54 Diabetes in Old Age

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Keypoints

- Diabetes affects 10–25% of elderly people (>65 years) worldwide, with particularly high rates in populations such as Pima Indians, Mexican-Americans and South Asians.
- Glucose tolerance worsens with age, the main factor being impairment of insulin-stimulated glucose uptake and glycogen synthesis in skeletal muscle.
- Factors precipitating hyperosmolar hyperglycemic syndrome include infections, myocardial infarction, stroke and drugs such as thiazides or glucocorticoids.
- Episodes of hypoglycemia resulting from insulin or sulfonylureas may be severe and prolonged, particularly because counter-regulatory responses are impaired in the elderly.
- High levels of disability are common in older people with diabetes and lead to heavy usage of health care resources and premature mortality.
- About 16% of elderly people with diabetes in the UK are registered blind or partially sighted (eight times more than the non-diabetic population) which justifies regular screening for undetected eye disease.
- Risk factors for foot ulceration affect 25% of elderly people with type 2 diabetes.
- Management strategies for many elderly people with diabetes are as in the younger population, with similar lipid-lowering and antihypertensive treatment schedules and aspirin or clopidogrel for patients with increased cardiovascular risk.
- Effective delivery of diabetes care depends on close cooperation between hospital and community, the involvement of diabetes specialists and practice nurses, and attention to all causes of disability and ill-health.
- Elderly people with diabetes in care homes are particularly vulnerable and require greater diabetes specialist input.

Introduction

Diabetes, the most common disabling metabolic disorder, imposes considerable economic, social and health burdens [1]. Many of these burdens fall heavily on older patients with diabetes, partly because type 2 diabetes mellitus (T2DM) and its co-morbidities are so much more common in that age group, and partly because of these subjects' special needs. Older people do not accept illness without question, however, and expect equity of access to treatment and services as for younger people. As those who are above pensionable age are, in most Westernized societies, a significant proportion of the voting public, they can be very persuasive in ensuring that there are political commitments to improving the organization and delivery of health care.

Within Europe, T2DM affects 10–30% of subjects above pensionable age and in the USA about 40% of all those with diabetes fall into this category [2]. Older people with diabetes use primary care services two to three times more than their counterparts without diabetes; in one Danish study [3], insulin-treated patients accounted for over half of the services provided, mainly because of macrovascular disease. The burden of hospital care is also increased two to three times in those with diabetes compared with the general aged population [4], with more frequent clinic visits and a fivefold higher admission rate; acute hospital admissions account for 60% of total expenditure in this group [5]. In the UK, some 5–8% of general hospital beds are occupied by patients with diabetes aged 60 years or more [6,7], accounting for 60% of all inpatients with diabetes [7]. Hospital admissions last twice as long for older patients with diabetes compared with age-matched control groups without diabetes, with the totals averaging 7 and 8 days per year for men and women, respectively [4,6,8]. Introducing insulin treatment increases costs fourfold, both in the community and in hospital, where bed occupancy rises to 24 days per year [4].

The management of T2DM and its common co-morbidity of macrovascular disease is complicated in elderly subjects because of the added effects of aging on metabolism and renal function, the use of potentially diabetogenic drugs and low levels of physical activity (Figure 54.1) [9,10]. Cardiovascular risk is particularly high because many risk factors of the metabolic syndrome can be present for up to a decade before T2DM is diagnosed (Figure 54.1) [11].

Textbook of Diabetes, 4th edition. Edited by R. Holt, C. Cockram, A. Flyvbjerg and B. Goldstein.

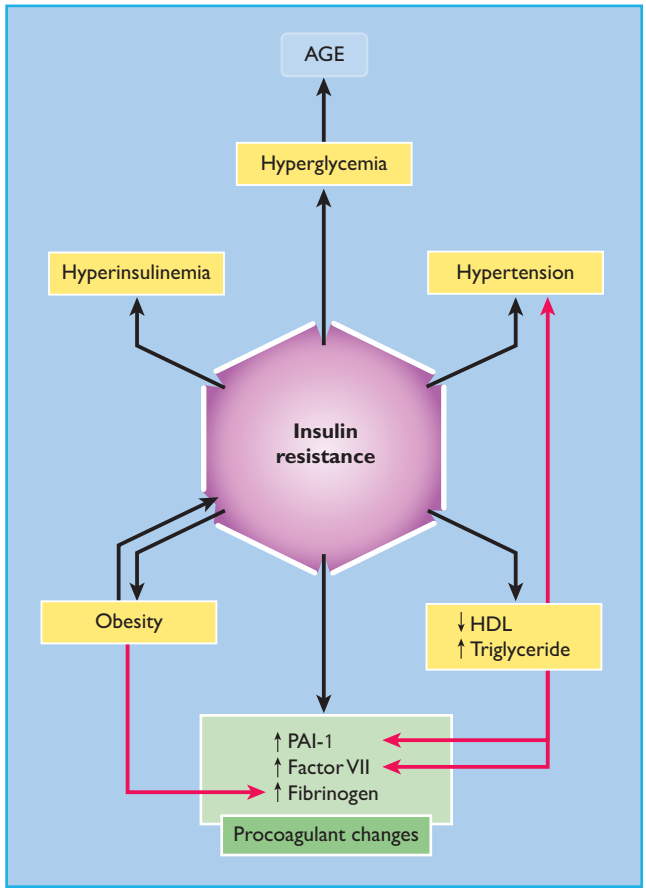

Figure 54.1 Features of the metabolic syndrome. Additional considerations that apply to the elderly population are described in the text. AGE, advanced glycation end-product; HDL, high density lipoprotein; PAI-1, plasminogen activator inhibitor1.

Table 54.1 Special characteristics of older subjects with diabetes.

High level of associated medical co-morbidities
Increased risk of cognitive dysfunction and mood disorder causing more complex decision-making
Varying evidence of impaired activities of daily living and lower limb function
Increased vulnerability to hypoglycemia
Increased risk of inpatient mortality
Unstructured specialist and primary care follow-up
Increased need to involve spouses and informal carers in management

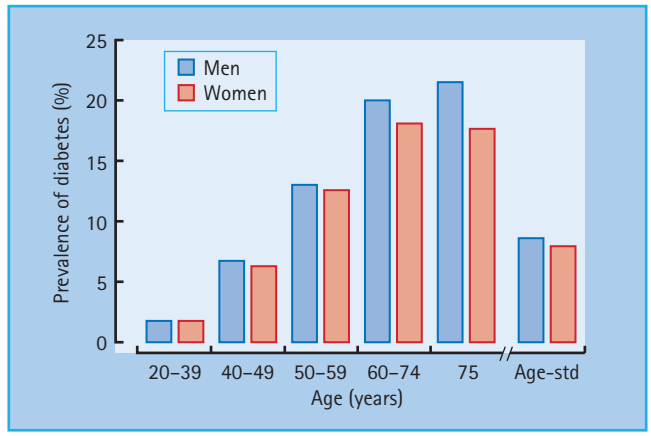

Figure 54.2 Prevalence of diabetes in men and women in the US population aged ≥20 years, based on the NHANES III study [14]. Subjects included those with previously diagnosed and undiagnosed diabetes (defined by fasting plasma glucose ≥7.0 mmol/L). Age-std, age-standardized.

It must be remembered that older people with diabetes, particularly those who are housebound or institutionalized, have special needs (Table 54.1). Overall, the quality of diabetes care for older patients appears to be improving in various countries [12,13], although the UK still seems to be alone in developing geriatric diabetes as a subspecialty.

Epidemiology of diabetes in aging populations

In 1997, there were approximately 124 million people with diabetes worldwide, of whom 97% had T2DM. By the time of publication of this edition, this number is projected to rise to 285 million. Aging is an important factor in the rapid worldwide rise of T2DM. In the USA, the number of new cases of diabetes in people aged 65–79 years was five times higher than in those aged less than 45 years of age [2]. The prevalence of diabetes begins to rise steadily from early adulthood, reaching a plateau in those aged 60 years or older; the data in Figure 54.2, from the Third National Health and Nutrition Examination Survey (NHANES III) in the USA [14], are representative of most developed countries. In some susceptible populations, T2DM may develop earlier; for example, among the Pima Indians prevalence peaks at 40 years of age in men and at 50 years in women, and declines after the ages of 65 and 55 years, respectively.

Overall prevalence rates of diabetes in the elderly are dominated by T2DM, which accounts for 95% of all cases in the UK and European countries, and for virtually all in populations such as the Pima Indians and Mexican-Americans. Some older patients who present clinically with T2DM may have slowly evolving autoimmune β-cell destruction that requires insulin treatment, so-called latent autoimmune diabetes of adults (LADA). This condition appears to be most prevalent in northern Europe and is rare in Asians and Africans.

