REVIEW

Diabetes Management

Older people with diabetes – avoiding hospitalization

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Practice points

- The prevalence of diabetes in older people is increasing.
- Geriatric syndromes such as cognitive impairment, physical dysfunction and frailty are emerging as a new category of complications in older people with diabetes.
- A disturbance in diabetes metabolic control (marked hyperglycemia or hypoglycemia), vascular complications or geriatric syndromes is the main risk factor that leads to hospitalizations.
- Comprehensive geriatric assessment is essential from the outset of diabetes care in older people.
- A multidisciplinary team approach with a multidimensional assessment and intervention to meet the complex need of older people with diabetes may help reduce acute hospitalization.

SUMMARY Diabetes phenotype in old age is characterized by increased prevalence of co-morbidities, geriatric syndromes and frailty. Interaction between geriatric syndromes and diabetes will have a synergistic effect to worsen adverse outcomes such as increased vascular complications, disability and hospitalization. Risk factors for hospitalizations include hypoglycemia, poor glycemic control, infections and acute exacerbation of the associated co-morbidities or geriatric syndromes. A large proportion of hospitalizations are preventable. Integrated care system between primary and secondary care to provide a holistic care for older people with diabetes with a focus on early and effective interventions, maintaining functional status and autonomy and promoting a good quality of life and well-being for each patient are warranted as part of any strategy to reduce hospitalization.

KEYWORDS
• diabetes • hospitalization • management • older people

Introduction

With increasing aging of the population and urbanization of lifestyle, the prevalence of diabetes is likely to increase especially in older people above the age of 75 years [1]. As a result, diabetes is increasingly becoming a disease of old age. Older people with diabetes are exposed to the interplay between metabolic dysfunction, vascular disease and the aging process in combination with other age-related disorders. Therefore, diabetes in old age is a disabling disease due to the traditionally associated vascular complications, coexisting morbidities and the increased prevalence of geriatric syndromes such as cognitive and physical dysfunction. Due to the complexity of diabetes in older people, it is associated with a substantial health burden on individuals and healthcare systems [2]. Older people with diabetes and their associated co-morbidities are at an increased risk of hospitalization with a long hospital stay [3]. In the USA, hospitalization attributable to diabetes

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costs 50% of the total direct medical expenditure for diabetes [4]. Appropriate management of older people with diabetes and the associated co-morbidities may differ substantially from the management of younger people with diabetes but without co-morbidities. This article reviews the diabetes phenotype in old age, risk factors for hospitalization and the management of diabetes with a focus on various aspects relevant to older people to optimize community care and look at ways to reduce hospitalization.

Epidemiology

As life expectancy increased due to a decline in cardiovascular mortality, the prevalence of diabetes is increasing [5]. The worldwide prevalence of diabetes increased with age from 12% in people aged 65–70 to 15% in those above the age of 80 years [6]. In France, the prevalence of diabetes peaks at the age of 75–79 years affecting 19.7% of men and 14.2% of women [7]. In the USA, more than 25% of the population aged ≥65 years have diabetes and more than 40% of adults with diabetes are older than 65 years. Projections by the Centre for Disease Control suggest that even if diabetes incidence rates level off, the prevalence of diabetes will double in the next 20 years, in part due to the aging of the population [8]. Other projections suggest that the number of cases of diagnosed diabetes in those aged ≥65 years will increase by 4.5-fold compared with threefold in the total population between 2005 and 2050 [9]. In care homes, the prevalence of diabetes is higher and affects around a third of residents [10]. Therefore, it appears that there is an epidemiologic shift for diabetes from being a disease of middle age to a disease of older people.

Diabetes phenotype in old age

Diabetes in old age is associated with a high co-morbidity burden with about 40% of older people with diabetes having at least three chronic conditions in addition to diabetes [11]. Diabetes is associated with accumulation of advanced glycation end products and increased atherosclerosis leading to premature aging and increased disability. On the other hand, geriatric syndromes are emerging as a third category of complications in addition to the traditional micro- and macrovascular disease in older people with diabetes **(Box 1)** [12]. Therefore, diabetes phenotype in old age is characterized by increased prevalence of physical and mental health dysfunction.

• Physical health

Malnutrition and anorexia are more common in older people with diabetes compared with those without [13]. Sarcopenic obesity, defined as excess body fat but loss of lean muscle mass, is common in older people with diabetes and is the most characteristic feature of frailty leading to muscle weakness, poor exercise tolerance and reduction in function [14]. Older people with diabetes tend to have an accelerated aging process that places them at greater risk of developing frailty at an earlier age [15]. Frailty refers to a condition of decreased reserve and resistance to stressors. It is defined as a clinical syndrome in which three or more of the following criteria are present: unintentional weight loss (≥4.5 kg in past year), self-reported exhaustion, weakness (grip strength), slow walking speed and low physical activity [16]. Development of frailty leads to a decline in function and eventual disability. It has been shown that about 28% of older people with diabetes require some help with activities of daily living (ADL) compared with only 16% of those without diabetes and only half of the cases of functional decline were explained by the traditional complications of diabetes such as coronary artery disease, stroke and peripheral vascular disease. The unexplained worsening in function could be due to muscle weakness and frailty [17]. Diabetes is associated with a twofold increased risk of being unable to perform daily physical tasks such as walking, doing house work or climbing stairs and 1.6-fold greater risk of difficulties performing basic personal care such as bathing, using the toilet, dressing and eating. Diabetes complications such as neuropathy, arthritis and vascular disease are contributors to physical disability in older people with diabetes [18,19]. The Study of Osteoporotic Fractures has shown that diabetes also increases the risk of falls (odds ratio [OR]: 2.78; 95% CI: 1.82–4.25). History of arthritis, musculoskeletal pain, depression, poor vision and peripheral neuropathy are the main predictors of falling among older people with diabetes [20]. Therefore, diabetes in old age can be associated with a decline in function and physical health in term of increased frailty and disability.

