

### **DECISION TO PRESCRIBE**

#### What am I trying to achieve?

- Prevent possible future cardiovascular events.
- Maintain quality of life.
- Maximise function or functional potential.

#### Is this what the patient wants?

 Discussing the potential risks and benefits with older people may help them decide which risk modifying factors they wish to implement.
If an older person believes that reducing cardiovascular risk is likely to improve quality or length of their life they may choose active treatment.

### Is there evidence that drugs will help achieve this?

There is undisputed evidence that antihypertensives reduce the risk of cardiovascular events in elderly people. The case for low-dose aspirin and statins is less certain. However clinical judgement will weigh the risks and benefits of these treatments taking into account the health and longevity of the elderly person.

#### Are there non-drug therapies?

 There is limited evidence of the cardiovascular effect of lifestyle modification in elderly people, however eating a healthy well balanced diet, increasing activity and smoking cessation is likely to help and have other health benefits.

#### Do potential benefits outweigh harms?

 The risks and benefits must be balanced for each individual older person. Older people with advanced chronological or physiological age or severe co-morbidities may not be suitable for intensive treatment. In contrast those older people in good health with a reasonable lifeexpectancy may be more suitable. There is less evidence about the management of cardiovascular risk in older people than younger age groups. Most elderly people over the age of 75 will have a five year cardiovascular risk of greater than 15% according to New Zealand Cardiovascular Risk Assessment guidelines. However calculation of risk, using the tables, can be useful when discussing risk modification with elderly people. In this article we discuss:

- Lifestyle modification
- Antihypertensives
- Statins
- Aspirin

### Lifestyle modification

Lifestyle modification may reduce cardiovascular risk but also has benefits for other common conditions in elderly people. A study showed a significantly lower mortality rate in older people who combined a diet rich in fruit and vegetables and low in saturated fat (the Mediterranean diet), with non-smoking, moderate alcohol consumption, and at least 30 minutes of physical activity per day.<sup>1</sup>

## Increasing physical activity is likely to be beneficial for elderly people

Although there is limited evidence about the effectiveness of exercise and physical activity in the prevention of cardiovascular disease, it is widely recommended because of other potential benefits for conditions such as hypertension, obesity, diabetes, and musculoskeletal disorders.<sup>2</sup> There is also some evidence that physical activity may reduce the risk of falls. In elderly people the

ability to participate in physical activity can often mean the difference between independent living and living with assistance.<sup>3</sup>

Variation in the ability of elderly people to become physically active requires the intensity, frequency and duration of physical activity to be adjusted to the capabilities of each individual. Gradual increase in activity is recommended because there is some evidence of an initial increased risk of adverse events, particularly in people who have been sedentary.<sup>2</sup> The social aspect of group physical activities may encourage elderly people to participate.

## Diet interventions and weight loss are often beneficial to elderly people

Although there is limited evidence of the effect of diet on cardiovascular risk in elderly people, eating more fruit and vegetables and reducing fat and salt intake is likely to be beneficial. Diet is part of therapy and more important for those with diabetes.

Weight loss may help modify cardiovascular risk in overweight individuals, and may be beneficial for other conditions that are common in elderly people such as osteoarthritis, and may also increase mobility.

## Reducing salt intake may reduce blood pressure but not overall cardiovascular risk

A Cochrane review found that salt restriction in adults produced a minimal decrease in blood pressure; however there was not enough evidence to show a decrease in cardiovascular mortality.<sup>4</sup>

It is possible that reduced salt intake would be more effective for lowering blood pressure in elderly people than in younger people, because arterial compliance decreases with age and any change in intravascular volume relating to sodium intake, could result in a greater change in blood pressure.<sup>5</sup>

Elderly people are prone to hyponatraemia but when associated with drugs, such as thiazides or SSRIs, it is usually a dilutional hyponatraemia. It is due to a failure to clear water.

#### Reducing total and saturated fat is recommended

There is evidence that modifying dietary fat intake by reducing total fat intake, or replacing some saturated fat with unsaturated fat, may reduce the incidence of cardiovascular events in the general population. However there is limited evidence that this also applies to older people. Older people are more at risk of unplanned weight loss than obesity and advice about reduction in dietary fat may be more suitable for those who are overweight or have dyslipidaemia.

## Increasing fruit and vegetable consumption is recommended

Diets that are rich in fruit and vegetables and low in saturated fat, such as the Mediterranean diet, have been shown to reduce cardiovascular risk in elderly people<sup>7</sup> as well as in the general population.<sup>8</sup>

## Smoking cessation is beneficial to elderly people

Smoking cessation is beneficial at all ages with immediate effect. The results of one study in elderly men showed the risk of all-cause mortality was the same in ex-smokers as in those who had never smoked. Smoking is one of the most modifiable risk factors for lung cancer, chronic obstructive pulmonary disease and cardiovascular disease.

Smoking cessation advice should be offered to all patients regardless of age or co-morbidity.

