Diabetes

This section is made up of edited extracts from the following publications (with permission from the authors and publisher) where further information can be found:

- Couzos S, Metcalf S, Murray RB. 'Diabetes' In: Aboriginal Primary Health Care: An evidence-based approach. 2nd Edition. Oxford University Press, Melbourne, September 2003.
- National Aboriginal Community Controlled Health Organisation (NACCHO) as lead agency of the Chronic Disease Alliance of Non-government Organisations. 'Prevention of Diabetes'. In: National Guide to a Preventive Health Assessment in Aboriginal and Torres Strait Islander Peoples. Feb 2003 (in press).

Readers are advised to refer to the full documents for detailed information on the prevention and management of diabetes, treatment goals and targets, case management, program implementation, data collection, and performance indicators.

Epidemiology and burden of disease

The overall prevalence of diabetes in the Aboriginal population lies between 10–30% and is generally 3–4 times higher at any age than the general population, with an earlier age of onset.[1] In northern Australia, the overall prevalence of type 2 diabetes is 4.5% to 19% in Aboriginal people rising to 40% in people older than 35 years of age.

Aboriginal and Torres Strait Islanders die from diabetes at an earlier age and at a higher rate than the general Australian population. They are 10 to 13.5 times more likely to die from diabetes than non-Indigenous Australians.[2]

Figure 1 below compares the number of deaths per 100 000 population over a 16-year period between Northern Territory Aborigines, Northern Territory non-Aborigines and the Australian population as a whole.[3]

The AusDiab Study (Australian Diabetes, Obesity and Lifestyle) recently documented the prevalence of diabetes in the general Australian population (12 000 persons from regions randomly selected across Australia). It found that 7.5% of Australians over the age of 25 years suffered from diabetes (of whom half were previously undiagnosed) and a further 10.6% had impaired glucose tolerance (IGT), whilst 5.7% had impaired fasting glycaemia (IFG), during 1999–2000. This study did not include sufficient Aboriginal and Torres Strait Islander people to report on their prevalence of diabetes.[4]

The AusDiab study in the general Australian population has confirmed that for every known case of diabetes, there is an undiagnosed case. Among the Aboriginal population, most studies support that the true prevalence of diabetes is twice that determined from known cases, though there will be great variation between sites due to different levels of screening activity in recent years.[1]

The incidence of diabetes has been less frequently reported. An eight-year follow-up study of a population in remote Central Australia (1987–95) indicated that 2% of the population developed diabetes every year. This contrasts with rates of 0.25% per year elsewhere. Obesity (BMI >33) increased the incidence to 5% per year.[5]

Hospital admission rates for diabetes are also more common in the Aboriginal population. There were 10–15 times as many hospital separations

for type 2 diabetes for Indigenous males and females compared with the total Australian population in 1998–9.[2]

Diabetes is a significant risk factor for cardiovascular disease — the primary cause of death among Aboriginal people with diabetes (67% of Aboriginal diabetic deaths were related to heart disease in 1997–99). However, the most common cause of death in a cohort of Aboriginal people with diabetes in the Northern Territory was renal failure. Infections were the next most common cause of death.[6]

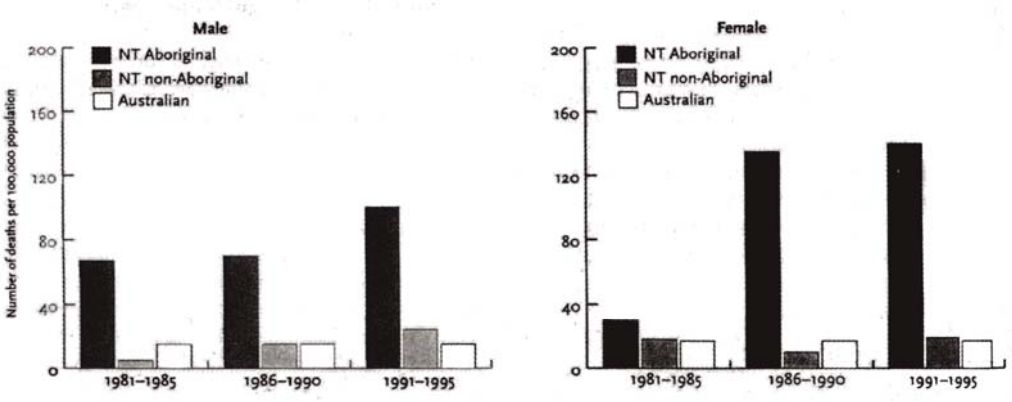

Figure 1: Diabetes: age-adjusted death rates, Northern Territory and Australia

The major types of diabetes

The diagnosis of diabetes 'is not based on the presence of a discrete physiological abnormality, but by an imperfectly chosen point on a continuum of glycaemia'.[7]

Type 1 diabetes is also known as insulin-dependent diabetes mellitus (IDDM). Ninety-nine per cent of diabetes seen in the Aboriginal or Torres Strait Islander population is type 2.[1] In comparison, around 10–15% of diabetes mellitus is type 1 in the general population.[4]

Type 2 diabetes, also known as maturity-onset diabetes or non-insulin-dependent diabetes, is the most common. In type 2 diabetes the pancreas can secrete excess amounts of insulin though it is insufficient to compensate for the insulin resistance.

Impaired glucose tolerance (IGT) is an intermediate metabolic state between diabetes and normal glucose control. Those with IGT are at higher risk of developing diabetes than the general population.[8] Some people with IGT will progress to diabetes, some will return to normal glucose tolerance and some will continue to have IGT. IGT, like diabetes, is commonly associated with hyperinsulinaemia and insulin resistance. Clinically significant microangiopathic renal and retinal complications are very rare in those with IGT.[9]

The use of glycated haemoglobin to diagnose diabetes has been explored as it has been shown that it can also predict the microvascular complications of diabetes.[10] However, there are limitations in the use of glycated haemoglobin to screen and diagnose diabetes. A number of expert committees around the world have not recommended the use of HbA1c (glycated haemoglobin) measurements to diagnose or screen for diabetes.[8,11]

Primary prevention: Summary

Three recently published studies have demonstrated that the development of diabetes in people with IGT can be prevented. The Diabetes Prevention

Study[12], conducted in Finland with a 3.2-year follow-up, showed that (intensive) individual diet and exercise intervention conducted by a dietitian could reduce the risk of diabetes by 58% ($p<0.001$) in a high risk population. This was achieved with seven sessions in the first year and regular three-monthly sessions after that, during which goals were set on how to lose weight (>5%), decrease total fat intake to <30% of energy, decrease saturated fat intake to <10% of energy, increase fibre intake to >15 g/1000 kcal consumed and to exercise for at least 30 min per day. The control group were set goals and given general written and oral information about diet and exercise initially and then annually, but no specific individualised programs were offered. The incidence of diabetes in the intervention group was significantly lower than the control group (11% vs 23%). Diabetes did not develop in any of the groups who achieved four or five goals, however, significantly more people were able to achieve these goals in the intervention group (49 in the intervention group vs 15 in the control group, $p<0.001$ for each of the goals). In those who did not achieve any of the goals the incidence of diabetes was 38% vs 31% respectively.

The Diabetes Prevention Program was a major clinical trial conducted in the United States over three years in a group with people with IGT and therefore at high risk of developing type 2 diabetes. The intensive lifestyle intervention included instruction on a low fat diet, exercising for 150 minutes per week and behaviour modification skills. The results show on average that this group had a 7% weight loss in the first year, sustained a 5% loss for the study's duration and maintained 30 minutes of exercise per day. A 58% reduction in the risk of developing type 2 diabetes was found compared to the control group who received only basic diet and exercise advice.[13]

The Da Qing study reported in 1997 that diet and exercise strategies can prevent the onset of type 2 diabetes in patients with IGT. Both strategies were equally effective in preventing the development of type 2 diabetes by 31–46% over six years, although the combination of diet and exercise was not any more effective than either strategy alone.[14]

In Aboriginal populations leanness appears to protect against diabetes in all age groups.[15] There is indirect evidence that traditionally oriented Aboriginal people display insulin resistance despite their leanness and that this is responsible for their predisposition for the Metabolic Syndrome upon adopting a Western lifestyle. A reversion to traditional hunter-gatherer lifestyle has been shown to greatly ameliorate the abnormalities of carbohydrate and lipid metabolism associated with diabetes and IGT.[16]

Dietary aspects other than the impact on BMI appear to be important. These include a sufficient intake of dietary fibre[17,64,18,19] and the consumption of vegetables, rice and pasta throughout the year.[20]

People with a high intake of dietary fat, especially saturated fat, are at increased risk of type 2 diabetes, whilst those who regularly consume fish derive some protection.[11]

Physical activity

The effect of physical activity in overweight individuals has been shown to be beneficial even if they remain overweight. In a prospective trial of middle-aged men the degree of physical activity required appeared to be moderate, of at least a 40-minute duration per week. The protective effect was greater in men at high risk for type 2 diabetes (reduced risk by 64%)

with the same level of physical activity and was still protective even at lower levels of activity.[21]

As mentioned above, the US and Finnish diabetes prevention studies found an important role for physical activity in the prevention of diabetes, though it was not possible to clearly differentiate the relative roles of diet and exercise.

