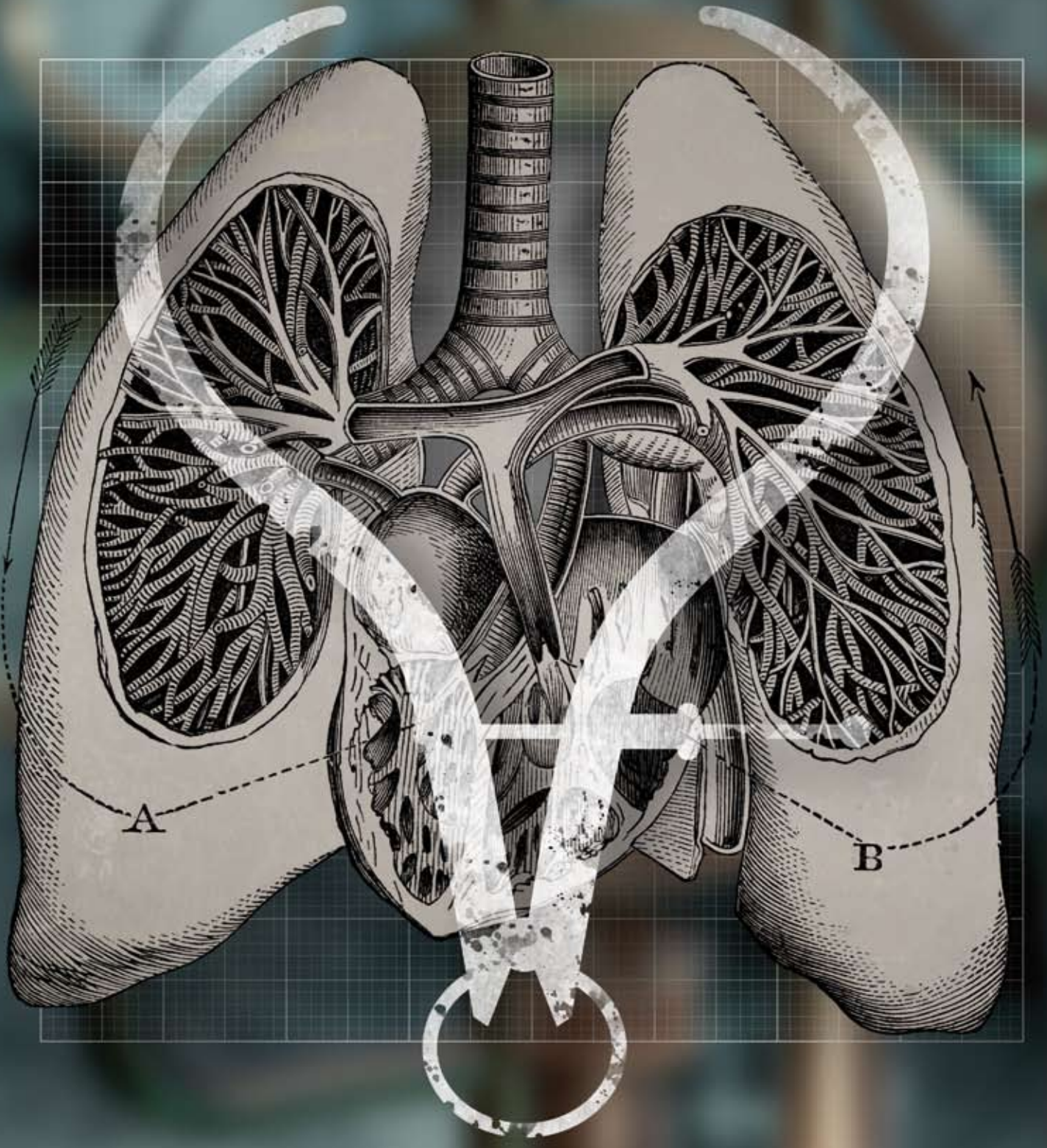
Assessing cardiovascular risk: **what the experts think**



Risk factors for cardiovascular disease

Cardiovascular disease is the leading cause of mortality in New Zealand, accounting for 40% of deaths annually.[1] Many cardiovascular-related deaths are premature and preventable.