• Mental health

Cognitive dysfunction and depressive symptoms are common in older people with diabetes. Incidence of vascular-type dementia increases in older people with diabetes due to the increased

prevalence of cerebrovascular disease, increased inflammation, endothelial dysfunction, oxidative stress and insulin resistance [21]. On the other hand, accelerated brain aging due to altered amyloid metabolism, increased protein glycation and direct cerebral glucotoxicity may explain the increased incidence of Alzheimer's-type dementia [22]. Repeated episodes of hypoglycemia may contribute to cognitive dysfunction [23]. Cerebral atrophy and hippocampal atrophy are reported more frequently in older people with diabetes and contribute to cognitive dysfunction especially impairment in immediate memory [24]. The risk of developing Alzheimer disease or vascular dementia is twofold in older people with diabetes compared with age-matched control subjects without diabetes [25]. It has been shown that the relative risk (RR) of Alzheimer's disease is 1.56 (95% CI: 1.41–1.73) or 56% increase, vascular dementia is 2.27 (95% CI: 1.94–2.66) or 127% increase and all types of dementia is 1.73 (95% CI: 1.65–1.82) or 73% increase [26]. Over 10 years, the risk of developing dementia is 5.3% (95% CI: 4.2–6.3) for the lowest co-morbidity score (-1) and 73.3% (95% CI: 64.8–81.8) for the highest (95% CI: 12–19) score. Age, microvascular disease, diabetic foot, cerebrovascular disease, cardiovascular disease, acute metabolic events, depression and education were most strongly predictive of dementia and constituted the risk score [27]. Depressive symptoms affect about 30% of older people with diabetes and up to 10% have major depression [28]. The prevalence of depressive symptoms is associated with the presence of diabetes complications such as impairment of ADL, disability, urinary incontinence and increased number of hospitalizations [28]. In the Health, Aging, and Body Composition Study, older people (70–79 years old) with diabetes showed increased incidence of depression compared with persons without diabetes (23.5 vs 19.0%; hazard ratio [HR]: 1.31; 95% CI: 1.07–1.61) [29]. Diabetes also increased the risk of prevalent depression (OR: 1.47; 95% CI: 1.16–1.83) and incident depression (OR: 1.40; 95% CI: 1.03–1.9) in a Spanish community-based study [30]. Diabetes-related distress, defined as patient concerns about disease management, support, emotional burden and access to care is another important condition distinct from depression [31].

Hospitalization risk

Older people with diabetes have five-times the risk of admission to hospital and stay twice as long as inpatients compared with those without diabetes [32]. In addition to the traditional vascular complications and acute metabolic decompensation of diabetes that lead to hospital admissions, there are other risk factors for hospitalization specific to older people with diabetes **(Box 2)**.

Box 1. Functional effects of diabetes in old age.

Physical function

- Malnutrition
- Frailty
- Falls and fractures
- Disability with limitation in performing activities of daily living
- Urinary incontinence
- Visual and hearing impairment
- Chronic pain

Mental function

- Depression
- Dementia

• Co-morbidity-related risk

Co-morbid conditions increase the likelihood of preventable hospitalizations among older people with diabetes. In a study of a random sample of Medicare beneficiaries, about 7% of all hospitalizations were classed as avoidable. The likelihood of a preventable hospitalization increased in the presence of ambulatory care sensitive conditions (ACSC) that could have been prevented with appropriate outpatient care. The likelihood of a preventable hospitalization increased in the presence of cardiovascular co-morbidities such as congestive heart failure, cardiomyopathy, coronary atherosclerosis, hypertension or cardiac dysrythmias and noncardiovascular co-morbidities such as chronic obstructive pulmonary disease, asthma, dementia, anxiety, depression and osteoporosis [33]. More recently, it has been shown that one-fifth of hospital admissions of older people (≥65 years) with diabetes were due to potentially preventable hospitalizations. Of these hospitalizations, 43.7% were due to acute conditions (most common was pneumonia 58.6% followed by urinary tract infections 28.2%) and 56.3% were due to chronic conditions (most common was congestive cardiac failure 77.0% and chronic obstructive pulmonary disease 14.1%). Congestive heart failure, respiratory and urinary tract infections and chronic obstructive pulmonary disease accounted for

89.1% of admissions. The risk of admission due to a chronic condition was consistently higher among patients with multiple chronic co-morbidities compared with those who had diabetes only suggesting that timely and effective comprehensive outpatient and community care, beyond glycemic control, may reduce the impact of co-morbidity on unnecessary hospitalization in older patients with diabetes [34].

• Hypoglycemia-related risk

In a retrospective study to assess the frequency and most common causes of hospitalization in older (≥65 years) compared with younger (<65 years) people with Type 2 diabetes mellitus in the USA, hypoglycemia was a common cause for diabetes-related hospitalizations (22.9%) and the age-specific rate was nearly 2.5-fold higher in older compared with younger people (38.3 vs 11.4%) [35]. In another study to estimate the rate of hospitalization due to adverse drug events in older people, nearly half of hospitalizations (48.1%; 95% CI: 44.6–51.6) involved adults ≥80 years old and the population rate of hospitalizations was 3.5-times higher among adults ≥85 years old compared with those 65–69 years of age (4.6 hospitalizations per 1000 persons, 95% CI: 2.5–6.8 vs 1.3; 95% CI: 0.7–1.8). About two-thirds of hospitalizations were due to unintentional overdoses (65.7%; 95% CI: 60.1–71.3). Insulin and oral hypoglycemic agents constituted 24.6% of drug-related hospitalizations. Nearly all hospitalizations attributed to hypoglycemic medications were for hypoglycemia (94.6%) due to unintentional overdoses. An estimated two-thirds of these hospitalizations (66.6%; 95% CI: 56.9–76.3) involved neurologic symptoms (loss of consciousness, seizures, changes in mental status or other neurologic sequel). Therefore, coordinated efforts to promote safe management of hypoglycemic medications may have the potential to reduce adverse events leading to hospitalization of older patients with diabetes especially those above the age of 80 years [36].

