FROM RESEARCH TO PRACTICE

Challenges and Strategies for Diabetes Management in Community-Living Older Adults

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The prevalence of diabetes is increasing, especially in older people, mainly because of an increase in life expectancy. The number of comorbidities also increases with increasing age, leading to a unique diabetes phenotype in old age that includes vascular disease, physical and neuropathic complications, and mental dysfunction. These three categories of complications appear to have a synergistic effect that can lead to a vicious cycle of deterioration into disability. Early assessment and appropriate, timely interventions may delay adverse outcomes. However, this complex phenotype constitutes a great challenge for health care professionals. This article reviews the complex diabetes phenotype in old age and explores management strategies that are predominantly based on the overall functional status of patients within this heterogeneous age-group.

With increasing aging of the population and urbanization of lifestyle, the global prevalence of diabetes is expected to rise from 8.4% in 2017 to nearly 10% by 2045 (1). Almost half of patients with diabetes (44%) are >65 years of age, with a prevalence that peaks (22%) at the age-group of 75–79 years (1). In older people, diabetes is a disabling disease as a result of vascular complications, coexisting multiple comorbidities, and an increased prevalence of geriatric syndromes such as cognitive and physical dysfunction, leading to increased risk of frailty and disability (2). Because of the complexity of diabetes in old age and the heterogeneous nature of this age-group (i.e., ranging from fit individuals living independently in the community to fully dependent people residing in a care home), comprehensive geriatric assessment is essential. Adoption of individualized management goals that aim to prevent loss of autonomy, preserve independence, and put quality of life at the heart of care plans is also essential. This article reviews the challenges and suggests management strategies for diabetes in this complex age-group. Its primary focus is on type 2 diabetes, which is the predominant form of the disease in aging populations.

Diabetes Phenotype in Old Age

In addition to the traditional diabetes-related vascular and neuropathic complications, physical and mental disabilities are only now emerging as important categories of complications in people with diabetes that affect older people disproportionately (3). Diabetes is directly associated with accelerated loss of muscle strength and muscle quality, increasing the risk of sarcopenia (4,5). Additionally, diabetes-related complications such as renal impairment and diabetes-associated comorbidities such as hypertension increase the likelihood of frailty (6,7). The combination of sarcopenia and frailty, often complicated by various types of neuropathy, mediate the pathway to physical disability and lower-limb dysfunction (3).

On the other hand, persistent hyperglycemia and recurrent episodes of hypoglycemia increase the risk of cognitive dysfunction and all types of dementia by twofold (8). Diabetes also increases the risk of incident depression by 27% (9). The combination of dementia and depression in older people with diabetes mediate the pathway to mental disability.

With the development of physical or mental disabilities, diabetes self-care will be compromised. For example, dementia may limit a patient’s ability to recognize or treat hypoglycemia, and depression may compromise self-care compliance leading to persistent hyperglycemia and increased risk of diabetes complications. As a consequence of dementia, poor communication with family members or caregivers may also delay the recognition of these problems. Meanwhile, physical disability manifested by disturbances in activities of daily living may compromise the safety of
performing a task such as self-administering insulin, create an inability to self-monitor glucose, and, in the case of frailty and particularly if associated with weight loss, increase the risk of hypoglycemia.

Synergistic and Reciprocal Relations

The vascular, physical, and mental categories of complications in older people with diabetes have synergistic and reciprocal relations among one another, leading to a vicious cycle and downhill deterioration to disability as shown in Figure 1. Some diabetes-related neuropathic complications (e.g., proximal motor neuropathy), although microvascular in origin, have been grouped with the “physical” category, reflecting the clinical consequences and symptom profiles associated with this complication.