The development of cardiovascular disease is associated with risk factors that an individual may be able to change or improve (i.e. modifiable) as well as factors that are fixed (i.e. non-modifiable). Modifiable risk factors include; smoking, lipid levels, physical activity, diet, blood pressure, alcohol intake, psychosocial stress and obesity. Non-modifiable risk factors include; age, gender, genetics, ethnicity and socioeconomic status. Knowledge of which risk factors are present can help target appropriate interventions and monitor response.

In addition to these risk factors, certain co-morbidities can also increase cardiovascular risk, including diabetes, chronic kidney disease, rheumatoid arthritis and depression.

Despite much being known about cardiovascular risk assessment, there are still areas which remain contentious and are not supported with conclusive evidence. Therefore we invited a group of practitioners, with expertise and interest in cardiovascular disease, to discuss some of these issues.

Questions focused on:

- Risk assessment tools in the current New Zealand guidelines – are they still appropriate to use? How up to date and relevant are they? Can they be used with confidence?
- Risk factors – how are factors such as obesity, ethnicity and renal function included in a risk assessment?
- Surrogate risk markers – e.g. lipoprotein (a) and high sensitivity C-reactive protein, is there any evidence for their use?

The experts:

Dr Sisira Jayathissa, General Physician and Geriatrician, Clinical Head of Internal Medicine, Hutt Valley DHB, Wellington.

Professor Jim Mann, Human Nutrition and Medicine, University of Otago, Consultant Physician (Endocrinology), Dunedin.

Associate Professor Stewart Mann, Cardiovascular Medicine, University of Otago, Wellington.

Professor Norman Sharpe, Medical Director, National Heart Foundation of New Zealand.

So, what did they say?

A summary of advice from the experts

The risk assessment tools included in the current New Zealand guidelines are well supported. Tools based on Framingham data are robust and take into account the essential elements for cardiovascular risk assessment. When used as outlined in the New Zealand guidelines, risk prediction can be performed with confidence for the majority of people.

- Do the basics and do them well for everybody. Use the current cardiovascular risk assessment tools without getting too tied up in the arguments about alternative tools and the use of emergent risk factors and surrogate markers.
- Use the available assessment tools as a prompt and use your clinical judgement at an individual level.
- Be definite in setting goals and reassessing time frames. Rather than saying to a patient: “Next time I see you, we will measure your blood pressure”, instruct them to: “Make an appointment in three months time to have your blood pressure checked”.
- Significant effort needs to go into lifestyle changes including smoking cessation. Acknowledge to the patient that it can be hard to maintain diet and exercise changes but that they are very important and worth persevering with.

- Beware of giving people false reassurance – clinicians have to give a true picture of the patient's cardiovascular risk. Remember not everybody understands numbers in the same way. You may need to explain risk in a variety of different ways to ensure it is understood.

Best Practice Tip: The Heart Foundation "Know Your Numbers" programme is a very useful tool for engaging with patients in primary care and motivating change, particularly as it shows the future lifetime risk trajectory and how high risk can be improved with lifestyle interventions and treatments. This programme is available online at: **www.knowyournumbers.co.nz**

Current cardiovascular risk assessment tools are supported

There has been some question over whether Framingham based tools should still be used for cardiovascular risk assessment and whether alternative tools should be used.

In the United Kingdom there is no consensus about which risk calculator should be used, rather a number are available including the Framingham risk score, QRISK®2 (based on a primary care cohort from the United Kingdom) and ASSIGN. Clinicians are advised to select the tool that is best suited to their requirements.[2]

QRISK®2 calculator available at: **http://qrisk.org**

ASSIGN calculator available at: **www.assign-score.com**

Current New Zealand guidelines for primary prevention of cardiovascular disease recommend risk management based on the Framingham risk score. It is available in different formats including risk charts and electronic calculators.

In your opinion are the current cardiovascular risk assessment tools outlined in the New Zealand Cardiovascular Guidelines Handbook (based on Framingham score) still up to date based on latest evidence?

