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## 2018 Clinical Practice Guidelines

## Diabetes in Older People

## Diabetes Canada Clinical Practice Guidelines Expert Committee

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## KEY MESSAGES

- Diabetes in older people is distinct from diabetes in younger people and the approach to therapy should be different. This is especially true in those who have functional dependence, frailty, dementia or who are at end of life. This chapter focuses on these individuals. Personalized strategies are needed to avoid overtreatment of the frail elderly.
- In the older person with diabetes and multiple comorbidities and/or frailty, strategies should be used to strictly prevent hypoglycemia, which include the choice of antihyperglycemic therapy and a less stringent glycated hemoglobin (A1C) target.
- Sulphonylureas should be used with caution because the risk of hypoglycemia increases significantly with age.
- DPP-4 inhibitors should be used over sulphonylureas because of a lower risk of hypoglycemia.
- Long-acting basal analogues are associated with a lower frequency of hypoglycemia than intermediate-acting or premixed insulin in this age group.

## KEY MESSAGES FOR OLDER PEOPLE WITH DIABETES

- No two older people are alike and every older person with diabetes needs a customized diabetes care plan. What works for 1 individual may not be the best course of treatment for another. Some older people are healthy and can manage their diabetes on their own, while others may have 1 or more diabetes complications. Others may be frail, have memory loss and/or have several chronic diseases in addition to diabetes.
- Based on the factors mentioned above, your diabetes health-care team will work with you and your caregivers to select target blood glucose and glycated hemoglobin (A1C) levels, appropriate glucose-lowering medications, and a program for screening and management of diabetes-related complications.

## Introduction

This guideline refers primarily to type 2 diabetes in the older person. There is limited information on the management of type 1 diabetes in the elderly, but this is included wherever appropriate. The definition of “older” varies, with some studies defining the elderly population as  $\geq 60$  years of age. Administrative guidelines frequently classify people  $>65$  years of age as older. Although there is no uniformly agreed-upon definition of older, it is generally accepted that this is a concept that reflects an age continuum starting

sometime around age 70 and is characterized by a slow, progressive impairment in function that continues until the end of life (1). There are many people with type 2 diabetes who are over the age of 70 who are otherwise well, functionally independent/not frail and have at least a decade of healthy life expectancy. These people should be treated to targets and with therapies described elsewhere in this guideline (see Targets for Glycemic Control chapter, p. S42 and Pharmacologic Glycemic Management of Type 2 Diabetes in Adults chapter, p. S88). This chapter focuses on older people who do not fall into any or all of those categories. Decisions regarding therapy should be made on the basis of age/life expectancy and the person's functional status. Where possible, evidence is based on studies where either the main focus was people over the age of 70 years or where a substantial subgroup, specifically reported, were in this age group.

## Diagnosis and Screening

As noted in the Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome chapter, p. S10, glycated hemoglobin (A1C) can be used as a diagnostic test for type 2 diabetes in adults. Unfortunately, normal aging is associated with a progressive increase in A1C, and there can be a significant discordance between glucose-based and A1C-based diagnosis of diabetes in this age group, a difference that is accentuated by race and gender (2) (see Monitoring Glycemic Control chapter, p. S47). Pending further studies to define the role of A1C in the diagnosis of diabetes in the elderly, other tests may need to be considered in some older people, especially where the elevation in A1C is modest (i.e. 6.5% to 7.0%). Because they are complementary, we recommend screening with both a fasting plasma glucose and an A1C in older people.

Screening for diabetes may be warranted in select individuals. In the absence of positive intervention studies on morbidity or mortality in this population, the decision about screening for diabetes should be made on an individual basis. Screening is unlikely to be beneficial in most people over the age of 80.

## Reducing the Risk of Developing Diabetes

Healthy behaviour interventions are effective in reducing the risk of developing diabetes in older people at high risk for the development of the disease (3). Acarbose (4), rosiglitazone (5) and pioglitazone (1,6) also are effective in preventing diabetes in high-risk

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elderly. Metformin may not be effective (3). Since several of these drugs have significant toxicity in the older adult (see below) and since there is no evidence that preventing diabetes will make a difference in outcomes in these people, there would appear to be little justification for drug therapy to prevent diabetes in older adults.