Box 2. Risk factors for hospitalization in older people with diabetes.

- Multiple co-morbidities
- Physical and cognitive dysfunction
- Frailty
- Hypoglycemia
- Uncontrolled diabetes
- Depression
- Falls and fractures
- Polypharmacy, noncompliance and medication errors
- Infections
- Lack of carer support
- Breakdown in community support package

• Falls-related risk

Diabetes increases fracture risk by 64% regardless of bone mineral density. In the Health, Aging, and Body Composition Study of 2979 participants aged 70–79 years, diabetes was associated with elevated fracture risk (RR: 1.64; 95% CI: 1.07–2.51) after adjustment for hip bone mineral density and fracture risk factors. Impaired fasting glucose was not significantly associated with fractures (RR 1.34; 95% CI: 0.67–2.67). Participants with diabetes and fractures were more likely to have reduced peripheral sensation (35 vs 14%), transient ischemic attack or stroke (20 vs 8%), a lower physical performance battery score (5.0 vs 7.0) and falls (37 vs 21%) compared with those with diabetes but without fractures ($p < 0.05$) [37]. Diabetes was also associated with a higher rate of injurious fall requiring hospitalization (HR: 1.48; 95% CI: 1.12–1.95) in models adjusted for age, race, sex, BMI and education. In those participants using insulin, compared with participants without diabetes, the HR was 3.00 (95% CI: 1.78– 5.07). Among participants with diabetes, a history of falling, poor standing balance score and poor glycemic control (HbA1c level ≥8%) were risk factors for an injurious fall requiring hospitalization [38]. Therefore, older people with diabetes may benefit from fracture prevention efforts, if they have greater risk factors for fractures and specific diabetic complications.

• Physical & mental function decline-related risk

In a prospective study of 2064 older (≥65 years) persons who participated in the National Health Interview Survey in Taiwan, older people with diabetes were significantly more likely to have limitations in performing ADL, worse self-rated health and had an increased risk of hospitalization. After adjustment for potential confounders, diabetes, ADL limitation and worse self-rated health independently predicted hospital admission within 1 year [39]. Cognitive decline may lead to inability to correctly manage medications and diabetes-related self-care. This may result

in increased hospitalization and increased need for assistance in personal care [40]. Decline in mood and depression has also been shown to be associated with ACSC-related hospitalization (HR: 1.41; 95% CI: 1.15–1.72) in a population-based study of 4128 patients with diabetes after adjustment for baseline demographic, clinical and behavioral factors [41].

• Compliance-related risk

It has been shown that low levels of medication compliance increase the risk of hospitalization in patients with diabetes (OR: 1.58; 95% CI: 1.38–1.81; $p < 0.001$) [42]. Ability to adhere to prescribed treatment regimens may be difficult because of the complexity of co-morbid medical conditions. Older people with diabetes may find it difficult to manage multiple complex treatment regimens due to depressed mood, cognitive dysfunction and high burden of illness. Therefore, interventions to improve patient adherence to therapeutic recommendations may help reduce hospitalization [42].

• Infections-related risk

The occurrence of pneumonia increases the risk of hospitalization in older people with diabetes. In a population-based case–control study, the adjusted RR for pneumonia-related hospitalization among persons with diabetes was 1.26 (95% CI: 1.21–1.31) compared with individuals without diabetes. Duration of diabetes ≥10 years (RR: 1.37; 95% CI: 1.28–1.47) and poor glycemic control with HbA1c ≥9% (RR: 1.60; 95% CI: 1.44–1.76) were associated with increased the risk of a pneumonia-related hospitalization [43].

Management

Management of diabetes in older people should take into account their heterogonous nature, complex needs, address their risk factors for hospital admission and adopt targets that are relevant to them to optimize their quality of life (QoL) and to reduce hospitalization.

Diagnosis

Symptoms of diabetes become less intense with increasing age and diabetes can be totally asymptomatic in up to 50% of cases [44]. Symptoms may also be grossly nonspecific such as increasing lethargy or tiredness and can be attributed to the aging process. One of the geriatric syndromes such as falls or urinary incontinence may be the first manifestation of diabetes in old age. The increased renal threshold of glucose and reduced thirst sensation with aging is associated with diminished perception of the traditional osmotic symptoms of diabetes such as polyuria and polydipsia. Therefore, diabetes may be diagnosed on a normal routine blood testing or nonketotic hyperosmolar coma may be a first presentation. Diagnostic criteria for diabetes are not age specific. Diabetes is diagnosed, if fasting plasma glucose is more than 7 mmol/l or the 2-h postprandial glucose is above 11.1 mmol/l regardless of age [45]. However, fasting blood glucose is less sensitive in diabetes diagnosis in old age and can miss up to a third of patients but postprandial hyperglycemia or the 2-h glucose tolerance test appear to capture undiagnosed cases [46]. HbA1c is another diagnostic test for diabetes with a cutoff level of more than 48 mmol/mol (>6.5%). It has the advantage of convenience to patients, less day-to-day variability, specificity for diabetes and it is standardized internationally. However, although HbA1c has high specificity (98.7%), its low sensitivity (46.8%) means that below threshold HbA1c may miss more than half of cases of diabetes [47].