# Antihypertensives, statins and low dose aspirin in elderly people

In the general population there is evidence that antihypertensives, statins and low dose aspirin can modify risk of cardiovascular events. While antihypertensives have good evidence of effectiveness in elderly people, the evidence for statins and low dose aspirin is either of poor quality or lacking.

## Reducing blood pressure reduces cardiovascular risk in the elderly

Many trials have shown significant benefits of treating hypertension in elderly people, to reduce the risk of cardiovascular events, especially stroke. All trials have resulted in marked reductions in morbidity associated with stroke and myocardial infarction (MI). However they report conflicting results on the reduction of all-cause mortality; some report a significant reduction and some show no significant reduction.

The recent HYpertension in the Very Elderly Trial (HYVET) was stopped early after researchers observed significant reductions in both overall mortality and stroke, in those receiving therapy.<sup>10</sup> The HYVET trial is novel in testing the hypothesis that treatment of hypertension at advanced age (over 80) does not reduce events. The hypothesis was proven wrong and marked benefit was observed.

Antihypertensives lower cardiovascular risk, reduce blood pressure and prevent cardiovascular events. They may also reduce the development of dementia, as it is likely that most dementia is mixed dementia, and reducing the vascular component delays onset of symptoms.

Once dementia has reached an advanced stage, active management of co-morbidities should be reconsidered as it may not increase quality of life.

Treatment decisions that can reduce the risk of antihypertensive treatment:

- Starting with the lowest dose and increasing gradually reduces the risk of postural hypotension.
- More frequent monitoring in elderly people can identify potential problems with treatment, especially intolerable side effects such as postural hypotension.
  Elderly people may see their side effects, such as impotence with thiazides, as an unavoidable part of treatment and not report them.
- Thiazides are a good first choice as they may be particularly effective in elderly people.<sup>11</sup>
- Calcium channel blockers are less influenced by age and ethnicity compared with other agents (e.g. ACE inhibitors) and this may present a benefit for their use in elderly people.<sup>12</sup>
- ACE inhibitors may be considered initially in elderly people with co-existing conditions such as chronic kidney disease or diabetes.<sup>11, 13</sup>
- Beta-blockers have been shown to be not as effective as other antihypertensive agents in elderly people.
  Initial therapy with beta-blockers should probably be limited to those people who have compelling indications for their use, such as coronary heart disease or congestive heart failure.<sup>11</sup>

### Modification of lipids may be beneficial

Data on primary prevention of cardiovascular events with statins in the elderly population is limited. Studies in older people report adverse effects inconsistently making it difficult to draw conclusions regarding the risk of treatment versus the benefit.

The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) showed no significant reduction in all-cause mortality, but suggested that statin therapy in high-risk elderly patients, can reduce coronary disease events.<sup>14</sup>

Other trials and sub-group analyses have shown a variable effect of statins on mortality as well as cardiovascular events.

Those with limited life expectancy due to co-morbidities will be unlikely to benefit from statin primary prevention. <sup>14</sup> Age alone is not a contraindication to drug therapy. <sup>2</sup>

The decision to treat elderly people with a statin should be made on an individual basis, taking into account cardiovascular risk assessment, patient choice, life expectancy and quality of life.

Treatment decisions that may reduce the risk of statin therapy:

- Start with low doses and increase gradually. Higher doses may place elderly people at increased risk of adverse effects.
- Monitoring therapy is especially important in elderly people. They are at increased risk of statin induced myopathy, even though the risk is still small. Patients should be advised to report any unexplained muscle pain, tenderness or weakness. This may occur without muscle enzyme rise.
- Elderly people are at risk of polypharmacy and may be taking drugs such as macrolides, amiodarone, cimetidine, or azoles (ketoconazole and itraconazole), which may increase the plasma concentration of statins.

### Atrial fibrillation and anticoagulation

Anticoagulation with warfarin lowers the risk of stroke in people with atrial fibrillation (AF). Treating 1000 people with AF for one year with warfarin rather than aspirin would prevent 23 ischaemic strokes.<sup>17</sup>

However warfarin is associated with increased risk of major bleed including cerebral haemorrhage. This is particularly so in those 80 years and over and in the initial few months of treatment. In a recent trial the cumulative incidence of major haemorrhage in this group was 13.1 per 100 patient years.<sup>18</sup>

## Low dose aspirin may be suitable for elderly people at high risk of cardiovascular events

The likelihood of benefit achieved from primary prevention with aspirin improves with increasing risk of cardiovascular events. Therefore in those at highest risk of cardiovascular events, the benefit of low dose aspirin prophylaxis outweighs the risks associated with aspirin therapy.