## Management

### Organization of care

As interprofessional interventions specifically designed for older adults have been shown to improve glycemic control, referrals to diabetes health-care (DHC) teams should be facilitated (7–9). Pay-for-performance programs improve a number of quality indicators in this age group (10,11). Telemedicine case management and web-based interventions can improve glycemic control, lipids, blood pressure (BP), psychosocial well-being and physical activity; reduce hypoglycemia and ethnic disparities in care; and allow for detection and remediation of medically urgent situations, as well as reduce hospitalizations (12–21). A pharmaceutical care program (e.g. monitoring of symptoms, medication counselling, facilitating communications with physicians/nurse practitioners by pharmacists) can significantly improve medication compliance, as well as the control of diabetes and its associated risk factors (22,23) (see Organization of Care chapter, p.S27).

### Self-management education and support

Self-management education and support programs are a vital aspect of diabetes care, particularly for older adults who may require additional education and support in light of other chronic conditions and polypharmacy (24). Recently, a population-based cohort study of older adults (≥65 years of age) living in Ontario found that attendance at a diabetes education program was associated with better quality of care, and better participation relating to education utilization and retinopathy screening (25). A review of diabetes self-management programs for older adults ≥65 years of age, identified that programs that emphasized tailored education and support, or psychological support resulted in greater reductions in A1C, when compared to group-setting education, review and feedback monitoring, or medical management (24) (see Self-Management Education and Support chapter, p. S36).

In the absence of frailty, intensive healthy behaviour interventions may be applicable for appropriate older adults. A 1-year intensive self-management healthy behaviours program (calorie reduction and increased physical activity) was associated with a statistically significant benefit on weight reduction, increased high-density lipoprotein cholesterol (HDL-C), decreased A1C and reduced waist

circumference in older adults ranging from 65 to 76 years of age (26). Diabetes self-management programs with access to geriatric teams (i.e. geriatricians, diabetes nurse educators, registered dietitians) can further improve glycemic control and self-care behaviours when compared to usual care, by assessing barriers and providing strategies and opportunities for ongoing support between clinic visits (27).

### Targets for glycemic control

The same glycemic targets apply to otherwise healthy older adults as to younger people with diabetes (see below), especially if these targets can be obtained using antihyperglycemic agents associated with low risk of hypoglycemia (see Targets for Glycemic Control chapter, p. S42). In older people with diabetes of several years' duration and established complications, intensive control reduced the risk of microvascular events but did not reduce cardiovascular (CV) events or overall mortality (28–31). Overall mortality was increased in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study. Therefore, in older people with longstanding diabetes and multiple comorbidities, intensive glycemic control is not advisable. While the initial report of the ACCORD-MIND substudy suggested that intensive control preserved brain volume but did not alter cognitive outcomes, subsequent follow up found no impact on either parameter (32). However, better glycemic control may be associated with less disability and better function (33,34). In cohort studies, it has been demonstrated that the best survival is present in elderly people with an A1C between 7.0% to 8.0%, and values above and below this range are associated with increased mortality (35,36). Table 1 outlines glycemic targets for the elderly across the health spectrum.

Recently, an A1C-derived average blood glucose value has been developed and offered to people with diabetes and health-care providers as a better way to understand glycemic control. While this is a valuable parameter in younger people, this variable and A1C may not accurately reflect continuous glucose monitoring (CGM) measured glucose values or glycemic variability in the older adult (37).

It has been suggested that postprandial glucose values are a better predictor of outcome in older people with diabetes than A1C or preprandial glucose values. Older people with type 2 diabetes who have survived an acute myocardial infarct (MI) may have a lower risk for a subsequent CV event with targeting of postprandial vs. fasting/preprandial glycemia (38). In people with diabetes with equivalent glycemic control, greater variability of glucose values is associated with worse cognition (39).

