Managing diabetes in older people

Mark Kennedy

As the Australian population ages, physicians are seeing an increasing number of older people with diabetes in primary care. While the broad aim of diabetes management in this patient group is still to control blood glucose levels and reduce the risk of diabetes-related complications, the prevalence of frailty and multimorbidity in elderly people make this a challenging task, and a balance needs to be found between achieving good diabetes control and avoiding adverse treatment effects and worsening of comorbidities. This article reviews the factors that need to be taken into account when treating elderly people with diabetes and suggests strategies that can be used to achieve the highest level of individualised care.

The proportion of the community in older age groups is increasing rapidly. In 2007–2008, 43% of Australians with diabetes were older than 65 years, and the prevalence of type 2 diabetes, which increases with age, was over 15% in the 65–69-year age group (Australian Institute of Health and Welfare, 2011).

Although older people with diabetes are at risk of the same microvascular complications as those at younger ages, absolute cardiovascular (CV) risk is much greater at a more advanced age. Older people with diabetes experience greater morbidity and mortality, and are more likely to have polypharmacy, cognitive impairment, depression, falls, urinary incontinence and impaired mobility than those without diabetes.

Individualising management

Older people with diabetes managed in primary care are a heterogeneous group, ranging from those living independently in the community to those in aged care facilities requiring full-time care. Their general health status can also range from fit and active to frail with many disabilities and comorbidities. In people over 65 years of age, the reported prevalence of multimorbidity has varied from 50% to 80%, and in those older than 80 years a prevalence of >70% has been reported (Fortin et al, 2005; 2010).

The broad goals of diabetes management in older people are not significantly different from those for younger people with the condition. Safely controlling glycaemia and reducing other risk factors for macrovascular and microvascular disease remain paramount. However, in frail elderly people with diabetes, avoidance of hypoglycaemia, hypotension, medication interactions and worsening of other comorbidities is often more important than mitigating long-term CV risk. Balancing the benefits of achieving glycaemic, blood pressure (BP) and lipid targets in elderly patients against these risks can be challenging. Appropriate targets must be determined on an individual basis at a particular point in time and reviewed often to consider additional factors that might change the appropriate target, such as increasing frailty, development of new comorbidities and changed home or social circumstances.

Glycaemic targets

Although elderly people are often included in large diabetes trials, studies specifically targeting elderly people with diabetes are more often observational than randomised and placebo-controlled. Nevertheless, relationships between poor glycaemic control in elderly people and increased mortality (Zoppini et al, 2008), CV events (Kuusisto et al, 1994) and retinopathy

Article points

1. Compared with their younger counterparts, older people with diabetes are at a higher risk of comorbidities, polypharmacy and mortality.

2. Diabetes management in this patient group needs to balance the benefits of achieving good control of blood glucose and other cardiovascular risk factors with the risks that such treatment confers.

3. Optimal management requires treatment specific to the individual, taking into account factors such as frailty, life expectancy, comorbidities and home support systems, as well as good communication between primary care team members and, often, those involved in secondary care.

Key words

– Comorbidities
– Diabetes
– Individualised care
– Older people
– Treatment targets

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1. There is little research into specific glycaemic targets for older people with diabetes; however, these should be weighed against the risk of adverse treatment effects, such as hypoglycaemia.

2. Higher glycaemic targets may be appropriate for people with lower life expectancy and longer diabetes duration, while lower targets may be beneficial in those who are still fit and active.

3. Similarly, while healthy diet and lifestyle are beneficial in all age groups, exercise may need to be avoided in frail people at risk of falls, and weight loss should be carefully monitored to avoid undernutrition.

(Zoppini et al, 2009) have been identified in these studies.

There is little specific research to provide the basis of optimal glycaemic targets for older people with diabetes. Risks of hyperglycaemia and hypoglycaemia in this age group make it important to individualise glycaemic goals, considering the need for CV risk reduction, overall health and projected life span. For elderly people, glycaemic targets may need ongoing adjustment taking into account many factors, such as those listed in *Box 1* (Inzucchi et al, 2012).

