant symptoms appear in people at risk for stroke, calling 111 is critical (as opposed to calling the family doctor or trying to get the patient to the hospital by car). One study reported that patients who went to the emergency room in an ambulance had a much shorter delay in getting treatment than those who went on their own. Receiving treatment early is critical in reducing the damage from a stroke.

***Determine Whether the Stroke Is Ischaemic or Hemorrhagic.*** As soon as the patient enters the hospital, diagnostic tests, particularly a CT scan, should be obtained to help determine whether the stroke is ischaemic or hemorrhagic.

***Determine The Need for Thrombolytic Agents.*** If the stroke is ischaemic, the next step is to determine if the patient would benefit from blood clot-busting agents (called thrombolytics). The following factors are helpful in making this decision:

* Estimating the time of onset of the stroke is critical in this decision. These agents are generally not beneficial if given more three hours after onset. In general, onset is when the patient first experiences any symptoms, even minor impairment. If the patient had had a previous TIA that completely resolved before the stroke, however, onset is dated from when the more recent symptoms developed.
* Patient or the family should tell the physician if the patient has been taking any blood-thinning agents.
* The patient or family should give the physician a thorough history of any accompanying medical or physical condition and any recent event, such as surgery or injury, which might contribute to the condition.
* CT scans will indicate if there are extensive early injuries, which might affect the decision to use these drugs.

***Give Supportive Treatment:***The patient should receive treatment to support basic life functions and to reduce stress, pain, and agitation. The following steps are also very important:

* *Maintain Adequate Delivery of Oxygen.* It is very important to maintain oxygen levels. In some cases, airway ventilation may be required. Supplemental oxygen may also be necessary for patients when tests suggest low blood levels of oxygen.
* *Managing Fever and Lowering Body Temperature (Hypothermia).* Fever should be aggressively treated, since strong evidence suggests that its presence predicts a poorer outlook. Some evidence, in fact, suggests that hypothermia (reducing body temperature) might protect nerve cells in stroke patients. Cooling is done through special cooling blankets, ventilators, or infusion of cool fluids. Unfortunately, there are severe side effects with even moderate hypothermia (30°C), which can include pneumonia, blood clotting disorders, heart rhythm disturbances, and others. Studies using mild hypothermia (32° to 34 °C), however, are reporting protection from developing brain injuries. In one, it was administered with nerve-protecting agents (calcium, magnesium, glutamate, and an antioxidant) within three hours of the stroke. Compared to patients without hypothermia, brain injuries were reduced by 45% to 74%, depending on how quickly the patients were treated.
* *Managing Blood Pressure.* Managing blood pressure is essential and complicated. Patients with stroke and pressures above 220 (systolic) or 120 (diastolic) should be treated. Lowering blood pressure too quickly can be dangerous, however in patients with both ischaemic and hemorrhagic strokes. In general, however, experts do not advise aggressively lowering elevated pressures below 220/120 in patients unless they have other conditions, such as a heart attack, that require pressure-lowering treatments. In patients who require thrombolytic agents, blood pressure should cautiously be lowered to 185/110 mm Hg. In most cases, blood pressure declines when these patients become stabilized.
* *Managing Increased Brain Pressure.* Hospital staff should watch carefully for increased pressure on the brain, which is a frequent complication of hemorrhagic strokes. It can also occur a few days after ischemic strokes. Early symptoms of increased brain pressure are drowsiness, confusion, lethargy, weakness, and headache. A number of medications, such as mannitol and other, may be given during a stroke to reduce pressure or the risk for it. Keeping the top of the body higher than the lower part, such as by elevating the head of the bed, can reduce pressure in the brain. However, this practice also lowers blood pressure in general, which may be very dangerous in patients with massive stroke. The experts in the study recommend keeping the bed level for all ischemic stroke patients. More work needs to be done to clarify this simple procedure.
* *Monitoring the Heart.* Heart attack and arrhythmias are potential complications of ischemic stroke. Patients must be monitored using electrocardiographic tracings.
* *Controlling Glucose Levels.* Elevated glucose (blood sugar) levels can occur with severe stroke and may be a marker of serious trouble. In general, it is advisable to lower glucose levels that are above 17 mmol/l, usually with insulin. It is not clear, however, if glucose-lowering treatments offer any advantage below this. Excessive lowering of glucose levels can have damaging effects on the brain, and a target of 11.1 mmol/l is currently used in the Waikato Hospital.