There are marked ethnic and geographic differences in the prevalence rates of diabetes amongst older people. In the UK and most developed countries, diabetes affects 9–17% of white subjects aged over 65 years and up to 25% of non-white people [15,16]; intriguingly, the prevalence of diabetes in elderly care homes in the UK is also 25% [17]. Among subjects aged over 60 years from NHANES III, Mexican-Americans showed a consist-

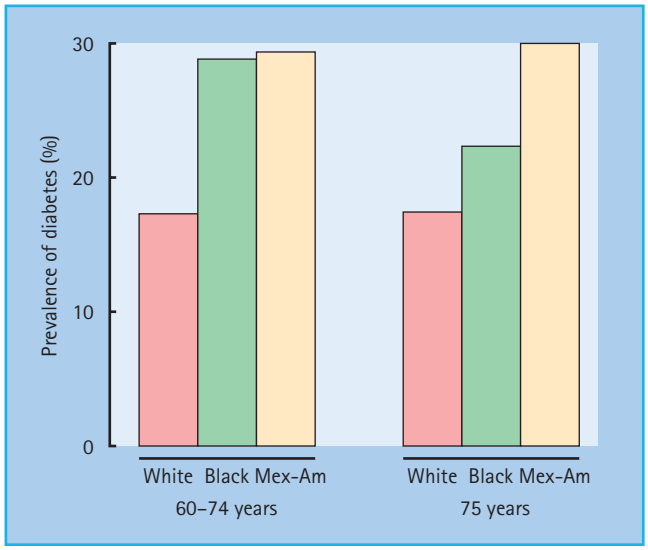

Figure 54.3 Prevalence rates for diabetes among elderly non-Hispanic white, non-Hispanic black and Mexican-American subjects. Data from the NHANES III study [14].

ently higher prevalence of diabetes than non-Latino white and black subjects (Figure 54.3) [14].

Etiology of diabetes in the elderly

T2DM accounts for virtually all of the age-related increase in the prevalence of diabetes. This is attributed to various combinations of insulin resistance and impaired insulin secretion that result in a progressive age-related decline in glucose tolerance, which begins in the third decade and continues throughout adulthood [18,19]. Plasma glucose levels at 1 and 2 hours after the standard 75-g oral glucose challenge rise by 0.3–0.7 mmol/L per decade, the increase being greater in women. Consistent with this, NHANES III found the prevalence of impaired glucose tolerance (IGT) to be 12% in subjects aged 40–49 years, rising to 21% in those aged 60–74 years [14].

Various factors contribute to age-related glucose intolerance (Table 54.2). Perhaps the most important is impairment of insulin-mediated glucose disposal, especially in skeletal muscle [19,20], which is particularly marked in obese subjects (Figure 54.4) [21]. Insulin receptor number and binding are not consistently affected by age, and so post-receptor defects are presumably responsible. Contributory factors in some cases include increased body fat mass, physical inactivity and diabetogenic drugs such as thiazides. In contrast to younger people with T2DM, fasting hepatic glucose production does not appear to be increased in either lean or obese elderly people with T2DM [21]. The ability of insulin to enhance blood flow is also considerably reduced in obese insulin-resistant subjects with diabetes; this may be etiologically important, as insulin-mediated vasodilatation is thought to account for about 30% of normal glucose disposal.

Table 54.2 Factors contributing to glucose intolerance in old age.

Impaired glucose disposal and utilization
• Insulin-mediated uptake into skeletal muscle
• Insulin-mediated vasodilatation in muscle
• NIMGU
Impaired glucose-induced insulin secretion
Other factors
• Obesity
• Physical inactivity
• Reduced dietary carbohydrate
• Diabetogenic drugs (thiazides, glucocorticoids)

NIMGU, non-insulin mediated glucose uptake.

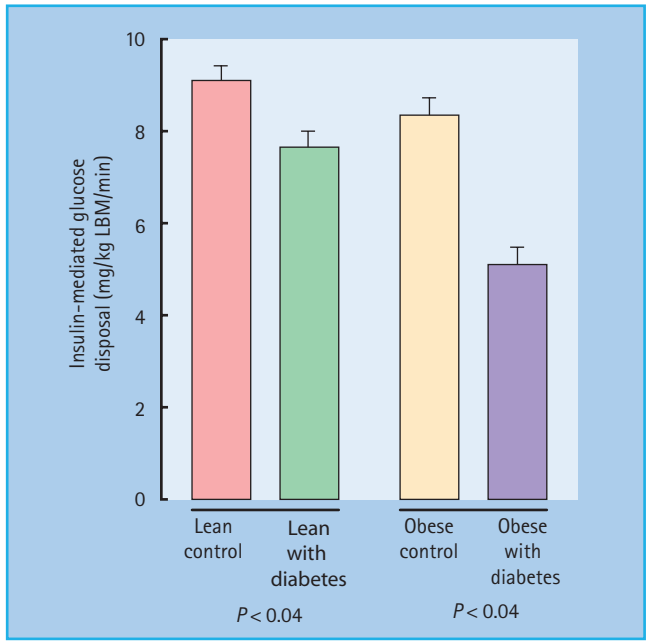

Figure 54.4 Insulin-mediated glucose disposal is decreased in elderly patients with type 2 diabetes. The euglycemic clamp technique was used to measure the glucose disposal rate in healthy lean and obese elderly controls, and in their counterparts with diabetes. LBM, lean body mass. From Meneilly *et al.* [21], with permission.

As well as insulin resistance, many elderly people with glucose intolerance show impairment of glucose-induced insulin secretion, especially in response to oral rather than intravenous glucose. In addition, recent studies have shown that glucose effectiveness (i.e. the ability of glucose to stimulate its own uptake in the absence of insulin) is decreased in healthy elderly subjects [22]. This non-insulin-mediated glucose uptake (NIMGU) accounts for 70% of glucose uptake under fasting conditions (primarily into the CNS) and for 50% of post-prandial glucose uptake (especially into skeletal muscle). This is therefore a potentially important new target for therapeutic intervention, as exer-

cise, anabolic steroids and decreased non-esterified fatty-acid (NEFA) levels can all enhance NIMGU and improve glucose tolerance, at least in younger patients [23].

Acute metabolic complications in elderly people with diabetes

Hyperglycemic states

Older subjects with diabetes can develop diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (formerly known as hyperosmolar non-ketotic coma [HONK]), which occurs predominantly in subjects aged over 50 years. In one study from Birmingham, UK, 22% of admissions with DKA were in subjects aged 60 years or more [24], while 13% of cases of hyperglycemic coma in all ages in Melbourne, Australia, were caused by hyperosmolar hyperglycemic state [25]. Many people with T2DM maintain enough residual insulin secretion to suppress lipolysis and ketogenesis, and so develop hyperosmolar hyperglycemic state instead of DKA; hyperosmolarity can worsen insulin resistance and may also inhibit lipolysis. The tendency to hyperosmolarity may be worsened in elderly people, who may not perceive thirst or drink enough to compensate for the osmotic diuresis, and are often taking diuretics [26].

Causes of hyperglycemia include infection (55% of cases in one series of hyperosmolar hyperglycemic state), myocardial infarction (MI), inadequate hypoglycemic treatment or diabetogenic drug treatment. Thiazide diuretics and glucocorticoids can increase blood glucose levels and may precipitate DKA; thiazide diuretics and furosemide (frusemide) appear particularly likely to cause hyperosmolar hyperglycemic state. A specific cause often cannot be identified – for example, in 38% of DKA cases in Birmingham [24]. Residents of care homes are at increased risk of hyperosmolar hyperglycemic state, which is associated with appreciable mortality [27].

Compared with the young, older patients have higher mortality and longer stays in hospital; they are also less likely to have had diabetes diagnosed previously, and more likely to have renal impairment and to require higher insulin regimens [28]. Death may occur from the metabolic disturbance or concomitant illnesses such as pneumonia and MI.

Investigation and treatment of hyperglycemic comas

The history and examination should pay special attention to previous diabetic symptoms, drug treatment, any precipitating infection (MI), possible MI or medication, evidence of heart failure and the degree of dehydration. Initial investigations are as for younger patients, including arterial blood gases and plasma osmolality (see Chapter 34).

Fluid, insulin and potassium replacement are discussed in general in Chapter 34. In elderly patients, intravenous saline can often be given at a rate of 500 mL/hour for 4 hours, then reducing to 250 mL/hour; faster infusion is needed if the patient is shocked, when a central line is invaluable to monitor filling pressure, particularly in the presence of cardiac failure or recent MI.