Adverse effects of treatment, particularly hypoglycaemia, can increase the risk of falls and exacerbate comorbidities, often affecting the level of independence in community living. On the other hand, impaired vision (Tai et al, 2006) and cognition (Cox et al, 2005), and sometimes dehydration, can accompany undertreated hyperglycaemia. This can increase the risk of falls and functional decline in older people with diabetes.

For elderly people with diabetes who are fit and active with a life expectancy beyond 10 years, HbA$_{1c}$ targets of 53 mmol/mol (7.0%) are often still very appropriate. However, a goal of 64 mmol/mol (8.0%) may be more appropriate in those with long-standing diabetes, particularly if there is coexisting or high risk of CV disease (CVD), because lower targets in this group may be associated with increased mortality, as was seen in the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial (Kirkman et al, 2012).

The potential benefits of diabetes medications that increase the likelihood of hypoglycaemia need to be carefully measured against the significantly increased risks associated with hypoglycaemia. Assessment of hypoglycaemic risk in older people is paramount because hypoglycaemia may lead to impairment in cognitive function and increase the risk of adverse CV events and cardiac autonomic dysfunction (Ligthelm et al, 2012). Recurrent severe hypoglycaemia has also been associated with increased rates of dementia (Whitmer et al, 2009). In frail elderly people, even mild hypoglycaemia can have severe consequences if it contributes to falls, fractures and loss of independent living.

Box 1. Factors to be considered in setting and reviewing glycaemic targets in older people with diabetes.

- Level of patient engagement
- Expected concordance with prescribed therapy
- Risks associated with hypoglycaemia and other adverse reactions
- Duration of diabetes
- Life expectancy
- Important comorbidities
- Known vascular complications
- Patient support systems

Lifestyle modification

Appropriate diet, loss of excess weight and regular aerobic and resistance exercise continue to be beneficial in the majority of older people with diabetes. Individualisation of advice in these areas is important, with due consideration given to comorbidities, family and social support. A randomised controlled trial of a specific dietary intervention in people with diabetes over the age of 65 years demonstrated significant improvements in both fasting blood glucose and HbA$_{1c}$ levels (Miller et al, 2002).

Older people with diabetes enjoy the same benefits from regular exercise as younger people in terms of maintenance of physical function, reduced CV risk and improved insulin sensitivity. However, for older people, there are extra benefits in terms of reductions in falls, depression and arthritic pain, and in terms of increased strength and balance, quality of life and survival (Christmas and Andersen, 2000; Heath and Stuart, 2002; Morey et al, 2002). Patients at high risk of falls can benefit from fall-prevention training focused on balance and muscle strengthening.

In obese older people with diabetes, a modest weight loss target of 5% of body weight through calorie reduction and increased exercise has been shown to be beneficial (American Diabetes Association et al, 2008; Kirkman et al, 2012). Careful monitoring of weight loss is important because there are also significant risks of

increased morbidity and mortality associated with undernutrition in older people (Wedick et al, 2002).

Pharmacotherapy

A recent review of meta-analyses, randomised controlled trials and evidence-based reviews identified a relative lack of specific data on diabetes pharmacotherapy options in older patient groups, although most large diabetes drug studies have included some people over the age of 65 years (Neumiller and Setter, 2009). The appropriate choice of therapy in older age groups requires careful individualisation taking into account frailty, renal function, weight status, risk of hypoglycaemia, cognitive function, home support systems and comorbidities, particularly chronic kidney disease, cardiac failure, liver dysfunction and CVD. Many guidelines for the treatment of diabetes in the elderly have as a central concept that doctors should base recommendations for treatment targets or interventions on life expectancy (Sinclair et al, 2011; American Diabetes Association, 2015). People whose life expectancy is limited (usually less than 5–10 years) are not considered likely to benefit from intensive glucose control, whereas those with longer life expectancy are more likely to benefit from more aggressive glycaemic control. This is supported by the observation that cumulative event curves for the intensive and conventional glycaemic control arms of the UKPDS (UK Prospective Diabetes Study) separated after 9 years (Kirkman et al, 2012).