Recent international guidelines have focused on functional status as a key factor in determining the target A1C in older people with diabetes (Table 2). There is an acceptance that as functional

**Table 1**  
Glycemic targets in older people with diabetes

Status	Functionally independent	Functionally dependent	Frail and/or with dementia	End of life
<b>Clinical Frailty Index*</b>	1–3	4–5	6–8	9
<b>A1C target</b>	≤7.0%	<8.0%	<8.5%	A1C measurement not recommended. Avoid symptomatic hyperglycemia or any hypoglycemia.
<i>Low-risk hypoglycemia</i> (i.e. therapy does <b>not</b> include insulin or SU)				
<b>A1C target</b>		7.1–8.0%	7.1–8.5%	
<i>Higher-risk hypoglycemia</i> (i.e. therapy includes insulin or SU)				
<b>CBGM</b>				
Preprandial	4–7 mmol/L	5–8 mmol/L	6–9 mmol/L	Individualized
Postprandial	5–10 mmol/L	<12 mmol/L	<14 mmol/L	

A1C, glycated hemoglobin; CBGM, capillary blood glucose monitoring; SU, sulfonylurea.

\* Clinical Frailty Score (1 - very fit to 9 - terminally ill). Please see Figure 1.

**Table 2**

Guideline recommendations for key clinical outcomes for older people with diabetes from Diabetes Canada (DC), American Diabetes Association (ADA) and International Diabetes Federation (IDF)

Measure	ADA	DC	IDF
A1C	Healthy: <7.5% Complex/Intermediate: <8.0% Very Complex/Poor Health: <8.5%	Functionally independent: ≤ 7.0% Functionally dependent: 7.1–8.0% Frail and/or dementia: 7.1–8.5% End of life: A1C measurement not recommended. Avoid symptomatic hyperglycemia and any hypoglycemia.	Functionally independent: 7.0–7.5% Functionally dependent: 7.0–8.0% Sub-level frail: <8.5% Sub-level dementia: <8.5% End of life: avoid symptomatic hyperglycemia
Blood Pressure	Healthy: <140/80 mmHg Complex/Intermediate: <140/80 mmHg Very Complex/Poor Health: <150/90 mmHg	Functionally independent with life expectancy >10 years: <130/80 mmHg Functionally dependent, orthostasis or limited life expectancy: individualize BP targets	Functionally independent: <140/90 mmHg Functionally dependent: <140/90 mmHg Sub-level frail: <150/90 mmHg Sub-level dementia: <140/90 mmHg End of life: strict BP control may not be necessary
LDL-C	<1.8 mmol/L	<2.0 mmol/L or >50% reduction from baseline	<2.0 mmol/L and adjusted based on CV risk

Adapted from ADA (42) and IDF (40).

A1C, glycated hemoglobin; BP; blood pressure; CV, cardiovascular; LDL-C, low density lipoprotein cholesterol.

independence is lost and/or life expectancy shortens, the benefit of lower glycemic targets is diminished and the risk of hypoglycemia increases (40–42). Therefore, it is functional status and life expectancy, rather than age itself, that helps determine glycemic targets, including A1C.

### Frailty

Diabetes is a marker of reduced life expectancy and functional impairment in the older person. People with diabetes develop disability at an earlier age than people without diabetes and they spend more of their remaining years in a disabled state (43,44). “Frailty” is a widely used term associated with aging and disability that denotes a multidimensional syndrome that gives rise to increased vulnerability. Frailty may have a biological basis and appears to be a distinct clinical syndrome. Many definitions of frailty have been proposed. The most commonly applied definition (Fried’s Frailty Phenotype) suggests that a person is frail when 3 or more of the following criteria are present: unintentional weight loss (>4.5 kg in the past year), self-reported exhaustion, weakness (diminished grip strength), slow walking speed and low physical activity (45). Progressive frailty has been associated with reduced function and increased mortality. Frailty increases the risk of diabetes, and older people with diabetes are more likely to be frail (46,47). When frailty occurs, it is a better predictor of complications and death in older people with diabetes than chronological age or burden of comorbidity (48).

The Clinical Frailty Scale, developed by Rockwood et al, has demonstrated validity as a 9-point scale from 1 (very fit) to 9 (terminally ill), which can help to determine which older people are frail (49) (Figure 1). In people with multiple comorbidities, a high level of functional dependency and limited life expectancy (i.e. frail people), decision analysis suggests that the benefit of intensive glycemic control is likely to be minimal (50). From a clinical perspective, the decision to offer more or less stringent glycemic control should be based on the degree of frailty. People with moderate or more advanced frailty (Figure 1) have a reduced life expectancy and should not undergo stringent glycemic control. When attempts are made to improve glycemic control in these people, there are fewer episodes of significant hyperglycemia but also more episodes of severe hypoglycemia (51).