Some older subjects with hyperosmolar hyperglycemic state need very small doses of insulin to reduce plasma glucose levels, although hypercatabolic or severely insulin-resistant states will require higher dosages.

Thrombotic complications may occur, especially in subjects with hyperosmolar hyperglycemic state; prophylactic anticoagulation with low dose subcutaneous heparin is therefore recommended.

Hypoglycemia

Older patients are particularly susceptible to hypoglycemia, and this problem is often exacerbated because old people may have been given little knowledge about the symptoms and signs of hypoglycemia [29]. Even health professionals may misdiagnose hypoglycemia as a stroke, transient ischemic attack, unexplained confusion or epileptic fit, as illustrated in the case history below.

Case history

A 76-year-old man was admitted with a left-sided hemiplegia. He was unconscious and the family was told by the emergency room staff that he had had a stroke and his prognosis was very poor. At this point, no-one had thought to assess his glucose concentration. When requested by the medical registrar, it was found to be 1.4 mmol/L. Following treatment with IV glucose, the man regained consciousness and he was able to leave hospital 1 hour later. He had taken his insulin but delayed his meal.

Personal communication from Richard Holt, University of Southampton

Patients with cognitive impairment or loss of the warning symptoms of hypoglycemia are especially vulnerable, as they may not recognize impending hypoglycemia and/or fail to communicate their feelings to their carers. Multiple factors underlie the increased susceptibility to hypoglycemia in the elderly, including recent discharge from hospital with altered sulfonylurea dosages, renal and hepatic impairment, excess alcohol and insulin therapy [30]. In addition, older subjects mount a diminished counter-regulatory response to hypoglycemia [31], and this may delay recovery.

The risk of hypoglycemia is highest with insulin, but prolonged hypoglycemia is an important clinical problem for older subjects taking glibenclamide and chlorpropamide [32]. Glibenclamide-induced hypoglycemia may be more pronounced because the drug accumulates within the β-cell, and its metabolites retain some hypoglycemic activity. The long elimination half-life (approximately 35 hours) of chlorpropamide causes it to accumulate with continued dosing; steady-state is not achieved for 7–10 days. Impaired renal function further prolongs hypoglycemia secondary to sulfonylureas that are cleared through the kidneys. Short-acting sulfonylureas, gliclazide and tolbutamide,

are less likely to cause hypoglycemia [33], although glipizide is considered by some to be unsafe in the elderly [34]. Newer oral agents such as the thiazolidinediones and the meglitinides may decrease the risk of hypoglycemia in the elderly, as may both rapid- and prolonged-acting insulin analogs.

In the elderly, serious hypoglycemia appears to carry a worse prognosis and higher mortality; permanent neurologic damage may occur, presumably because of an already compromised cerebral circulation. Most sulfonylureas have caused fatal hypoglycemia, most commonly chlorpropamide or glibenclamide [35]. Other factors predisposing to fatal hypoglycemia include alcohol consumption, poor food intake, renal impairment and potentiation of hypoglycemia by other drugs.

Treatment and prevention of hypoglycemia are as described in Chapter 33. Many old people cannot treat hypoglycemia themselves [28]. The educational program should focus on detecting and treating hypoglycemia, with advice to others about how to manage cases of unresponsive hypoglycemia. In view of the additional vulnerability of older people to hypoglycemia, extra caution is required when there is a history of recurrent symptoms, drowsiness is present, the patient is on relatively large doses of insulin or when their diabetes care is delegated to an informal carer. This increased risk must be balanced by a lower threshold for admission to hospital when hypoglycemia is suspected. In this setting, a glucose level <4 mmol/L may warrant admission.

Chronic diabetic complications in the elderly

Diabetes in older subjects carries considerable morbidity, mainly through its long-term complications. For example, in a 6-year study of 188 patients aged over 60 years in Oxford [36], the reported incidence rates of ischemic heart disease, stroke and peripheral vascular disease (PVD) were 56, 22 and 146 cases per 1000 person-years, respectively. These were slightly higher than the rates in the Framingham study [37], presumably because of the older age of the Oxford patients. Retinopathy occurred at a rate of 60 cases and cataract at 29 cases per 1000 person-years, while the rate of proteinuria (albumin concentration >300 mg/L) was 19 per 1000 person-years. These incidence rates appeared to be unrelated to sex or duration of diabetes, but stroke and PVD rose significantly with age.

The age-dependence of chronic diabetic complications was also investigated in a cross-sectional study of patients with T2DM aged 53–80 years [38]. Logistic regression demonstrated a significant rise in the prevalence of retinopathy with aging, independent of the effects of metabolic control, duration of disease and other risk variables. Age also increased the prevalence of peripheral neuropathy, hypertension and erectile dysfunction. An independent contribution of age per se to retinopathy, however, was not reported by Ballard *et al.* [39] from Minnesota, USA (who found a positive relationship with persistent proteinuria only), or by Knuiman *et al.* [40], who studied patients with both type 1 diabetes (TIDM) and T2DM and found independent associations of age with renal impairment, macrovascular complications and sensory neuropathy only.

Diabetic eye disease and visual loss

Cataract, age-related macular degeneration and diabetic retinopathy remain the major causes of blindness and partial-sight registration in most developed countries (see Chapter 36) [41]. All these conditions are common in elderly patients with diabetes.

Cataract, the most frequent cause of deteriorating vision in the elderly, is more common in subjects with diabetes, even at the time of diagnosis; its presence is associated with premature death [16]. Age-related macular degeneration is also frequent in older patients with diabetes and is an important cause of central visual loss [42]. Risk factors include atherosclerosis, diastolic blood pressure >95 mmHg or antihypertensive medication, and elevated serum cholesterol. Most older patients with diabetes have diabetic retinopathy of some degree, although about 5% show no evidence of retinal damage even after 15 years of the disease [42]. The main sight-threatening consequence of diabetic retinopathy in this population is maculopathy and particularly macular edema (see Chapter 36).

In Nottingham, UK, 16% of elderly people with diabetes are registered blind or partially sighted which is approximately eight times more than among their counterparts without diabetes [43]. The Welsh Community Diabetes Study [44] found that visual acuity was impaired in 40% of elderly subjects with diabetes, compared with only 31% of controls without diabetes ($P < 0.007$). Factors significantly associated with visual loss in people with diabetes included advanced age, duration of diabetes, female sex, a history of foot ulceration and treatment with insulin. Reduced visual acuity was also significantly associated with poorer quality of life, as measured by the SF-36 questionnaire.

Screening for retinopathy

This is particularly important in the elderly, as deteriorating vision may be accepted by the patient as part of aging. Diabetic retinopathy may be the presenting feature of the disease in older people. Elderly people with diabetes need annual measurements of visual acuity and retinal photography; where the latter may not be available or feasible, patients should undergo dilated-pupil fundoscopy by experienced observers. Exudative maculopathy (hard exudates at or within one disc diameter of the macula) is easy to detect, but macular edema is practically impossible to detect by routine ophthalmoscopy; instead, slit-lamp stereoscopic fundoscopy is required to measure retinal thickness. Mydriasis is usually a short-term intervention and, in the great majority of cases, is not associated with any major problems, even in older people. It is always important to know whether patients have a history of glaucoma before mydriasis, as this requires a different approach, often under specialist supervision. This highlights the importance of measuring the corrected visual acuity, which is decreased by maculopathy (see Chapter 36). Indications for referral to an ophthalmologist

are generally identical to those in younger patients (see Table 36.3).

Prevention and management of diabetic retinopathy

The benefits of tight glycemic control in slowing the progression of diabetic retinopathy have been convincingly proven in both T1DM and T2DM, by the Diabetes Control and Complications Trial (DCCT) and UK Prospective Diabetes Study (UKPDS) trials, respectively [45,46]. In the UKPDS, the risk of retinopathy progressing was reduced by 25% when HbA_{1c} was maintained at <53 mmol/mol (7.0%) [46], while improved blood pressure control also reduced risk by 37% [47]. Although there have been no specific intervention studies in elderly patients with T2DM, it seems reasonable to extrapolate the general principles to this population. Problems with hypoglycemia and postural hypotension, however, prevent many elderly subjects from achieving tight glycemic and blood pressure control.

Laser photocoagulation should be used as indicated in Chapter 36; it halves the risk of severe visual loss with macular edema and exudative maculopathy (if visual acuity is 6/9 or better), which otherwise reaches 50–70% after 5 years [48–50]. It has been calculated that screening and treating diabetic retinopathy would prevent 56% of blind registrations resulting from this condition.