Because of the high prevalence of diabetes in the Aboriginal population, and its great impact on morbidity and mortality, its prevention is very important. This will need to be multifaceted, combining individual counselling for high-risk people with population approaches (such as store food policies, amenities for exercise and promoting a healthy lifestyle). Promotion of improvements in other fundamental socioeconomic determinants of health is also likely to be important, though how best to achieve this is unclear. In general community control and self-determination is thought to be crucial.

People with the metabolic syndrome and/or IGT have the highest risk of progressing to full diabetes and its complications and should be targeted for more intensive interventions.

Primary prevention with medication

The US Diabetes Prevention Program reported in 2002 that metformin (850 mg twice daily) reduced the incidence of diabetes over 2.8 years by 31% compared with placebo. Metformin was used by those who were at high risk for diabetes with high fasting and post-load glucose levels (high enough for IFG or IGT but not diagnostic for diabetes). The protective effect was such that 14 people would need to be treated with metformin over three years to prevent one of them from becoming diabetic, at the expense of higher rates of gastrointestinal symptoms.[13] At this stage CARPA is not recommending this as routine treatment for IGT, though future studies may change this.

Other factors

There is evidence that low birth weight and poor growth by 12 months of age can increase the risk of developing IGT and type 2 diabetes — a link described by the 'thrifty-phenotype' hypothesis.[22,1] The understanding of this relationship (sometimes referred to as the 'Barker hypothesis') is evolving and is beyond the scope of this summary.

Screening

For most people diabetes is asymptomatic and will only become known after testing. Given that diabetes is common in Aboriginal populations, that there are effective treatment options and that early detection is relatively easy, CARPA recommends annual screening for diabetes for all Aboriginal adults.

[Editor: The optimal age at which to start screening can be debated. Type 2 diabetes occasionally occurs at ages less than 15 years, but is not common. Screening people in their early teen years is consequently more likely to lead to false positive results than screening at an older age. As a pragmatic compromise the screening age has been kept the same as that used for other components of the Adult Health Check.

Attempts at annual screening lead to many people actually getting two-yearly screens. Two-yearly screening would be fine but it may not fit with local management issues like staff turnover, and staff feeling that they

are responsible for it. There is also value in keeping it linked with other well- person checks that may be more clearly appropriate annually, such as smoking. PHC delivery issues probably favour annual screening as part of opportunistic Adult Health Check.]

Extensive experience in remote and urban Indigenous health practice tells us that effective screening and management of cases needs local population registers, coordinated care-planning, recall systems, input from a range of health professionals and a good relationship between the health service and the people with diabetes.

A US study concluded that type 2 diabetes screening may be cost-effective if it involves screening high-risk subpopulations and commences at a younger age.[23] No cost effectiveness study for diabetes screening has been reported in Australia.

The Australian National NHMRC Evidence Based Guidelines for type 2 Diabetes (2002) recommend that diabetes screening should be offered to all Aboriginal peoples and Torres Strait Islanders aged 35 years and over, but may need to be commenced at a younger age in some regions.[24] Most primary care providers to the Aboriginal population have already introduced diabetes screening at a younger age (around 18 years).[25]

A fasting blood glucose is currently the most widely recommended screening test for diabetes. The diagnostic criteria for diabetes have been based on the levels of hyperglycaemia that adequately predict the development of microvascular complications of diabetes.[26] Diabetes is present if the fasting plasma glucose is greater than or equal to 7.0 mmol/L. In the absence of symptoms this has to be confirmed on a subsequent day. A random or casual plasma glucose >11.1 mmol/L (with symptoms or repeated on a subsequent day) is retained as a diagnostic criterion.

A fasting blood glucose may be less than ideal in the field because of logistic difficulties. In these instances, a random plasma glucose from venous blood is an alternative.

Should the diagnostic level of fasting glucose also be used to screen for diabetes?

This issue was investigated in detail in the Australian National NHMRC Evidence Based Guidelines for Type 2 Diabetes 2002. A fasting plasma glucose cut-off of 5.5 mmol/L best defined the upper limit of normality, and values above this indicated that further diagnostic testing was required (an oral GTT). Applying the guideline-recommended protocol of measuring fasting plasma glucose in people with risk factors to the general Australian population would result in 77% of people with diabetes being identified (with a specificity of 83%) but 25% of those tested would also require an oral GTT.[24] This has been adopted in the CARPA protocol.

Random blood glucose for screening diabetes

The SANDS study questioned the value of a random blood glucose as a screening tool and concluded that, if the cut-off was 7.5 mmol/L (meaning that at this level a diagnostic oral GTT was performed), the test would fail to diagnose 60% of those with undiagnosed diabetes. The investigators were able to justify the use of a random blood glucose cut-off of 5.5 mmol/L in screening for diabetes, confirming the diagnosis with an oral GTT.[27] This has been adopted in the CARPA protocol acknowledging that it will often need to be followed up with diagnostic tests. With very high prevealence rates, many people will be diagnosed (>11.1, later confirmed)

by random BGL testing and it is very important to make the screening process easy to implement.

Finger-prick blood glucose useful as a screening test

Capillary glucose levels may be slightly different to venous blood levels.[8] Blood glucose meters are frequently unreliable and very few evidence-based guidelines recommend their use for screening. The Australian National NHMRC Evidence Based Guidelines for Type 2 Diabetes 2002 clearly recommended that blood glucose meters not be used to screen for diabetes. However, although a venous sample is preferred, CARPA realises that there can be an advantage of having instant feedback, and the option of using a glucometer may increase the amount of screening that is performed. [Editor: Our experience is that a major barrier to Adult Health Checks is its uptake and promotion by primary health care staff during their clinical work, despite theoretical support.] If other blood tests are being done, for example as part of an Adult Health Check, then the glucometer should not be used.

A lower (5 mmol) throshold for triggering further diagnostic testing is recommended to allow for a 10% inaccuracy in the glucometer reading. Similarly, a high reading of 12 mmol is recomended as being likely to indicate diabetes, all results in between need follow up.

Case management

Relationship with the health service

As emphasised in the tips for managing chronic disease and in the diabetes protocol, a trusting relationship between the health professionals and the patient is very important. This is primarily based on our (CARPA) experience, but also supported by research into compliance issues.

Lifestyle changes

Weight loss

Weight loss in obese patients with diabetes can improve glycaemic control and reduce the need for oral hypoglycaemics or insulin. Weight reduction can also reduce blood pressure in obese hypertensive subjects and can improve hyperlipidaemia.

In one meta-analysis investigating the effect of weight loss in those with diabetes, dietary strategies alone had the greatest effect on glycated haemoglobin levels (a 2.7% reduction). A combination of diet plus behavioural therapy plus exercise also had a strong effect on reducing glycated haemoglobin, even though only a small degree of weight loss was achieved.[28] Recognition that improved glycaemic control can occur in the absence of achieving a target weight is important in relation to compliance issues, health promotion and evaluation of programs.

For the general population calorie restriction diets and appetite suppressant drugs have good short-term effects, but most of this weight is regained a few months after treatment.[29] A recent systematic review concluded that fat-restricted diets are no better than calorie-restricted diets in achieving long-term weight loss in overweight or obese people (general population).[30] Others have concluded that a combination of advice on diet and physical activity, supported by behaviour therapy, is more effective than diet or physical activity alone. Strategies that involve family support, personal contact with therapist, mutliple inteventions and walking programs appeared most effective.[31]

[Editor: As a person increases their exercise, body fat will decrease but the net effect on weight or BMI may be less than expected because of increased muscle mass.]