"The Framingham engine may appear a little crude as it requires only basic information from patient history and easily available tests. However, it remains a powerful tool for population prediction and it is difficult to show significant improvement by allowing for inclusion of any one new risk factor."– Stewart Mann

"Most cardiovascular risk assessment tools are based on Framingham data, therefore the debate about which is better probably has little merit. There is no good evidence that any of the other tools currently available perform any better than that in current use in New Zealand."– Jim Mann

"An ideal tool for New Zealand would be based on our own population data including ethnic sub-groups."– Sisira Jayathissa

The Framingham score is used to predict the absolute risk of coronary events in populations free of cardiovascular disease. Risk calculators based on Framingham data are the most widely used and researched. Validation studies have demonstrated that the Framingham risk prediction is well calibrated for New Zealand, Australia and the United States. Although in New Zealand a 5% additional risk is added for certain ethnicities, e.g. Māori, Pacific peoples and people from the Indian subcontinent. In Europe and the United Kingdom risk prediction is poorer due to over-estimation.[3]

Clinical judgement can account for limitations in risk prediction

There are limitations associated with the use of any of the available risk prediction tools. Interpretation of the calculated risk requires clinical judgement to adjust for other known factors that the risk calculator does not take into account. Once the risk elements have been

incorporated into the prediction tool; age, gender, blood pressure, cholesterol, smoking and diabetes, then each patient should be evaluated on an individual basis. The factors that need to be kept in mind include:

- Family history of premature cardiovascular disease
- Obesity
- Ethnicity
- Socioeconomic factors
- Renal function
- Age <35 years and >75 years

What are the main limitations of the current assessment tools?

"Underestimation of risk in certain groups may occur, especially in people with a family history of premature cardiovascular disease, in people who are obese and in certain ethnic groups. It has been suggested that such individuals might be moved up the risk scale. The extent to which this improves the risk estimate has not been established but could be taken into account when discussing risk with individual patients." – Jim Mann

"The identification of 'at risk' people is critical. Assessment tools should be viewed as a prompt to enable this. Doctors need to consider additional risk factors relevant to each patient such as abnormal renal function and obesity."– Sisira Jayathissa

The Framingham risk score (the basis for the New Zealand risk charts) calculates risk based on age, gender, blood pressure (systolic), cholesterol level (total cholesterol:HDL cholesterol ratio), smoking status and presence of diabetes mellitus. In addition, the New Zealand risk charts allow for adjustments to be made in groups where underestimation of risk is likely, e.g. for certain ethnic groups and family history.[4]

Many studies have attempted to identify additional risk factors that could improve prediction beyond the Framingham risk score. However, some commentators believe that issues with study design, analysis or reporting cast some doubt on the strength of these factors as predictors.[5]

Possible additional risk factors include:

- Body mass index, waist circumference, waist-hip ratio
- Deprivation, living standards
- Alcohol intake (excessive or binge drinking)
- Surrogate markers including; high sensitivity CRP, lipoprotein (a), uric acid

Triglycerides have been included in studies of risk factors, however, they have only a weak effect on cardiovascular risk assessment. Apart from one or two rare disorders, they are likely to be, for the most part, an indirect measure of poor lipid particle clearance, e.g. insulin resistance.

Some risk factors are not independent. For example, social deprivation, smoking, stress and alcohol misuse are interrelated, as are ethnicity, obesity, dyslipidaemia and diabetes. The strength of the relationship between dependent factors is unknown.[2]

Family history

The New Zealand guidelines account for family history of cardiovascular disease by adding an additional 5% to the calculated five-year cardiovascular risk. Family history is defined as premature coronary heart disease or ischaemic stroke in a first-degree relative (father or brother <55 years, mother or sister <65 years).[4]

"Caution is required with family history as there are widely different interpretations of what qualifies for a positive family history. Both the Framingham and INTERHEART studies showed that family history added virtually nothing to prediction once the classic risk factors had been included."– Stewart Mann

The INTERHEART study found nine risk factors that collectively accounted for over 90% of the population-attributable risk of an initial acute myocardial infarction. The factors were; abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits, vegetables and alcohol and regular physical activity.[6]

The study also found that 90.4% of myocardial infarctions could be attributed to the risk factors described above and this only rises to 91.4% when family history is added. This indicates that although family history is an independent risk factor for myocardial infarction, most of the attributable risk can be accounted for through the other risk factors studied. Family history appeared to be a more significant risk factor in younger people.[6]

Obesity

Obesity needs to be considered in conjunction with other risk factors, such as raised blood pressure, glucose and lipid levels. If these factors are also present then management can include addressing these factors along with lifestyle issues. However, if the patient is obese without other associated factors then management could be based on diet and exercise alone.