Treatment

Cardiovascular complications remain the main cause of mortality affecting about 50–75% of all deaths in patients with diabetes [48]. Therefore, hyperglycemia should not be treated in isolation but a holistic view of the collective cardiovascular risk reduction should be adopted. On the other hand, geriatric syndromes involving decline in physical and mental function is an emerging complication of diabetes in old age and should be addressed in the management plan of this age group **(Box 3)**. Management of cardiovascular risk factors should include both lifestyle modification and pharmacological interventions.

• Lifestyle modification

Lifestyle modification includes changes in diet, weight reduction in obese individuals, smoking cessation and regular exercise to reduce visceral obesity and improve insulin sensitivity. Smoking cessation may be the single most effective means of reducing mortality in high-risk populations [49]. A diet that is rich in fiber and potassium and low in saturated fat and refined carbohydrates and salt improves the lipid profile and significantly lowers blood pressure [50]. The achievement of ideal body weight, with reduction of obesity in overweight persons and increasing

muscle mass in frail ones, through diet changes and exercise will reduce the overall cardiovascular risk and will have a favorable effect on the metabolic profile of lipids, glycemia and blood pressure. Lifestyle interventions improve insulin sensitivity and the metabolic risk factors for cardiovascular disease [51]. Additional benefits of exercise for older people may include increased muscle strength and improved walking balance. The Look Action for Health in Diabetes (AHEAD) study in the middle aged and older people with Type 2 diabetes showed that weight loss and improved fitness lowered the risk for loss of mobility [52].

• Hyperglycemia

Although the evidence in reducing microvascular disease by tight glycemic control is established, there is no convincing evidence that reducing blood glucose to near normal levels results in lower cardiovascular events. Early data from the UKPDS which included 5102 newly diagnosed patients with diabetes, mean (SD) age 54 (8), showed equivocal results with a nonsignificant (p = 0.052) 16% reduction in myocardial infarction with tight glycemic control but significant reduction by 39% (p = 0.01) in the metformin group, which included only 342 obese patients [53]. Data from the three more recent prospective trials failed to show macrovascular benefits of tight glycemic control but increased risk of hypoglycemia **(Table 1)**. The ACCORD, [54] ADVANCE [55] and VADT [56] studies included 10,251, mean (SD) age 62.2 (6.8), 11,140, mean (SD) age 66 (6) and 1791, mean (SD) age 60.5 (9), Type 2 diabetes patients, respectively, with coexisting risk factors and history of cardiovascular complications. The ACCORD study was prematurely discontinued after 3.5 years of follow-up due to excess mortality in the intensive therapy arm (5 vs 4%). The ADVANCE study demonstrated a 10% reduction in composite of micro- and macro-vascular events (HR: 0.90; 95% CI: 0.82–0.98; p = 0.01) over a 5 years follow-up, but it did not remain significant after adjustment for reduction in nephropathy. The VADT study showed no significant reduction in the cardiovascular events (HR: 0.88; 95% CI: 0.75–1.05; p = 0.14). However, in the UKPDS follow-up study, risk reduction of myocardial infarction emerged after 10 years (HR: 0.85; 95% CI: 0.74–0.97; p = 0.01) [57]. The UKPDS included only patients with newly diagnosed diabetes and excluded those with significant cardiovascular disease or those above the age of 65 years. In contrast, participants in the three more recent studies were older, had longer duration of diabetes, high use of insulin (among 35–50% of subjects) and a third (32–40%) already had preexisting heart disease suggesting that their cardiovascular disease was already established before intervention minimizing the benefit of tight glucose control. In frail older patients, the benefit of blood glucose control diminishes in the presence of other co-morbidities. In older people (75–79 years) with diabetes, blood pressure control appears to be more beneficial than blood glucose control and the benefit from both therapies proportionally declines with increasing level of co-morbidities and functional impairment [58]. Therefore, in older people who are frail with multiple co-morbidities and functional impairment, tight control may be more harmful by inducing hypoglycemia. It is important to address individual goals of therapy, guided by patient preferences, life expectancy, co-morbidities and the influences of therapy on QoL.

• Hypertension

A target BP around 140 mmHg systolic is reasonable in older patients with diabetes. It has been shown that BP control to maintain systolic BP between 130–140 mmHg is associated with reduction of adverse cardiovascular outcomes compared with uncontrolled systolic BP more than 140 mmHg among hypertensive patients (age ≥50 years) with diabetes. The INVEST study concluded that controlling systolic BP less than 130 mmHg was not associated with better cardiovascular outcomes than usual control of 130–140 mmHg in individuals ≥55 years, mean (SD) age 66 (6), and it was associated with slightly increased risk of mortality (11.0% in the tight vs 10.2% in the usual control groups, respectively [adjusted HR: 1.20; 95% CI: 0.99–1.45; p = 0.06]) [59]. Tight BP control (target <120 mmHg systolic) was also not beneficial and was associated with adverse outcomes in older people (40–79 years) with diabetes [60]. The ONTARGET also had similar conclusions for older individuals, mean (SD) age 66 (7), 57% of whom were ≥65 years old [61]. Two meta-analyses of older people with diabetes did not show benefits for myocardial infarction or mortality with BP less than 140 mmHg [62,63]. In the very old patients (>80 years), targets may be even more relaxed.