Diabetic foot disease

Amputation of a limb remains an important and expensive health problem in the diabetic population, with the elderly being particularly affected [51]. A Dutch study [52] identified increasing age and a higher level of amputation as important factors that increased both the duration and costs of hospitalization (estimated at over £10 000 per hospitalization, lasting an average of 42 days). The 3-year survival following lower-extremity amputation is about 50% [53]; in about 70% of cases, amputation is precipitated by foot ulceration [54]. The principal antecedents include peripheral vascular disease, sensorimotor and autonomic neuropathy, limited joint mobility (which especially prevents older people from inspecting their feet) and high foot pressures (Table 54.3) [51]. Most elderly people with diabetes are at increased risk of developing foot ulcers. Peripheral sensorimotor neuropathy, the primary cause or contributory factor in most cases, becomes more common with increasing age and affects 25% of patients with T2DM aged 80 years or more [55]. As well as the common symptoms of numbness, neurogenic pain, "pins and needles" and hyperesthesia (all typically worse at night), peripheral neuropathy often causes gait disturbances, falls and other foot injuries. Concomitant visual loss worsens the situation [56]. A trivial foot injury in a patient with severe neuropathy can eventually lead to Charcot arthropathy; most of these patients have had diabetes for at least 10 years, and many are elderly (see Chapter 44).

Table 54.3 Risk factors for foot ulceration in the elderly.

Peripheral sensorimotor neuropathy
Automatic neuropathy
Peripheral vascular disease
Limited joint mobility
Foot pressure abnormalities, including deformity
Previous foot problems
Visual loss
History of alcohol abuse

Treatment of painful neuropathy in older patients is often difficult. Recent-onset symptoms may remit with improved metabolic control, but pain associated with loss of sensation and of greater than 6 months' duration generally requires specific therapy. Localized pain may respond to topical application of capsaicin cream (0.075%), which depletes pain fibers of the neurotransmitter, substance P. Other drugs include tricyclic antidepressants (e.g. amitriptyline) and antiepileptics, such as carbamazepine and gabapentin (now licensed for this indication). Alternative treatments include transcutaneous nerve stimulation or acupuncture, as described in Chapter 38.

Ischemia, secondary to PVD and perhaps microcirculatory disturbances [57], is the other main contributor to diabetic foot ulceration. Macrovascular disease becomes more common with advancing age. As discussed in Chapter 39, atheromatous lesions in diabetes are more diffuse and involve vessels below the knee more often than in individuals without diabetes. Medial arterial calcification is common, especially in association with somatosensory and autonomic neuropathy; this change can affect Doppler ultrasound measurements of blood pressure in the foot and cause a misleadingly high ankle pressure index.

As in younger patients, many older people with diabetes and critical or worsening limb ischemia, or ischemic ulcers that are slow to heal, will benefit from surgical revascularization (angioplasty or arterial reconstruction). Appropriate cases should be referred early for surgery, ideally through joint protocols developed by the diabetes specialist and the vascular surgeon [58]. A reasonable life expectancy is considered important by surgeons, as concomitant cardiac and cerebrovascular disease kill 50% of patients within 5 years [59]. Following proximal arterial reconstruction, the 5-year patency averages 70% and may exceed life expectancy in patients with major co-morbidities; for distal reconstruction surgery, 5-year limb salvage rates approach 85% [59].

Strategies to prevent diabetic foot ulceration are based on a multidisciplinary approach to identifying, educating and treating high-risk patients; as discussed in Chapter 44, these measures can effectively reduce diabetes-related amputation rates. Many elderly patients have great difficulty in performing the most basic routine foot care [60], often because of poor vision and reduced mobility. In such cases, spouses and other carers must be involved to prevent and treat foot lesions. Education needs to be concise and repeated regularly; video presentations may also be helpful.

Coronary heart disease and arterial disease

Angina, MI, heart failure, stroke and intermittent claudication are substantially more common in elderly subjects with diabetes than in age-matched control groups without diabetes. Mortality is particularly high following MI, especially because of acute pump failure and later onset of left ventricular failure.

Many elderly patients with diabetes may present with atypical symptoms, including "silent ischemia" (which carries a worse prognosis than in the non-diabetic population); even MI may be painless and present non-specifically as a fall, breathlessness, malaise or hypotension.

Investigation and management of cardiovascular disease is covered in detail in Chapter 41.

Erectile dysfunction

Erectile dysfunction becomes more common in older adults and occurs earlier and more commonly in men with diabetes after 60 years of age; 55–95% of men with diabetes are affected, compared with 50% of their counterparts without diabetes [61]. It is often neglected, or attributed to a diminished quality of life or depressive illness. Vasculopathy, autonomic neuropathy, hormonal dysregulation, endothelial dysfunction and psychogenic factors have all been implicated, as have certain drugs (notably cimetidine, beta-blockers and spironolactone) and a high alcohol intake.

Investigation should generally proceed as for younger men, beginning with an interview with the patient and his partner, where appropriate. For many older patients, extensive testing is often avoided. Treatments include oral sildenafil (which achieved erections in 67% of elderly men in one study [61]), a vacuum tumescence device, misoprostol urethral pellets and self-administered intracorporeal injection of vasoactive drugs (e.g. prostaglandin E_1). The latter is relatively successful, but up to 50% of men eventually discontinue because of pain or loss of effect or interest [62].

Mental illness in elderly people with diabetes

Cognitive impairment and dementia

Diabetes and cognitive dysfunction are related and have evoked some interest over the last decade (Table 54.4). Impaired cognitive function has been demonstrated in elderly subjects with diabetes, but these studies were mostly not population-based, excluded subjects with dementia and generally used a large battery of tests to show the deficit [63]. Community-based studies in the UK (Melton Mowbray [64], Nottingham [43] and South Wales [65]) have shown worse cognitive function in elderly subjects with diabetes, using simple instruments such as the Folstein Mini-Mental State Examination (MMSE), Hodkinson's Abbreviated Mental Test (AMT), and the Clock Test. These are easily learned, bedside screening tests of mental status which test several cognitive domains such as memory, orientation, calculation, language and, in the case of the MMSE and Clock Tests, also test planning skills and visuospatial function.

Table 54.4 Background to relationship between diabetes and cognitive disorders. Reproduced from European Diabetes Working Party for Older People [92], with permission.

Professional and public concern about the impact of diabetes on cognition
Long-term influence of hyperglycemia and hypoglycemia on cerebral function unknown
Pathophysiologic mechanisms involved uncertain, but may involve both vascular, inflammatory and neuronal mechanisms
No current agreement on the most optimum method to detect or assess cognitive deficits in diabetes
Clinical relevance of the changes observed uncertain

Impaired glucose tolerance has also been shown to be associated with cognitive dysfunction [66]. It has been suggested that certain components of the metabolic syndrome (hyperglycemia, dyslipidemia, hypertension) may each contribute to memory disturbance in T2DM [67], and that hyperinsulinemia is associated with decreased cognitive function and dementia in women [68]. The Rochester study [69] has demonstrated that the overall risk of dementia is significantly increased for both men and women with T2DM; excess risk for Alzheimer disease achieved significance in men only. Poor glucose control may be associated with cognitive impairment, which recovers following improvement in glycemic control [70]. In other cases, vascular or "mixed" dementias are probably responsible.

Cognitive dysfunction in older subjects with diabetes has wide implications including increased hospitalization, less ability for self-care, reduced likelihood of specialist follow-up and increased risk of institutionalization [71]. Impaired cognitive function should be borne in mind when treating elderly subjects with diabetes, as it has implications for their safe treatment; it may cause difficulty with glycemic control because of erratic taking of diet and medication, including hypoglycemia when the patient forgets earlier administration of hypoglycemic medication and takes more.

Depression

Depression in diabetes is a serious co-morbidity associated with poor outcome and high health care expenditure (see Chapter 55). The presence of a major depressive disorder significantly increases the risk of diabetes [72], this association being apparently independent of age, gender or coexistent chronic disease [73]. Moreover, depression was the single most important indicator of subsequent death in a group of people with diabetes admitted into hospital [74]. Failure to recognize depression can be serious, as this is a long-term life-threatening disabling illness that can significantly damage quality of life. It is also associated with

worsening diabetic control [75] and decreased treatment compliance (see Chapter 55) [76].

The relationship between diabetes and depression is complex and may result from the presence of a chronic medical condition in a susceptible individual. There are also complex neuroendocrine and cytokine changes in both conditions that may provide an explanation to link these two conditions (see Chapter 55).