The three categories of complications are likely to share part of a common pathophysiologic mechanism, suggesting that they are a manifestation of a single but complex phenotype (10). For example, the correlation between physical frailty and depression is substantial and suggests that psychological vulnerability is an important component of frailty (11). A recent meta-analysis has shown that the relationship between depression and frailty is reciprocal (12). Similarly, longitudinal data from the Survey of Health Ageing and Retirement in Europe (SHARE) showed a reciprocal relationship between physical frailty and cognitive impairment (13). Depressive symptoms are associated with increased risk of all types of dementia (14). The SHARE study demonstrated the other direction of this relationship, with lower memory performance at a given age predicting subsequent 2-year increases in depressive symptoms (15). Physical frailty may be an intermediate stage or mediate the associations between diabetes and both dementia and depression (16,17). Similarly, frailty and vascular disease appear to have a bidirectional relationship (18). Frailty predicts vascular disease, and vascular disease is associated with an increased risk of incident frailty (19). Frailty and sarcopenia are associated with reduced muscle mass and increased visceral fat, which lead to atherosclerosis via a complex interplay of factors, including increased insulin resistance, proinflammatory cytokines, reduced physical activity, increased oxidative stress, and mitochondrial dysfunction, increasing the risk of vascular disease (20). Also, vascular disease is linked to both cognitive dysfunction and depression (21,22) (Figure 1).

Clinical Presentation and Diagnosis

Clinical diagnosis of diabetes in old age may not be straightforward. Symptoms may be absent in up to 50% of cases, and, when present, they are usually nonspecific such as general fatigue, which may be attributed to old age (23). Geriatric syndromes or diabetes-related complications such as falls or urinary incontinence and hyperglycemic hyperosmolar state, respectively, may be the first manifestation of diabetes. Osmotic symptoms are less prominent because of the increased renal threshold for glucose filtration (reducing the intensity of polyuria) and impairment of thirst sensation (reducing the intensity of polydipsia).

Diagnostic criteria for diabetes are the same regardless of age and are based on high fasting plasma glucose (FPG) ≥7 mmol/L (126 mg/dL) or 2-hour plasma glucose during oral glucose tolerance test (OGTT) ≥11.1 mmol/L (200 mg/dL) (24). Clinicians should be aware that, in older adults, FPG is less sensitive in diagnosing diabetes, but the 2-hour plasma glucose with OGTT appears to capture most cases (25). An A1C ≥6.5% (48 mmol/mol) is another diagnostic test for diabetes. It has the advantages of less day-to-day variability, high specificity for diabetes diagnosis (98%), and international standardization. However, it has a low sensitivity (46.8%), which means that it can miss ≥50% of diabetes cases (Table 1) (26). Because of the asymptomatic nature of diabetes in old age, testing for A1C should be included in the routine annual checkups of older people. In patients with normal A1C but for whom there is clinical suspicion of diabetes, a random blood glucose or 2-hour plasma glucose during OGTT is required.
Diabetes Management

In general, interventions should be functionally dependent, starting with tighter metabolic control in independent people, with gradual relaxation of targets as patients’ functional level declines (Figure 2). Considering the often-complex phenotype of diabetes in old age, management should be focused on early assessment and reducing the risks of the three major complication categories (Table 2) (27–30).

Vascular Disease

Managing vascular disease risk includes treatment of risk factors such as hyperglycemia, hypertension, and dyslipidemia (31).

Hyperglycemia

Tight glycemic control will have a cardiovascular benefit after at least 10 years of treatment; however, the risk of hypoglycemia increases by 1.5- to 3-fold with tight control (32). For fit, independent patients, an HbA1C goal of 7.0–7.5% (53.0–58.5 mmol/mol) is acceptable because hypoglycemia risk increases with HbA1C levels below this target range. For frail, dependent patients with multiple comorbidities, a target HbA1C of 8.0–9.0% (63.9–74.9 mmol/mol) is reasonable to avoid side effects of medications and the risk of hypoglycemia (32).