The Hypertension in the HYVET which included older people ≥80 years of age with sustained systolic BP more than 180 mmHg, 7% of whom had diabetes, showed a significant 33.7% (HR: 0.66; 95% CI: 0.53–0.82; p < 0.001) reduction in cardiovascular events with BP control (target BP: 150/80 mmHg). However, the individuals included in HYVET were healthier than those in the general population with a low base line rate of known cardiovascular disease (11.5%), myocardial infarction (3.1%) or heart failure (2.9%). Therefore, the results may not apply to all older persons, especially those with multiple co-morbidities or living in care homes [64]. In another community study of the very old (≥85 years old), there was a U-shaped relationship with systolic blood pressure of 164.2 mmHg (95% CI: 154.1–183.8 mmHg) being associated with the lowest mortality suggesting that the optimal systolic blood pressure for this age group could be more than 140 mmHg [65]. Thiazide diuretics, angiotensin receptor blockers, angiotensin converting enzyme inhibitors and calcium channel blockers are reasonable first choice agents although higher doses of diuretics could worsen blood glucose and lipid levels. Most patients will require more than one antihypertensive agent for BP control.

Box 3. Diagnosis and assessment of diabetes in old age – special considerations.

Diagnosis

- Symptoms may be absent in up to 50% of patients
- Osmotic symptoms are less prominent
- Other symptoms may be nonspecific such as fatigue or lethargy
- A change in memory may be a first sign
- Fasting blood glucose may be normal in up to a third of cases
- Postprandial or 2-h oral glucose tolerance test is more reliable
- HbA1c is specific but less sensitive diagnostic test

Assessments

Comprehensive geriatric assessment should be performed on initial diagnosis and annually including assessment of:

- Cognitive function
- Screening for depression
- Assessment for frailty
- Falls risk
- Activities of daily living ability
- Presence of urinary incontinence and chronic pain
- Nutritional status
- Medication compliance and polypharmacy
- Social circumstances

• Dyslipidemia

There are no large clinical trials of lipid-lowering interventions specifically in older people with diabetes. Post-hoc analysis of the Heart Protection Study, which included patients who had diabetes and were between 40 and 80 years, showed a significant 25% risk reductions of cardiovascular events [66]. A meta-analysis of 18,686 people with diabetes in 14 trials of statin therapy for primary prevention showed a similar 20% RR reduction in major adverse vascular outcomes in older (≥65 years) compared with younger (<65 years) people [67]. Cardiovascular prevention with statins emerges fairly quickly (within 1–2 years) suggesting that statins may be indicated in nearly all older people with diabetes except those with very limited life expectancy. In the very elderly (>80 years), cholesterol targets are not yet very clear. A review of observational studies including 13,622 participants showed that low total cholesterol (<5.5 mmol/l) was associated with the highest mortality rate in those more than 80 years old [68]. The routine use of a fibrate or niacin in addition to a statin therapy failed to further reduce cardiovascular events and is not recommended [69,70]. From the above evidence, lowering cholesterol with statin therapy seems to be beneficial in older people with diabetes, however, it may not be suitable for frail elderly with limited life expectancy.

• Aspirin therapy

Aspirin has been shown to reduce cardiovascular morbidity and mortality in patients with a history of cardiovascular disease [71]. However, evidence for aspirin use in primary cardiovascular risk prevention is still not clear. A meta-analysis of aspirin treatment in patients with diabetes in primary prevention studies demonstrated a trend toward a 10% reduction in the cardiovascular events [72]. Presence of diabetes per se does not justify aspirin use. However, most of older patients with diabetes will have a high burden of cardiovascular risk factors and likely to benefit from aspirin therapy. Therefore, aspirin use should be considered selectively in older patients with diabetes and high cardiovascular risk but after assessment of their bleeding risk [73].

Avoiding hospitalization

Many hospitalizations of older people with diabetes can be avoided. Risk factors that precipitate hospitalizations should be addressed in the care plan for each patient.

• Avoiding medication-related hospitalization

Older people with diabetes are heterogeneous individuals with varying degrees of co-morbidity and function level. The guidelines are largely disease specific, age neutral and driven by numerical surrogates such as HbA1c or blood pressure levels but do not necessarily consider hard end points and outcomes relevant to older people such as physical function, disability or QoL [74]. Indiscriminate application of guidelines may lead to overtreatment and polypharmacy with potential harm and increased hospitalization in this age group. For example, elderly individuals are more liable to experience adverse effects to antihypertensive medications such as rennin angiotensin aldosterone system (RAAS) blockers leading to acute kidney injury, hyperkalemia or hypotension with further deterioration of renal function especially in those already known to have chronic kidney disease (CKD). Withdrawal of RAAS blockers in elderly patients (mean age: 73.3 years) with stage 4 and 5 CKD has been shown to improve kidney function [75]. A gradual decrease of BP is also an essential strategy in treating elderly patients with hypertension to avoid accelerated drop in BP with subsequent falls. BP should be measured lying and standing and patients asked about orthostatic symptoms to avoid orthostatic hypotension. It is important to realize that the presence of orthostatic symptoms such as dizziness, light headedness or faintness is associated with increased risk of falls (OR: 8.21; 95% CI: 4.17–16.19) rather than orthostatic hypotension per se [76]. Avoidance of hypoglycemia is essential especially in those with impaired kidney or liver function, which delay the clearance of hypoglycemic medications [77]. Glycemic goals should be regularly reviewed and hypoglycemic medications adjusted with increasing age of the patients especially with the onset of cognitive impairment or frailty. Declining body function associated with weight loss, malnutrition and frailty may lead to reduced body needs of hypoglycemic medications and increased risk of hypoglycemia. Hypoglycemic medications have been safely withdrawn in a cohort of frail nursing home older patients with Type 2 diabetes, mean (SD) age 84.4 (6.8) years [78] and in another group of older patients in the community, mean (SD) age 86.5 (3.2) years attending outpatient clinic without deterioration of their glycemic control [79]. The main characteristics of these patients were significant weight loss, increased co-morbidities including dementia and polypharmacy with recurrent hypoglycemia [79]. Therefore, patients with these criteria appear to be suitable candidates for a trial of hypoglycemic medication withdrawal. Higher doses of statins should be used with caution in frail elderly patients, who may be more susceptible to drug-related myopathy as statin toxicity is dose related. The use of nonsteroidal anti-inflammatory drugs should be used carefully in older people with diabetes especially those with CKD due to the increased risk of acute kidney injury. Older patients with diabetes who require imaging with radio contrast agents use should be well hydrated before undertaking the test and their kidney function carefully monitored thereafter.