Diabetes and depression share similar symptomatology (e.g. fatigue, irritability and sexual dysfunction). This may delay or confuse the diagnosis, although the commonly used diagnostic assessment scales are unlikely to be invalidated. Enquiries about well-being, sleep, appetite and weight loss should be part of the routine history, with a more comprehensive psychiatric evaluation if appropriate. A Geriatric Depression Scale (GDS) score of >5 can be regarded as indicative of probable depression [77]. While the GDS-15 may be the scale of choice for older people without cognitive impairment, it does not perform as well in those with dementia. Depression in diabetes can be treated successfully with pharmacotherapy, and/or psychologic therapy, but blood glucose levels should be monitored closely especially with pharmacotherapy. Goals for treating patients with depression and diabetes are twofold:

1 Remission or improvement of depressive symptoms; and
2 Improvement of poor glycemic control if present [78].

The preferred first-line treatment is a selective serotonin reuptake inhibitor (SSRI) or a serotonin norepinephrin reuptake inhibitor and psychotherapy. Treatment with SSRIs, such as fluoxetine, may improve symptoms and consequently metabolic control although close observation for side effects and changes to glycemic control are needed [79].

There have been reports of an increase in T2DM following treatment with antipsychotic medication which is often prescribed for older people with mental illness. This use of antipsychotics often goes beyond the license of these drugs but nevertheless has been recommended by groups such as the US Expert Consensus Panel for Using Antipsychotic Drugs in Older Patients to treat psychosis and anxiety [80]. It is estimated that as many as half of all repeat prescriptions for antipsychotics occur in people aged over 65 years [81]. Between 38–43% and 60–80% of all elderly patients living in nursing homes or old age psychiatry units, respectively, receive antipsychotics. Around 20% of people aged over 80 years are affected by dementia and 25–50% of these develop psychotic symptoms that require treatment with antipsychotics.

A systematic review of 17 studies examined the relationship between treatment with several antipsychotic agents and the risk of developing diabetes; olanzapine had an increased odds ratio but the risk for risperidone was small [82]. Data are still relatively limited in the elderly but suggest that the relative risk is less than for younger people with schizophrenia. Nevertheless, it seems prudent to undertake regular monitoring of weight, glucose and lipid profile [83].

Disability

Disability in elderly people with diabetes

Chronic diabetic complications often cause considerable disability in older people. For example, a community-based survey from Nottingham, UK [43], found significant disability in 80% of 98 elderly inner-city patients with diabetes (mean age 73 years); common problems included visual impairment (especially cataract) and previous amputation.

One in four of subjects with diabetes aged over 65 years in the Welsh Community Diabetes Study [65] required assistance with personal care, while older people with diabetes had significantly lower levels of well-being in most of the domains of the SF-36 health status questionnaire. Moreover, one in three subjects with diabetes had been hospitalized in the previous 12 months (twice the rate of those without diabetes), and subjects with diabetes had significantly increased levels of both physical and cognitive disability.

Mortality in elderly subjects with diabetes

People with diabetes die prematurely, mostly from cardiovascular disease. Early reports suggested that excess rates among people with diabetes fell progressively with age, especially in those aged 65 years and over. This has been confirmed largely by the Verona Study, in which the standardized mortality ratio declined from a range of 2–3.5 for middle-aged subjects with diabetes to 1.75 in those aged 65–74 years and 1.3 in patients older than 75 years; at all ages, the impact of diabetes on the standardized mortality ratio was more pronounced in women [84]. A recent systematic review of the relationship between mortality and age has suggested a higher incidence of premature death in older subjects with diabetes [85]. Cardiovascular mortality is primarily responsible, accounting for 42% of the overall mortality in the Verona Study. In the Melton Mowbray, UK, study [86], excess mortality rose substantially in subjects with diabetes aged over 65 years, and impaired glucose tolerance was associated with a relative risk of death of 1.7.

Age remains the strongest predictor of mortality; the contributions of classic cardiovascular risk factors are uncertain in older subjects with diabetes. A Finnish study [87] concluded that smoking, hypertension, low high-density lipoprotein (HDL) cholesterol and high total cholesterol did not affect overall mortality. In the Verona Study, long-term metabolic control was a better predictor of outcome, and subjects with more variable glycemic control (measured by the coefficient of variation of fasting plasma glucose) had lower survival rates, especially in those aged over 75 years [88].

Methodologic variations have prevented a consensus from being reached across different diabetic populations. Unequivocal evidence of increased mortality would argue for a more sustained

commitment to diabetic health care provision; otherwise, future care strategies should focus on reducing morbidity and disability.

Clinical features of diabetes in the elderly

The presentation of diabetes in older people is varied and often insidious, which may delay diagnosis (Table 54.5) [1]. Many cases are detected by finding hyperglycemia during investigation for co-morbidities or acute illnesses. Some patients do not have classic features of either DKA or hyperosmolar hyperglycemic state, but present with a "mixed" disturbance of moderate hyperglycemia (blood glucose levels 15–25 mmol/L) and modest acidosis (arterial blood pH ≈7.2), but without marked dehydration or altered consciousness.

Recognition of the diverse, atypical and often cryptic symptom profile of hyperglycemia in older subjects can be helpful in making an early diagnosis (Table 54.5). Worryingly, however, even when hyperglycemia is recognized in hospital, about half of elderly subjects receive no further evaluation or treatment of diabetes [89].

Diagnosis of diabetes in the elderly

Diagnostic criteria are as in younger subjects. Mortality may be higher in those subjects diagnosed with diabetes on the basis of a 2-hour glucose value than with the new fasting criteria alone [90]. Moreover, isolated post-load hyperglycemia with normal fasting glucose (<7.0 mmol/L) is associated with increased fatal cardiovascular disease and heart disease in elderly women [91].

Some elderly patients have hyperglycemia secondary to acute illness, diabetogenic therapy or other stress-inducing disorders. This can be identified because the HbA_{1c} is normal, but the oral glucose tolerance test (OGTT) should be employed where doubt exists. Retesting following an acute illness may sometimes prevent a false diagnosis from being made. Particular difficulties may intrude: a true fasted sample may be difficult to obtain (and may be normal [90]), while an OGTT may be declined because it is time-consuming and inconvenient.

Table 54.5 Presentations of diabetes in older people.

Asymptomatic (coincidental finding)
Classic osmotic symptoms
Metabolic disturbances
• Diabetic ketoacidosis
• Hyperosmolar hyperglycemia syndrome
• "Mixed" metabolic disturbance
Spectrum of vague symptoms
• Depressed mood
• Apathy
• Mental confusion
Development of "geriatric" syndromes
• Falls or poor mobility: muscle weakness, poor vision, cognitive impairment
• Urinary incontinence
• Unexplained weight loss
• Memory disorder or cognitive impairment
Slow recovery from specific illnesses or increased vulnerability
• Impaired recovery from stroke
• Repeated infections
• Poor wound healing

Management of diabetes in the elderly

Prioritizing diabetic care

Ideally, elderly patients with diabetes should be treated as rigorously as younger subjects. Few studies have focused specifically on the elderly but a comprehensive set of evidenced-based clinical guidelines for T2DM in older people has been developed [92], and these provide a logical pathway for clinical decision-making in older people.

In older people, diabetes can cause much physical and mental impairment, and the individual's problems must be targeted effectively. Approaches such as the five-step evaluation shown in Table 54.6 [58] can help to shape the content of the care package.

Despite their numerous problems [65], about two-thirds of older people with diabetes are suitable for strategies to improve or optimize glycemic control (Figure 54.5). It is important to identify "frail" patients (i.e. those who are especially vulnerable to a wide range of diverse outcomes secondary to the effects of aging, chronic diabetic complications, physical and cognitive decline, and the presence of other medical co-morbidities). The Frailty Model of Diabetes [58] can assist clinical decision-making by defining factors (e.g. recurrent hypoglycemia, cardiac disease and reduced recovery from metabolic decompensation), which may herald disability and often directly threaten independence, yet may have preventable or reversible components. In clinical practice, the presence of a mobility disorder or severe restriction of activities of daily living, or the presence of several co-morbid-

Table 54.6 Prioritizing diabetes care in older adults: a five-step approach.