### Monitoring glycemic control

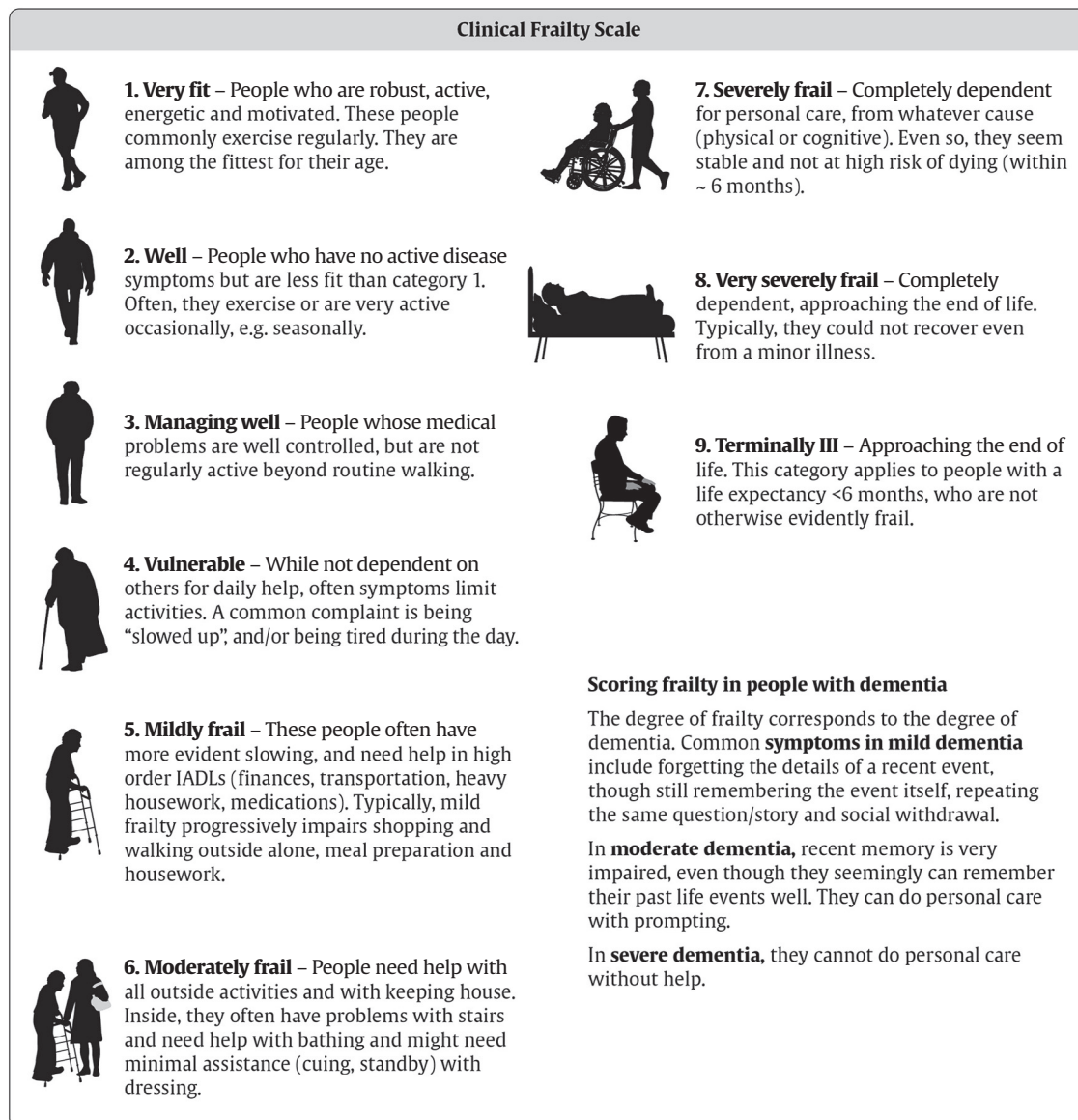
The same general principles pertain to self-monitoring of blood glucose (SMBG) in older people, as they do for any person with

