Guidelines Review

# New Zealand Cardiovascular Guidelines:

# Best Practice Evidence-based Guideline: The Assessment and Management of Cardiovascular Risk December 2003

*<http://www.nzgg.org.nz/guidelines/0035/CVD_Risk_Full.pdf>*

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**Introduction**

The New Zealand Guideline for the Assessment and Management of Cardiovascular Risk was published in December 2003, replacing separate guidelines for management of dyslipidaemia and hypertension and incorporating a section on cardiovascular risk in diabetes. The guideline was developed under the auspices of the New Zealand Guidelines Group (NZGG) in partnership with the National Heart Foundation, the Stroke Foundation of New Zealand and the Ministry of Health. Members of the guideline development team were from these organisations with other members nominated by a variety of stakeholders.

The guideline is for use principally by primary care practitioners and is intended to address the gap between evidence and practice that is known to exist. Assessment and management of people with known cardiovascular disease (CVD) is fully covered but a major feature is the description of a framework to guide opportunistic screening for identifying those at high risk of future CVD and instituting appropriate treatments. The structure of the screening process has the clear intent of redressing the socioeconomic inequalities in CVD that are evident in New Zealand and which have widened over the last several decades, especially in Maori but also in Pacific peoples and those with ethnic origin in the Indian Subcontinent.[1-4]

The guidelines describe appropriate pharmacologic treatments but also have a strong focus on lifestyle interventions, including physical activity, cardioprotective diet patterns, weight management, and smoking cessation. CVD defined in this guideline is a composite of angina, myocardial infarction, coronary death, ischaemic stroke, transient ischaemic attack and peripheral vascular disease.

The whole document, including the evidence base, is 220 pages with 750 references. A seven page summary contains key messages and risk assessment tables and a practical version with an extra section on atrial fibrillation and risk of stroke is included in a handbook for primary care practitioners, published in June 2005. All documents are freely downloadable from the NZGG.[5] This review will not attempt to cover the whole guideline but the essential elements of the risk assessment process are presented. Because of the special relevance to laboratory practice, some comparisons are made with information presented in the 2005 Australian Guidelines on Lipid Management, which also have a strong focus on absolute risk.[6] Details of therapeutic interventions, whether pharmacologic or lifestyle, are not considered and assessment of blood pressure is mentioned only to indicate suggested target levels. However, it should be recognised that recommendations on lifestyle interventions are a strong feature of the guideline.

**Principle of risk assessment**

The fundamental principle of the guideline is that risk assessment is based on considering all relevant risk factors and expressing risk in absolute terms. Absolute risk is the likelihood that an individual will have a cardiovascular event over a given time period, e.g. 15% over 5 years. Risk reduction is also expressed in absolute terms. Decisions to use pharmacologic treatment in addition to lifestyle measures and

the intensity of treatment are strongly based in the magnitude of absolute risk, the absolute risk reduction achievable by treating all risk factors and the number needed to treat to prevent a cardiovascular event.

The 1993 and 1996 New Zealand Guidelines on Management of Dyslipidaemia were pioneering in use of absolute risk.[8] This approach should now be mandatory in order to cut across the misleading information often quoted in clinical trials and drug advertising, in which risk reduction is often quoted only in terms of relative risk. For example 'cardiovascular events were reduced by 25% in the group treated with high dose statin' is a meaningless statement unless the actual risk of the control group is stated. Unfortunately, some recent guidelines do not emphasise absolute risk and thus are inefficient and uneconomic.[9] Table 1 shows the different levels of absolute benefit that can be achieved at the same level of relative risk reduction in subjects at different levels of absolute risk. This is a key message.

Steps in risk assessment

1. **Select people for risk assessment**. Table 2 shows recommended ages for initiating cardiovascular risk assessment in those without known CVD. People with diabetes should have risk assessment at the time of diagnosis. People at high risk will have one or more of the risk factors shown in Table 3.