Diet

A diet high in fibre can lower total cholesterol by 10% in those with type 2 diabetes[32] and can improve glycaemic control if ingested in large quantities, but may be unacceptable.[33]

A diet high in monounsaturated fat and low in carbohydrate can produce a more desirable plasma glucose, lipid and insulin profile in the short term.[34,35,36] Modifying the frequency of meals and reducing their size so that there is 'nibbling versus gorging' may alter carbohydrate absorption, resulting in better glycaemic control.[37]

The avoidance of sugar in the diabetes diet has been aggressively promoted in the past. However, simple sugars like sucrose (common sugar) and fructose (fruit sugar) do not need to be avoided as they have not been shown to adversely affect the blood glucose level any differently from complex carbohydrates[33], nor do they affect the lipid profile.[32] There is no reason to recommend that people with diabetes avoid naturally occurring fructose in fruits, vegetables, and other foods.

The health promotion of appropriate diet and physical activity in several Aboriginal communities in Central Australia was associated with reduced rates of glucose intolerance over a seven-year intervening period.[38] In the Kimberley, involvement in diet and/or exercise strategies was associated with protection from increases in plasma glucose.[39]

Activity

In patients with type 2 diabetes exercise may improve glycaemic control, hypertension and total serum cholesterol levels. A meta-analysis of randomised controlled trials demonstrated that exercise in those with type 2 diabetes can reduce glycated haemoglobin from a weighted mean of 8.31% to 7.65% (over a mean period of 18 weeks) without any significant change in BMI (mean weight 83 kg), compared with control groups with no exercise.[40] The physical activity to achieve this outcome was three 45-minute moderate-intensity aerobic workouts per week (similar to goals specified in Australian guidelines).[41]

A community-based exercise program for a Native American population with type 2 diabetes was able to demonstrate reduced weight and improved metabolic control after 37 weeks of exercise for approximately two hours per week.[103]

Smoking

Smoking is a potent risk factor for vascular disease, and it is particularly important for those at high risk of cardi-vascular disease, such as those with diabetes, to be encouraged to quit. See the chapter on tobacco and smoking for more detail.

Alcohol

People with diabetes should avoid more than about 20 g/day (two standard drinks). Alcohol consumed in large amounts provides a heavy caloric load, encourages obesity, adds to psychological stress, damages the liver and pancreas and raises blood pressure and lipids — all factors which complicate management. Alcohol can cause severe and life-threatening hypoglycaemic episodes, particularly among diabetics on insulin or long-

acting sulphonylureas, and can significantly complicate infections such as pneumonia.

Glycaemic control

Glycaemic control in type 2 diabetes can prevent microvascular disease (small vessel damage seen in the retina and kidneys) and macrovascular events (damage to large conduit vessels such as coronary, cerebrovascular and peripheral vessels) in obese patients.

In those with type 2 diabetes, a six-year Japanese study — which compared intensive insulin therapy with conventional insulin therapy — demonstrated a beneficial effect in preventing macrovascular disease in the intensively treated group. This was noted despite no change in lipid profiles and hypertension status between the type 2 diabetes groups, and no difference in weight from baseline after six years. The average BMI (BMI = 21) of the participants was, however, much less than usually seen in patients with type 2 diabetes, and no blinding was reported.[42]

This study also demonstrated that intensive insulin therapy (three or more daily injections) in patients with type 2 diabetes significantly prevented microvascular complications to a greater degree than conventional insulin therapy (one or two daily injections of intermediate insulin).

The UK Prospective Diabetes Study (UKPDS) reported 10 years of follow-up in those with type 2 diabetes, but did not demonstrate reduced diabetes-related deaths, stroke, amputation, death from peripheral vascular disease, or all-cause mortality from intensive insulin nor oral hypoglycaemic treatment (sulphonylureas) when compared with conventional dietary therapy. The median HbA1c values over 10 years were significantly lower in the intensive than in the conventional group (7.0% compared with 7.9%). This degree of glycaemic control appeared to make no difference in influencing the absolute risk for fatal myocardial infarction, heart failure, or angina. The aggregate absolute risk for myocardial infarction (fatal and non-fatal infarction as well as sudden death) was of borderline significance in favour of intensive glycaemic control. Consequently, the UKPDS did not support the theoretical risk that exogenous insulin adversely affected cardiovascular status.[43]

The situation was quite different and unexpected in overweight type 2 diabetes clients (median baseline BMI = 32) treated with metformin in the UKPDS. These patients were treated so that fasting blood glucose remained below 6.0 mmol/L, and were kept on monotherapy until marked hyperglycaemia occurred. Intensive blood glucose lowering lead to significantly reduced macrovascular events. There was a 36% lower risk of all-cause mortality, and 39% lower risk of myocardial infarction. The reduction for aggregate macrovascular disease (stroke, peripheral vascular disease, infarction, and sudden death) was 30% greater in the metformin group over 10 years than conventional treatment. Metformin lead to significantly less weight gain than sulphonylurea or insulin therapy while achieving the same degree of glycaemic control.[44]

The UKPDS demonstrated that intensive glycaemic control in those with type 2 diabetes, either through insulin or sulphonylureas, can significantly decrease the risk of aggregated microvascular complications (in mildly obese or non-obese clients with type 2 diabetes with median baseline BMI = 27) when compared with conventional treatment such as regular dietary advice. The absolute risk reduction was 2.8 events prevented per 100 patients over 10 years. This means that 36 clients with

type 2 diabetes need to be intensively treated in order to prevent one microvascular event over 10 years, when compared with dietary treatment alone. However, most of the benefit was due to reduced retinal complications. The progression of retinopathy after 12 years was reduced by 21%. The need for retinal photocoagulation was also significantly reduced when compared with diet therapy. However, reno-protection from improved glycaemic control in type 2 diabetes was not confidently demonstrated. Whilst intensive treatment with sulphonylurea therapy or insulin lead to a 67% risk reduction in the proportion of patients who had a two-fold increase in plasma creatinine, the result was not significantly different from progression in the diet-treated group over 10 years. The progression of microalbuminuria and overt proteinuria varied between the groups but differences remained insignificant after 15 years. The progression to renal failure was reduced but the difference between the treatment groups was also insignificant. Intensive therapy was also less protective for other microvascular endpoints such as differences in ankle reflexes, or autonomic markers.[43]

There is a special case for insulin treatment in those who have recently had a myocardial infarct. In the DIGAMI study, intensive insulin therapy started within 24 hours of infarct (mean age 68 years) and continued thereafter; this significantly reduced mortality over 3.4 years compared with conventional therapy. The absolute reduction in mortality was 11%, implying one saved life for nine patients treated for 3.4 years.[45]

Oral hypoglycaemic drugs

The timing for the introduction of oral hypoglycaemic drugs has to be negotiated with the person with diabetes and should be influenced by the severity of their diabetes (e.g. fasting BGL) and the presence of symptoms or complications.

In patients with type 2 diabetes, metformin is the drug of choice,[46,47] Metformin produces a reduction in fasting (15–20%), post-prandial (45%) and glycated haemoglobin by 1.2%, which is similar to suphonylurea drugs.[46] Further, long-term therapy reduces plasma triglyceride concentrations by 10–20% and reductions in total cholesterol and LDL have been reported, independent of its glycaemic effect.[32,48] In comparison to sulphonylureas, metformin does not cause weight gain or increase insulin concentrations.[46,47] A systematic review also concluded no increased risk of lactic acidosis from metformin.[49]

Alpha-glucosidase inhibitors such as Acarbose can be used as first-line therapy with diet and exercise, or in combination with sulfonylureas to lower hemoglobin A1c concentrations an additional 0.5–0.9%.[50] These agents inhibit polysaccharide digestion and therefore glucose absorption, which decreases post-prandial hyperglycaemia. They have only modest anti-diabetic action and hence a limited role.

The thiazolidinediones are a new class of oral agents that decrease insulin resistance. Troglitazone belongs to this class, but was withdrawn in the US in March 2000 due to associated liver injury. Newer agents have been approved in Australia (rosiglitazone and pioglitazone) for mono or combined therapy with metformin or sulphonylurea. These agents lower hemoglobin A1c concentrations an additional 0.6–0.8% compared with baseline, alone, in combination or with insulin. There is no evidence to indicate they are better than other drugs.