diabetes (Monitoring Glycemic Control chapter, p. S47). The person with diabetes, or family or caregiver must have the knowledge and skills to use a home blood glucose monitor and record the results in an organized fashion. Additionally, the person with diabetes, and/or members of the health-care team, must be willing to review and act upon the SMBG results, in addition to the A1C results. In selected cases, continuous glucose monitoring (CGM) may be employed to determine unexpected patterns of hypoglycemia or hyperglycemia, which may result in significant changes in therapy (see below). Since the correlation between A1C values and CGM-derived mean glucose values is much less in the elderly than younger patient populations, the 2 measures may be used in a complementary manner to assess glycemic control in the future (37).

Particularly relevant to the older adult is the fact that glucose monitoring is the only way to confirm, and appropriately treat, hypoglycemia. Therefore, for older people treated with sulfonylureas, meglitinides and/or insulin, the ability to obtain SMBG at the time of symptoms consistent with hypoglycemia is essential. On the other hand, monitoring is often conducted when it is not required. Regular monitoring is generally not needed in well-controlled subjects on antihyperglycemic agents that rarely cause hypoglycemia (see Monitoring Glycemic Control chapter, p. S47).

Unfortunately, aging is a risk factor for severe hypoglycemia with efforts to intensify therapy (52). Recent data suggests that a substantial number of clinically complex older people have tight glycemic control, which markedly increases their risk of hypoglycemia (53). Asymptomatic hypoglycemia, as assessed by CGM, is frequent in this population (54). This increased risk of hypoglycemia appears to be due to an age-related reduction in glucagon secretion, impaired awareness of hypoglycemic warning symptoms and altered psychomotor performance, which prevents the person from taking steps to treat hypoglycemia (55–57). Although it has been assumed that less stringent A1C targets may minimize the risks of hypoglycemia, a recent study using CGM suggests that older people with higher A1C levels still have frequent episodes of prolonged asymptomatic hypoglycemia (58). If these data are replicated in subsequent studies, the assumptions underlying higher A1C targets for functionally impaired people with diabetes will need to be revisited.

The consequences of a moderate-to-severe hypoglycemic episode could include a fall and injury, seizure or coma, or a CV event (59). A1C values <6.5% and >8.0% are associated with an increased risk of fractures (60). Episodes of severe hypoglycemia may increase the risk of dementia (61), although this is controversial (62). Conversely, cognitive dysfunction in older people with diabetes has clearly been identified as a significant risk factor for the development of severe hyperglycemia (62–64).



**Figure 1.** Clinical frailty scale. Adapted with permission from Moorhouse P, Rockwood K. Frailty and its quantitative evaluation (49).

### Nutrition and physical activity

Nutrition education can improve metabolic control in ambulatory older people with diabetes (65). Although nutrition education is important, weight loss may not be, since moderate obesity is associated with a lower mortality in this population (66). Amino acid supplementation may improve glycemic control and insulin sensitivity in these people, although this is controversial (67,68).

Older women with diabetes have a greater decline in walking speed when compared to a control group without diabetes (69). In the older population with diabetes, higher levels of physical activity are associated with greater survival (70). Physical training programs can be successfully implemented in older people with diabetes, although comorbid conditions may prevent aerobic physical training in many patients, and increased activity levels may be difficult to sustain. Prior to instituting an exercise program, elderly people should be carefully evaluated for underlying CV or musculoskeletal problems that may preclude such programs. Aerobic exercise improves arterial stiffness and baroreflex sensitivity, both surrogate markers of increased CV morbidity and mortality (71,72).

While the effects of aerobic exercise programs on glucose and lipid metabolism are inconsistent (73–75), resistance training has been shown to result in modest improvements in glycemic control, as well as improvements in strength, body composition and mobility (76–80). Exercise programs may also reduce the risk of falls and improve balance in older people with diabetes with neuropathy (81,82).

Unfortunately, it appears difficult to maintain these healthy behaviour changes outside of a supervised setting (83).