2. **Measure and record risk factors**. This includes age, gender, ethnicity, smoking history, fasting lipid profile, fasting plasma glucose, the average of two sitting blood pressures, family history, waist circumference and body mass index. People with diabetes require $HbA_{1c}$, urinary albumin:creatinine ratio, serum creatinine and date of diagnosis.

3. **Risk assessment**. Cardiovascular risk is assumed to be more than 20% over 5 years in those who have had a previous cardiovascular event, in those with genetic lipid disorders, in those with diabetes and overt nephropathy (albumin:creatinine ratio $\geq$ 30 mg/mmol or albumin >200 mg/L) or diabetes with other renal disease.

   Cardiovascular risk in all other people is calculated with risk tables[6] or with an electronic decision support tool.[10] Both are based on the Framingham risk equation for first

**Table 1.** Absolute risk reduction at fixed relative risk reduction. The degree of reduction in absolute risk following an intervention is highly dependent on the prior risk in that individual.

| Absolute risk in controls | Number of events in 1000 controls | Number of events in 1000 treated | Relative risk reduction | Absolute risk reduction |
|---|---|---|---|---|
| 40% | 400 | 280 | 30% | 12% |
| 20% | 200 | 140 | 30% | 6% |
| 10% | 100 | 70 | 30% | 3% |
| 1% | 10 | 7 | 30% | 0.3% |

**Table 2.** Recommended age levels for initiating cardiovascular risk assessment in subjects without known CVD.

| | Men | Women |
|---|---|---|
| Maori, Pacific and Indian* subcontinent peoples | 35 years | 45 years |
| People with known cardiovascular risk factors or at high risk of developing diabetes | 35 years | 45 years |
| Asymptomatic people, without known risk factors | 45 years | 55 years |

* Indian, including Fijian Indian, Sri Lankan, Afghani, Bangladeshi, Nepalese, Pakistani, Tibetan

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**Table 3.** Factors associated with a high risk of CVD, which identify people who should be selected for early screening.

| Family risk factors |
|---|
| • Diabetes in a first degree relative (parent or sibling)<br>• Premature coronary heart disease or ischaemic stroke in a first degree relative (father or brother <55 years, mother or sister <65 years) |
| **Personal risk factors** |
| • Gestational diabetes, polycystic ovary syndrome, current or recent smoking<br>• Prior blood pressure ≥160/95 mmHg, prior TC:HDL ratio ≥7.0<br>• Known impaired glucose tolerance (IGT) or impaired fasting glucose (IFG)<br>• BMI ≥30 kg/m$^2$ or truncal obesity (waist ≥100 cm in men or ≥90 cm in women) |

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cardiovascular events.[11]

People with very elevated single risk factors (total cholesterol (TC) >8 mmol/L or TC:HDL-C ratio >8 or blood pressure consistently >170/100 mmHg) are considered to have a risk of at least 15% over 5 years but should have a full assessment as risk may be higher than this.

4. Steps 4-6 involve deciding appropriate lifestyle and drug interventions, setting individual-specific realistic targets, arranging follow up and monitoring. All treatment decisions are based on an individual's 5 year absolute risk as detailed below.

**Adjustment of risk**

The guidelines acknowledge that where risk is determined from the Framingham equation, risk will be underestimated in some individuals. The pragmatic decision was made to increase estimated absolute risk by one risk category (5%) in the following cases:

- People with a family history of premature coronary heart disease or ischaemic stroke in a first-degree male relative before the age of 55 years or a first degree female relative before the age of 65 years
- Maori
- Pacific peoples or people from the Indian subcontinent
- People with both diabetes and microalbuminuria
- People who have had type 2 diabetes for more than 10 years or who have $HbA_{1c}$ consistently greater than 8%
- People with the metabolic syndrome

The adjustment is made once only for people who have more than one criterion i.e. the maximum adjustment is 5%. This may still underestimate risk in diabetes and some ethnic groups, especially in those under 35 years, and further work on these issues is under way.