1	Functional assessment, including cognitive testing and screening for depression
2	Vascular risk assessment, especially vascular prophylaxis and lifestyle modification
3	Metabolic targeting ("single disease" or "frailty" models)
4	Devise appropriate interventions for diabetes-related disabilities
5	Assess suitability for self-care or carer assistance

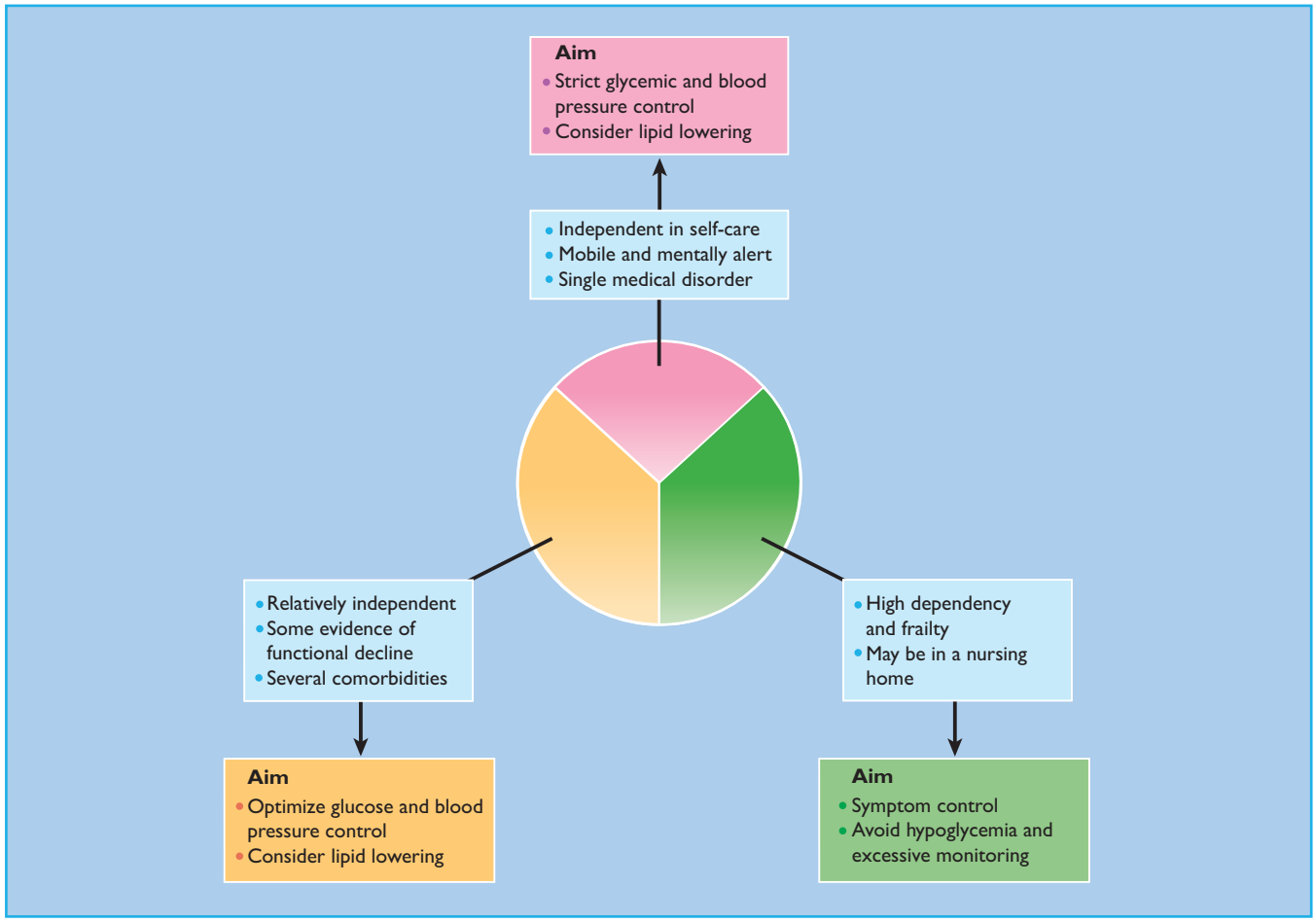

Figure 54.5 Matching treatment aims to functional assessments in elderly people with diabetes.

ities, and/or advanced age (>80 years) will increase the risk of becoming confined to a chair or bed by two- to threefold over 2 years [93].

Treatment targets for older people with diabetes

Table 54.7 lists metabolic and cardiovascular treatment targets appropriate for "strict" and "optimal" therapy, using evidence derived from large-scale clinical trials (referenced in full in Sinclair [58]); caveats about applying these data to the elderly are acknowledged comprehensively in the European Diabetes Working Party for Older People [92]. The European Guidelines have provided a series of glycemic targets to guide treatment (see box).

Because of the increased risk of hypoglycemia, a more realistic target HbA_{1c} in frailer subjects is often <64 mmol/mol (8.0%), which will still reduce hyperglycemic malaise and may decrease the risk of some vascular complications. There are conflicting data about the relationship between advancing age and HbA_{1c}: in a French study of telecom workers aged 18–80 years, HbA_{1c} rose with age but then fell in males [94]. In a smaller study of 93 subjects, however, advancing age was not related to glycated hemoglobin or fasting plasma glucose [95]. This is an area requiring further study.

As well as glycemic and blood pressure control, lipid-lowering therapy should be considered for subjects up to the age of 80 years. Thromboembolic prophylaxis (e.g. with aspirin [75 mg/

European guidelines for the management of glycemic control in older people with diabetes

For older patients with T2DM, with single system involvement (free of other major co-morbidities), a target HbA_{1c} (DCCT aligned) range of 7.0–7.5%* should be aimed for. Evidence level 1+; Grade of recommendation A. *The precise target agreed will depend on existing cardiovascular risk, presence of microvascular complications and ability of the individual to self-manage*

For older patients with T2DM, with single system involvement (free of other major co-morbidities), a fasting glucose range of 6.5–7.5 mmol/L can be regarded as indicating good control. Evidence level 2++; Grade of recommendation B

*IFCC HbA_{1c} 53–58 mmol/mol

Table 54.7 Treatment targets for elderly patients with diabetes.

Blood glucose levels
No specific studies in older people with diabetes
UKPDS: HbA_{1c} <53 mmol/mol (7%); fasting blood glucose <7 mmol/L

Blood pressure
UKPDS: ≤140/80 mmHg (not based on older subjects)
HOT Study: diastolic lowering to ≤83 mmHg
SHEP Study: systolic <150 mmHg
Syst-Eur study: systolic BP <160 mmHg

Blood lipid levels
No specific studies in older people with diabetes
LIPID, CARE, 4S, VA-HIT studies
- Total cholesterol <5 mmol/L
- High density lipoprotein (HDL) cholesterol >1.0 mmol/L
- Triglycerides <2.0 mmol/L

Aspirin use
ATS study: 75–325 mg/day reduced major cardiovascular events in high-risk patients by 25%
HOT study: 75 mg/day reduced major cardiovascular events by 15% and myocardial infarction by 36%

Key to clinical trials: ATS, Antiplatelet Trialists' Study; CARE, Cholesterol and Recurrent Events Study; HOT, Hypertension Optimal Treatment study; LIPID, Long-term Intervention with Pravastatin in Ischemic Disease; 4S, Swedish Simvastatin Survival Study; SHEP, Systolic Hypertension in the Elderly Program (US); Syst-Eur, Systolic Hypertension in Europe Trial; UKPDS, UK Prospective Diabetes Study; VA-HIT, Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial.

day] or clopidogrel [75 mg/day] [96] if aspirin is not tolerated) is appropriate in older subjects with diabetes and macrovascular disease or risk factors such as hypertension, obesity, albuminuria or cigarette smoking. Atrial fibrillation is more common in older subjects with diabetes, but there is no specific evidence to support full warfarin anticoagulation in this advanced age group.

Evaluation of cardiovascular risk

Evaluation of cardiovascular risk provides prognostic information and helps to target therapy for the primary and secondary prevention of coronary heart disease (CHD). The available methods estimate risk (e.g. 10–20%) over a 5- or 10-year period, and include the New Zealand tables [97] and data from the Framingham [98] and Seven European Countries studies [99]; all are limited by the lack of data from subjects over 74 years of age.

Reducing triglyceride levels may also help to reduce overall cardiovascular risk in older subjects. In a New Zealand study, subjects with T2DM aged over 70 years had an increased mortality if they were hyperlipidemic [100], while the Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT) study showed that treatment with gemfibrozil lowered cardiovascular mortality by over 20%; three-quarters of the latter subjects were aged 60–74 years, and 25% had diabetes [101].

A more recent study provides convincing evidence of benefit irrespective of age: the Heart Protection Study [102] included adults with diabetes aged 40–80 years treated with 40 mg simvastatin or placebo over a 5-year period. Treatment led to an average fall in low density lipoprotein (LDL) cholesterol of 1.0 mmol/L and resulted in a highly significant reduction of 27% in the incidence of first non-fatal MI or coronary death, and a 25% reduction in first non-fatal or fatal stroke. Evidence of benefit was observed as early as 12 months of treatment.