### Noninsulin antihyperglycemic agents

In lean older people with type 2 diabetes, the principal metabolic defect is impairment in glucose-induced insulin secretion (84). Initial therapy for these individuals could include agents that stimulate insulin secretion without causing hypoglycemia, such as dipeptidyl peptidase-4 (DPP-4) inhibitors. In older people with obesity and type 2 diabetes, the principal metabolic defect is resistance to insulin-mediated glucose disposal, with insulin secretion being relatively preserved (85–87). Initial therapy for older people

with obesity and diabetes could involve agents that improve insulin resistance, such as metformin.

There have been no randomized trials of metformin in the older person with diabetes, although clinical experience suggests it is an effective agent. Metformin may reduce the risk of cancer in older people with diabetes (88,89). There is an association between metformin use and lower vitamin B12 levels, and monitoring of vitamin B12 should be considered in older people on this drug (90–92). Alpha-glucosidase inhibitors are modestly effective in older people with diabetes, but a substantial percentage of individuals cannot tolerate them because of gastrointestinal side effects (93–96). Thiazolidinediones (TZDs) are effective agents, but are associated with an increased incidence of edema and congestive heart failure (CHF) in older people (97–100). Rosiglitazone, but not pioglitazone, may increase the risk of CV events and death (101–104). These agents also increase the risk of fractures in women (97,104–106). When used as monotherapy, they are likely to maintain glycemic targets for a longer time than metformin or glyburide (100). Interestingly, drugs that increase insulin sensitivity, such as TZDs and metformin, may attenuate the progressive loss in muscle mass that occurs in older people with diabetes and contributes to frailty (107).

Sulphonylureas should be used with great caution because the risk of severe hypoglycemia increases substantially with age (108,109) and appears to be higher with glyburide (110–112). Gliclazide and glimepiride are preferred over glyburide in the elderly because they are associated with a lower frequency of hypoglycemia and CV events (113–119). A long-acting formulation of gliclazide resulted in equivalent glycemic control and the same frequency of hypoglycemic events as regular gliclazide in the older adult (115), and appears to result in a lower frequency of hypoglycemic events than glimepiride (116). Meglitinides (repaglinide and nateglinide) are associated with a lower frequency of hypoglycemia in the older person compared to glyburide (120–122) and may be considered in individuals with irregular eating habits.

DPP-4 inhibitors (alogliptin, linagliptin, saxagliptin and sitagliptin) are similarly effective and safe in young and older people with diabetes, cause minimal hypoglycemia when used alone (or with metformin) and do not result in weight gain (123–132). Large numbers of older people have been enrolled in studies of these drugs, including those over 75 and with multiple comorbidities. When compared to sulphonylureas in monotherapy or in combination with metformin, DPP-4 inhibitors result in equivalent glycemic control but result in much lower rates of hypoglycemia (133–137). When added to insulin, linagliptin may improve glycemic control without increasing the risk of hypoglycemia (138). Saxagliptin, alogliptin and sitagliptin do not increase the overall risk of CV events, pancreatitis or pancreatic cancer, but the risk of heart failure may be increased with saxagliptin (139–142) (see Treatment of Diabetes in People with Heart Failure chapter, p. S196).

The efficacy of the glucagon-like peptide-1 (GLP-1) receptor agonists (liraglutide, lixisenatide and dulaglutide) with respect to blood glucose, A1C and weight reduction is independent of age. These agents are well tolerated in the elderly with a similar side effect profile to younger people with diabetes, although there may be a higher risk of gastrointestinal side effects. There is a low risk of hypoglycemia when used as monotherapy or with metformin (143–148). Lixisenatide is not associated with an increase in CV events in elderly people who have recently had a similar event (149), and liraglutide and semaglutide improve CV outcomes in older people with diabetes and pre-existing cardiovascular disease (CVD) (150,151) (see Pharmacologic Glycemic Management of Type 2 Diabetes chapter, p. S88).

Colesevelam is generally well tolerated in the older person with diabetes and has a modest impact on A1C and lipid values (152).