**Metabolic syndrome**

The presence of the metabolic syndrome is one of the factors that dictate increasing the absolute risk by 5%, with metabolic syndrome defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), published in 2001 (Table 4).[12] There has been considerable recent controversy about the separate value of the metabolic syndrome as a predictor of cardiovascular risk. Some argue that because all definitions of the metabolic syndrome include established risk factors there is doubt about whether or not the syndrome contributes to prediction of cardiovascular risk more than its individual components.[13,14] Others consider that the metabolic syndrome confers risk independent of the Framingham risk score because of its association with non-traditional atherogenic risk factors linked to insulin resistance, such as elevated triglyceride (TG) rich lipoproteins, small dense LDL, postprandial lipaemia, endothelial dysfunction, inflammation and the prothrombotic state.[15] The debate has been intensified by new definitions of the metabolic syndrome which will include a significantly greater proportion of the population.[16,17] The view has recently been expressed that while the Framingham risk assessment may be a better predictor of short term risk than the metabolic syndrome, the latter may be a useful tool for early identification of people who are at long term high risk but who currently have apparent low risk.[18] This might especially apply in younger subjects. A similar view has been expressed to this reviewer (personal

**Table 4.** List of factors associated with the metabolic syndrome. The 2001 NCEP ATP III definition of the metabolic syndrome requires three of five factors to be present.

| Risk Factor | Sex | Defining Level |
|---|---|---|
| Abdominal Obesity | Men | ≥100 cm waist circumference |
| | Women | ≥90 cm waist circumference |
| Fasting Triglycerides (TG) | | ≥1.7 mmol/L |
| HDL-C | Men | <1.0 mmol/L |
| | Women | <1.3 mmol/L |
| Blood Pressure | | Systolic ≥130 mmHg or Diastolic ≥85 mmHg |
| Fasting Glucose | | ≥6.1 mmol/L |

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communication, Professor Jim Mann, Human Nutrition Department, University of Otago) and these factors are likely to feature strongly in the deliberations of an expert group recently convened in New Zealand to consider and redefine cardiovascular risk in diabetes and associated conditions.

**Emerging risk factors**

The guideline group reviewed emerging risk factors, including homocysteine, apolipoprotein B (apoB), LDL particle size, microalbuminuria without diabetes, Lp(a), prothrombotic factors and high sensitivity CRP (Hs-CRP). None of these were considered to be suitable for inclusion in risk assessment, either because their independent predictive value was not quantified, there was insufficient data on the effectiveness of interventions or assays were poorly standardised.

Little has emerged since 2003 to make a compelling case for routine use of these emerging risk factors, especially for the most studied, Hs-CRP. The National Heart Foundation of Australia position statement on lipid management 2005 has reached a similar conclusion about Hs-CRP.[6] No current guideline is recommending routine use of Hs-CRP in risk assessment and even the American Heart Association statement recommends very limited optional use.[19] There have been recent challenges to the concept that Hs-CRP has any useful predictive value.[20,21] It is the opinion of this reviewer that, while Hs-CRP may provide useful epidemiological data and insights into atherogenesis, it is unlikely to be very useful in classifying individuals because of significant biological and analytical variability.[22,23]

ApoB has been recommended for use in specialist practice[24] and the evidence that the ApoB/ApoA1 ratio is a strong risk factor for CVD and may be a suitable target for lipid-lowering therapy has been extensively reviewed in a series of articles in a recent symposium.[25]

**Measurement of risk factors**

The guidelines recommend that a fasting lipid profile (TC, LDL-C, HDL-C, TC:HDL-C ratio and TG) be measured, together with fasting glucose. The TC:HDL-C ratio is used in the risk tables. A further lipid measurement is taken prior to instituting drug treatment or intensive lifestyle treatment and LDL-C is the main target of treatment. If there is a difference of more than about 0.8-1.0 mmol/L in the results for TC a third determination of lipids is recommended, and the average of the three is used as the baseline. This is intended to minimise analytical and biological variability.