Retinopathy

The prevalence of retinopathy increases progressively with the duration of both type 1 and type 2 diabetes, and with poor glycaemic control and younger age at original diagnosis. Retinopathy rates and severity have decreased with better screening, improvements in glycaemic control and better treatments for retinopathy (Vallance et al, 2008).

Regular screening by optometrists or ophthalmologists from diagnosis and at least once or twice yearly according to presence and severity of retinopathy and/or other eye disease is essential. These examinations also screen for and monitor cataracts and glaucoma, both of which are more common in older people with diabetes. Poor vision has many consequences, including increased risk of falls and accidents, social isolation and difficulties with monitoring blood glucose and administering oral and injectable therapies.

Nephropathy

The prevalence of at least moderate albuminuria in people who have had diabetes for 10 years is at least 25% and has been reported to be as high as 40% in some studies (Newman et al, 2005; Parving et al, 2006). Since the advent of angiotensin-converting enzyme inhibitor treatments effective at reducing development and progression of nephropathy, screening at least annually for diabetic nephropathy has generally been recommended.

The prevalence of at least moderate albuminuria at the time of diagnosis of type 2 diabetes may be higher in older people, making it essential to screen from the time of diagnosis (Mykkänen et al, 1994). There may be other causes for this higher prevalence, including longer periods of undiagnosed diabetes or other coexisting conditions, such as benign nephrosclerosis.

Diabetic foot disease

Foot pathology is a cause of significant morbidity in people with diabetes, and its prevalence is much higher in older people. Both vascular and neurological disease can contribute to the development of foot disease in people with diabetes. Additionally, many older people with diabetes have difficulty seeing or reaching their feet, making adequate self-inspection and foot care difficult or impossible.

Regular foot examination by general practitioners, practice nurses or podiatrists is essential and should also include assessment of the individuals' ability to see and reach their feet, and enquiry into other family members or carers who might be able to assist with regular foot examination in the home. Detailed neurological examination and assessments for peripheral artery disease should be performed at least annually. Regular review by a podiatrist

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1. Appropriate choice of pharmacotherapy in older people requires careful individualisation, taking into account life expectancy, frailty, renal function, weight status, risk of hypoglycaemia, cognitive function, home support systems and comorbidities.

2. The risk of both retinopathy and nephropathy increases with the duration of diabetes, and thus older people with diabetes require at least annual screening for these conditions from diagnosis onwards.

3. Regular examination for diabetic foot disease is also required, particularly for people with difficulties in seeing or reaching their feet, and annual examination for neuropathy and peripheral artery disease is also recommended.

for those considered to be at high risk of diabetic foot complications is recommended.

CV risk reduction

Both diabetes and age are major risk factors for coronary heart disease (CHD), so it is not surprising that CHD is the greatest cause of death in older people with diabetes. As well as glycaemic control, risk reduction should address smoking cessation, if relevant, and good control of hypertension and dyslipidaemia. As with glycaemic goals, goals for hypertension and lipid management in elderly people with diabetes should be individualised based on comorbidities, life expectancy, cognitive state and patient preference.

Smoking cessation

In people with diabetes, smoking is an independent risk factor for all-cause mortality. Whenever possible, smoking cessation should be a priority in discussions with older people with diabetes. Smoking cessation even after the age of 65 years has been associated with reductions in mortality as well as significant improvements in a range of functional parameters (LaCroix and Omenn, 1992).

Treatment of hypertension

There is some evidence to support BP lowering up to the age of about 80 years in people with type 2 diabetes. In the BP arm of the UKPDS, people with hypertension and type 2 diabetes up to the age of 75 years were randomised to a tight control arm or a less tight control arm (UKPDS Group, 1998). The final mean BP was 144/82 mmHg in the tight control group and 154/87 mmHg in the less tight control group. Over 9 years, people in the tight control group showed significant reductions in morbidity and mortality, specifically diabetes-related death, fatal and non-fatal stroke, congestive cardiac failure and microvascular complications. The tightly controlled participants were treated with atenolol or captopril, but the study was not sufficiently powered to determine which agent was superior.