"Some co-morbidities of obesity will be detected through standard cardiovascular risk assessment. Others, most importantly pre-diabetes, will not. Obese patients require measurements in addition to those routinely recorded as part of cardiovascular risk assessment. The most appropriate clinical measurements for assessing obesity are BMI in conjunction with waist circumference. It is a false assumption that higher BMIs are acceptable in some ethnic groups, particularly Maori and Pacific peoples."–Jim Mann

"Obesity appears to exert an influence on calculable risk when it is associated with higher blood pressure or glucose intolerance (which of course is not infrequent). The preferred index for obesity remains controversial. The waist circumference (or waist-to-hip ratio) is likely to prove more predictive but may be as much of a risk marker (indicating a genetic dysmorphic pattern associated with other risks such as low HDL/high triglyceride) as a usefully modifiable risk factor."– Stewart Mann

Ethnicity

New Zealand cardiovascular guidelines identify Māori, Pacific peoples and people from the Indian subcontinent as high-risk groups that should be targeted for risk assessment. It is recommended that risk assessment should be started ten years earlier than for New Zealand Europeans and that an upward adjustment of 5% in five-year cardiovascular risk is made for these ethnic groups.

There are differences in cardiovascular risk factors between ethnic groups such as rates of smoking and diabetes, and possibly differences in blood pressure and lipid levels. There is work being undertaken to develop New Zealand specific cardiovascular risk prediction equations which consider ethnicity.[7]

Socioeconomic factors

"Socioeconomic factors are undoubtedly important and should be kept in mind. Framingham may not have measured these well enough. The INTERHEART study did include them and identified them as important. Some socioeconomic factors will be accounted for by ethnicity and some track closely with other classic risk factors (studies from the United Kingdom have shown that the main reason for the socioeconomic gradient is a correlated prevalence of the classic risk factors). Hopefully, local studies will include this and be able to weight it as an independent variable appropriately."– Stewart Mann

The Living Standards and Health Survey 2006/07 found that adults experiencing severe hardship were 60% more likely to have coronary heart disease than those with good or very good living standards or experiencing no deprivation. They were also twice as likely to be current smokers and 20–25% more likely to be obese.[8]

One-quarter of Pacific people (24%), approximately 16% of Māori, 7% of Europeans and 6% of Asians reported any degree of hardship. Over 5% of Pacific and 3% of Māori reported severe hardship; this response was much less prevalent (approximately 1%) among the European and Asian ethnic groups.[8]

Renal Function

The link between chronic kidney disease and increased cardiovascular disease is not always recognised. The estimated glomerular filtration rate (eGFR) is now automatically reported by most laboratories in New Zealand and can be used to screen for chronic kidney disease. The eGFR can be considered in the overall cardiovascular risk assessment.

> "Impaired renal function is clearly a risk factor but numbers have not been large enough to include in population equations."– Stewart Mann

It is increasingly recognised that chronic renal dysfunction alone is an independent risk factor for the development of cardiovascular disease.[9]

The eGFR can be used to screen for chronic kidney disease. Most patients with an eGFR <60 mL/min/1.73 m^2 die of cardiovascular causes and not due to progression to end stage renal disease.[10] An eGFR <60 mL/min/1.73 m^2 indicates the need for measures to reduce cardiovascular risk.[2]

A meta-analysis found that people with an eGFR <60 mL/min/1.73 m^2 had a 43% greater risk of stroke than those with a normal eGFR and that Asians were at higher risk than those of non-Asian ethnicity.[10] This supports the use of a low baseline eGFR as a risk marker. When eGFR is <60 mL/min/1.73 m^2, established strategies such as blood pressure reduction should be used to prevent future strokes and reduce cardiovascular risk in people with renal insufficiency.

See "Making a difference in chronic kidney disease", BPJ 22 (Jul, 2009).

Younger (<35 years) and older (>75 years) people

Risk calculators become less accurate at the extremes of age (under 35 years and over 75 years).