Patients should not be started on the glitazones if there is any history of underlying chronic liver disease, e.g. cirrhosis, and probably chronic

hepatitis. Treatment should be avoided if the ALT is more than 2–3 x upper limit of normal [Editor: Which is tricky as many of our patients have fatty liver with mild elevations in ALT which will actually improve on any BG lowering treatment]. It is recommended to check LFTs at four weeks, then three monthly and, if the ALT becomes more than three times the upper limit of normal, treatment should be ceased. Prescribing requires monitoring alanine amino transferase (ALT) e.g. two-monthly testing in the first 12 months of therapy.[51]

Most patients with type 2 diabetes over time will require multiple oral hypoglycaemic therapy for glycaemic control.[52]

Insulin (in type 2 diabetes)

Those with type 2 diabetes can become insulin-deficient over time because of the progressive decline in pancreatic beta-cell function and will require insulin therapy to achieve optimal glycaemic goals.[53] The UKPDS Group reported that, over six years, 53% of type 2 diabetics treated with sulphonylureas required additional insulin therapy to reach glycaemic goals (fasting plasma glucose <6 mmol/l).[54]

When insulin is used in those with type 2 diabetes very high doses are often required, and consequent increased weight gain can be a problem.[55]

The use of insulin in poorly controlled type 2 diabetes patients is controversial and there appears to be no consensus on the optimal commencement time. The decision can be based on when poorly controlled type 2 diabetes becomes symptomatic, or oral therapy fails to achieve target glycaemic control. If there is persistant ketonuria, this strongly suggests a need for exogenous insulin. [Editor: However, because insulin use requires an additional level of patient education and motivation, it is crucial to involve the patient, and possibly their carers, in the decisions about using insulin. This may take more than one attempt.]

The main aim of introducing insulin therapy in patients with type 2 diabetes is to optimise glycaemic control in order to prevent microvascular diabetic complications and to relieve the symptoms of poorly controlled hyperglycaemia. The protective effect of insulin was no different from that achieved with oral sulphonyureas in the 10-year UKPDS, although the rate of a major hypoglycaemic event every year was almost twice as high (2% per year) when using insulin. Due to the risk of complications, significant co-morbidity (e.g. cerebrovascular disease, ESRF, cardiac failure) should be considered a possible contraindication to tight control in type 2 diabetes. [Editor: Seek specialist advice re risks and benefits.]

Three meta-analyses have confirmed that combined insulin and oral hypoglycaemic (sulphonylurea) therapy in type 2 diabetes results in lower insulin doses than insulin alone to achieve similar glycaemic control.[56,57,58] In addition, combined therapy improved glycaemic control in type 2 diabetes patients without a significant change in body weight. Reductions in glycated haemoglobin of 1.0–1.5% with lower insulin doses were seen in the combined insulin groups.

Common combinations include sulphonylureas plus evening or bedtime intermediate or long-acting insulin. The combination of sulphonylurea plus metformin plus insulin has been used infrequently, and is therefore less well studied. [Editor: The UKPDS data compares early introduction of insulin with standard non-insulin–based management. This is a different issue to the use of insulin in ‘failed’ oral Tx. A common problem seen in clinical practice is; what is the best strategy when diet and oral drugs have failed? There are only a few options (can be combined):

- Check and reinforce compliance with diet, exercise and oral drugs
- Switch to or add insulin (which will improve glycaemic control, which is a beneficial thing)
- Leave glycaemic control and focus on other CV risk factors to decrease overall risk

One of the major changes in the fourth edition of the CARPA STM is the promotion of nocturnal insulin in this situation.]

Monitoring glycaemic control

Glycated haemoglobin measurement is the accepted gold standard for monitoring glycaemic control. Australian guidelines recommend that HbA1c be measured every three–six months for insulin-treated patients and every six–12 months for patients with type 2 diabetes who are not on insulin.[59]

Glycated haemoglobin (expressed as %HbA1c) is measured from red blood cells and, because cell turnover occurs every three months or so, there is little value in performing the test at intervals less than three months.[60]

The optimal glycaemic goal is a HbA1c <7%, although the lower the glycaemic threshold, the lower the risk of complications. This may be unrealistic for some people and less stringent treatment goals may be appropriate for patients with limited life expectancies, in the very young or older adults, and in individuals with comorbid conditions.[61] [Editor: A goal of HbA1c <7% will not be achievable for many people, and could lead to a further sense of failure for staff and patients. In the protocol we stress that any decrease is in HbA1c is beneficial and suggest 8% as a more realistic target.]

An evaluation of a point-of-care glycated haemoglobin testing program (DCA 2000) in 42 ACCHSs, in which 2315 Aboriginal people with diabetes were monitored, showed that point-of-care HbA1c testing served as a catalyst to enhance patient self-management, was acceptable to Aboriginal health workers, produced acceptable results, and led to more opportunistic testing.[62,63] [A] Medicare rebate to cover the cost of cartridges was introduced in 2000 (item No 73840, $14.15 per tests, 4 x per year).

Self-monitoring of glucose

Self-monitoring is useful for adjusting insulin requirements. For those not needing insulin it is unlikely to be useful unless it leads to changes in lifestyle, treatment, motivation or sense of control.

A meta-analysis of trials of self-monitoring of BGL in type 2 diabetes did not provide evidence for reduction of glycated haemoglobin, nor was there any effect on body-weight.[64] Most of the trials involved clients who were not on insulin. However, there have been some more recent studies that suggest a small improvement in HbA1c might be attributable to self-monitoring in type 2 diabetes.[65]

The benefits for patients with type 2 diabetes in relation to quality of life remain to be proven. No matter how hard some patients try to achieve glycaemic control, their blood glucose values continue to fluctuate in an alarming way. This can lead to despair and learned helplessness.[66]

Self-testing for glycouria is unpredictable in relation to glycaemia.

Blood pressure and renal disease

Treatment for hypertension

Hypertension is very common in those with diabetes, thought to be twice that in those without diabetes. Hypertension in patients with diabetes is associated with accelerated progression of both microvascular (retinopathy and nephropathy) and macrovascular (CHD, stroke, peripheral vascular disease) complications.[67] The AusDiab study showed that there is nearly one untreated and possibly undiagnosed Australian with hypertension for every person on treatment.[4]

Lowering blood pressure in those with diabetes is effective at reducing both macrovascular and microvascular events. Weight loss (even small reductions such as 3–9% of body weight), increase in physical activity[68], and reduction of sodium intake[69] have been shown to improve blood pressure control.[70] A reduction in alcohol consumption from more than two standard drinks per day reduces blood pressure of both hypertensive and normotensive people according to two systematic reviews.[70,71] (Most of the hypertension studies have been conducted in the general population without diabetes.) Non-pharmacological measures should be encouraged as first-line therapy.

Treatment of hypertension in those with diabetes (with or without pre-existing heart disease) is effective at reducing cardiovascular morbidity (AMI, stroke) and cardiac death.[72] This was shown in several systematic reviews.[73,74,75]

In the UK Prospective Diabetes Study (UKPDS) study, lowering the mean BP to 144/82 mmHg (‘tight blood pressure control’ compared with less tight control of 154/87 mmHg) achieved significant reductions (44%) in fatal and non-fatal stroke compared with less tight BP control over nine years. The 21% reduction in risk for myocardial infarction was not statistically significant, but when all macrovascular diseases were combined — including myocardial infarction, sudden death, stroke, and peripheral vascular disease — the group assigned to tight blood pressure control had a statistically significant (34%) reduction in risk compared with the group assigned to less tight control.[76] Combination therapy with more than one agent was required in one third of those with type 2 diabetes in the UKPDS group assigned to tight BP control.

Treatment of hypertension in the UKPDS also significantly prevented microvascular complications in those with type 2 diabetes by 36%. This was mainly due to a significant reduction in the risk of requiring retinal photocoagulation over a median 7.5 years of treatment. Six clients with type 2 diabetes need to have their blood pressure intensively controlled over 7.5 years, in order to prevent a two-step retinopathy progression in one of them. The magnitude of this benefit appears greater than that achievable through intensive glycaemic control. The deterioration of visual acuity can also be prevented suggesting the prevention of diabetic maculopathy. Renal complications could not be prevented by tight BP control.[76]

The tighter the control of BP in those with type 2 diabetes, the greater the reduction in cardiovascular events.[72] The HOT study demonstrated that in patients with diabetes a lower diastolic blood pressure (<80 mmHg) led to a 51% reduction in major cardiovascular events (fatal and non-fatal myocardial infarction and strokes and all other cardiovascular deaths) over 3.8 years, compared with a diastolic blood pressure of <90 mmHg.[77]

The HOPE Study (3577 with diabetes, of whom 98% were type 2, mean age 65 years, mean BMI 28.5, mean baseline BP 142/80 mmHg) was largely a primary prevention trial for those with diabetes. It compared the use of ramipril

with placebo and found the risk of the aggregate of cardiovascular death, myocardial infarction, or stroke was significantly reduced by 25% over 4.5 years. There was also a significant relative risk reduction in total mortality (24%), myocardial infarction (22%) and stroke (33%).[78]