Metformin therapy appears to be associated with lower long-term (≥2 years) cardiovascular mortality compared with sulfonylureas in patients with or without multiple morbidities (33,34). Pioglitazone has been shown to reduce the risk of major adverse cardiovascular events (MACE) and recurrent stroke in patients with a history of ischemic stroke (35). However, pioglitazone should be carefully used in patients with heart failure (HF) because it increases the risk of peripheral edema, weight gain, and HF (36). α-Glucosidase inhibitors as add-on therapy significantly reduced the risk of myocardial infarction (MI), whereas sulfonylureas may be associated with increased cardiovascular risk, but there have been no large randomized trials to confirm this (37,38). Dipeptidyl peptidase-4 (DPP-4) inhibitors have shown mixed safety results, with mostly marginal but nonsignificant increases in HF risk, especially with saxagliptin (39). Meta-analysis of the glucagon-like peptide 1 (GLP-1) receptor agonists trials showed a significant risk reduction for all-cause mortality, cardiovascular mortality, and incidence of MI but no effect on stroke or HF (40). Another meta-analysis of the trials of sodium–glucose cotransporter 2 (SGLT2) inhibitors showed a significant reduction of MACE and hospitalization for HF and a slowing of the progression of renal disease (41). The advantages and disadvantages of antidiabetic medications in older people are summarized in Table 3, and their cardiovascular safety and benefits are shown in Table 4.

Hypertension

A target systolic blood pressure (SBP) of 140 mmHg is reasonable in older people with diabetes because it is associated with a reduction of cardiovascular risk compared with SBP >140 mmHg. Several meta-analyses have concluded that lower SBP of <130 mmHg is not associated with better cardiovascular outcomes because cardiovascular benefits appear to reach a plateau after attaining an SBP of 140 mmHg. More intensive SBP reduction to <130 mmHg may be beneficial in patients with high risk of stroke, but this is likely to be associated with a significant increase in serious adverse events (42–44).

The recently published SPRINT (Systolic Blood Pressure Intervention Trial) showed that treating to an SBP target <120 mmHg compared with an SBP target <140 mmHg resulted in significantly lower rates of fatal and nonfatal MACE (hazard ratio [HR] 0.66, 95% CI 0.51–0.85) and death from any cause (HR 0.67, 95% CI 0.49–0.91) in older people ≥75 years of age. However, this study did not enroll older people with diabetes, stroke, heart failure, dementia,

### TABLE 1 Clinical Presentation, Diagnosis, and Assessment of Diabetes in Older People

<table>
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<tr>
<th>Clinical presentation</th>
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<td>Osmotic symptoms are less prominent because of an increased renal threshold for glucose (reducing the intensity of polyuria) and impairment of thirst sensation (reducing the intensity of polydipsia).</td>
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<tr>
<td>Diabetes can be asymptomatic in up to 50% of older patients.</td>
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<td>When symptoms are present, they may be nonspecific such as being generally unwell, fatigued, or lethargic and can mistakenly be attributed to aging.</td>
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<td>A diabetes complication such as visual loss or neuropathy or an unexplained fall may be the first presentation.</td>
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<th>Diagnosis</th>
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<td>Fasting glucose in the early stages of diabetes may be normal.</td>
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<td>Two-hour plasma glucose during OGTT appears to capture undiagnosed cases.</td>
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<td>A1C is specific but less sensitive (i.e., a normal A1C may miss cases of diabetes).</td>
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<th>Assessment</th>
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<td>In addition to screening for macrovascular and microvascular complications, comprehensive geriatric assessment should be performed on diagnosis, including screenings for:</td>
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<td>Vascular disease</td>
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<td>Physical and neuropathic function</td>
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<td>Mental/cognitive function</td>
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limited life expectancy of <3 years, unintentional weight loss (>10% of body weight during the preceding 6 months), or who resided in a nursing home (45).

Individuals with these conditions may not benefit from such intensive treatment and may be at increased risk of adverse events. It has been shown that higher SBP is positively correlated with mortality in healthier and functionally capable older people, but negatively correlated with mortality in frail and functionally less able populations, and particularly in those with slow gait speeds (46). Therefore, it appears logical to base blood pressure targets on overall function, with tighter control targets for fit individuals and more relaxed targets for frail individuals.

However, caution should be undertaken in intensive blood pressure reduction, especially in those with systolic hypertension, which may cause postural drop in blood pressure and an increased risk of falls. It has been shown that a higher daily dose of antihypertensive medications is independently associated with a greater risk of falls (relative risk 1.07, 95% CI 1.02–1.11, P = 0.004) (47). Therefore, risk reduction and prevention strategies for falls should be discussed with patients when commencing or increasing antihypertensive therapy.