A relatively recent clinical trial comparing different antihypertensive regimens in the prevention of CHD and other cardiovascular events was terminated early because of the obvious significant benefits on mortality being achieved with an amlodipine-based regimen. This study involved subjects up to age 79 years, and in those with T2DM benefits were similarly realized [103]. These included the incidence of the composite endpoint (total cardiovascular events and procedures) compared with the atenolol-based regimen (hazard ratio 0.86; 95% CI 0.76–0.98; $P = 0.026$). In addition, fatal and non-fatal strokes were reduced by 25% ($P = 0.017$), PVD by 48% ($P = 0.004$) and non-coronary revascularization procedures by 57% ($P < 0.001$).

Angiotensin-converting enzyme (ACE) inhibitors can also improve cardiovascular outcome. The Micro-HOPE study investigated the effects of ramipril on macrovascular and microvascular disease in people aged over 55 years over a 4.5-year period [104]. All subjects were at high cardiovascular risk because of a previous event (e.g. stroke, MI, PVD) or diabetes together with another cardiovascular risk factor such as hypertension or dyslipidemia. Primary endpoints (stroke, or fatal or non-fatal MI) were significantly reduced from 20% to 15%, while all-cause mortality fell by 24%.

Several other recent studies have looked at the benefits of tighter glucose regulation in a wide range of subjects (including older subjects) with T2DM [105–107]. Excess cardiovascular mortality was demonstrated in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) in the intensive group where the average HbA_{1c} was 46 mmol/mol (6.4%) [105], whereas in the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) study [106] excess mortality was not demonstrated. Neither study indicated any benefit in reducing cardiovascular outcomes despite similar reductions in HbA_{1c} in the intensive groups. A further study in American veterans [107] with T2DM (average HbA_{1c}: 52 mmol/mol [6.9%] in the intensive group) also failed to show benefit at a level of HbA_{1c} in the range usually aimed for by most clinicians. The rates of hypoglycemia were significantly more common in the intensive groups in all studies.

For older people, these results pose several dilemmas in management: first, they do not answer the important clinical question of how to reduce cardiovascular risk, and, secondly, what is the optimal level to aim for which substantially reduces microvascular risk yet avoids severe hypoglycemia. For now we must continue to aim for realistic targets (similar to younger adults) for all those older patients who do not have marked evi-

Table 54.8 Principal aims in managing older people with diabetes.

Medical
Freedom from hyperglycemic symptoms
Prevent undesirable weight loss
Avoid hypoglycemia and other adverse drug reactions
Screen for and prevent vascular complications
Detect cognitive impairment and depression at an early stage
Achieve a normal life expectancy for patients where possible
Patient-orientated
Maintain general well-being and good quality of life
Acquire skills and knowledge to adapt to lifestyle changes
Encourage diabetes self-care

Table 54.9 Care plan for initial management of diabetes in an elderly person.

1	Establish realistic glycemic and blood pressure targets
2	Provide an estimate of cardiovascular risk over 5 years
3	Ensure consensus with patient, spouse or family, GP, informal carer, community nurse or hospital specialist
4	Define the frequency and nature of diabetes follow-up
5	Organize glycemic monitoring by patient or carer
6	Refer to social or community services as necessary
7	Provide advice on stopping smoking, increasing exercise and alcohol intake

dence of frailty. Intensified treatment in this latter category is not justified at present on the basis of these recent intervention studies.

The principal aims of managing diabetes in older adults are listed in Table 54.8. The priority of each may change with time, the development of complications or the need for external help. An initial diabetes care plan should be drawn up for the individual patient (Table 54.9). The guidelines of the International Diabetes Federation (IDF) for managing T2DM [108] appear equally applicable to older subjects although more detailed specialist guidance is now available [92]. Patients with T1DM are managed as in younger individuals.

Lifestyle modification

Dietary and lifestyle advice are given as for middle-aged subjects, including an exercise program if possible. These measures may be sufficient for subjects with minimal symptoms, whose initial random glucose levels lie between 8 and 17 mmol/L. If metabolic targets are not reached by 6–8 weeks, oral therapy is required [109].

Active management of other cardiovascular risk factors, especially hypertension and dyslipidemia, is necessary from the outset (Table 54.7).

Oral hypoglycemic agents

Sulfonylureas

Sulfonylureas are often used initially in elderly people with diabetes failing on diet, because they are generally well tolerated. Their main hazard is hypoglycemia. This is a particular problem with glibenclamide, the use of which has been associated with more fatalities than other sulfonylureas, including chlorpropamide; it must be strictly avoided in the elderly. Glipizide can cause prolonged hypoglycemia in older people and has been linked to hypoglycemic deaths in elderly Swedish subjects [34]. Gliclazide has a relatively low risk of hypoglycemia; it may be less likely to cause weight gain, the other common problem with sulfonylureas, and it is undoubtedly safer than glibenclamide [33]. A modified-release once-daily preparation of gliclazide is now available. Tolbutamide carries the lowest risk of hypoglycemia and can be used in those with mild renal impairment (serum creatinine <150 μmol/L (estimated glomerular filtration rate [eGFR] <42 mL/min/1.73 m^2 based on a 75-year-old non-black male) [110]. If compliance is uncertain, glimepiride may be useful, because the effective daily dose for all patients is one tablet before breakfast; however, there are no good comparisons between this and gliclazide.

With all sulfonylureas, the maximal glucose-lowering effect is about 4–5 mmol/L. Patients with very high glucose levels will not therefore achieve adequate glycemic control.

Metformin

Metformin is predictable and safe if it is used correctly and its contraindications are respected: these include renal impairment (serum creatinine >120 μmol/L, eGFR <54 mL/min/1.73 m^2 based on a 75-year-old non-black male), hepatic or cardiac failure, critical limb ischemia and severe acute illness. Accordingly, some 40–50% of older subjects are ineligible for the drug.

Particular advantages of metformin are that it does not cause hypoglycemia or weight gain on its own, and is inexpensive. Its glucose-lowering effect is similar to sulfonylureas, including in the elderly. The usual daily dose required is approximately 1.7 g, and it is as effective in the lean as in the overweight. Metformin was the only antidiabetic drug shown to reduce macrovascular events in the UKPDS, and all-cause mortality and combined diabetes-related endpoints were significantly lower with metformin than with insulin or sulfonylurea in obese subjects [111].

Acarbose

Acarbose has a weak hypoglycemic effect, including in elderly subjects. Slow introduction of the drug (e.g. 25 mg with the first mouthful of one meal per day initially) can help to diminish gastrointestinal side effects (bloating and flatulence) which often limit its use. Its main contraindications are inflammatory bowel disease and subacute obstruction. Acarbose can be combined with metformin, sulfonylureas or insulin.

Thiazolidinediones

Thiazolidinediones (TZDs) reduce insulin resistance by activating the peroxisome proliferator activated receptor γ (PPARγ). They lower glucose by 3–4 mmol/L and, as monotherapy, they reduce HbA_{1c} by 5–15 mmol/mol (0.5–1.4%). Although they do not cause hypoglycemia, their main problems are mild edema, dilutional anemia (in <5% of subjects) and weight gain, with a twofold increased risk of heart failure for which they are contraindicated. TZDs can be given in combination with metformin, sulfonylureas and glinides, and pioglitazone can be given with insulin in the UK (see Chapter 29). Several meta-analyses suggest that rosiglitazone treatment may be associated with an increased risk of MI although this has not been demonstrated for pioglitazone. Both TZDs are associated with an increased fracture risk, mainly in women, and this is an additional factor to consider when screening older people with osteoporosis for treatment with a TZD. They are safe in mild to moderate renal impairment; the liver damage associated with troglitazone (now withdrawn) does not appear to extend to rosiglitazone or pioglitazone, but frequent monitoring of liver function is required, especially during the first 12 months of treatment; this is a drawback for many older subjects.

Rosiglitazone and pioglitazone have comparable hypoglycemic effects and the latter shows a modest improvement in lipid profile; up to 6–8 weeks may elapse before the full beneficial actions are seen. These drugs can be given once daily, which is helpful for older patients.

Non-sulfonylurea insulin secretagogues (glinides)

Repaglinide is a benzoic acid derivative of the meglitinide class which predominantly lowers post-prandial hyperglycemia. It has a rapid onset of action and a lower risk of hypoglycemia than the sulfonylureas, and achieves better post-prandial glucose profiles. Repaglinide is predominantly metabolized in the liver to inactive metabolites and is safe in mild to moderate renal impairment. Tablets can be missed if meals are omitted, and it may be effectively combined with metformin and with thiazolidinediones (where license permits). Initially, 0.5 mg can be given with each meal (1 mg for subjects transferring from other oral agents), increasing to 4 mg with each meal.