For blood pressure the average of two seated measurements is recommended and this should be repeated on three separate occasions prior to the initiation of either intensive lifestyle modification or drug treatment.

**Intensity of treatment according to absolute risk**

The goal for everyone is to reduce 5 year cardiovascular risk and the higher the risk the more aggressive the management of all modifiable risk factors should be. The guidelines state that there is no ideal or normal blood lipid level but optimal levels are indicated (Table 5). The same concept applies to blood pressure targets (Table 6). These levels reflect data from clinical trials. The rationale for targeting blood pressure and lipid lowering drug treatment to patients at high absolute risk, irrespective of their blood pressure or cholesterol level is well explained in a recent review.[26] This emphasises that terms such as hypertension and hypercholesterolaemia have limited

**Table 5.** Optimal levels of lipoprotein fractions for high risk individuals according to the New Zealand Cardiovascular Guidelines.

| Lipid Fraction | Value |
|---|---|
| TC | <4 mmol/L |
| LDL-C | <2.5 mmol/L |
| HDL-C | >1 mmol/L |
| TC:HDL-C Ratio | <4.5 |
| TG | <1.7 mmol/L |

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value. Thus, in the context of all risk factors, it may be more appropriate to lower cholesterol with drugs in one individual with LDL-C 3.5 mmol/L than in another with LDL-C 4.5 mmol/L.

For those at very high risk, determined clinically, the aim is to achieve maximal risk reduction to <15% through multiple interventions. Intensive lifestyle therapy and pharmacologic treatment should be started concurrently and the optimal levels for lipids and blood pressure should be targets of treatment for these people. The potential absolute risk reduction is large and the number needed to treat (NNT) to prevent an event is low (Table 7). This table emphasises the key concepts of absolute risk. For example, it is clear that a 25% relative risk reduction achieved by reducing LDL-C in a low risk individual has a very small benefit, requiring large numbers to be treated to prevent a single event.

For those with no previous clinical history of CVD but with 5 year cardiovascular risk calculated from tables to be high, greater than 15%, the goal is to reduce risk to less than this figure. The intensity of treatment should be individualised to each person according to risk and the optimal levels are not necessarily targets. For those with risk over 20%, immediate pharmacologic therapy and intensive lifestyle intervention should be started concurrently but if risk is 15-20% a 3 month trial of specific lifestyle intervention is recommended with pharmacologic treatment recommended if risk remains over 15%. Intensive lifestyle intervention usually requires referral to a health professional specifically trained in this area while specific lifestyle intervention is under guidance of the general practitioner.

In those with moderate risk, 10-15%, pharmacologic treatment is not usually recommended but clinical judgement should be exercised. Specific lifestyle interventions are recommended to further reduce risk. When risk is <10% general lifestyle advice is recommended in the form of educational material.

The guidelines indicate that it may be difficult to reach optimal levels in some people, even when their risk indicates that these may be an appropriate goal. The simultaneous improvement of several risk factors is considered to be a better approach than the aggressive pursuit of further small reductions in LDL-C or blood pressure. While reductions in LDL-C of 25-35% can be achieved by the standard doses of statins used in trials, for every doubling of the dose of any statin above standard only an approximate further 6% reduction in LDL-C can be obtained.[27,28]

**Management of people with diabetes, hyperglycaemic states or the metabolic syndrome**

Measurement of fasting glucose is part of the risk factor assessment and an oral glucose tolerance test (OGTT) is recommended for those with IFG, defined as 6.1-6.9 mmol/L. The guideline group considered that an OGTT is also indicated in some people with risk factors for diabetes who have fasting glucose 5.5-6.0 mmol/L.