## WHAT ARE THE DRUGS USED TO TREAT STROKE PATIENTS?

1. **Acute ischaemic stroke**

*Intravenous Thrombolytics.* Clot-busting, or thrombolytic, drugs break up existing blood clots. They are among the important treatments for heart attacks, and are now also being used for ischaemic (not hemorrhagic) stroke. Their benefits for treating stroke patients appear to be more limited than for heart attacks, however, and only a minority of stroke patients is given these agents. More needs to be learned about the risks and benefits of thrombolytics for stroke. The standard thrombolytic drug is recombinant tissue plasminogen activator (Alteplase). Before the thrombolytic is given, a CT scan must also first confirm that the stroke is not hemorrhagic. If the stroke is ischemic, a CT scan can also suggest if injuries are very extensive, which might affect the use of thrombolytics. Thrombolytics must be administered within three hours of a stroke (but not after that period) to have any effect. Unfortunately, most stroke patients arrive at the hospital more than 4.5 hours after an attack and therefore are not eligible for treatment. Thrombolytics carry a risk for haemorrhage and so may not be warranted for patients with existing risk factors for bleeding. They should not be used in patients who are experiencing seizures. The drug may be appropriate in more patients than previously thought, however, including older people, those with a history of stroke, and those with high blood pressure. More research is needed to confirm this.

*Intra-Arterial Thrombolytics*. Researchers are investigating catheter based clot removal directly into an artery in the brain. Early studies suggest this approach may allow effective treatment up to six hours after a stroke and improve recovery in more patients.

*Anti-Platelet Agents.* Typically, an anti-platelet agent (most often aspirin) is initiated within 48 hours of an ischaemic stroke and continued in low doses as maintenance. Studies suggest that antiplatelet therapy can reduce the risk for a second stroke by 25%. Aspirin has some modest effect in preventing a second stroke and is recommended within 48 hours of a first stroke in doses of between 50 and 325 mg. Note, patients should not be given an aspirin until a diagnosis of ischaemic or hemorrhagic stroke has been determined. Aspirin increases the risk for bleeding in patients with hemorrhagic stroke and taking it would preclude important clot-busting drugs in appropriate patients with ischaemic stroke. On an ongoing basis, experts now recommend that most patients take a daily low-dose aspirin to prevent a second stroke. If patients had already taking aspirin for preventing heart disease, it is not clear if they should take if after a first stroke.

*Anticoagulants.* Anticoagulants thin blood and may be useful under certain circumstances. The anticoagulant warfarin is a potent anticoagulant and needs to be monitored carefully. Studies have been mixed on its value for protecting against future stroke.

1. **acute haemorrhagic stroke**

*Calcium Channel Blockers.* Early administration of calcium channel blockers, such as nimodipine (Nimotop), can improve functional outcome. One of the most common and serious dangers after a subarachnoid hemorrhagic stroke is spasm of the blood vessels near the ruptured site, which closes off oxygen to the brain. Calcium causes contraction of the smooth muscles of the blood vessels, and calcium channel blockers are drugs that relax the blood vessels. The drugs work best if it is administered within six hours of the stroke. Calcium channel blockers are not useful for ischemic stroke, although they can be used in combinations with blood pressure lowering agents to prevent them.

*Antifibrinolytic Drugs.* Drugs called antifibrinolytics (e.g., tranexamic acid, epsilon amino-caproic acid or an equivalent) are used to stop bleeding. They have been investigated for years for subarachnoid hemorrhagic stroke but, at this time, they do not appear to improve outlook.

1. **surgical interventions for stroke**

*Hemicraniectomy* is surgical removal of a bone patch from the skull to relieve pressure. The bone is stored under sterile conditions and re-implanted a few months later. It may have be a life-saving option for some patients with severe stroke that has resulted in swelling and injury to a large area in the brain. Studies are showing some benefits for high-risk patients, but more information is needed to determine specific conditions that will respond to this treatment. (In one study, for example, patients with subarachnoid haemorrhage had a poor outlook after this procedure.)