The MICRO-HOPE substudy assessed the effect of ramipril in those with diabetes, plus at least one other cardiovascular risk factor (total cholesterol >5·2 mmol/L, HDL cholesterol <0·9 mmol/L, hypertension, known microalbuminuria, or current smoking). Subjects had no overt proteinuria when therapy commenced. Ramipril significantly reduced the risk of overt nephropathy by 24%, and combined overt nephropathy, laser therapy or dialysis by 16% over 4.5 years, when the baseline blood pressure on average was 142/80 mmHg.[78]

Other studies have shown that the progression of microalbuminuria to persistent proteinuria can be reduced by ACEI or Angiotensin Receptor Blockers (ARB) in both hypertensive and normotensive patients with type 1 diabetes and in hypertensive type 2 diabetics[79,80] With ACEI, the risk of a doubling of the serum creatinine was reduced by half over a median follow-up of three years, as was the combined risk of death, dialysis or transplantation in type 1 diabetics. A systematic review of trials also confirmed that ACEI can arrest or reduce the albumin excretion rate in microalbuminuric normotensive diabetics, as well as reduce or prevent an increase in blood pressure in both type 1 and type 2 diabetics.[81]

Overall, the control of hypertension reduces microvascular complications in those with type 2 diabetes more than glycaemic control does.[82] The number of patients with type 2 diabetes who need to be treated over 10 years to prevent one patient developing any complication was 6.1 (95% CI interval 2.6 to 9.5) and to prevent death from a cause related to diabetes 15.0 (12.1 to 17.9).[76] No studies have as yet shown a reduction in end stage renal failure (ESRF) incidence or mortality from renal failure, due to hypertension treatment in patients with type 2 diabetes.

Target blood pressure

The American Diabetes Association recommend a target blood pressure goal of <130/80 mmHg if it can be safely achieved. There is no threshold value for blood pressure, and risk continues to decrease well into the ‘normal’ range. Behavioural and lifestyle therapy is warranted for the first three months if BP is between 130–140 mmHg systolic or 80–90 diastolic, before commencing antihypertensives, and those with BP >140/90 should be commenced at the same time as lifestyle advice.[67]Australian Guidelines recommend a target <130/85 mmHg.[83]

Blood pressure should be measured at least annually in those with diabetes. However, most health care providers will measure blood pressure more frequently than this. Several evidence-based guidelines suggest measuring blood pressure at every clinic visit in patients with diabetes.[83,67]

Choice of medication

There is evidence that ACE inhibitors have renal protective effects, as demonstrated by their ability to reduce proteinuria and prevent renal deterioration more effectively than other classes of anti-hypertensive agents in diabetic patients. They do not adversely affect glucose control, they favourably affect lipids and they reduce left ventricular hypertrophy.

The Australian Diabetes Society recommends that ACE inhibitors are the drug of choice in diabetic patients with microalbuminuria (with or without

hypertension) or overt nephropathy, while beta-blockers or calcium channel blockers were recommended for diabetic patients without nephropathy but with angina. The NT Coordinated Care Trial hypertension guidelines have concluded that the favourable lipid profile associated with ACEI use and the higher absolute cardiovascular risk in Aboriginal populations support the first-line use of ACEI regardless of diabetes. Since the introduction of ARB's the American Diabetes Association recommend either ACEI or ARB in hypertensive patients with microalbuminuria or clinical albuminuria/ nephropathy.[67]

Ischaemic heart disease

Aspirin prophylaxis

There is good evidence that aspirin can prevent adverse vascular outcomes in those with diabetes. Aspirin is protective in those with diabetes who do not have heart disease (primary prevention) and in those with pre-existing heart disease (secondary prevention). Twenty-six poeple with diabetes needed to be treated with aspirin (75–325 mg/day) over a median of two years to prevent against a 'vascular event' (non-fatal myocardial infarctions, non-fatal strokes, or vascular deaths)[84]

Three primary prevention trials — including the Physicians Health Study,[85] the Early Treatment Diabetic Retinopathy Study (ETDRS)[86] and the Hypertension Optimal Treatment (HOT)[87] trial — all reported that aspirin reduced the risk for acute myocardial infarction in those with diabetes, and to a similar degree to those without diabetes.

A collaborative overview of 145 trials reported secondary prevention against cardiovascular disease and death from aspirin in subgroups with diabetes. Diabetic subjects had risk reductions that were comparable to non-diabetic individuals.[88]

The American Diabetes Association guidelines recommend aspirin therapy for all patients with diabetes.[89] Contraindications include aspirin allergy, bleeding tendency, anticoagulant therapy, recent gastrointestinal bleeding and clinically active hepatic disease. Australian guidelines also recommend aspirin (75–325 mg/day) for people with type 2 diabetes.[90]

Lipids

(Also see the separate chapter on lipids.)

Lipid abnormalities — such as elevated low-density lipoprotein (LDL) cholesterol, and reduced high-density lipoprotein (HDL) cholesterol — increase the risk of cardiovascular disease in those with or without diabetes.[90] Hypertriglycerideamia is more common in those with diabetes or IGT, and is an independent risk factor for cardiovascular disease. Alcohol intake (even modest quantities) can exacerbate hypertriglycerideamia.

Lipid-lowering agents can reduce the risk of cardiovascular disease in those with diabetes. Reduced risk has been shown in those without pre-existing heart disease (primary prevention) and in those with previous acute myocardial infarction (AMI) or angina (secondary prevention).[84]

Several studies have confirmed that lipid-lowering drugs protect against CV events in those with diabetes who had previous AMI or angina. The Scandinavian Simvastatin Survival Study, or '4S', showed that the relative risk reduction of a major cardiovascular event was of equal magnitude to that observed in non-diabetic patients (55%, 95% CI 24–73%) over a median of 5.4 years.[91] The LIPID study reduced cardiovascular events in diabetics over 6.1 years by 16%, but this was not statistically significant. The

Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT), led to a 24% decrease in cardiovascular events in diabetic subjects with prior cardiovascular disease over 5.1 years.[92]

Weight loss has been associated with improvements in triglyceride levels, a reduction in total and LDL cholesterol and increases in HDL cholesterol.[93] There have also been reports of a beneficial effect of exercise on the lipid profile.[32,94] Because physical activity is recommended and shown to be of benefit in weight loss, it is recommended for all patients with diabetes.[41]

Dyslipidaemia will improve with a low saturated fat diet replacing saturated fats with carbohydrate and monounsaturated fats.[93] This will also reduce the risk of coronary heart disease.[94]

Australian guidelines recommend those with diabetes have annual assessment of serum lipid levels to assess cardiovascular risk. Lipid-lowering therapy should be initiated immediately in those with existing coronary heart disease and a total cholesterol >4 mmol/L. In all those with diabetes, lipid-lowering therapy should be implemented if dietary advice is ineffective in reducing total cholesterol to target levels after six weeks (and total cholesterol is >6.5 mmol/L). A total cholesterol <4 mmol/L (LDL cholesterol <2.5 mmol/L) is the recommended target. Almost all guidelines recommend screening using fasting serum specimens for determination of HDL cholesterol and triglyceride levels in those with diabetes (even though TGs are only affected by non-fasting).[32] When the patient is on drug therapy, lipid profiles should be repeated every two months to assess progress until stable and satisfactory. Choice of therapy is detailed in the Australian Lipid Management Guidelines,[94] Australian cardiovascular drug guidelines[95] and NHMRC Diabetes Guidelines.[32]

[Editor: Note that the lipid protocol in the CARPA STM regards diabetics as being in the highest risk group, along with those who have had a myocardial infarct. This is outside the scope of many current guideline recommendations. We believe the combination of: the high incidence of ischaemic heart disease, the high-risk state of most Aboriginal patients with diabetes (by virtue of other components of the metabolic syndrome and the efficacy of lipid treatment as primary prevention of ischaemic heart disease), make earlier and more aggressive use of lipid-lowering medication warranted.]

Diabetic retinopathy

Diabetic retinopathy is a specific microvascular complication of diabetes characterised by microaneurysms, haemorrhages and other abnormalities in the retina leading to bleeding and new vessel formation in the eye and, ultimately, blindness. The associated macular oedema occurs from the increased permeability of retinal vessels. The early changes can only be detected by eye examination. The case for regular screening and treatment of diabetic retinopathy is well described in the OATSIH Specialist Eye Health Guidelines.[96]

There is little data on the prevalence of diabetic retinopathy in Aboriginal populations. However, based on unpublished studies from around Australia, the crude prevalence of diabetic retinopathy in those with diabetes did not differ between Aboriginal and non-Aboriginal populations (8–35%).[97] It is uncertain what proportion of blindness in the Aboriginal population is due to diabetes, though we would now expect it to overtake trachoma as the leading cause.