**Table 6.** Suggested target blood pressure levels according to the New Zealand Cardiovascular Guidelines.

| | Systolic Blood Pressure | Diastolic Blood Pressure |
|---|---|---|
| People without clinical CVD | <140 mmHg | <85 mmHg |
| People with diabetes or CVD | <130 mmHg | <80 mmHg |
| People with diabetes and overt nephropathy, diabetes and microalbuminuria or diabetes with other renal disease | Aggressive blood pressure control to a target of <120/75 mmHg is recommended | |

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**Table 7.** Absolute risk determines the significance of relative risk reduction; the table shows the number of patients needed to be treated for 5 years by one, two and three interventions respectively at various levels of absolute risk to prevent one CVD event. (The figure within brackets shows the number of CVD events prevented per 100 people treated for 5 years). Based on the conservative estimate that each intervention (e.g. lowering blood pressure, lowering LDL-C and aspirin therapy) reduces relative risk by about 25% over 5 years.

| 5-year absolute risk of CVD | Benefits: NNT to prevent one event (CVD events prevented per 100 people treated for 5 years) | | |
|---|---|---|---|
| | 1 intervention (25% relative risk reduction) | 2 interventions (45% relative risk reduction) | 3 interventions (55% relative risk reduction) |
| **30%** | **13** (7.5) | **7** (14) | **6** (16) |
| **20%** | **20** (5) | **11** (9) | **9** (11) |
| **15%** | **27** (4) | **15** (7) | **12** (8) |
| **10%** | **40** (2.5) | **22** (4.5) | **18** (5.5) |
| **5%** | **80** (1.25) | **44** (2.25) | **36** (3) |
| **<2.5%** | **≥ 160** (≤ 0.6) | **≥ 88** (≤1.125) | **≥ 72** (≤ 1.5) |

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This would include people of non-European ancestry, those with a family history of diabetes, a past history of gestational diabetes or other features of the metabolic syndrome. This lower range of fasting glucose is consistent with that specified for proceeding to an OGTT in the Australian National Health and Medical Research Council (NHMRC) guideline for screening for type 2 diabetes.[29] The difference is that the NHMRC guideline recommends screening with fasting plasma glucose (FPG) in those with one or more risk factors for diabetes rather than measuring FPG in the context of a cardiovascular risk assessment but in practice many would be likely to receive a full cardiovascular risk assessment as part of good primary care.

One significant difference is that age is included as a risk factor in the NHMRC guideline but when there are no other known risk factors it is set at ≥55 years for both men and women. The age is set at ≥45 years if there are other risk factors but this may not be low enough to ensure detection of diabetes or IGT in some people. The age for Aboriginal people, Torres Strait Islanders and other high risk ethnic groups is set at ≥35 years. The New Zealand guideline recommends screening based on age, sex and ethnicity as it is a screening program for cardiovascular risk rather than for diabetes. There is no particular age specified in the current Australian lipid and blood pressure guidelines.

Those with diabetes are started on treatment according to their absolute risk in the same way as those without diabetes. Measures to improve glycaemic control begin immediately and the recommended target for $HbA_{1c}$ is <7.0% for most people. Details of glycaemic management are in a separate guideline. The targets for blood pressure are lower (Table 6) but the optimal levels for lipids are the same as for those without diabetes. Whether or not the lipid targets should be more stringent will be reviewed in the light of new trial evidence.

**Follow up after risk assessment**

The guidelines recommend lipid monitoring every 3 months for those on lipid lowering drug treatment, until levels are controlled, then every 6 months. For those at lower risk who are being treated with lifestyle advice, the full risk assessment, with laboratory tests, is recommended at an interval of 5 years (10 years for very low risk).

**Monitoring for adverse effects of statins**

Baseline alanine aminotransferase (ALT) is recommended prior to initiating statin treatment and at the first 3 month follow up, with testing thereafter if indicated clinically. Both creatinine and ALT are required before using a fibrate. The guideline recommends that with increases in ALT up to three times the upper limit of the reference interval it is usually possible to continue the statin but increased monitoring and discussion with a specialist is required for greater increases.