> "The Heart Foundation's 'know your numbers' tool is very useful for dialogue with young people at high relative but low absolute risk where efforts should concentrate on lifestyle rather than medicines." – Stewart Mann
>
> "Future health promotion efforts should be focussed on targeting 'at risk' people at very young ages as atheroma deposition and changes to the brain start below age 35 years. Older people need to be assumed as having high risk due to their age and associated co-morbidities". – Sisira Jayathissa

Caution with surrogate markers – they may be unproven or obsolete

It may be tempting to include additional factors such as lipoprotein (a), homocysteine or high sensitivity C-reactive protein (hsCRP) into a calculation of cardiovascular risk. However, these factors are not supported with conclusive evidence of improved risk prediction and priority should be given to the basic risk factors as in Framingham.

What is the current thinking on the role of cardiovascular risk markers such as lipoprotein (a), homocysteine and hsCRP?"

Lipoprotein (a)

"Lipoprotein (a) is still not widely measured but high levels are associated with higher risk. We do not appear to have specific tools to deal with it effectively."– Stewart Mann

"If someone has a family history of premature cardiovascular disease and no obvious risk factors, measurement of lipoprotein (a) is an appropriate, though costly, test. Nicotinic acid is currently the only available therapeutic agent to treat elevated lipoprotein (a) levels and large doses are required. A slow release preparation is now available and is relatively free of adverse effects. Because of the difficulty in treating raised levels of lipoprotein (a) it is important to ensure that other risk factors are effectively treated."– Jim Mann

Routine measurement of lipoprotein (a) is not indicated as part of a cardiovascular risk assessment in primary care.

Lipoprotein (a) is a modest, independent risk factor for atherosclerotic cardiovascular events, especially myocardial infarction. There are no clinical trials that have adequately tested the hypothesis that lipoprotein (a) reduction reduces the incidence of first or recurrent cardiovascular events. Lipoprotein (a) levels are also difficult to alter. Therefore, widespread screening for elevated lipoprotein (a) is not indicated and treatment of lipoprotein (a) levels should only be considered in specific circumstances.[11] A high level would usually prompt a more aggressive approach to other risk factors, rather than treating the level itself. If the clinical approach is otherwise clear based on other definite risk factors, then measuring lipoprotein (a) has little additional value.

Homocysteine

"Three very large trials have shown no benefit from reducing homocysteine levels with folate supplementation to lower cardiovascular risk."–Stewart Mann

Routine measurement of homocysteine is not indicated as part of a cardiovascular risk assessment in primary care.

It is hypothesised that high homocysteine levels cause endothelial damage and contribute to progression of cardiovascular disease. Treatment with folic acid (0.5 to 5 mg/day) lowers homocysteine, and therefore a decreased risk or slowing of cardiovascular disease progression would be expected. However, results from meta-analyses show that folic acid supplementation fails to decrease cardiovascular events despite homocysteine lowering. Folic acid supplementation actually appeared to increase cardiovascular risk in patients with high homocysteine levels at baseline. This suggests that folic acid may affect atherosclerotic disease progression through pathways that are independent of homocysteine lowering.[12] Folic acid supplementation is not recommended as a means to prevent or treat cardiovascular disease or stroke.[12]

Vitamin B supplements; cyanocobalamin (B12), folic acid (B9) and pyridoxine (B6), are also used to lower homocysteine levels. However, there is also no evidence to support their use in lowering homocysteine levels to prevent cardiovascular events.[13]

High sensitivity CRP

"HsCRP is undoubtedly a powerful risk marker (and may act as a useful surrogate for calculated absolute risk). However, genetic variations in hsCRP levels are not associated with variations in risk. Treatments for other risk factors, e.g. statins, tend to reduce hsCRP as well and we do not have a pharmaceutical that reduces it alone and specifically to test its relevance as a risk factor." – Stewart Mann

Routine measurement of hsCRP is not indicated as part of a cardiovascular risk assessment in primary care.

Inflammatory processes significantly contribute to atherogenesis (plaque formation in the aterial lining). It is unclear whether hsCRP is a non-specific marker that is increased in response to the inflammation or whether it directly contributes to the progression of atherosclerosis and its clinical consequences. Observational studies, although inconclusive, have suggested that hsCRP has only a small, or no, incremental contribution to cardiovascular risk prediction compared to traditional risk factors.[14]

HsCRP may be temporarily raised by inflammation and in addition, there is significant biological variation in levels (approximately 30–40% compared with most other lipid markers such as cholesterol and HDL which are 6–10%). Therefore, a raised level should be followed up with a repeat test when the patient is well.