**Dyslipidemia**

The evidence for statin therapy for older people with diabetes is generally extrapolated from studies conducted in younger populations with or without a diagnosis of diabetes. The PROSPER (Prospective Study of Pravastatin in the Elderly at Risk) trial was designed for older people aged 70–82 years (10.5% with diabetes), who had either preexisting vascular disease (secondary prevention) or elevated risk of vascular disease because of smoking, hypertension, or diabetes (primary prevention). It showed 15% lower incidence of cardiovascular end points in the statin group (48). Similar results were shown in the Heart Protection Study (primary prevention), which included 20,536 patients between the ages of 40 and 80 years (28% were >70 years old, and 28% of all study patients had diabetes) (49).

The magnitude of risk reduction in older people appears to be similar to younger patients (50). However, the absolute benefit of statin therapy depends on an individual’s baseline risk and is likely to be higher in older age, as demonstrated in the post hoc analysis of the CARDS (Collaborative Atorvastatin Diabetes Study) primary prevention trial, which compared the efficacy and safety of atorvastatin in 1,129 patients aged 65–75 years with that in 1,709 younger patients. Relative risk reduction of cardiovascular events was similar in both groups (38% in the older group vs. 37% in the younger group), but the absolute risk reductions were 3.9 vs. 2.7%, and the numbers needed to treat were 21 and 33, respectively, reflecting the higher absolute risk in older people, with a similar safety profile in both groups (51).

Therefore, the evidence for statin therapy is established for older people with diabetes up to the age of 80 years whether they do not have underlying heart disease (primary prevention) or already have established heart disease (secondary prevention). Observational studies have shown some extra evidence of benefit, although not significant, for those >80 years of age (52). There was also a trend toward mortality benefit in those aged 80–85 years compared with those >85 years of age (52). However, there are no clear data for benefit for those >85 years of age.
Physical and Neuropathic Complications

Diabetes is associated with an increased risk of sarcopenia and frailty, which mediate the pathway to physical dysfunction and physical disability (53). Exercise training and adequate nutrition are important interventions to slow down the progression of physical decline and maintain functional capacity (54).

Resistance exercise training has been shown to be effective in reducing muscle mass loss and improving the performance status of older people with diabetes (55). A large, European, randomized controlled trial (the MID-Frail [Multi-Modal Intervention in Diabetes in Frailty]) in prefrail and frail older adults (>70 years of age) with type 2 diabetes has shown that twice-weekly resistance training with nutritional education leads to significant improvement in physical performance as measured by the Short Physical Performance Battery and a reduction of healthcare costs (56).

Diabetes-related peripheral neuropathy can increase the risk of frailty and is likely to play a role in other complications such as balance disorders and falls risk (57).

Diabetes nutritional therapy has been shown to reduce the risk of frailty (58). Dietary protein supplementation (1.0 g/body weight/day) combined with resistance exercise training increase muscle hypertrophy, muscle strength, muscle mass, and performance (59). Vitamin D supplementation of at least 400 IU/day has also been shown to increase muscle strength, especially in people who are deficient in vitamin D or those who are ≥65 years of age (60). A diet rich in vitamin D and the amino acid leucine were associated with an increase in muscle mass and improvement in muscle function (61). A Mediterranean diet, which includes an especially high intake of vegetables and fruits, was associated with a reduced risk of frailty syndrome in older women with type 2 diabetes (62).

Mental/Cognitive Dysfunction

Diabetes is associated with increased risks of dementia and depression, which mediate the pathway to mental dysfunction and mental disability. Management should focus on the prevention of factors involved in increasing the risk of mental dysfunction such as reduction of insulin resistance through achieving ideal body weight and regular

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<th>TABLE 2 Screenings for the Three Main Categories of Complications in Older People With Diabetes (27–30)</th>
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<td>Category</td>
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<td>Vascular disease</td>
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<td>Physical and neuropathic complications</td>
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<td>Mental dysfunction</td>
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exercise training, prevention of persistent hyperglycemia, and avoidance of recurrent episodes of hypoglycemia and other diabetes-related complications.