In the HOT (Hypertension Optimal Treatment) trial, people aged up to 80 years with hypertension, and many also with diabetes,

were randomised into three groups, the aim being to achieve diastolic BP under 90 mmHg, 85 mmHg and 80 mmHg, respectively (Hansson et al, 1998). There were significant reductions in CV morbidity and mortality in the tightest controlled group.

People enrolled in clinical trials tend to be relatively fit and healthy, usually with a single specific disease being the "target" of the trial. However, this does not correlate with many of the elderly people with type 2 diabetes seen in primary care, which raises concerns over the applicability of these trials to many patients in the community.

Treatment of dyslipidaemia

There is some evidence in favour of cholesterol lowering up to the age of about 84 years in people with type 2 diabetes. In the HPS (Heart Protection Study), people aged up to 80 years were recruited and followed for a mean of 4 years (HPS Collaborative Group, 2002). Treatment with simvastatin resulted in a 27% reduction in the incidence of first non-fatal myocardial infarction (MI), and a 25% reduction in first incidence of fatal or non-fatal stroke, compared with placebo.

In CARDS (Collaborative Atorvastatin Diabetes Study), people aged up to 75 years with type 2 diabetes, no CHD but one other risk factor for CHD (e.g. hypertension or smoking) were randomised to atorvastatin or placebo (Colhoun et al, 2004). Compared with placebo, the risk reduction in the atorvastatin group was 37% for a CHD event, 48% for stroke, 31% for coronary revascularisation and 27% for death.

In the FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) trial, people aged up to 75 years with type 2 diabetes received fenofibrate or placebo (Keech et al, 2005). The initial primary endpoint of coronary mortality was later broadened to include non-fatal MI. After 5 years, there was no significant reduction in fatal MI or total mortality. There was a 24% reduction in non-fatal MI and a 21% reduction in coronary revascularisation. Fenofibrate was also associated with a reduction in albuminuria progression and in retinopathy needing laser treatment, but there were slight increases in

pancreatitis and pulmonary embolism compared to the placebo group.

Recent European guidelines for type 2 diabetes in older people (Sinclair et al, 2011) make the following recommendations about lipid therapy:

1. A statin should be offered as primary prevention if absolute 10-year CV risk is >15%.
2. A statin should be offered if there is an abnormal lipid profile in the setting of proven CVD.
3. Statin therapy should be considered to reduce stroke risk as part of secondary prevention of CVD.
4. A fibrate should be considered if triglyceride levels remain >2.3 mmol/L after at least 6 months of statin treatment.

Aspirin therapy

At this time there is insufficient evidence to recommend routine use of aspirin to older people with diabetes for primary prevention of CVD or stroke. However, all people with type 2 diabetes should be offered aspirin at a dose of 75–325 mg daily for secondary prevention (Sinclair et al, 2011).

Cognitive impairment and dementia

Diabetes is associated with an increased risk of dementia and cognitive decline (Alonso et al, 2009; Rawlings et al, 2014). However, many older people with cognitive decline and dementia, particularly in the early stages, are undiagnosed. It is recommended that people aged ≥70 years should be screened for cognitive impairment, using a tool such as the Mini Mental State Examination, at diabetes diagnosis and then at regular intervals thereafter (Sinclair et al, 2011).

Optimal glycaemic management and prevention of repeated hypoglycaemia in older people with diabetes may reduce the risk of developing cognitive impairment or dementia (Abbatecola et al, 2006; Whitmer et al, 2009).

Depression

Depression is more prevalent in older people with diabetes than in those without the condition (Anderson et al, 2001; Maraldi et al, 2007). Depression in people with diabetes has not only been associated with worse glycaemic control, less home monitoring of blood glucose and higher weight, but also accelerated rates of CHD (Lustman et al, 1998). Depression is often undiagnosed and untreated in older people with diabetes (Newman and Hassan, 1999). Early diagnosis and appropriate treatment may lead to better glycaemic control (Lustman et al, 1998; Lustman and Clouse, 2002).

