

Reducing risk in type 2 diabetes a practical approach

Fear of the complications of diabetes can hang like a shadow over the lives of people with this condition. Effective prevention and management of these complications requires sound knowledge not only of the specific complications themselves, but also of the risk factors for their development in an individual patient.

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Even before patients are diagnosed with diabetes they are at increased risk of morbidity and mortality from macrovascular disease (ischaemic heart disease, stroke and peripheral vascular disease). Prediabetic risk arises from the many atherosclerotic risk factors inherent in the metabolic syndrome. Once diabetic hyperglycaemia ensues, the patient acquires the additional risks of microvascular disease, including retinopathy, nephropathy and neuropathy (see the box on page 16). Because patients with hyperglycaemia are often asymptomatic for years, many have evidence of either microvascular or macrovascular complications at the time of diagnosis.

Importantly, the complications of diabetes do not develop in isolation. The effects of one complication may profoundly impact on others. For example, the insidious onset of worsening hypertension

as a consequence of diabetic nephropathy accelerates the progression of the underlying nephropathy as well as the macrovascular complications and diabetic retinopathy. Similarly, the development of peripheral neuropathy may be of relatively limited consequence until worsening peripheral vascular disease further compromises the capacity of the skin of the foot to recover from injury. This results in an amputation rate that is much higher than predicted from the severity of the individual complications themselves. Hence risk surveillance and management is especially important in patients known to have complications due to their diabetes. Strong evidence now supports rigorous targets for glycaemic control, blood pressure and lipid management (Table 1), particularly in patients at high risk of diabetes.¹⁻³

Added to the risks mentioned above are those

IN SUMMARY

- Even before patients are diagnosed with diabetes they are at increased risk of macrovascular disease.
- The complications of diabetes do not develop in isolation so the effects of one complication may profoundly impact on others.
- Attention to detail is essential to detect and manage effectively the risk factors and complications of diabetes.
- The ability to view the patient 'globally', directing attention to where treatment is most likely to be of benefit and least likely to cause harm, is the key to diabetes management.
- Multifactorial approaches to diabetes care appear to be the most effective.

derived from treatment complications, be they medication-related hypoglycaemia, drug side effects from the inevitable polypharmacy or risk of hospitalisation. During their management, patients with diabetes often experience numerous adverse psychosocial outcomes, such as depression, social stigmatisation, limited employment opportunities and economic disadvantage due to the high medication costs. These factors potentially worsen both medical outcomes and quality of life.

Golden rules of diabetes risk reduction

Here we briefly elucidate a series of practical tips, or 'golden rules', for reducing the risk and severity of complications in patients with type 2 diabetes. For a lighter perspective on diabetes management, we have included Newnham's own formulaic laws that outline some of the practicalities encountered when managing patients with diabetes (see the box on page 17).

Prevention of diabetes

- **Remember that prevention is better than cure.**

Diabetes confers an inherent risk for macrovascular disease that is independent of the standard coronary risk factors. The only way to prevent this risk is to stop the onset of diabetes itself. Advise first degree relatives of patients with type 2 diabetes about screening and risk minimisation. Such advice should also be provided to women with a history of polycystic ovary syndrome and/or gestational diabetes (conditions that are associated with an increased likelihood of developing diabetes) and to at-risk ethnic groups such as Aboriginal and Torres Strait Islanders, Indians and Asians.

- **Prescribe exercise at every visit as lifestyle interventions work.**

Exercise is a major therapeutic intervention for both prevention and management of patients with type 2 diabetes, particularly if accompanied by weight loss. Unlike most of the other treatments available, exercise can also improve wellbeing and reduce macrovascular risk. Regular exercise and weight loss of 5% were shown to reduce the development of diabetes by 58% in patients with impaired glucose tolerance.⁴ A standard 150 minutes of regular exercise per week typically reduced HbA_{1c} by 1 to

Risk reduction in type 2 diabetes

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Patients with hyperglycaemia are often asymptomatic for years, and thus many have evidence of either microvascular or macrovascular complications at the time of diagnosis of type 2 diabetes. In addition, the complications of diabetes do not develop in isolation, and the effects of one complication may profoundly impact on others. Risk surveillance and management is especially important in patients who are known to have diabetic complications.

1.5% in patients with type 2 diabetes.⁵

- **Don't miss the secondary causes of diabetes.**

Failure to diagnose underlying Cushing's syndrome, acromegaly, haemochromatosis or pancreatic disease in patients can result in poor outcomes and a lost opportunity for diabetes prevention in these patients.