• Avoiding geriatric syndromes-related hospitalization

Geriatric syndromes such as functional disability, falls, sepsis, depression and cognitive

Table 1. Cardiovascular benefits in the recent diabetes studies.

Parameter	ACCORD	ADVANCE	VADT	UKPDS follow-up
Number of patients	10,251	11,140	1791	3277
Mean (SD) age (years)	62.2 (6.8)	66 (6)	60.5 (9)	62 (8)
HbA1c (intensive vs standard, %)	6.4 vs 7.5	6.5 vs 7.3	6.9 vs 8.4	7.9 vs 8.5 (Su/Ins) 8.4 vs 8.9 (Met)
Duration of diabetes on start of study (years)	10.0	8.0	11.5	Newly diagnosed on start of intervention study
History of cardiovascular disease	35%	32%	40%	Patients with significant CVD were excluded
Cardiovascular outcome	Harmful effect	No benefit	No benefit	Beneficial effect

CVD: Cardiovascular disease; Ins: Insulin; Met: Metformin; Su: Sulfonylurea.
Data taken from [54–57].

dysfunction are risk factors for hospitalization of older people with diabetes **(Figure 1)**. Therefore, comprehensive geriatric assessment should be performed when older patients are first diagnosed with diabetes and included in their annual reviews with efforts made to reduce aggravation of geriatric syndromes. Diabetes is a risk factor for falling (OR: 2.25; 95% CI: 1.21–4.15; p = 0.010) [80]. Exercise programs may help reduce disability and risk of falls. Targeted training including gait, balance and functional strength exercises has been shown to improve gait speed, balance, muscle strength and joint mobility in patients with diabetes [81]. Resistance training increases muscle mass, strength and power that leads to increased mobility and a decreased risk of falling [82]. Patients should be directly asked about the occurrence of falls and assessed for their gait and balance, which can be tested by the timed 'get-up-and-go' test that involves asking the patient to stand up and walk for 3 m then turn round, walk back to the chair and sit down. Impaired mobility is diagnosed if this takes more than 30 s. Patients diagnosed with impaired mobility or had history of falls should be referred for exercise training program. As malnutrition is associated with frailty and subsequent disability, nutrition should part of regular assessment in addition to regular exercise to help reduce muscle mass loss, delay frailty and prevent disability. Good glycemic control may reduce the incidence of sepsis and pneumonia risk may be reduced by annual vaccination [83]. In one study, the presence of depression was the strongest predictor of hospitalization and subsequent mortality [84]. The coexistence of diabetes and depression is associated with increased healthcare use, increased healthcare costs and adverse health outcomes [85]. Patients with depression may have problems with medication taking or self-care management, leading to persistent hyperglycemia and increased risk of diabetic complications [86]. Depression is also a contributor to functional disability as a result of decreased physical activity and less likelihood of seeking medical care [87]. Therefore, screening and treatment of depression should be a routine part of patient management. Patient Health Questionnaire (PHQ-9) is a brief tool and provides a two-step process to assess the presence of depressive symptoms. The first step (two questions) can be used for quick screening and it has 97% sensitivity and 67% specificity [88] **(Table 2)**. Diabetes-related education and social services support can help reduce diabetes-related distress [89]. Cognitive dysfunction is also associated with a decline in self-care needs. Increasing cognitive dysfunction has been shown to be associated with increasing difficulties in self-care needs such as compliance with medications, diet, exercise, feet inspection and monitoring blood glucose levels [90]. Dementia is also associated with increasing prevalence of severe hypoglycemia needing assistance [91]. Therefore, the occurrence of unexplained recurrent hypoglycemia or if the patients are struggling or having difficulties with self-care management clinicians should be alerted to the possibility of cognitive dysfunction development **(Box 4)**. Therefore, tests of cognition should be included in the functional assessment of all older patients with diabetes. The Mini-Cog test is a simple screening tool for dementia which has a sensitivity of 86.4% (95% CI: 64.0–96.4%) and a specificity of 91.1% (95% CI: 85.6–94.6%) and takes only 3 min to perform [92] **(Table 2)**.

• Avoiding hospitalization from care homes

Diabetes affects around a third of care home residents and increases the risk of nursing home admission by threefolds [10,93]. Factors that predict institutionalization are cognitive decline and low social support such as absence of a carer at home [94]. Due to the high prevalence of cognitive dysfunction, frailty and limited life expectancy in care home residents with diabetes, less intensive glycemic control with lower dosages of hypoglycemic medications and a simple regimen of insulin may reduce treatment errors and risk of hypoglycemia that could lead to hospitalization. Due to the increased prevalence of dementia and increased co-morbidities in care home population, the incidence of hypoglycemia is likely to be high reaching up to 41.9% in one study over 1-year period (median: 2; range: 1–10 episodes per patient per year) [95]. It is important that care home staff are trained to recognize symptoms of hypoglycemia in older people, due to the predominance of neurological rather than autonomic symptoms, in order to intervene early before serious consequences that lead to hospitalization occur. Hypoglycemia may present with symptoms such as dizziness or visual disturbances or present in a similar way to dementia where patients become confused, agitated or have behavioral changes resulting in misdiagnosis [96]. Residents in care home with diabetes and dementia will have complex