Nateglinide is a recent meglitinide which has a faster and shorter duration of insulin secretory activity than repaglinide but is less effective as monotherapy or in combination than rapaglinide.

Insulin

Recent improvements in the organization of care between hospital and primary care, and the expanding roles of diabetes specialist nurses and general practice nurses, have made it easier and safer to use insulin in the treatment of older people with diabetes [112]. The main indications in the elderly are T1DM or T2DM where metabolic targets have not been achieved with diet, exercise and oral agents. It should also be used following acute MI (see Chapter 41), acute stroke, hyperglycemic coma and major surgery (see Chapter 32).

The main disadvantage of insulin is hypoglycemia, although the UKPDS found that fewer than 2% of subjects treated with insulin experienced a major hypoglycemic episode. Reported benefits include improvements in well-being and possibly quality of life [113–115] and in cognitive function [70], partly following improved glycemic control; however, others have found lower treatment satisfaction in insulin-treated patients [116].

Some guidelines for insulin treatment in the elderly are suggested in Table 54.10. Rapidly acting insulin analogs such as insulin lispro or insulin aspart may cause less hypoglycemia and weight gain, and can be given after eating where timing may be

Table 54.10 General guidelines for insulin treatment in older people.

	Indications	Advantages	Disadvantages
Once-daily insulin	Frail subjects Very old (>80 years) Symptomatic control	Single injection Can be given by carer or district nurse	Control usually poor Hypoglycemia common
Twice-daily insulin	Preferred if aiming for reasonable glycemic control Suitable for T1DM	Low risk of hypoglycemia Easily managed by most older people with diabetes	Normoglycemia difficult to achieve Fixed meal times reduce flexibility Expensive
Basal/bolus insulin	Well-motivated individuals For acute illness in hospital	Enables tight control Can reduce microvascular complications Flexible meal times	Frequent monitoring required to avoid hypoglycemia
Insulin plus oral agents	If glycemic control is unsatisfactory with oral agents alone To limit weight gain in obese subjects	Limits weight gain by reducing total daily insulin Increased flexibility	May delay conversion to insulin in thin or type 1 patients

unpredictable (e.g. because of memory disorder). In patients with T1DM, premixed insulins given twice daily may achieve reasonable glycemic control, although nocturnal hypoglycemia may be troublesome because of the longer-acting component of the pre-supper dose (see Chapter 27).

In older patients with T2DM, a twice-daily regimen of human isophane insulin can be used, adding short-acting insulin to cover meals if necessary. The newly introduced long-acting insulin analogs (e.g. insulin glargine and insulin detemir) have more reproducible pharmacokinetics and a "peakless" action profile, and may prove safer in older subjects. Once-daily insulin regimens alone are now little used, except where glycemic control is not a priority or injections are impracticable.

Insulin can usefully be combined with an oral agent in patients failing to be controlled by diet and oral agents. A suitable regimen is a night-time dose of intermediate-acting insulin (e.g. isophane) together with metformin, which causes less weight gain and hypoglycemia and better glycemic control than twice-daily insulin or combinations of glibenclamide with insulin or metformin [117]. The use of insulin in the elderly varies enormously even in developed countries. For frail subjects including those within care-home settings, complex regimens should be avoided so the use of longer-acting insulin analogs during the day often combined with oral agents is a feasible alternative.

Low-vision aids are available to help to inject insulin, and some insulin pens have audible clicks for counting doses.

Diabetic patients in care homes

In many developed countries the numbers of care-home residents are increasing and the prevalence of diabetes in this setting will inevitably increase. Recent surveys suggest that 7–27% of care-home residents in the UK and USA have diabetes. The wide range is partly because of differences in the diagnostic criteria used [17,118–120]; the prevalence of IGT may be as high as 30% [17]. People with diabetes in care homes should receive care commensurate with their health and social needs [121]. The best possible quality of life and well-being should be maintained, without unnecessary or inappropriate interventions, while helping residents to manage their own diabetes wherever feasible and worthwhile.

Metabolic control should reduce both hyperglycemic lethargy and hypoglycemia, with a well-balanced dietetic plan that prevents weight loss and maintains nutritional well-being. Foot care and vision require screening and preventive measures to maintain mobility and prevent falls and unnecessary hospital admissions.

At present, residents with diabetes in care homes appear to be generally vulnerable and neglected, with high prevalences of macrovascular complications and infections (especially skin and urinary tract), frequent hospitalization and much physical and cognitive disability. Known deficiencies of diabetes care include lack of individual management care plans and dietary supervision, infrequent review by specialist nurses, doctors and ophthalmologists, and poor knowledge and training for care staff [120,121].

Table 54.11 Some recommendations for improving diabetes management in care homes.

Screen on admission for diabetes and regularly thereafter
Policies must include strategies to minimize hospital admission, metabolic decompensation, pressure-sore development, pain, diabetes-related complications, infections and weight loss
All residents with diabetes must have an annual review and access to specialist services
Care-home diabetes policies must be developed nationally, locally and at the level of the resident with diabetes
Research based on interventional strategies is needed

Various strategies can improve diabetes care in this setting (Table 54.11) [117,122,123]. The impact of these initiatives is being followed on outcomes including well-being, metabolic control, access to regular review, rates of hospitalization and diabetic complications such as amputation and visual loss. A UK Task and Finish Group of Diabetes UK is revising previous guidelines and will be publishing new guidance at the beginning of 2010.

Modern diabetes care for older people

Structured diabetes care is particularly important for older people who are often neglected at present [124]; with the current shift in health care from hospitals to the community, GPs will have an increasingly important role [125,126]. This will require considerable motivation by the GP, effective screening for diabetes program and close liaison with diabetes specialist nurses (see Chapter 56). A shared-care approach, with GPs working in partnership with hospital-based diabetic and surgical specialists and based around agreed clinical protocols, is particularly valuable for older people.

A modern geriatric diabetes service (Figure 54.6) is based on a "multidimensional intervention" model [58]. This emphasizes the importance of early intervention in diabetic complications and of establishing rehabilitation programs for patients disabled by various complications such as amputation, peripheral neuropathy, immobility, falls, stroke and cognitive change. "Critical event monitoring" denotes monitoring periods of ill-health or social care need where patient vulnerability is high and opportunity for intervention is paramount (e.g. admission to hospital, amputation or stroke).

Health care must be cost-effective, which presents a difficult challenge for diabetes, because of its high prevalence, long duration of impact and wide spectrum of complications and emotional and psychologic sequelae; in older subjects, the challenge is even more complex because of the many other confounding factors.

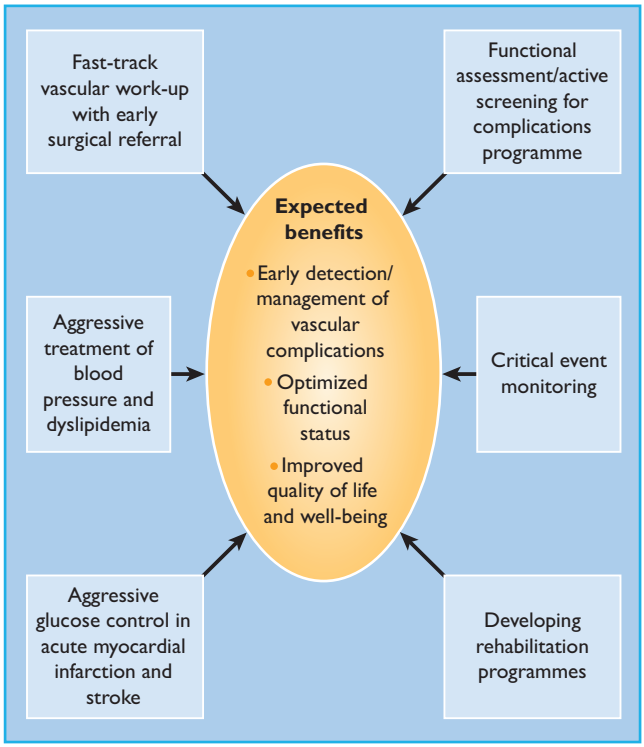

Figure 54.6 Components of a modern strategy for managing diabetes in the elderly.

Recent studies [127–129] have suggested that aggressive treatment of diabetes in older individuals is not warranted because of their reduced life expectancy; however, implementing the strategies outlined above seems likely to reduce acute hospitalization, outpatient costs and long-term disability. Only well-organized prospective clinical trials will be able to determine how best to manage diabetes in older people.

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