Macrovascular disease in patients with diabetes⁶

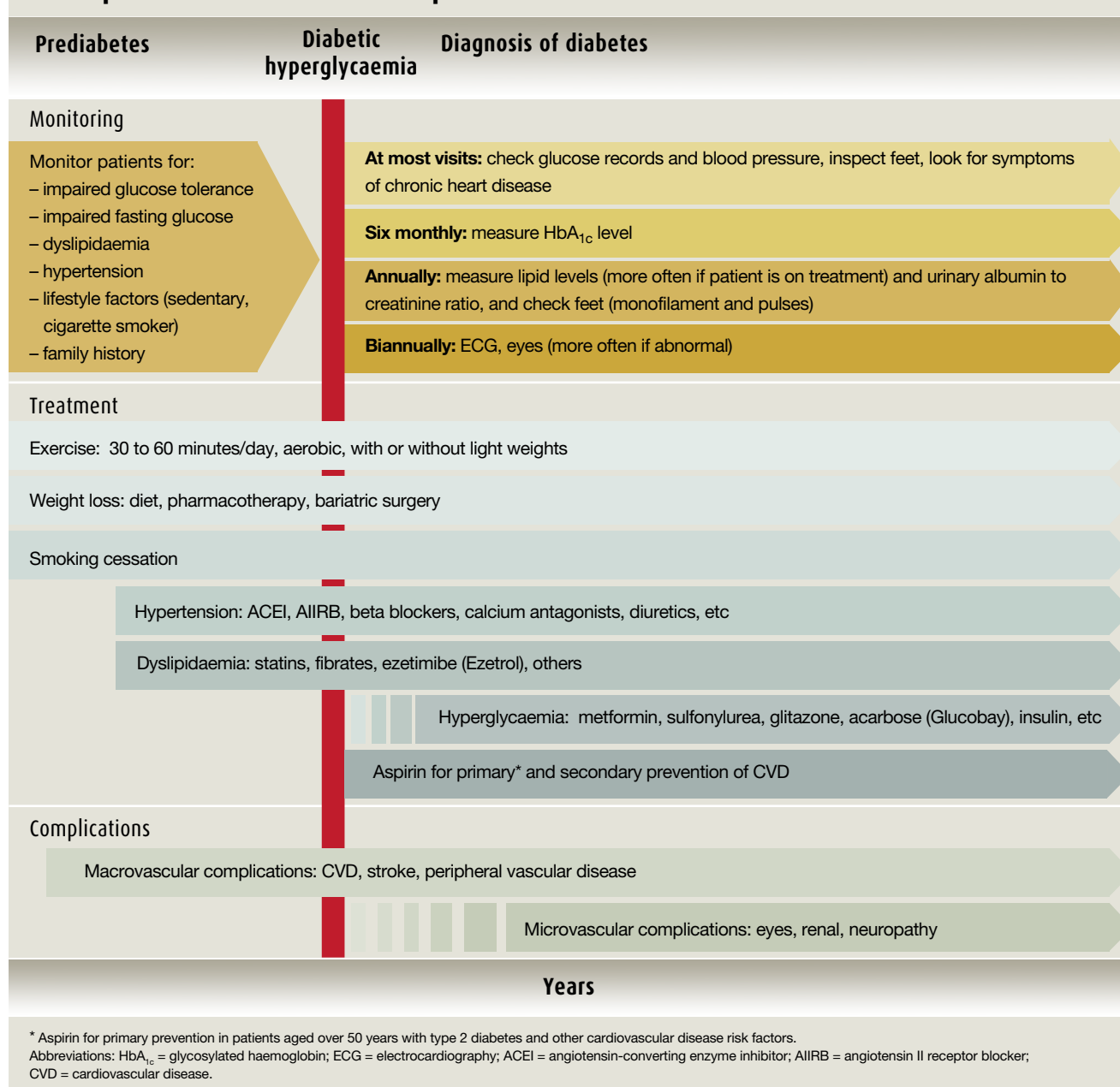
- Ask patients about coronary symptoms (chest pain, shortness of breath, lethargy) at every visit. Patients with diabetes may not suffer typical anginal pain and coronary disease is often painless.

New onset dyspnoea or tiredness may be the only presenting feature and should be investigated with non-invasive stress testing (thallium study or an echocardiographic stress test).

- Be alert for atrial fibrillation. Patients with type 2 diabetes have an increased

risk of stroke as well as atrial fibrillation. Careful assessment of the patient's pulse is a simple and inexpensive method of detecting this major risk factor for stroke and should be a routine examination in patients with diabetes.