Only good glycaemic and blood pressure control and laser photocoagulation treatment are known to prevent and slow the progression of diabetic retinopathy. Timely laser therapy reduces the rate of vision loss by 80–90% among patients with proliferative retinopathy over two years and this underlies the rationale for regular screenign for diabetic retinopathy.[96]

Given that around 20% of those with type 2 diabetes have retinopathy at the time of diagnosis, screening for retinopathy should be started at the time of diagnosis. The rate of progression of early retinopathy to high-risk stage is thought to be only about 1% per year.[96] However, we recommend that in the Aboriginal and Torres Strait Islander population retinal and eye examinations should be conducted every year, as some will be missed in some years and other eye conditions will be detected as long as visual acuity is measured as part of the screening (especially since those with poor glycaemic control or proteinuria are at greater risk of retinopathy progression). This is consistant with other reviews and guidelines.[96,98] Examinations will be required more frequently if retinopathy is progressing, and women with pre-existing diabetes who become pregnant should have close follow-up throughout pregnancy.[99]

Screening should include visual acuity with vision worse than 6/12 leading to referral.[96] Screening can be done by appropriately skilled clinicians, or better as part of an organised system of retinal photography. Non-mydriatic fundal photography has enabled retinal screening to take place without the need for on-site ophthalomologists. It requires the use of a specialised camera, and photographs can be taken through a dilated or non-dilated (non-mydriatic) pupil. An ophthalmologist in the referral centre can then assess photographs.

Indirect ophthalmoscopy is sensitive and specific enough but requires specialised experience and skill not usually found in primary health care settings. Screening for DR with a camera is generally more sensitive and specific than direct ophthalmoscopy.[100]

Retinal photography has the advantage of possible immediate patient feedback and the permanent record allows quality assurance and monitoring of progressive changes. A systematic review of DR screening techniques supports retinal photography with mydriasis as the preferred method.[101] It has been evaluated in remote Aboriginal community screening programs and found to be as good or better than indirect fundoscopy.[102] There are now a number of regions successfully using retinal cameras for DR screening in Australia.

A number of studies have concluded that screening people with diabetes for retinopathy is cost effective, especially compared to the cost of caring for people that would otherwise be blind.[103,104] The marginal gains in cost utility of annual over second or third yearly screening were modest in a US model, though annual screening was more cost-effective for populations who are at high risk for retinal complications (with poor glycaemic control).[105]

Infections

People with poorly controlled diabetes are prone to infections.[9] Infections increase insulin resistance and worsen diabetes control and should be considered in the differential diagnosis of a sudden deterioation in glycaemic control.

Infections in Aboriginal patients with diabetes are very common. The age-adjusted relative risk for hospital admission resulting from infection for Aboriginal patients with diabetes presenting to health services in Central Australia was nearly three times greater than for those who did not have diabetes. Infection was the most common reason for attendance at a health service. Infections accounted for 21% of deaths in Aboriginal patients with diabetes followed for seven years (late 1980s). Furthermore, deaths occurred at a young age, with a median of 55 years.[106] Infection with diabetic foot complications was the commonest cause for admission in Central Australia between 1992 and 1997.[107]

Those with diabetes should receive advice regarding the early presentation of soft tissue infections and symptomatic urinary tract infections. Pneumococcal and influenza vaccination is recommended for Aboriginal patients with diabetes regardless of age.

Feet

This is discussed in detail the following separate chapter.

References

1. De Courten M, Hodge A, Dowse G, King I, Vickery J, Zimmet P. Review of the epidemiology, aetiology, pathogenesis and preventability of diabetes in Aboriginal and Torres Strait Islander population. Canberra: International Diabetes Institute and Commonwealth Department of Health and Family Services, 1998.
2. Edwards RW, Madden R. The Health and Welfare of Australia's Aboriginal and Torres Strait Islander Peoples. AIHW. Cat No 4704.0. Canberra: ABS, 2001; 99–109.
3. Condon J & Dempsey K. NT mortality in the Northern Territory 1979–1997. Darwin: Territory Health Services Epidemiology Branch, 1999.
4. Dunstan D, Zimmet P, Welborn T, Sicree R, Armstrong T, Atkins R, Cameron A, Shaw J, Chadban S. Diabesity and Associated Disorders in Australia 2000. The Accelerating Epidemic! Final report of the Australian Diabetes, Obesity and Lifestyle Study. Melbourne: International Diabetes Institute, 2001.
5. Daniel M, Rowley KG, McDermott R, Mylvaganam A, O'Dea K. Diabetes incidence in an Australian aboriginal population. An 8-year follow-up study. Diabetes Care 1999 Dec; 22(12):1993–8
6. Phillips CB, Patel MS, Weeramanthri TS. High mortality from renal disease and infection in Aboriginal Central Australians with diabetes. Aust J Publ Health 1995; 19:482–6.
7. McCance DR, Hanson RL, Pettit DJ, Bennett PH, Hadden DR, Knowler WC. Diagnosing diabetes mellitus: do we need new criteria? Diabetologia 1997; 40:247–55.
8. World Health Organization. Definition, Diagnosis and Classification of Diabetes mellitus and its Complications. Report of a WHO Consultation, 1999.
9. WHO Study Group. Prevention of diabetes mellitus. Technical Report Series 844. WHO, Geneva, 1994; 26–7.
10. Diabetes Control and Complications Trial (DCCT) Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in IDDM. N Eng J Med 1993; 329:977–86.
11. Diabetes Australia Guideline Development Consortium. National Evidence-based Guidelines for the Management of Type 2 Diabetes Mellitus. Sydney: Australian Centre for Diabetes Strategies, Prince of Wales Hospital, 2000. Public Consultation Draft.
12. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Slaminen V, Uusitupa M. Prevention of Type 2 diabetes mellitus by changes in lifestyle among

subjects with impaired glucose tolerance. New England Journal of Medicine 2001; 344(18):1343–50.
13. Diabetes Prevention Program Research Group. Reduction in the incidence of Type 2 diabetes with lifestyle intervention or metformin. New England Journal of Medicine 2002; 346(6):393–403.
14. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing Type 2 diabetes in people with IGT: the Da Qing IGT and diabetes study. Diabetes Care 1997; 20:4:537–44
15. Rowley KG, Best JD, McDermott R, Green EA, Piers LS, O'Dea K. Insulin resistance syndrome in Australian Aboriginal people. Clin Exp Pharmacol Physiol 1997 Sep–Oct; 24(9–10):776–81.
16. O'Dea K. Westernisation, insulin resistance and diabetes in Australian Aborigines. Med J Aust 1991; 4:155:258–64.
17. Salmeron J, Ascherio A, Rimm EB, Colditz GA, et al. Dietary fibre, glycaemic load and risk of NIDDM in men. Diabetes Care. 1997; 20:545–50.
18. Wolever TM, Hamad S, Gittelsohn J, Gao J, Hanley AJ, Harris SB, Zinman B. Low dietary fiber and high protein intakes associated with newly diagnosed diabetes in a remote Aboriginal community. Am J Clin Nutr 1997; 66:6:1470–4.
19. Buyken AE, Toeller M, Heitkamp G, Vitelli F, Stehle P, Scherbaum WA, Fuller JH. Relation of fibre intake to HbA1C and the prevalence of severe ketoacidosis and severe hypoglycaemia. EURODIAB IDDM Complications Study Group. Diabetologia 1998; 41:8:882–90.
20. Williams DE, Wareham NJ, Cox BD, Byrne CD, Hales CN, Day NE. Frequent salad vegetable consumption is associated with a reduction in the risk of diabetes mellitus. J Clin Epidemiol 1999 Apr; 52(4):329–35
21. Lynch J, Helmrich SP, Lakka TA, Kaplan GA, Cohen RD, Salonen R, Saloanen JT. Moderately intense physical activities and high levels of cardiorespiratory fitness reduce the risk of Type 2 diabetes in middle aged men. Arch Intern Med 1996; 156:12:1307–14.
22. Hales CN, Barker DJ, Clark PM, Cox LJ, Fall C, Osmond C, Winter PD. Fetal and infant growth and IGT at age 64. BMJ 1991; 303:1019–22.
23. CDC Diabetes Cost-Effectiveness Study Group. The cost-effectiveness of screening for type 2 diabetes. CDC Diabetes Cost-Effectiveness Study Group, Centers for Disease Control and Prevention. JAMA 1998 Nov 25; 280(20):1757–63
24. Colagiuri S, Zimmet P, Hepburn A, Colagiuri R. Evidence Based Guidelines for Type 2 Diabetes: Case Detection and Diagnosis. Canberra: Diabetes Australia & NHMRC, 2002.
25. VACCHO WPHC, Apunipima WPHC, North Qld WPHC, NT Coordinated Care Trials, Kimberley Aboriginal Medical Services, etc.
26. Welborn TA. Diabetes and IGT: using the new criteria [editorial]. Med J Aust 1993; 158:8:516–17.
27. Welborn TA, Reid CM, Marriott G. Australian Diabetes Screening Study: impaired glucose tolerance and non-insulin-dependent diabetes mellitus. Metabolism 1997 Dec; 46(12 Suppl1):35–9
28. Brown SA, Upchurch S, Anding R, Winer M, Ramirez G. Promoting weight loss in type II diabetes. Diabetes Care 1996; 19:6:613–24.
29. Glanville J, Glenny AM, O'Meara S, Melville A, Sharp F, Sheldon T, Wilson C. The prevention and treatment of obesity. Effective Health Care Bulletin April 1997; 3:2. http://www.york.ac.uk/inst/crd/ehcb.htm [accessed 9 May 2002].
30. Pirozzo S, Summerbell C, Cameron C, Glasziou P. Advice on low-fat diets for obesity (Cochrane Review). In: The Cochrane Library. Issue 2. Oxford: Update Software, 2002.