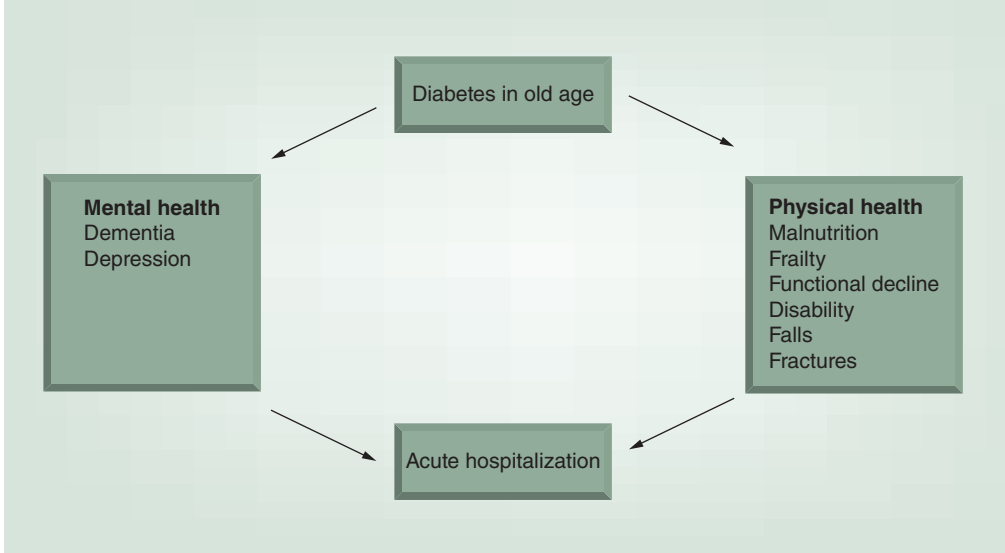

Figure 1. Diabetes phenotype in old age. Diabetes in older people is associated with a decline in both mental and physical health that leads to the development of geriatric syndromes and the effects of geriatric syndromes may contribute to acute hospitalization.

needs due to unpredictable behavioral changes as the decline in cognitive function continues. For example, hydration should be maintained due to impaired thirst sensation to avoid risk of volume depletion and hyperglycemic crises. In insulin-treated patients, the new class of long-acting insulin analogues may be a good option as they have less risk of hypoglycemia and can be conveniently injected once daily [97]. Patients who have erratic eating patterns and unpredictable caloric intake could be managed with hypoglycemic medications that have less risk of hypoglycemia or an insulin regimen where short-acting insulin analogues are administered only after meal consumption, thus preventing insulin-induced hypoglycemia if a meal is missed or only partly consumed. It is important to realize that hypoglycemia threshold in older people may be higher than usually defined less than 3.9 mmol/l. In an interview study of British patients, the lowest tolerated blood glucose level was more than 4 mmo/l in all patients with a mean (SD) of 6.7 (1.3) mmol/l and range 5–9 mmol/l [98]. Short-term glycemic targets are more important than long-term HbA1c due to limited life expectancy. For example, the implementation of a HbA1c level of less than 8% in frail nursing home patients resulted in a significant increase in the rate of severe hypoglycemia requiring emergency department visits (2.9

Table 2. Quick screening tools for dementia and depression.

Task	Score
Dementia (Mini-Cog test)†	
Ask the patient to repeat three items such as lemon, key and balloon, then provide a clock face:	
– Ask the patient to draw the numbers of the clock face	1 mark
– Ask the patient to draw the hands of the clock to show the time as ten to three	1 mark
– Ask the patient to recall the three items	1 mark for each item
Depression (PHQ-9)‡	
Ask the patient, over the past 2 weeks how often has been bothered by the following:	Not at all 0 mark
– Little interest in doing things	Several days 1 mark
– Feeling down, depressed or hopeless	More than half the days 2 marks
	Nearly every day 3 marks

†Mini-Cog score 0–3 out of maximum 5 defines cognitive impairment.
‡PHQ-9 score ≥3 out of 6 indicates possible depression and full PHQ9 score is needed.
PHQ: Patient health questionnaire.

episode per 100 patient years; RR: 3.03; 95% CI: 1.17–7.82) [99]. Maintaining a random blood glucose more than 5 but less than 15 mmol/l is a reasonable target to avoid hypoglycemia, symptomatic hyperglycemia that may lead to infections and incontinence resulting in hospitalization and also to maintain good cognition and general well-being [100]. Polypharmacy (taking >4 drugs) is common (84%) in a British care home study of residents with diabetes with a high proportion (59%) of residents prescribed drugs for cardiovascular disease prevention, which may be inappropriate in this disabled population with limited life expectancy. Polypharmacy may lead to increased risk of drug errors, hypoglycemia and hospitalization. Therefore, regular medication review of care home residents with diabetes should be undertaken as it has the potential to reduce costs, minimize adverse drug reactions and reduce hospitalization [101].

• Avoiding health system-related hospitalization

A multidisciplinary approach with access to comprehensive geriatric care is essential. In the hospital, a dedicated older patients' diabetes service resulted in a reduction of the length of stay by 81% (from a mean [SD] 2.7 [6.6] days before to 0.5 [2.9] days after introduction of the service) [102,103]. Discharge plans from hospital should include a problem list and a management plan that is communicated appropriately to the community care team for the patient to prevent readmission [104]. A nurse case manager devoted to diabetes could be very efficient in the general follow-up of patients in the community [105]. A systematic and a multidisciplinary team approach to care with a focus on providing patients with support to cope with their disease will help to improve outcome. Long-term telephone support for disease management and improvement of physical activity and nutrition has been shown to reduce hospitalizations and to improve QoL of older patients with diabetes living in the community [106]. Diabetes education is an integral part of diabetes care. Development of educational programs that are specific to the needs of older people with diabetes and adapted to their cognitive and physical dysfunctions as well as regular exposure of their carers to education and training would provide the means to better knowledge and care [107]. Introducing advanced nurse practitioners in care homes has positive impact on improving staff confidence and in reducing hospital admissions [108]. A holistic approach to patients' care starting with screening for diabetes of residents newly admitted to care homes and individualized care plans which minimize invasive interventions and take QoL at the heart of patient care is recommended [109] **(Box 5)**.