Development of diabetes and its complications: when to intervene



- **Perform an ECG every two years in patients with diabetes who are over 50 years old.** Investigate definite and nonspecific changes. An ECG may reveal unsuspected prior infarction or nonspecific ST–T wave changes due to significant coronary artery disease (CAD) in asymptomatic patients.
- **Consider prescribing statins plus ACE inhibitors or angiotensin II receptor blockers.** Statins plus ACE inhibitors or angiotensin II receptor blockers may reduce CAD events, even in patients with ‘normal’ lipids and blood pressure. These medications may be more cost effective in terms of the magnitude of risk reduction than manipulation of glycaemic medications that achieve only modest improvements in glycaemic control.
- **Don’t forget to prescribe aspirin.** Most current guidelines suggest that patients over 50 years of age with type 2 diabetes and other risk factors for CAD take low dose aspirin.¹ Aspirin use reduces cardiovascular events, even in patients with retinopathy provided such patients are under expert surveillance.⁷
- **Remember that patients at high risk benefit the most from risk reduction.** With most of the risk interventions mentioned above, patients at highest risk of experiencing a cardiovascular event are the ones most likely to benefit from effective risk factor reduction.

For example, treatment of patients at low risk of CAD (e.g. 6% risk over five years) with a medication that is known to reduce the relative risk of CAD by 33% (e.g. a statin) requires treatment of 50 patients to prevent one CAD event, whereas only 10 patients at high risk of CAD (30% risk over five years) need to be treated to prevent one event. Both low and high risk groups have a similar risk of side effects so that the cost to benefit treatment ratio is much more favourable for high risk patients.

Microvascular disease

- **Inspect the patient’s feet at most visits.** Checking the feet enables detection of feet at risk of ulceration, unsuspected infections and pressure areas while also reinforcing the importance of careful foot management to the patient. Palpation of peripheral pulses to detect peripheral vascular disease and the nylon monofilament examination to detect clinically significant neuropathy are simple and rapid tools for identifying patients whose feet are most likely to benefit from expert podiatric management. It is also worth being alert for possible musculoskeletal complications of longstanding diabetes that affect the hands and feet, such as diabetic cheiroarthropathy (Figure 1) and the less common Charcot or neuropathic arthropathy.

Table 1. Recommended management targets for patients with type 2 diabetes^{1-3*}

Glycaemia

- Fasting blood glucose: 5.0 to 7.2 mmol/L
- 1 to 2 hour postprandial glucose: <10 mmol/L
- HbA_{1c}: <7.0%

Lipids

- Total cholesterol: <4.0 mmol/L
- Triglycerides: <1.5 mmol/L
- HDL cholesterol: >1.0 mmol/L
- LDL cholesterol: <2.5 mmol/L

Blood pressure

- <130/80 mmHg
- <120/85 mmHg if microalbuminuria present
- <125/75 mmHg if ≥1 g proteinuria/day

*These targets are for patients who do not have known cardiovascular disease. For those with known cardiovascular disease, targets should be more stringent (e.g. aim for a calculated LDL cholesterol of <1.8 mmol/L).

- **Inspect the patient’s eyes regularly: doctor not looking equals patient not seeing.** Diabetic retinopathy is usually asymptomatic until visual loss develops. Early detection and appropriate laser therapy in cases of vision-threatening

Newnham’s laws of diabetes management

Newnham’s first law

Number of medications required to manage type 2 diabetes $\propto \frac{K(1 + \text{number of diabetic complications} + \text{number of CVD risk factors})}{G \times \text{exercise} \times \text{nutrition}}$

Where K = ‘keenness’ of physician and G = government restriction on availability of medications

Newnham’s second law

Patient compliance $\propto \frac{C(\text{patient education} + \text{socioeconomic status})}{\text{number of medications} + \text{inconvenience} + \text{cost}}$

Where C = patient’s level of trust in his or her caring team



Figure 1. Limited joint mobility or 'diabetic cheiroarthropathy' becomes increasingly prevalent with diabetes' duration and is possibly associated with an increased risk of microvascular complications. Contractures of the metacarpophalangeal, proximal interphalangeal and distal interphalangeal joints result in the positive 'prayer sign' pictured. Similar changes probably contribute to the development of pressure areas in the diabetic foot. Patients with diabetes have an increased risk of frozen shoulder and other joint disorders.