Recently, data have become available on the use of sodium/glucose cotransporter 2 (SGLT2) inhibitors (canagliflozin, empagliflozin and dapagliflozin) in the older person (153–160),

although the numbers of participants over 70 years of age in these studies is not nearly as large as those with DPP-4 inhibitors. The studies have been done on participants without complex comorbidities, so it is not clear what the outcomes would be in less robust older people. These drugs are often contraindicated in the older adult due to reductions in glomerular filtration rate (GFR). They appear slightly less effective in terms of reductions in A1C in the older adult, likely because of lower GFRs in this age group. Although information is limited, the older person with diabetes may be more susceptible to dehydration and fractures than younger people treated with these agents, suggesting that they should be used cautiously. There does not appear to be an increased risk of bladder or skin infections, relative to younger patient populations. There have been no head-to-head studies of these drugs in comparison to DPP-4 inhibitors, specifically in the older person with diabetes. In a recent study of empagliflozin in participants with established CVD, the positive impact on CV outcomes was greater in those over, rather than under the age of 65 years, and the impact on renal outcomes was similar in both age groups (158,161). Canagliflozin also appears to have a greater impact on CV outcomes in people over age 65, but the increased risk of amputation and fractures give cause for concern (162). If subsequent studies confirm this finding and establish the safety of these compounds, they may be used more widely in the older age group. Because there is a much larger body of evidence with DPP-4 inhibitors to date in this age group, they should generally be used before SGLT2 inhibitors. Currently, empagliflozin could be considered for people <75 years with evidence of CVD, relatively preserved renal function and no other complex comorbidities.

#### *Insulin therapy*

Insulin regimens in the older adult should be individualized and selected to promote patient safety. Insulin absorption is similar from the arm and abdomen, and a skin lift is not required to optimize absorption (163). The abdomen is the preferred site for self-injection because it is easier for the older person to landmark. The clock drawing test and other cognitive assessments can be used to predict which elderly people are likely to have problems with insulin therapy (164,165). In older people, the use of prefilled insulin pens as an alternative to conventional syringes (166,167) minimizes dose errors and may improve glycemic control.

Pre-mixed insulin analogues can be administered after meals (168–170) and result in better and more durable control than basal insulins alone (171), but at the expense of more hypoglycemia and greater weight gain (172,173). When compared to premixed insulin, the combination of detemir and repaglinide results in equivalent glycemic control, with less weight gain, hypoglycemia and glycemic variability (174).

Basal-bolus injection regimens may be associated with greater improvements in glycemic control, health status and mood than twice-daily injections of long-acting insulin (175), although premixed insulin analogues can result in equivalent glycemic control to basal-bolus regimens (176). The addition of glargine to noninsulin antihyperglycemic agents results in improved control and a reduced frequency of hypoglycemia when compared to escalation of non-insulin antihyperglycemic agents (177). Both detemir insulin and glargine insulin U-100 have similar effectiveness in young and older people and result in a reduced rate of hypoglycemia when compared to 30/70 insulin or neutral protamine Hagedorn (NPH) (178–182). Glargine insulin U-300 is associated with a lower frequency of hypoglycemia than glargine U-100 in the older person (183). The kinetics of insulin degludec are similar in young and old people with diabetes (184). Older people appear to have less nocturnal hypoglycemia with insulin degludec than glargine U-100 (185).

Recently, it has been demonstrated that simplification of the insulin regimen in older people with type 2 diabetes by switching

multiple-dose insulin regimens to once-a-day glargine U-100 with or without noninsulin antihyperglycemic agents results in equivalent glycemic control and a reduced risk of hypoglycemia (186). This strategy should be more broadly applied in older people with multiple comorbidities and/or frailty.

In the future, older adults may be using newer technology for insulin administration. A randomized controlled trial of basal-bolus injection therapy vs. continuous subcutaneous insulin infusion (CSII) therapy in older people with type 2 diabetes found no difference in glycemic variability, treatment satisfaction, rates of hypoglycemia or glycemic control (187,188). People with type 1 diabetes <75 years of age who are highly functional have improved glycemic control and reduced symptomatic hypoglycemia using CSII (189–191). The ability to use more advanced pump features and the basal/bolus ratio appears to be similar in younger and older people (191). There is no data as yet favouring one pump device over another.