Baseline creatine kinase (CK) before statin treatment is not recommended and is subsequently required only if there are muscular symptoms. With moderate increases (3-10x upper limit) CK should be monitored weekly and specialist advice sought. Reduction in dose of statin or temporary discontinuation may be required and severity of symptoms is a guide, even if the elevation in CK is modest. Statin therapy should be stopped if CK levels are more than 10x upper limit.

There was considerable debate about these recommendations for monitoring adverse effects of statins, especially with regard to baseline CK, but they are essentially the same as those stated in a recent report from the Statin Safety Assessment Taskforce on the safety of this class of drug.[30] This taskforce recommends that the necessity for monitoring liver function tests should be reviewed, as the accumulated evidence is that the risk of serious liver dysfunction caused by statins is very low and in any case is unlikely to be detected by monitoring. However, they indicated that monitoring should continue until the manufacturers and regulatory agencies agree to revise their current statements on adverse effects of statins. The view on CK was that it is not routinely necessary to obtain a pre-treatment baseline, in contrast to the recommendation in Australian guidelines.

**Comparison with Australian and other guidelines**

As far as this reviewer can ascertain, there is no integrated Australian guideline on cardiovascular risk assessment. However, the 2005 Lipid guideline[6] and the 2004 hypertension guideline[31] both completely endorse the concept of absolute risk in guiding treatment, thus requiring that a full cardiovascular assessment be carried out. Both guidelines recommend that the New Zealand risk tables or calculator can be used for risk assessment but, in agreement with the New Zealand guidelines, emphasise that this Framingham-based calculation has limitations. They recommend that local risk prediction tools be developed, a view endorsed by others.[32] The emphasis is similar to that in the New Zealand guidelines, that the inequities in cardiovascular health obvious in groups with lower socioeconomic status need to be addressed.

The level of absolute risk at which pharmacologic treatment is recommended in both these Australian guidelines is >15% over 5 years or >10% in those with a significant family history or the metabolic syndrome and this is essentially the same as the New Zealand guideline. Target blood pressures are similar in the Australian and New Zealand guidelines.

The lipid guideline does have some significant differences from the New Zealand guideline. The most important is the inclusion of evidence from recently published trials that there is benefit in lowering LDL-C to <2 mmol/L in high risk subjects with existing coronary heart disease. The guideline has stopped short of completely endorsing this as a mandatory target but states:

"***The results of these trials suggest a target LDL-C of <2.0 mmol/L for this patient population. The validity of this suggestion of a lower LDL-C target will be reviewed in the light of upcoming results from additional trials that are currently in progress."***

Otherwise the lipid targets stated for LDL-C and HDL-C are the same as the optimal levels in the New Zealand guideline but are slightly lower for TG at 1.5 mmol/L. There is a difference in emphasis in that the levels are stated as targets. It is implied in the lipid guideline and is explicit in the blood pressure guideline that every effort should be made to reach the targets.

The NCEP recommends a target for LDL-C of 1.8 mmol/L in high risk subjects[28] while the Joint British Societies recommend <2.0 mmol/L or a 30% reduction, whichever is lower.[33] The European guidelines on CVD prevention, also published in 2003, indicate that LDL-C <2.5 mmol/L is a goal of therapy for patients with clinically established CVD and for patients with diabetes but for asymptomatic high risk patients only when this goal can be reached with moderate doses of lipid lowering drugs.[34] They recommended against using very high dose therapy to achieve the goal because the merit had not been shown at the time of publication and this view is consistent with the New Zealand guideline. There are opinions that levels of LDL-C should be a low as 0.8 mmol/L for high risk individuals and 1.5 mmol/L for primary

prevention[35] but these opinions lie well outside guidelines based on absolute risk and absolute benefit. A recent review has examined the independent relationship between LDL-C and major cardiovascular outcomes in patients with LDL-C below 3.4 mmol/L.[36] In an interesting analysis it concludes that the evidence as presented does not demonstrate that titrating lipid therapy to achieve proposed low targets is beneficial or safe, because of avoidable limitations in the studies.