Exercise and nutrition appear to maintain cognitive function in older people with diabetes (63). Structured aerobic or resistance training for a period of 12 weeks has been shown to promote several aspects of cognitive function, including improved attention and concentration in people with diabetes (64).

Glycemic control with avoidance of A1C variability or hyperglycemic fluctuations also may have a long-term positive effect on cognitive function (65,66). In the Look AHEAD (Action for Health in Diabetes) study, an intensive lifestyle intervention significantly reduced the incidence of depressive symptoms (HR 0.85, 95% CI 0.75–0.97, \( P = 0.02 \)) and preserved better function in the intervention group \( (P < 0.01) \) (67). Although this study included relatively younger participants with a mean age of 58.7 years (SD 6.8) at baseline, the range was wide (45–76 years), and the follow-up period was relatively long (9.6 years) (67). At baseline, 31.9% of participants were between the ages of 45 and 54 years, 51.5% were 55–64 years of age, and 17.0% were ≥65 years of age, which may suggest that, after the specified follow-up period, the study likely included a significant proportion of older people ≥65 years of age. Moderate-intensity physical activity may help to relieve stress and depressive symptoms in older people with diabetes (68). Greater adherence to the Mediterranean diet and daily tea drinking has also been shown to have a beneficial effect on depressive symptoms (69).

**Special Considerations in Old Age**

Delivering care for older people with diabetes is complex and constitutes a challenge to health care professionals (70). Special considerations unique to this age-group should be considered when formulating their individualized care plans.

**Hypoglycemia**

Symptomatic mild and severe hypoglycemia are not only associated with increased risk of cardiovascular events, all-cause hospitalization, and all-cause mortality (71), but are also linked to concerns about driving competence, socialization issues, self-care capacity, serious falls, physical and cognitive status, and impairments in emotional well-being and quality of life (72).

Hypoglycemia is more common in older than in younger people with diabetes because it is associated with comorbidities, geriatric syndromes, polypharmacy, long duration of diabetes, and the hepatic and renal dysfunction.
that increase with prevalence in older age. In a prospective, observational study of 3,810 people in primary care, 11% of participants reported having at least one episode of hypoglycemia of any severity in a 12-month period. People 70 years of age reported more episodes than those <60 years of age (12.8 vs. 9.0%, P <0.01). Significant differences were also seen for symptomatic episodes without the need for help (9.2 vs. 5.6%) and symptomatic episodes that required medical assistance (0.7 vs. 0.1%) (73). Continuous glucose monitoring has shown that asymptomatic hypoglycemia is common in this population regardless of A1C level (74).

Severe hypoglycemic episodes may lead to serious acute consequences such as stroke, MI, acute cardiac failure, and ventricular arrhythmias, and recurrent episodes of hypoglycemia lead to chronic complications such as physical and cognitive dysfunction, frailty, disability, and increased mortality (75,76).

Recognition of hypoglycemia may be a challenge for health care professionals because of the nonspecific nature of symptoms in old age (77). Therefore, educational programs for health care professionals, patients, and caregivers should be in place to facilitate early recognition of the atypical presentation of hypoglycemia. Patients should be regularly reviewed to identify factors that increase the risk of hypoglycemia such as polypharmacy, and medications with less hypoglycemic potential should be chosen where appropriate.

**Care Homes**

Residents with diabetes in care homes are more likely than older people living in the community to be frail and to have multiple comorbidities, advanced dementia, possible behavioral problems, and erratic eating patterns, which increase their risk of hypoglycemia. These patients are potentially at risk for harm from insulin and oral glucose-lowering agents, and hypoglycemic events are likely to be underreported (78).