*Emergency Surgery for Hemorrhagic Strokes.* Emergency surgery for a hemorrhagic stroke usually involves locating and removing large blood clots. In the past, such procedures had little effect on survival. Advances, however, are improving outcome when surgery is performed very early. Cerebellar bleeds causing pressure on the brainstem, and pressure leading to swollen ventricles (hydrocephalus) are the most amenable to surgery.

## HOW IS STROKE RECOVERY MANAGED?

Using a Stroke Specialist Physician as the primary physician after a stroke, rather than some other specialist or primary care doctor, significantly increases the chance for survival. In any case, patients or their families should be persistent in requesting the best care possible during this important early period. Being treated initially in a stroke unit instead of a general ward plays a strong role for better long-term quality of life. Rehabilitation services aimed at patients living at home are also very effective in improving independence. Patients or their families should seek patient advocates or support associations.

*Reducing the Risk for Non-Neurologic Complications after a Stroke*

In addition to problems brought on by neurologic damage, stroke patients are also at risk for other serious problems that reduce their chances for survival. They include the following:

* Blood clots in the legs (deep vein thrombosis).
* Pulmonary embolism (a blood clot that travels to the lungs).
* Pneumonia.
* Widespread infection.
* Heart problems.
* Urinary tract infections.

*Candidates for Rehabilitation:* In all, 90% of stroke survivors experience varying degrees of improvement after rehabilitation. There is pressure to send elderly stroke victims directly to a nursing home rather than try rehabilitation first, although one study found that patients were three times more likely to return home from rehab units than from nursing homes. Not all patients, however, need or benefit from formal rehabilitation:

* If the stroke is severe, intensive training would not be very helpful
* If the stroke is mild, patients often improve on their own.

*Positive factors that help predict good candidates for rehabilitation:*

* A patient should be able to sit up for at least an hour.
* The patients should be able to learn and be aware.
* Spasticity may be a good sign, because it indicates live nerve action.
* Patients who are able to move their shoulders or fingers within the first three weeks after having a stroke are more likely to recover the use of their hands than patients who cannot perform these movements. The ability to feel light pressure on the affected hand, however, makes no difference for future hand movement.
* Family members or close friends are available to be active participants in the rehabilitation process.

*Factors that might predict a poor response to rehabilitation:*

* Dysphagia (the inability to swallow) is associated with a higher mortality rate, possibly because of increased risk for infection and malnutrition. (Dysphagic patients who are given nutrition using a stomach tube may improve more than those who are fed using a feeding tube inserted down through the nose.)
* Incontinence.
* The inability to recognise nonspeech sounds that occur right after a stroke.
* A poor hand grip that is still present after three weeks is an indicator of severe problems.
* Having had very severe seizures after the stroke.

*Factors that do not rule out rehabilitation:*

* About 30% of patients experience aphasia (an impaired ability to speak), which is particularly distressing. It is necessary to understand that this disability does not necessarily impair the ability to think.
* Although confusion is common among people who have had strokes, partial or even complete recovery is very possible.

*Some Approaches to Rehabilitation:* Physical therapy should be started as soon as the patient is stable, as early as two days after the stroke. Some patients will experience the fastest recovery in the first few days but many will continue to improve for about six months or longer. Because stroke affects different parts of the brain, specific approaches to managing rehabilitation vary widely among individual patients:

*Retraining muscles.* One approach is based on training different muscles to replace those that have been impaired by damaged brain cells. In one small but important 2000 study, 13 stroke victims who had right-side paralysis had their non-paralyzed arm immobilized so that they were forced to use their paralyzed arm. Eleven of the patients experienced improvement in their impaired arms. The affected side of their brains also appeared to become more active. More studies are necessary. Physical exercise relating to the disability caused by the stroke is, in any case, important and may actually help repair the brain.