Effect of calcium supplementation and low vitamin D levels is still unclear

Recent studies have raised concern that calcium supplementation (without vitamin D) may increase cardiovascular risk. Other observational studies have shown an association between low vitamin D levels and increased risk of cardiovascular events, in particular stroke. Many older people receive calcium or vitamin D supplements or both. It is therefore important to understand their effects on overall cardiovascular risk.

What is the current advice about the use of calcium supplements in patients with cardiovascular disease? Is vitamin D protective?

"Some studies have suggested adverse cardiovascular outcomes with calcium supplementation but this is not universally accepted. A systematic review showed neutral effects of calcium on cardiovascular disease.[15] It may be reasonable to avoid calcium supplements in patients with established cardiovascular disease until further evidence becomes available." – Sisira Jayathissa

"Calcium supplements should be avoided in general, in favour of a healthy balanced diet, and particularly so in people with cardiovascular disease or those at high risk. They remain a consideration for older people with high fracture risk where the benefits for some individuals in terms of bone health may outweigh any small increase in cardiovascular risk."–Norman Sharpe

"Vitamin D deficiency is common and we know improvement in vitamin D level is good for bones, muscles and other bodily functions. However, based on current evidence it is difficult to recommend routine vitamin D supplementation for cardiovascular protection."– Sisira Jayathissa

The evidence is limited as no randomised trials have focused primarily on the effect of vitamin D and calcium supplementation on cardiovascular end-points. The best evidence comes from trials that were designed to explore other issues. The available secondary and observational evidence suggests a possible cardiovascular disease prevention benefit of vitamin D (at moderate to high doses) and no benefit of calcium supplementation (either alone or in combination with vitamin D).[15,16]

While vitamin D supplementation may be associated with reduced cardiovascular disease risk, the evidence is limited and not sufficient to justify widespread vitamin D supplementation.[16]

A systematic review provides some reassurance that calcium supplements are unlikely to be associated with cardiovascular harm,[15] as suggested by local New Zealand studies, which found an increased risk of cardiovascular events in people receiving calcium without vitamin D.[17,18]

Further studies are required to establish the potential role of calcium and vitamin D supplementation in the prevention of cardiovascular disease.[15]

Aspirin for primary prevention is not routinely indicated for patients with diabetes

Recent studies have cast doubts on the widespread use of aspirin for primary prevention and its routine indication in people with diabetes.

Is there a place for aspirin in primary prevention, particularly in patients with diabetes?

"Aspirin is not generally recommended for primary prevention but is still a consideration for those identified at high risk in discussion between patient and doctor."–Norman Sharpe

"Aspirin should not be used routinely in primary prevention of cardiovascular events in diabetes. Good quality clinical trials and meta-analyses have shown lack of benefit of aspirin in primary prevention. However, aspirin could be considered on an individual basis if the patient has very high cardiovascular risk."– Sisira Jayathissa

"Recent studies showing little benefit of regular prophylactic aspirin in primary prevention have included large numbers of people at low absolute risk. It is still likely that people at higher risk, e.g. >15% five-year cardiovascular risk, may benefit and the Heart Foundation recommendations are to continue this practice here. Other trials are in process to examine this. The cardiovascular risk in diabetes has, in my view, been overplayed as evidenced by cardiovascular disease rates in some recent trials being a fraction of what was initially predicted. The concept that a diagnosis of diabetes confers equivalent risk to a cardiovascular event is not tenable. Many diabetics are therefore at low or intermediate risk, although a significant number have other risk factors which might well render aspirin useful."–Stewart Mann

See "Aspirin for primary prevention of cardiovascular disease", BPJ 25 (Dec, 2009).

A meta-analysis of randomised controlled trials, evaluating the benefits and harms of low-dose aspirin in people with diabetes and no cardiovascular disease, has shown no clear benefit of aspirin use. Until further research evidence becomes available, at present the use of low dose aspirin in the primary prevention of major cardiovascular events in people with diabetes remains unproven.[19]

Dietary inclusions and nutritional supplements may have value as part of lifestyle and diet modification

There is evidence that some dietary inclusions, e.g. nuts, may have a beneficial effect on reducing cardiovascular risk, however use of such products is not widely advocated.