Box 4. Early diagnosis of dementia or depression.

Screening for depression or dementia should be part of the annual review and earlier if patients developed one of the following:

- Noncompliance with medications
- Diminished skills for performing insulin injections
- Difficulties in checking own blood glucose
- Patient is unable to interpret blood glucose results or make decisions regarding adjusting insulin doses
- Eating pattern becomes erratic with increasing missed meals
- Frequent or unexplained hypoglycemia
- Patient is forgetting how to recognize or treat hypoglycemia
- Patients are struggling with general self-care
- Noncompliance with dietary requirements
- Social isolation and reluctance to seek medical care

Conclusion

The epidemiology of diabetes is shifting toward old age due to the increasing aging of the population and reduced mortality. Physical and cognitive dysfunctions are emerging as a new category of diabetes complications in older people in addition to the traditional vascular complications. Unlike other chronic conditions, diabetes care is dependent on patient ability to perform self-care tasks, which may be compromised by both cognitive and physical disability. Older people with diabetes are heterogeneous group ranging from a fit individual living independently in the community to a fully dependent frail person with multiple co-morbidities living in a care home. Because of the complexity of diabetes in old age, comprehensive geriatric assessment is important on the initial examination of older people with diabetes with an individualized goal of therapy aiming to prevent loss of autonomy, preserve function and independence, reduce risk of hospitalization and promote good QoL. Integrated care system between primary and secondary care is essential. This should have a multidimensional approach with an emphasis on early diagnosis of

diabetes, optimizing diabetes care, screening for complications, structured education programs for patients and their carers, immunizations against common respiratory infections, early intervention for vascular disease and measures to reduce and prevent acute exacerbations in geriatric syndromes. Implementing these strategies may help reduce acute hospitalization, lower healthcare costs and prevent long-term disability.

Future perspective

The benefit of glycemic control in older people with diabetes is still not very clear. It appears that there is a good evidence for tight glycemic control in younger people with new onset diabetes who have less co-morbidity and low prevalence of cardiovascular disease. Older people, however, are heterogeneous in terms of their biological age and functional status. Tight glycemic control will continue to be the aim in those fit and independent older people but not suitable for those who are frail and at a high risk of hypoglycemia. Therefore, there is a need for clinical trials specifically designed for older people with diabetes to explore the real benefit of tight glycemic control in this diverse group. It remains true that multifactorial intervention is the standard goal with a greater benefit of BP and cholesterol lowering followed by glycemic control and aspirin use. Comprehensive geriatric assessment including physical and mental health assessment will continue to be essential in view of the increasing age of the population and the epidemiologic shift of diabetes toward older age. Frailty and geriatric syndromes are an emerging new category of complications in older people with diabetes and will need interventions beyond glycemic control. There remains a lack of intervention studies that aim to reduce disability and improve QoL in older people with diabetes. Diabetes in old age is associated with increased

Box 5. Reducing the risk of hospitalization of older people with diabetes.

- Screening and early diagnosis of diabetes
- Comprehensive geriatric assessment on diagnosis
- Avoid tight glycemic or BP control in frail older people to reduce risk of hypoglycemia and hypotension leading to falls
- In care home residents, short-term glycemic targets (random blood glucose >5 but <15 mmol/l) are more important than long-term HbA1c
- Regular outpatient review to prevent acute exacerbation of ACSC
- Targeted exercise and resistance training for those at risk of falls
- Fracture risk assessment and treatment of osteoporosis
- Adequate nutrition review to avoid muscle loss and frailty
- Early screening and treatment for depression and dementia
- Regular education programs suitable for patients with cognitive dysfunction and including their carers
- Regular immunization of common respiratory infections
- Continuity of care in the community
- In hospital, dedicated diabetes service for older people to reduce LOS with clear discharge plans to the community care team to reduce readmission
- Nurse case manager for diabetes
- Integration of primary and secondary care services
- Individualized care plans with specific goals for each patient
- Medications:
- Avoid polypharmacy
- Avoid medications with high risk of hypoglycemia
- Avoid dual blocking of the RAAS
- Avoid use of high doses of statins
- Careful use of NSAID and radio contrast agents
- Consider withdrawal of RAAS blockers in patients with stage 4 or 5 CKD
- Consider withdrawal of hypoglycemic medications in frail older people with Type 2 diabetes who have significant weight loss and tight glycemic control or frequent hypoglycemia.

ACSC: Ambulatory care sensitive conditions; CKD: Chronic kidney disease; LOS: Length of stay; RAAS: Rennin–angiotensin–aldosterone system.

prevalence of both physical and mental disabilities leading to frailty, which will compromise the QoL of older people. A focus on improvements in function may be of more clinical importance in frail older people with diabetes than attention to metabolic control alone. The proposed MID-Frail study will evaluate the clinical, functional, social and economic impact of a multimodal intervention (resistance training exercise, diet and education) in frail and prefrail subjects aged ≥70 years with Type 2 diabetes compared with usual clinical practice [110]. This may have an impact on reducing functional decline, promoting independence and reducing hospital admissions. There will be a need for more integration of services between primary and secondary care to insure that the multidisciplinary team approach needed is in place to meet the complex needs of the growing number of older people with diabetes.

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