In people at lower risk of cardiovascular events, the excess bleeding risks, such as gastrointestinal bleeds or haemorrhagic stroke associated with aspirin, may outweigh any benefit of reduced cardiovascular outcomes. A meta-analysis showed aspirin to increase the risk of gastrointestinal bleeding by a factor of 1.5–2.0. However higher rates (up to double) may be expected in elderly patients. The risk of bleeding may be higher in elderly people due to underlying conditions such as gastric ulcer or drug interactions, including concomitant NSAID or anticoagulants.

People with uncontrolled blood pressure may be at greater risk of a cerebral haemorrhage with aspirin therapy<sup>2</sup> and

the beneficial effects of low dose aspirin therapy may be attenuated in patients with poorly controlled blood pressure.<sup>15</sup>

Enteric coated preparations do not seem to reduce the risk of gastrointestinal bleeding.<sup>2</sup>

Factors relating to the use of low dose aspirin:

- Only use low dose aspirin in patients at high risk of cardiovascular events when the benefits outweigh the risks.
- Risks of bleeding are increased in elderly people taking other drugs such as NSAIDs or anticoagulants, or with underlying clinical conditions such as peptic ulcer or uncontrolled blood pressure.
- Enteric coated preparations are not protective.
- Doses as low as 75mg are effective.

### **Summary**

Older people have a high absolute risk of cardiovascular disease and therefore appear to have the most potential to benefit from cardiovascular risk reduction. However they are often also at increased risk of adverse drug events and the decision to treat must be made on a case by case basis, taking into account the likely benefits and risk of treatment and the person's values.

Lifestyle measures should be implemented where possible as they may be beneficial to cardiovascular and other aspects of a patient's health.

Older people with advanced chronological or physiological age or severe co-morbidities may not be suitable for intensive treatment. In contrast older people in good health with a reasonable life-expectancy have a greater capacity to benefit from treatment and less risk of adverse effects.

#### References

- Knoops K, de Groot L, Kromhout D, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly men and women. JAMA 2004; 292(12): 1433-1439.
- SIGN (Scottish Intercollegiate Guidelines Network). 97: Risk estimation and the prevention of cardiovascular disease. Available from: http://www.sign.ac.uk/pdf/sign97.pdf Accessed December 2007.
- Takahasi P, Okhravi H, Lim L, Kasten M. Preventive health care in the elderly population: A guide for practicing physicians. Mayo Clin Proc 2004: 79: 416-427.
- Hooper L, Bartlett C, Davey Smith G, Ebrahim S. Advice to reduce dietary salt for the prevention of cardiovascular disease. Cochrane Database Syst Rev 2003(3): CD003656.
- Appel L, Espeland M, Easter L, et al. Effects of reduced sodium intake on hyoertension control in older individuals. Arch Intern Med 2001; 161: 685-693
- Hooper L, Summerbell CD, Higgins JPT, et al. Reduced or modified dietary fat for preventing cardiovascular disease. Cochrane Database Syst Rev 2000(2): CD002137.
- Trichopoulou A, Orfanos P, Norat N, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. BMJ 2005; 330(991).
- 8. Hu F, Willett W. Optimal diets for prevention of coronary heart disease. JAMA 2002; 288(20): 2569-2577.
- Menotti A, Mulder I, Nissinen A, et al. Cardiovascular risk factors and 10-year all-cause mortality in elderly European male populations. Eur Heart J 2001. 22: 573-579
- Imperial College. Trial stops after stroke and mortality significantly reduced by blood pressure-lowering treatment for those aged 80 and over: Trial of 3845 patients stops early. Imperial

- College news release. Available at: http://www3.imperial.ac.uk/newsandeventspggrp/imperialcollege/newssummary/news\_7-8-2007-14-8-13?newsid=15654. Accessed December 2007.
- Chobanian A. Isolated systolic hypertension in the elderly. N Engl J Med 2007; 357(8): 789-796.
- Epstein BJ, Vogel K, Palmer BF. Dihydropyridine calcium channel antagonists in the management of hypertension. Drugs 2007; 67(9): 1309-1327.
- Kapoor J, Chaudry S, Agostini J, Foody J. Systolic hypertension in older persons: how aggressive should treatment be? Prog Cardiovasc Dis 2006; 48(6): 397-406.
- Ali R, Alexander K. Statins for the primary prevention of cardiovascular events in older adults: A review of the evidence. Am J Geriatr Pharmacother 2007; 5(1): 52-63.
- Hayden M, Pignone M, Phillips C, Mulrow C. Aspirin for the primary prevention of cardiovascular events: A summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002; 136(2): 161-174.
- Mahe I, Leizorovicz A, Caulin C, Bergmann J. Aspirin for the prevention of cardiovascular events in the elderly. Drugs Aging 2003; 20(3): 999-1010.
- 17. van Walraven C, Hart R, Singer D, et al. Oral anticoagulants vs aspirin in nonvalvular atrial fibrillation: An individual patient meta-analysis. JAMA 2002; 288(19):2441-8.
- Hylek E, Evans-Molina C, Shea C, et al. Major haemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. Circulation 2007; 115(21): 2689-96.