There is strong clinical opinion within New Zealand that the lower targets for LDL-C should be adopted immediately for high risk subjects and that the potent statins required to reach these levels should be more freely available.[37] This view is valid and any revision of the New Zealand guidelines must consider the new trial data, but cost benefit is also likely be scrutinised. It is the opinion of this reviewer that the new trials do show incremental benefits of low LDL-C, achieved with high dose, potent statins, but the NNT is relatively high, even for composite endpoints in high risk patients, and benefits in mortality have not been demonstrated compared with treatment to less stringent targets. There may be a better pay off in finding and treating with multiple interventions the substantial proportion of those at high risk who are not yet on any treatment i.e. addressing the gap between evidence and treatment mentioned in both the Australian 2005 lipid guideline and the New Zealand cardiovascular guideline. Whatever the case, very low LDL-C levels should not be regarded as a compulsory target for all.

There has been a view in the literature that those with diabetes have a cardiovascular risk equivalent to those without diabetes who have already had an event.[38] In fact those with diabetes are a heterogeneous group and both the Australian and New Zealand guidelines recommend individual risk assessment. However, a specific recommendation in the Australian guideline is that those with diabetes and LDL-C over 2.5 mmol/L after lifestyle modification should be considered for statins or for fibrate therapy if TG are over 2.0 mmol/L. This takes into account recent trial evidence that aggressive lipid lowering is of benefit in diabetes but the Australian guideline also notes the need for the development of an appropriate absolute risk tool specifically for Australian people and there is work in progress in New Zealand to similarly develop better cardiovascular risk assessment in diabetes.

A further difference between the two Australian guidelines and the New Zealand guideline is that there are well defined age brackets in the New Zealand guidelines at which to commence risk assessment. There appears to be no age guidance in the current Australian guidelines, except for Torres Islanders and Aboriginals, set at 18 years. Age 45 years for the general population was suggested in the 2001 lipid guidelines but there was criticism that the combination of age and risk factors in those guidelines was confusing and could lead to misclassification of risk.[39]As universal screening is not advocated in the current Australian guideline, presumably the decision has been left to doctors in the context of opportunistic screening.

British guidelines indicate that risk assessment should begin at age 40 years.[33] European guidelines do not specify any age but the implication of the text is that cardiovascular risk assessment may be done in 20-30 year old subjects.[34] Both the European and the British guidelines have an element of forward prediction. The latter has only three age categories in the tables for assessing absolute risk, <50, 50-59 and >60 but the risk is actually set as if age is 49, 59 and 69 years respectively. The European guidelines explicitly state that if the risk factor profile of young adults projected to age 60 years will exceed a high risk threshold, the information should be used to guide early lifestyle intervention and close follow up.

The NCEP guidelines current in the United States consider that screening for lipids should start from age 20 years without being explicit about a comprehensive cardiovascular assessment, although they do recognise absolute risk as important.[28] The value of early screening for lipids was considered by the NZGG in the context of picking up familial hypercholesterolaemia but it was considered that this was not an efficient strategy. Recent opinion confirms this view, with case finding through families being a better option.[40]

There is concern in New Zealand that application of the guidelines as stated will fail to detect younger people who may have currently low absolute risk but who are at high future risk of both diabetes and cardiovascular events, especially in the context of the obesity epidemic and in Maori and Polynesian populations. A current expert group is likely to consider such issues as part of the aforementioned brief to strengthen guidelines on assessment of cardiovascular risk in diabetes.