Polypharmacy

Older people with diabetes are often prescribed multiple medications to control blood glucose, BP and lipid levels, as well as comorbidities such as osteoarthritis, gastro-oesophageal reflux disease, cardiac failure, chronic obstructive pulmonary disease and constipation. One recent study found that middle-aged and older people with type 2 diabetes were prescribed a mean of 8.4 different drug compounds per day (Bauer and Nauck, 2014).

Adverse reactions to these medications may exacerbate comorbidities and adversely affect quality of life, as well as impairing individuals' ability to self-manage their diabetes. Older people are more prone to problems related to their treatment because of the higher number of medications used and because of a decline in cognitive and physical functioning (Denneboom et al, 2007). Polypharmacy in elderly people with diabetes may be associated with adverse effects specific to diabetes, such as hypoglycaemia, and those associated with poor adherence, as well as an increased risk of drug interactions and other serious or common side effects (Peron et al, 2015). Taken together, these effects of polypharmacy can significantly worsen quality of life and sometimes lead to disability or premature death (Dardano et al, 2014).

It is important that medication lists are regularly reviewed and updated when necessary (Kirkman et al, 2012). Medication reviews can be helpful and can increase the proportion of treatment consistent with recommended guidelines (Denneboom et al, 2007; Castelino et al, 2010).

Falls

Falls are common in elderly people and are a major contributor to loss of independence in many

Page points

1. To date there is little evidence to support the use of aspirin for primary prevention of cardiovascular disease; however, all people with type 2 diabetes should be offered aspirin for secondary prevention.

2. Cognitive impairment and depression are both associated with diabetes and, in particular, poor glycaemic control; therefore, older people with diabetes should be regularly screened for these conditions.

3. Polypharmacy is more common in older people with diabetes and can exacerbate comorbidities, make diabetes management more difficult and reduce quality of life. Medications should, therefore, be regularly reviewed and adjusted.

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1. Falls are common in older people with diabetes. While good glycaemic control can reduce the risk of falls by delaying diabetes complications, this is counteracted by an increased risk of hypoglycaemia, which leads to falls itself.

2. Treatment targets should thus take into consideration the frailty of the individual, with stricter targets appropriate only in people who are otherwise healthy and independent.

3. Older people often have comorbidities that affect adherence to treatment, such as cognitive decline; however, adherence can be improved with interventions that reduce dosing demands, involve a multidisciplinary team, provide ongoing monitoring and feedback, and are spread over multiple sessions.

people. Falls are even more common in elderly people with diabetes for many reasons, including muscle weakness, loss of vision, peripheral and/or autonomic neuropathy, declining renal function, hypoglycaemia and comorbidities such as osteoarthritis.

Good glycaemic control may reduce the risk of falls by preventing or delaying progression of some diabetes complications, but intensive glycaemic control, with the increased risk of hypoglycaemia that it confers, can increase the risk of falls. Appropriate glycaemic and BP targets for elderly people must be set to balance the risks associated with poor or too intensive control. The primary care team can also help identify other contributions to an individual's risk of falls, some of which may be reduced with appropriate strengthening, balance and exercise programs.

Frailty

Frailty is more prevalent with increasing age and is associated with a higher risk of falls, functional decline, reduced mobility, recurrent hospitalisation, increased likelihood of needing institutional care and death. Frailty also has a major impact on the risk–benefit balance of many treatment options for diabetes and comorbidities.

In considering frailty in elderly people with diabetes, it can be useful to think of a spectrum of frailty from two extremes:

- Those who have type 2 diabetes as their only significant disease and are otherwise fit, healthy and living independently. For people at or near this end of the spectrum, if age-specific evidence is not available, recommended targets for primary prevention to match evidence-based targets for younger people can usually be considered, in consultation with the individual patient.
- Those who are frail and elderly and have significant comorbidities, such as arthritis, high dependency levels or significant dementia. For those people at or near this end of the spectrum, it is often more appropriate to aim for symptom control, taking care to avoid hypoglycaemia, symptomatic hyperglycaemia and intensive monitoring, always in consultation with the patients and/or their carers.