31. Thorogood M, Hillsdon M, Summerbell C. Cardiovascular disorders: changing behaviour. Clinical Evidence Dec 2001; Issue 6. BMJ Publishing Group, London, 2001. http://www.clinicalevidence.org [Accessed 9th May 2002].
32. Lipids Expert Working Group. Evidence-based Guideline for management of Lipid Abnormalities in Type 2 Diabetes. Part 7. Consultation Draft. December 2001.
33. American Diabetes Association Evidence-Based Nutrition Principles and Recommendations for the Treatment and Prevention of Diabetes and Related Complications. Diabetes Care 2002; 25:S50–S60.
34. Garg A, Bonanome A, Grundy SM, Zhang Z, Unger RH. Comparison of a high carbohydrate with a high monounsaturated fat diet in patients with Type 2 diabetes. N Eng J Med 1988; 319:829–34.
35. Campbell LV, Marmot PE, Dyer JA, Borkman M, Stolien LH. The high monounsaturated fat diet as a practical alternative for Type 2 diabetes. Diabetes Care 1994; 17:177–82.
36. Lerman Garber I, Ichazo Cerro S, Zamora Gonzalez J, Cardosos Saldana G, Posada Romero C. Effect of a high monounsaturated fat diet enriched with avocado in Type 2 diabetes patients. Diabetes Care 1994; 17:311–15.
37. Jenkins DJ, Jenkins AL. Nutrition principles and diabetes: a role for ‘lente carbohydrate’? Diabetes Care 1995; 18:1491–8.
38. Rowley KG, Gault A, McDermott R, Knight S, McLeay T, O’Dea K. Reduced prevalence of Impaired Glucose Tolerance and no change in prevalence of diabetes despite increasing BMI among Aboriginal people from a group of remote homeland communities. Diabetes Care 2000; 23:7:898–904
39. Rowley KG, Daniel M, Skinner K, Skinner M, White GA, O’Dea K. Effectiveness of a community-directed ‘healthy lifestyle’ program in a remote Australian aboriginal community. Aust N Z J Public Health 2000 Apr; 24(2):136–44
40. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA 2001 Sep 12; 286(10):1218–27.
41. Bauman A, Bellew B, Vita P, Brown W, Owen N. Getting Australia Active. Towards better practice for the promotion of physical activity. National Public Health Partnership, Melbourne Australia, March 2002. http:// www.nphp.gov.au/sigpah [accessed 10 May 2002].
42. Ohkubo Y, Kishikawa H, et al. for the Kumamoto Study. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with Type 2 diabetes: a randomised prospective 6-year study. Diabetes Res Clin Pract 1995; 28:103–17.
43. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998; 352:837–53.
44. UKPDS. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998; 352:9131:854–65.
45. Malmberg K. Prospective randomised study of intensive insulin treatment on long-term survival after acute myocardial infarction in patients with diabetes mellitus. DIGAMI (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction) Study Group. BMJ 1997 May 24; 314(7093):1512–5.
46. Campbell IW, Howlett HCS. Worldwide experience of metformin as an effective glucose lowering agent: a meta-analysis. Diabetes-Metabolism Reviews 1995; 11(suppl1):S57–62. [Also: CRD: abstracts of quality assessed systematic reviews.]
47. Bailey C, Turner R. Metformin (review article). N Engl J Med 1996; 334:9:574–9.
48. DeFronzo RA, Goodman AM, and the Multicentre Metformin Study. Efficacy of metformin in patients with Type 2 diabetes. N Eng J Med 1995; 333:541–9.

49. Salpeter S, Greyber E, Pasternak G, Salpeter E. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus (Cochrane Review). In: The Cochrane Library. Issue 2. Oxford: Update Software, 2002.
50. Campbell LK, White JR, Campbell RK. Acarbose: its role in the treatment of diabetes mellitus. Annals of Pharmacotherapy 1996; 30(11):1255–62.
51. O'Moore-Sullivan TM, Prins JB. Thiazolidinediones and type 2 diabetes: new drugs for an old disease. MJA 2002; 176:381–6.
52. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. JAMA 1999 Jun 2; 281(21):2005–12.
53. Mudaliar S, Edelman SV. Insulin therapy in type 2 diabetes. Endocrinol Metab Clin North Am 2001 Dec; 30(4):935–82.
54. Wright A, Burden, FAC, Paisey RB, Cull CA, Holman RR, for the UK Prospective Diabetes Study Group. Sulfonylurea Inadequacy. Efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the UK Prospective Diabetes Study (UKPDS 57). Diabetes Care 2002; 25:2:330–6.
55. Henry RR. Glucose control and insulin resistance in Type 2 diabetes. Ann Intern Med 1996; 124:(1pt2):97–103.
56. Johnson JL, Wolf SL, Kabadi UM. Efficacy of insulin and sulfonylurea combination therapy in type II diabetes: a meta-analysis of the randomised placebo-controlled trials. Arch Intern Med 1996; 3:156:259–64291.
57. Pugh JA, Wagner ML, Sawyer J, Ramirez G, Tuley M, Friedberg SJ. Is combination sulfonylurea and insulin therapy useful in Type 2 diabetes patients? A meta-analysis. Diabetes Care 1992; 8 :15:953–9.
58. Peters AL, Davidson MB. Insulin plus a sulphonylurea agent for treating type 2 diabetes. Ann Intern Med 1991; 1:115:45–53. [Reviewed by American College of Physicians. ACP Journal Club 1991 Nov–Dec; 115:75.]
59. NSW Health. The principles of diabetes care and guidelines for the clinical management of diabetes mellitus in adults. Sydney: NSW Health Department,1996; 14.
60. Colman PG, Colagiuri S. Diagnosis and monitoring of diabetes mellitus. Common sense pathology. Unit 42. NSW: Royal College of Pathologists, February 1997.
61. American Diabetes Association Standards of Medical Care for Patients With Diabetes Mellitus Diabetes Care 2002; 25:S33–S49.
62. Brice G, Bellis-Smith N, Daley L. for the National Aboriginal Community Controlled Health Organisation. From 'major threat' to 'major opportunity'? Pilot project to assess the use of on-site Haemoglobin A1C testing for managing persons with diabetes (using the Bayer DCA 2000 analyser) in Australian Aboriginal Community Controlled Health Services: June 1999 to August 2000. Canberra: NACCHO, 2001.
63. Shephard M, Gill J. Results of a Quality Assurance Program for Monitoring On-site Haemoglobin A1c Testing in Aboriginal Community Controlled Health Services. Presentation at the 2002 National Indigenous Diabetes Conference, Cairns, May 2002. Community Point-of-Care Centre, Renal Unit Flinders Medical Centre and the RCPA Quality Assurance Programs Pty Ltd, Bedford Park SA 5042.
64. Coster S, Gulliford M C, Seed P T, Powrie J K, Swaminathan R. Self-monitoring in type 2 diabetes mellitus: a meta-analysis. Diabetic Medicine 2000; 17(11):755–61. See also full report: Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminathan R. Monitoring blood glucose control in diabetes mellitus: a systematic review. Health Technol Assess 2000; 4(12):i–iv, 1–93.
65. Karter AJ, Ackerson LM, Darbinian JA, D'Agostino RB Jr, Ferrara A, Liu J, Selby JV. Self-monitoring of blood glucose levels and glycemic control: the Northern California Kaiser Permanente Diabetes registry. Am J Med 2001 Jul; 111(1):1–9.
66. Gallichan M. Self-monitoring of glucose by people with diabetes: evidence-based practice. BMJ 1997; 313:964–7.316.