Careful attention to the hypoglycemic regimen of individuals residing in care homes is required. For example, sulfonylureas should be avoided in these patients. Long-acting basal insulin analogs may be a good option because they have less risk of hypoglycemia and can be conveniently injected once daily (79). In a 150-facility, cross-sectional study of 2,258 Italian nursing home patients with a mean age of 82 years (SD 8) and type 2 diabetes, of whom 1,138 had dementia, rapid- and long-acting insulin analogs were associated with reduced odds of severe hypoglycemia compared with sulfonylurea monotherapy or combined metformin and sulfonylurea therapy in patients with, but not those without, dementia (80). The reasons for this finding may be related to the ability to flexibly adjust insulin doses according to patients’ irregular eating habits (80). Short-acting insulin analogs can also be administered after meals rather than before and can therefore be omitted when a meal is not consumed.

Care homes should have a policy for diabetes care, including diabetes screening on admission and individualized care plans for residents (81). These care plans should be tailored to patients’ needs, which requires giving consideration to their values, preferences, life expectancy, and comorbidities, as well as the impact of diabetes management (e.g., polypharmacy and glucose monitoring) on their quality of life (82).

**Polypharmacy**

Polypharmacy is associated with increased risks of frailty and dementia (83,84). Many frail older patients with diabetes are treated inappropriately with multiple medications to achieve inappropriately tight glycemic control (85). Polypharmacy in these patients may lead to drug errors and unnecessary hospital admissions (86).

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**TABLE 4 Cardiovascular Safety of Antidiabetic Medications**

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<th>Types of Medications</th>
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| Older agents         | - Metformin appears to have cardiovascular benefits and can be safely used in patients with HF with low risk of lactic acidosis.  
- Pioglitazone has shown cardiovascular benefits and can be used in patients with compensated HF, but regular monitoring for HF exacerbation is required.  
- α-Glucosidase inhibitors may have cardiovascular benefits when added to metformin.  
- Sulfonylureas may increase cardiovascular events, but there have been no large randomized trials to confirm this.  
- Insulin appears to have a neutral cardiovascular effect. |
| Newer agents         | - DPP-4 inhibitors have neutral effects on cardiovascular events; however, hospitalization for HF significantly increases with saxagliptin, nonsignificantly increases with alogliptin, and is neutral with sitagliptin.  
- SGLT2 inhibitors may reduce cardiovascular events and hospitalization for HF and slow the progression of renal failure.  
- GLP-1 receptor agonists reduce cardiovascular events, including mortality, but have no clear effects with regard to stroke prevention. |

**Notes**

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Therapy deintensification opportunities are missed in about 20% of older patients with tight glycemic control, putting them at increased risk of adverse outcomes (87). Deintensification opportunities are also missed in older patients who are hospitalized with diabetes-related complications (88). Deintensification or withdrawal of antidiabetic medications has been shown to be safe in frail older patients with type 2 diabetes who had significant weight loss, tight glycemic control, comorbid dementia, and recurrent hypoglycemia, without causing deterioration in their glycemic control (89,90). These approaches provide increasing evidence for revising future clinical guidelines to take into account the need for therapy deintensification with advancing age (91).

Simplification of insulin regimens is another option to reduce polypharmacy and side effects and improve quality of life. In an intervention study, multiple daily insulin injections were switched to a once-daily injection regimen with or without the addition of noninsulin agents. This change resulted in fewer hypoglycemic episodes, stable A1C levels, and improvement in diabetes-related distress scores (92).

Conclusion

Diabetes is increasingly becoming a disease of older age because of overall population aging and increased life expectancy. The phenotype of diabetes in old age is complex and associated with three main categories of complications, including vascular disease, physical and neuropathic complications, and mental dysfunction. Therefore, the assessment of older people with diabetes on diagnosis and annually thereafter should be comprehensive and should include screenings for these complications. Early and timely intervention is required to delay progression into disability.

Older people are a highly heterogeneous population, and diabetes management should therefore be individualized with variable metabolic targets based on overall function. More attention should be considered for those at increased risk of hypoglycemia, those with unnecessary polypharmacy, and frail individuals living in care homes. Improving nutrition and maintaining physical activity are important to help delay disability. Quality of life should be at the heart of diabetes management plans.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

Author Contributions

Both authors researched data, wrote the manuscript, and reviewed/edit the manuscript. A.J.S. is the guarantor of this work and, as such, had full access to all the data reported and takes responsibility for the integrity of the review.

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