Concordance with recommended treatment

Adherence to recommended management is particularly challenging for people with type 2 diabetes (Cramer, 2004; Bezie et al, 2006). Pharmaceutical treatment regimens are often complex, involving multiple different medications and additional self-care recommendations, including diet control, regular exercise, self-monitoring of blood glucose, foot care and attendance at multiple appointments with many different health professionals. These are a significant burden for many people. Elderly people often have additional issues relating to cognitive decline, poor health literacy, increased likelihood of adverse reactions because of polypharmacy and physical difficulty reading labels or opening medication, which can worsen adherence. Poor adherence to recommended diabetes pharmacotherapy has been identified as a significant limiter of the effectiveness of diabetes therapeutic strategies (McDonald et al, 2002).

A recent study showed that people were four times less likely to adhere to prescribed medication for every unit increase in the total number of prescribed medications, and nine times less likely to adhere if the treatment required more than once-daily dosing (Jarab et al, 2014). Adherence was also three times less likely if the participants reported concerns about adverse reactions; however, it was twice as likely if participants had at least one microvascular complication.

A number of reviews have examined the effectiveness of different interventions in improving adherence to prescribed treatments in chronic medical conditions (Kripalani et al, 2007; Viswanathan et al, 2012; Zullig et al, 2013). Adherence is increased most consistently with behavioural interventions that reduce dosing demands, involve a multidisciplinary team, provide ongoing monitoring and feedback, and are spread over several sessions.

A simple strategy can be proposed to try to improve medication adherence in older people with diabetes, as outlined in *Table 1*.

Nursing home residents

Diabetes in nursing home populations is extremely common, with prevalence rates varying from 5.8%

to over 26%, depending on the type of facility, age range and gender of residents, and the way in which diabetes is diagnosed (Zhang et al, 2010; Moore et al, 2012; Szczerbinska et al, 2015). Priorities when treating frail nursing home residents with diabetes are less about prevention of long-term macrovascular and microvascular complications and more about maximising quality of life, preserving autonomy and avoiding hospitalisation (Sinclair, 2011). This requires a focus on avoiding acute diabetes complications, such as hyperglycaemia, hypoglycaemia, infection and dehydration. It also requires a careful consideration of factors such as cognitive impairment, risk of falls and nutrition status when determining individual management strategies.

Conclusions

Older individuals with diabetes experience greater morbidity and mortality than those without diabetes and have higher risk of polypharmacy, cognitive impairment, depression, falls, urinary incontinence, impaired mobility and persistent pain.

The broad goals of diabetes management in older people are not significantly different from those of younger people with the condition. Safe control of glycaemia and management aimed at reducing the other risk factors for macrovascular and microvascular disease remain paramount. However, particularly in frail elderly people with diabetes, the risk–benefit analysis of various interventions is often far more complicated, requiring good communication between primary care team members and often also with those involved in secondary care. In frail elderly people with diabetes, avoidance of hypoglycaemia, hypotension, medication interactions and worsening of other comorbidities can often be more important than tight control of individual CV risk factors. Issues such as polypharmacy, mental illness, risk of falls, frailty and medication adherence all need to be considered as part of the management plan. ■

Table 1. Strategy for improving medication adherence in older people with diabetes.

Explanation	● Careful and simple explanations about: – The purpose and importance of each medication – When and how each medication should be taken
Medication dosing	● Minimise the number of tablets to be taken ● Minimise the frequency with which tablets need to be taken ● Once-daily tablet treatments are preferable if available ● Combination preparations are preferable if available
Side effects	● Prescribe with strong focus on using medications with minimal side effects
Labelling	● Ensure instruction labels are readable by and understandable to the patient ● Ensure packaging is accessible to the patient ● Ensure the patient is able to read the label
Dispensing aids	● Consider pre-filled tablet dispensing systems: – If normal packaging is difficult – If forgetting whether tablets have been taken is an issue
Family and/or carers	● Enlist the help of family members or carers to assist with medication taking

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