67. American Diabetes Association Treatment of Hypertension in Adults With Diabetes. Diabetes Care 2002; 25:S71–S73.
68. Halbert JA, Silagy CA, Finucane P, Withers RT, Hamdorf PA, Andrews GR. The effectiveness of exercise training in lowering blood pressure: a meta-analysis of randomised controlled trials of 4 weeks or longer. J Hum Hypertens 1997 Oct; 11(10):641–9.
69. Fodor JG, Whitmore B, Leenen F, Larochelle P. Lifestyle modifications to prevent and control hypertension. 5. Recommendations on dietary salt. Canadian Hypertension Society, Canadian Coalition for High Blood Pressure Prevention and Control, Laboratory Centre for Disease Control at Health Canada, Heart and Stroke Foundation of Canada. CMAJ 1999 May 4; 160(9 Suppl):S29–34.
70. Ebrahim S, Smith GD. Lowering blood pressure: a systematic review of sustained effects of non-pharmacological interventions. J Public Health Med 1998 Dec; 20(4):441–8.
71. Campbell NR, Ashley MJ, Carruthers SG, Lacourciere Y, McKay DW. Lifestyle modifications to prevent and control hypertension. 3. Recommendations on alcohol consumption. Canadian Hypertension Society, Canadian Coalition for High Blood Pressure Prevention and Control, Laboratory Centre for Disease Control at Health Canada, Heart and Stroke Foundation of Canada. CMAJ 1999 May 4; 160(9 Suppl):S13–20.
72. Sigal R, Malcolm J. Cardiovascular disease in diabetes. Clinical Evidence. Issue 6. London: BMJ Publishing Group, 2001.
73. Fuller J, Stevens LK, Chaturvedi N, Holloway JF. Antihypertensive therapy for preventing cardiovascular complications in people with diabetes mellitus (Cochrane Review). In: The Cochrane Library. Issue 2. Oxford: Update Software, 2002.
74. Lievre M, Gueyffier F, Ekbom T, Fagard R, Cutler J, Schron E, Marre M, Boissel JP.Efficacy of diuretics and beta-blockers in diabetic hypertensive patients. Results from a meta-analysis. The INDANA Steering Committee. Diabetes Care 2000 Apr; 23 Suppl 2:B65–71.
75. Grossman E, Messerli FH, Goldhourt U. High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal. Arch Int Med 2000; 160:2447–52.
76. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998 Sep 12; 317(7160):703–13.
77. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, for the HOT Study Group. Effects of intensive blood pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. Lancet 1998; 351:1755–62.
78. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Lancet 2000 Jan 22; 355(9200):253–9.
79. Lewis, EJ, Hunsicker, LJ, Clarke, WR, et al. Renoprotective effect of the angiotensis-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001; 345:851.
80. Brenner, BM, Cooper, ME, de Zeeuw, D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001; 345:861.
81. Lovell HG. Angiotensin converting enzyme inhibitors in normotensive diabetic patients with microalbuminuria (Cochrane Review). In: The Cochrane Library. Issue 2. Oxford: Update Software, 2002.
82. O’Connor PJ, Spann SJ, Woolf SH. Care of adults with type 2 diabetes mellitus. A review of the evidence. J Fam Pract 1998 Nov; 47(5 Suppl):S13–22.

83. Hypertension Expert Working Group. Evidence-based Guideline for the Diagnosis and Management of Hypertension in Type 2 Diabetes. January 2001. http://www.diabetesaustralia.com.au/submission-documents.htm [Accessed 19 June 2002]
84. Sigal R, Malcolm J. Cardiovascular disease in diabetes. Clinical Evidence. Issue 6. London; BMJ Publishing Group, 2001; 438.
85. Steering Committee of the Physicians Health Study Research group. Final report on the aspirin component of the ongoing Physicians Health Study. N Eng J Med 1989; 321:129–35.
86. Early Treatment Diabetic Retinopathy Study (ETDRS) Investigators. Aspirin effects on mortality and morbidity in patients with diabetes mellitus. Report 14. JAMA 1992; 268:10:1292–300.
87. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, Menard J, Rahn KH, Wedel H, Westerling S: Effects of intensive blood-pressure lowering and low dose aspirin on patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomized trial. Lancet 1998; 351:1755–62.
88. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy—I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ 1994 Jan 8; 308(6921):81–106.
89. American Diabetes Association. Position Statement: Aspirin Therapy in Diabetes. Diabetes Care 2002; 25:S78–S79.
90. Macrovascular Disease Expert Working Group. Evidence Based Guideline for the Prevention and Detection of Macrovascular Disease in Type 2 Diabetes. Consultation Draft, January 2001.
http://www.diabetesaustralia.com.au/submission-documents.htm [accessed 14 June 2002].
91. Pyorala K, Pederson TR, Kjekshus J, Faergman O, et al., for Scandinavian Simvastatin Survival Study Group. Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. Diabetes Care 1997; 20:4:614–20.
92. Rubins HB, Robins SJ, Collins D, Fye CL, Anderson JW, Elam MB, Faas FH, Linares E, Schaefer EJ, Schectman G, Wilt TJ, Wittes J: Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol: Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. N Engl J Med 1999; 341:410–18.
93. American Diabetes Association. Management of Dyslipidemia in Adults With Diabetes. Diabetes Care 2002; 25:S74–S77.
94. National Heart Foundation and Cardiac Society of Australia and New Zealand. Lipid Management Guidelines — 2001. MJA 2001; 175: Supplement: S57–S85.
95. Writing Group. Therapeutic Guidelines: Cardiovascular. 3rd Edition. Victoria: Therapeutic Guidelines Limited, 1999.
96. Specialoist Eye Health Guidelines for use in Aboriginal and Torres Strait Islander Populations, Cataract, Diabetic Retinopathy, Trachoma. Office of Aboriginal and Torres Strait Islander Health, Commonwealth of Australia, 2001.
97. Taylor HR. Eye health in Aboriginal and Torres Strait Islander communities. Report of a review commissioned by Commonwealth Minister for Health and Family Services, Hon. Dr Michael Wooldridge, MP. Commonwealth of Australia, 1997; 69–79.
98. Couzos S, Murray R, Metcalf S. In Aboriginal Primary Health Care: An evidence-based approach. Ed Couzos S, Murray R. Oxford University Press, 1999.
99. American Diabetes Association. Diabetic Retinopathy Diabetes Care 2002; 25:S90–S93.
100. Siu SC, Ko TC, Wong KW, Chan WN. Effectiveness of non-mydriatic retinal photography and direct ophthalmoscopy in detecting diabetic retinopathy. Hong Kong Med J 1998; 4:367–70.

101. Hutchinson, A, McIntosh, A, Peters, J, O'Keeffe, C, Khunti, K, Baker, R, Booth A. Effectiveness of screening and monitoring tests for diabetic retinopathy: a systematic review. Diabet Med 2000; 17:495–506.
102. Diamond, JP, McKinnon, M, Barry, C, Geary, D, McAllister, IL, House, P, Constable, IJ. Non-mydriatic fundus photography: A viable alternative to fundoscopy for identification of diabetic retinopathy in an Aboriginal Population in rural Western Australia. Australian and New Zealand Journal of Ophthalmology 1998; 26:109–15.
103. Javitt JC, Aiello LP. Cost-effectiveness of detecting and treating diabetic retinopathy. Annals of Internal Medicine 1996; 124:164–9.
104. Martin JD, Yidegiligne HM. The cost-effectiveness of a retinal photography screening program for preventing diabetic retinopathy in the First Nations diabetic population in British Columbia, Canada. Int J Circumpolar Health 1998; 57:S379–82.
105. Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. JAMA 2000 Feb 16; 283(7):889–96.
106. Phillips CB, Patel MS, Cabaron Y. Utilisation of health services by Aboriginal Australians with diabetes. Diabetes Res Clin Pract 1993; 3:20:231–9.
107. Ewald D, Patel M, Hall G, Hospital separations indicate increasing need for prevention of diabetic foot complications in Central Australia. Aust J Rural Health 2001; 9:275–9.
108. Heath G, Leonard B, Wilson R, Kendrick JS, Powell K. Community-based exercise intervention: Zuni diabetes project. Diabetes Care 1987; 10:5 579–83.