Is there any evidence for nutritional supplements targeted at reducing cardiovascular risk such as flaxseed, walnuts or omega-3 fatty acid?

"All these products and others may have some value in improving the quality of the diet as a part of lifestyle modification."– Sisira Jayathissa

"A diet that favours significant contributions from fruit, vegetables and unprocessed nuts confers some lowering of risk. There is an absence of evidence (and in some cases, evidence of absence) of 'benefits' from nutritional supplements, which should be clearly stated on product information."– Stewart Mann

"There is no doubt that a healthy lifestyle including an appropriate dietary pattern is a cornerstone of treatment of all those at risk of cardiovascular disease. However, there is little evidence for unique benefits of individual foods. Nuts may be the single exception. There is evidence that those regularly consuming nuts may be at reduced risk of subsequent cardiovascular events, an effect which seems to be independent of potentially confounding factors. They have a favourable effect on several clearly described risk factors though if recommending nuts patients should be advised to avoid heavily salted and roasted nuts. They are sometimes roasted in saturated fat!

There is limited evidence that omega 3 fatty acids given as supplements, as well as the regular consumption of oily fish, may reduce subsequent cardiovascular events in those with established cardiovascular disease. There is no convincing evidence of benefit of any other nutrient supplements. " – Jim Mann

A mean daily consumption of 40 g to 100 g of raw nuts, e.g. almonds, walnuts, hazelnuts, pecans, pistachios and peanuts* may reduce cardiovascular risk and reduce blood lipid levels.[20]

Nut consumption improves blood lipid levels, particularly among people with higher LDL-cholesterol or with lower body mass index. It is not clear why nuts are less effective in lowering blood cholesterol concentration among people who are obese.[20]

The cardiovascular disease prevention benefits of nuts are likely to be due to a number of effects in addition to cholesterol lowering. Other beneficial effects include improved endothelial function and lowered oxidative stress. Nut consumption is also associated with a lower risk of developing type 2 diabetes and research has shown that frequent, moderate raw nut consumption does not lead to weight gain.[20]

Increasing the consumption of nuts as part of a healthy diet can be expected to favourably affect blood lipid levels (at least in the short-term) and has the potential to lower cardiovascular risk.[20]

* Peanuts are members of the legume family, but have a comparable nutrient profile to nuts and are associated with the same beneficial cardiovascular effects.[20]

Looking ahead

"The New Zealand Cardiovascular Risk Assessment Guidelines were updated as outlined in the Cardiovascular Guidelines Handbook 2009. The assessment of absolute risk is still based on the Framingham data and this has been validated for New Zealand. However, within the next year or two we will have the opportunity to rewrite the risk equation using New Zealand specific data obtained from primary care. These data have linked risk assessment with outcomes in a large population sample aggregated in recent years. Beyond that, the remaining challenge is to move beyond risk assessment to effective management and ensure that high risk individuals do indeed have effective long term intervention and support to reduce their absolute risk and improve their outlook."– Norman Sharpe

References

1. Hay D. Cardiovascular disease in New Zealand. A summary of recent statistical information. National Heart Foundation of New Zealand; 2004.
2. Clinical Knowledge Summaries. Cardiovascular risk assessment and management. Version 1.6. December 2008. Available from: www.cks.nhs.uk (Accessed Nov, 2010).
3. Eichler K, Puhan MA, Steurer J, Bachmann LM. Prediction of first coronary events with the Framingham score: A systematic review. Am Heart J 2007;153:722-31.
4. New Zealand Guidelines Group. New Zealand cardiovascular guidelines handbook: a summary resource for primary care practitioners. 2nd ed. Wellington: New Zealand Guidelines Group; 2009. Available from www.nzgg.org.nz (Accessed Nov, 2010).
5. Tzoulaki I, Liberopoulos G, Ioannidis JPA. Assessment of claims of improved prediction beyond the Framingham risk score. JAMA 2009;302(21):2345-52.