The New Zealand guideline does not specifically address the issue of increased risk of CVD related to chronic kidney disease (CKD), although the importance of management of blood pressure is explicit and there is special emphasis on the increased risk with diabetes and renal disease. The Australian lipid guideline outlines the general importance of CKD as a risk factor but notes that there is little trial data of statin therapy in those with CKD. Pending the results of trials, it recommends that decisions to start statins should be on an individual basis with caution in dosage because of the increased risk of myositis. The widespread availability of estimated Glomerular Filtration Rate (e-GFR) may be helpful

in this context. A recent publication from the American Heart Association and the National Kidney Foundation recommends screening for CKD with estimates of e-GFR and microalbuminuria in all those at high risk of CVD.[41]

**Significance of the guideline for laboratory practice**

The implication of the New Zealand guideline and the Australian lipid management guideline is that conventional reference intervals for lipid fractions are misleading and should be discarded in favour of an approach that reflects the concept of absolute risk i.e. that a very high risk subject will require intensive lipid lowering therapy at a level of cholesterol and LDL-C that may require only lifestyle advice in a low risk subject.

Some laboratories in New Zealand have already discarded reference intervals in favour of the optimal levels stated in the guideline but accompanying comments have not always been consistent and there has been concern that the optimal levels are being regarded as targets for all, irrespective of actual risk. Recently bpac$^{nz}$ (best practice advocacy centre http://www.bpac.org.nz/)[42] has suggested a possible standard for reporting. This is still in draft form but soon will be circulated to laboratory directors.The intent is that the optimal levels from the current guideline would replace the reference interval but must be clearly labelled as optimal and the results would be accompanied with a comment along the lines of:

***"For total cholesterol below 8 mmol/L all decisions to treat should be based on an individual's cardiovascular risk. For most patients on lipid-modifying drug treatment the optimal levels are recommended targets, but these should also be individualised. For very high risk patients the LDL-C target may be even lower, <2.0 mmol/L."***

The other laboratory issue raised by the New Zealand and Australian guidelines is that of the definition of IFG. The New Zealand guideline uses 6.1-6.9 mmol/L to define IFG and this range is also used in the parameters of the metabolic syndrome. The guideline allows that in individuals at high risk of diabetes, fasting glucose in the range 5.5-6.0 mmol/L does not exclude diabetes and requires that an OGTT be performed. This is consistent with the Australian recommendations for screening for diabetes.[29] Using 5.5 mmol/L as a cut-point for screening is not the same as defining this level as the threshold for IFG, but there is potential for confusion.[43] The situation is further confused by the recommendation of the American Diabetes Association (ADA)[44] that the range for IFG be extended to 5.6-6.9 mmol/L and the incorporation of this range in the new definition of the metabolic syndrome from the International Diabetes Federation (IDF).[16] There has been considerable controversy over the ADA recommendation.[45-48] To this reviewer's knowledge, no official body in Australia or New Zealand has yet endorsed the ADA definition of IFG and nor has the World Health Organisation. IFG remains as 6.1-6.9 mmol/L in the British guidelines.[33] However, the IDF definition of the metabolic syndrome is being used widely, including in the Australian 2005 lipid guideline. The issue of how IFG is defined needs to be addressed in future guidelines and laboratory practice in reporting needs to be consistent.

**Summary and future directions**

Since the New Zealand guideline was published in 2003 there has been further trial data, especially with regard to lipid lowering in high risk subjects and in those with diabetes. This data may lead to recommendations for more stringent goals of treatment in any revision of the guideline but the basic principles of assessment and management stated remain sound. More work is required on developing better tools for assessing risk in younger subjects and various ethnic groups and these issues are similar in Australia and New Zealand. There is always a need to ensure that the messages in guidelines are widely disseminated and the laboratory workforce must be aware of ways that value can be added to our reports to lend support to these and future guidelines.

**Conflict of interest**: Dr Crooke was a member of the guideline development team, nominated by the New Zealand Society for the Study of Diabetes.

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