Table 2. Tips for managing polypharmacy risks in patients with type 2 diabetes

- Prioritise treatment
- Use once daily medications if possible, e.g. extended release metformin (Diabex XR), glimepiride (Amaryl, Aylide, Diapride, Dimirel), modified release gliclazide (Diamcron MR)
- Consider economics
- Use half tablets if possible
- Use dosing boxes or pharmacist packaging of medications
- Use drug combinations
 - ACE inhibitor or angiotensin II receptor blocker in combination with thiazides (numerous examples)
 - metformin and glibenclamide (Glucovance)
 - simvastatin and ezetimibe (Vytorin)
 - rosiglitazone and metformin (Avandamet)
 - amlodipine and atorvastatin (Caduet)

retinopathy are the keys to management. For many patients without significant retinopathy, the convenience of local optometrical review facilitates regular checks compared with the more formal ophthalmological consultation that requires referral, appointments and travel (which may be difficult in patients following pharmacological mydriasis). Surveillance should start when a patient is diagnosed with type 2 diabetes.

- **Think renal: microalbuminuria, ACE inhibitors or angiotensin II receptor blockers.** Diabetic nephropathy develops silently and insidiously but is a major risk factor for the

development of both renal failure and vascular disease. ACE inhibitors and angiotensin II receptor blockers have been shown to decrease the rate of progression of diabetic kidney disease both before and after the development of microalbuminuria. The albumin to creatinine ratio on a first-voided urine sample is a simple and convenient tool for detecting early nephropathy and should be performed annually. If the result is positive, the patient should be followed up with formal urine collection. The presence of persistent microalbuminuria is a strong indication for aggressive management of vascular risk factors.

Table 3. Tips on pharmacotherapies for diabetes and its risk factors

Glycaemic management

Metformin

- First line therapy in obese patients
- Avoid in patients who have severe renal, pulmonary or hepatic problems or cardiac disease
- Withhold in patients having angiograms
- Withhold in patients with anorexia or diarrhoea
- Occasionally check vitamin B₁₂ levels

Glitazones

- Warn patients about weight gain
- Avoid or cease this treatment in patients with chronic heart failure or oedema

Hypertension and cardiovascular disease management

ACE inhibitors or angiotensin II receptor blockers

- Check renal function within one to two weeks of starting therapy
- Use with care in patients with renal impairment or taking potassium sparing diuretics

Beta blockers

- Effective but underused in patients with diabetes
- Use with particular care in patients with poor awareness of hypoglycaemia and/or autonomic neuropathy or peripheral vascular disease
- Check postural blood pressures in patients with diabetes on antihypertensive therapy

Lipid management

- Combined statin and fibrate therapy can, in rare cases, cause myositis. Warn patients to cease both these medications if they develop a flu-like illness or muscular aches and pains. In particular, check patients' creatine kinase levels before and after starting this combination.

Glycaemic control

- **Remember that the degree of glycaemic control achieved is usually more important than the treatment used to attain it.**

Metformin may be an exception as this medication seems to reduce complications in obese patients with type 2 diabetes more effectively than sulfonylurea or insulin treatment.⁸ One study of pioglitazone therapy in patients at high risk for CAD was stopped prematurely because of a significant decrease in the composite secondary end point of all-cause mortality, myocardial infarction and stroke in the pioglitazone group.⁹ However, the predefined primary composite endpoint of all-cause mortality, nonfatal myocardial infarction, silent myocardial infarction, stroke, acute coronary syndrome, surgical intervention on coronary or leg arteries and leg amputation did not achieve statistical significance. In this study there was a significantly increased rate of heart failure in the pioglitazone group.⁹

- **Achieve good glycaemic control early.** Glycaemic control is often achieved very slowly, with adjustments to the patient's therapy being made only during infrequent medical attendances. Persistent hyperglycaemia is itself toxic to beta cells and may hasten the gradual decline of beta cell function that characterises type 2 diabetes. Provide patients with clear targets and a plan summarising how glycaemic control can be achieved rapidly. This approach often requires telephone support.
- **Ask the patient about symptoms of hypoglycaemia.** Although hypoglycaemia is less frequent in patients with type 2 diabetes than in those with type 1 diabetes, it remains a significant risk factor of aggressive glucose lowering treatments, particularly in elderly patients with comorbidities or in patients who have an erratic oral intake. In the UK

Prospective Diabetes Study, approximately 3.6% of patients taking insulin suffered severe hypoglycaemia each year while on intensive therapy.¹⁰

Associated conditions and polypharmacy

- **Expect depression and ask about it.** In a typical clinic population, over 15% of patients with diabetes will be suffering from clinical depression and this often interferes with attainment of therapeutic targets.¹¹
- **Manage the polypharmacy.** Tips for managing diabetes-associated polypharmacy are outlined in Tables 2 and 3.

Conclusion

Attention to detail is essential to detect and manage effectively the risk factors and complications of diabetes. Also important is the ability to view the patient 'globally', directing attention to where treatment is most likely to be of benefit and least likely to cause harm. Multifactorial approaches to diabetes care appear to be the most effective.¹²

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