Some questions remain unanswered

Some issues in cardiovascular risk assessment remain controversial and there is not always a clear or universally accepted viewpoint.

The influence of current cardiovascular medication on risk assessment

"The role of treatment in re-assessment of risk level is an unanswered (and possibly unanswerable) question. It is no longer possible to study an untreated population comparable to a treated one. Past studies have shown that some risks are reduced immediately and completely by effective treatment, e.g. stroke risk in hypertension, but others, e.g. coronary disease in hypertension, may take longer to reduce. Certainly, studies of people with treated hypertension show that they remain at higher risk than those with comparable levels of blood pressure who were never hypertensive, but there could be many confounding factors here." – Stewart Mann

Uric acid as a risk marker

"This issue (using serum uric acid as a marker of cardiovascular risk) is still somewhat controversial. Some studies have shown independent association of uric acid and increased cardiovascular risk but other studies have come to a different conclusion. The main link between raised uric acid levels and cardiovascular disease is hypertension. In a small study of young adults, reduction in uric acid levels has produced improvement in hypertension. Uric acid has been linked to metabolic syndrome and diabetes. There is not sufficient evidence to consider treating isolated high uric acid levels in low risk adults. Doctors should instead focus on treating the known risk factors."– Sisira Jayathissa

"Gout appears to be increasing in Māori and Pacific peoples so uric acid as a risk marker is perhaps important in these groups." – Jim Mann

Research surrounding the link between uric acid, allopurinol and hypertension is currently underway, which may provide new data to help understand this association.

See "Genes, fructose, allopurinol and gout" BPJ 32 (Nov, 2010) and "Gout in the Māori community" BPJ 13 (May, 2008).

6. Yusuf S, Hawken S, Ôunpuu S, et al, on behalf of the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364:937–52.
7. Grey C, Wells S, Riddell T, et al. A comparative analysis of the cardiovascular disease risk factor profiles of Pacific peoples and Europeans living in New Zealand assessed in routine primary care: PREDICT CVD-11. N Z Med J 2010;123(1309):62-75.
8. Ministry of Health. Living standards and health: New Zealand 2006/07. Wellington: Ministry of Health; 2010.
9. Post TW, Gibson CM, Henrich WL. Chronic kidney disease and coronary heart disease. UpToDate. 2010. Available from: www.uptodate.com (Accessed Nov, 2010).
10. Lee M, Saver JL, Chang K-H, et al. Low glomerular filtration rate and risk of stroke: meta-analysis. BMJ 2010;341:c4249.
11. Rosenson RS, Stein JH. Lipoprotein(a) and cardiovascular disease. UpToDate 2010. Available from: www.uptodate.com (Accessed Nov, 2010).
12. Miller ER, Juraschek S, Pastor-Barriuso R, et al. Meta-analysis of folic acid supplementation trials on risk of cardiovascular disease and risk interaction with baseline homocysteine levels. Am J Cardiol 2010;106:517–27.
13. Martí-Carvajal AJ, Solà I, Lathyris D, Salanti G. Homocysteine lowering interventions for preventing cardiovascular events. Cochrane Database Syst Rev 2009;4:CD006612.
14. Morrow DA. Screening for cardiovascular risk with C-reactive protein. UpToDate 2010. Available from: www.uptodate.com (Accessed Nov, 2010).
15. Wang L, Manson JE, Song Y, Sesso HD. Systematic review: vitamin D and calcium supplementation in prevention of cardiovascular events. Ann Intern Med 2010;152:315-23.
16. Gore J. Do vitamin D and calcium supplements prevent cardiovascular events? Journal Watch Cardiology 2010;March 24. Available from: www.jwatch.org (Accessed Nov, 2010).
17. Bolland MJ, Barber PA, Doughty RN, et al. Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial. BMJ. 2008;336:262-6.
18. Reid IR, Ames R, Mason B, et al. Randomised controlled trial of calcium supplementation in healthy, nonosteoporotic, older men. Arch Intern Med. 2008;168:2276-82.
19. De Berardis G, Sacco M, Strippoli G, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials. BMJ 2009; 339:b 4531.
20. Sabaté J, Oda K, Ros E. Nut consumption and blood lipid levels: A pooled analysis of 25 intervention trials. Arch Intern Med 2010;170(9):821-7.