*Speech therapy and sign language.* Intense speech therapy (about 9 hours a week for three months) after a stroke is important for recovery. (The less intense the program, the less chance for success.) While professional speech therapy progresses, the patient's caregivers should use and encourage the patient in non-verbal communications, such as pantomime, facial expressions, and pen and paper. Learning and using the sign-language alphabet may be helpful both in communicating and improving small-motor dexterity.

*Biofeedback techniques combined with physical therapy.* This combination has been beneficial in certain cases. Electrical stimulation of the throat, for example, may help patients with dysphagia recover their ability to swallow faster. Stimulation of the wrist and finger is also showing promise for improving motor capabilities.

*Swallowing exercise.* A very promising 2002 study reported that swallowing improved when patients performed a simple exercise three times a day for six weeks. They lay flat and raised their heads three times, holding them up for one minute with a minute rest in between. This was followed by 30 consecutive head lifts.

*Attention training.* Problems in attention are very common after strokes. Direct retraining teaches patients to perform specific tasks using repetitive drills in response to certain stimuli. (For example, they are told to press a buzzer each time they hear a specific number.) A variant of this approach trains patients to relearn real-life skills, such as driving, carrying on a conversation, or other daily skills. For example, in one study, small electric cars were used in a lab to teach driving.

*Occupational training.* Occupational therapy is important and improves daily living activities and social participation.

***Drug Therapy for Rehabilitation****:*

* Dantrolene, baclofen, and botulinum (Botox) injections have shown some promise in relieving spasticity.
* In one small study, the drug bromocriptine, normally used for Parkinson's disease, was helpful for patients with severe speech problems, improved their ability to pronounce multi-syllable words and to form sentences.
* Some patients experience intractable hiccups, which can be very serious. Among the drugs used for this condition are chlorpromazine and baclofen.
* Studies have reported that dextroamphetamine or methylphenidate (Ritalin), an amphetamine used in attention deficit disorder, may help patients recover speech and motor skills when combined with physical therapy.
* Certain drugs commonly taken for conditions associated with stroke may actually slow recovery. They include drugs used for high blood pressure, including clonidine and prazosin, anticonvulsant drugs, the antipsychotic drug haloperidol, and the common anti-anxiety drugs benzodiazepines.

*The Emotional State of the Patients.* Strong motivation with the goal of independence after rehabilitation is important for recovery. Unfortunately, depression is very common after a stroke, both as a direct and indirect result of the stroke: Strokes that affect the right hemisphere in the brain particularly increase the risk for depression. Patients can certainly become depressed by the great changes in their ability to function. A peculiar stroke-induced condition, known as post-stroke crying or neurologic emotionalism, is a neurologic not a psychologic disorder.

If depression is prolonged, it can impair recovery. One study showed that people who suffered strokes and became depressed were three times more likely to die within ten years than stroke victims who were not depressed. There is a significantly increased risk of suicide in patients with stroke, especially in women and those under age 60. Antidepressants, particularly fluoxetine (Prozac) and similar so-called SSRI drugs, have been beneficial in relieving post-stroke crying and to improve recovery in general, and mood in particular, in patients who are depressed. Antidepressants may also help restore mental abilities. Some physicians also recommend agents called tricyclic antidepressants, including amitriptyline (Elavil) and nortriptyline (Pamelor). In one 2000 study nortriptyline (Pamelor) not only improved mood but also had positive effects on mental functioning, suggesting perhaps that some dementia associated with stroke may actually be due to depression. Tricyclics may also be useful for neurologic emotionalism.

Anxiety disorder is also common and debilitating. Some research, in fact, indicates that many patients suffer from feelings identical to post-traumatic stress syndrome. The two disorders often overlap, but drug treatments for each differ and may offset the other.

It should be noted that many drugs for psychologic disorders affect the central nervous system and can actually delay rehabilitation. Skilled professional help is needed to determine the most effective and safest treatments.

*The Emotional State of the Caregiver.* The caregiver's emotions and responses to the patient are critical. Patients do worse when caregivers are depressed, over-protective, and not knowledgeable about the stroke. Unfortunately, in one study, over half of the caregivers themselves were depressed, particularly if the stroke victims were left with dementia or abnormal behaviour.