Finally, older people with diabetes are at increased risk for falls and fractures, and insulin therapy and sulfonylureas increase this risk (192,193).

## Prevention and Treatment of Complications

### Hypertension

Treatment of isolated systolic hypertension or combined systolic and diastolic hypertension in older people with diabetes is associated with a significant reduction in CV morbidity and mortality and microvascular events. The number needed to treat (NNT) reduces with increasing age (194–198). Treatment of isolated systolic hypertension may also preserve renal function in older people with diabetes (199). Several different classes of antihypertensive agents have been shown to be effective in reducing the risk of CV events and end stage renal disease (ESRD), including thiazide-like diuretics, long-acting calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) (194–204). Any of these agents is a reasonable first choice (200–202). Although the calcium channel blocker amlodipine may be associated with an increased risk of congestive heart failure (CHF) (202), the combination of ACE inhibitor and amlodipine appears to reduce CV events more than the combination of an ACE inhibitor and hydrochlorothiazide (205). Cardioselective beta blockers and alpha-adrenergic blockers are less likely to reduce CV risk than the above agents (200–203). ACE inhibitors may be particularly valuable for people with diabetes and >1 other CV risk factor (206).

In the ACCORD study, more intensive control of blood pressure (BP) (systolic BP <140 mmHg vs. <120 mmHg) in participants with type 2 diabetes at high risk for CV events, did not improve CV outcomes and resulted in more side effects (207). In older people with diabetes, systolic BP <130 mmHg and diastolic BP <67 mmHg may predict an increased mortality rate (36,208). As a result, there has been discussion about altering the systolic BP target for the elderly to 140 mmHg; however, Hypertension Canada in collaboration with Diabetes Canada have maintained the target BP <130/80 mmHg in diabetes (see Treatment of Hypertension chapter, p. S186), although this should be modified for people with diabetes with multiple comorbidities and limited life expectancy. The current guidelines from other international organizations and Diabetes Canada are shown in Table 2. There has been significant improvement in the number of older people treated for hypertension, and therapies being used are more consistent with current clinical practice guidelines (209).

### Dyslipidemia

The treatment of dyslipidemia with statins for both primary and secondary prevention of CV events has been shown in most, although

not all, studies to significantly reduce CV morbidity and mortality in older people with diabetes (210–218). In people with diabetes with limited life expectancy, consideration should be given to stopping or not starting these medications, as these people are unlikely to receive benefit. Current guidelines from other international organizations are shown in Table 2. The data on the use of fibrates in this patient population are equivocal (219,220), although they may reduce albuminuria and slow GFR rate loss (221).

### Erectile dysfunction

Type 5 phosphodiesterase (PDE) inhibitors appear to be effective for the treatment of erectile dysfunction in carefully selected older people with diabetes (222–224). (See Sexual Dysfunction and Hypogandism in Men with Diabetes chapter, p.S228.)

### Depression

Depression is common in older people with diabetes, and a systematic approach to the treatment of this illness not only improves quality of life, but reduces mortality (225). While screening for depression is not recommended, maintaining a high index of suspicion is advisable.

### Osteoporosis

Type 1 diabetes is associated with low bone density although the mechanism of bone loss is unknown. The Nord-Trondelag Health Survey from Norway showed a significant increase in hip fracture rates among females with type 1 diabetes compared to females without diabetes (relative risk [RR] 6.9, 95% confidence interval [CI] 2.2–21.6) (226). In the Iowa Women's Health Study, women with type 1 diabetes were 12.25 times more likely to report having had a fracture compared to women without diabetes (227). The relationship between type 2 diabetes and osteoporosis is less clear. In some studies, people with type 2 diabetes had a higher bone mineral density than control populations (228,229); however, other studies have not found significant differences (230,231).

### Dementia

Diabetes increases the risk of dementia in older people with diabetes, including both vascular dementia and Alzheimer's disease (62,232,233). This risk appears to be increased in women treated with unopposed estrogen therapy (233). As yet, there is no clear evidence that any particular intervention (i.e. healthy behaviour interventions, treatment of risk factors, etc.) will prevent dementia in this cohort.

### Polypharmacy

Older people with diabetes are frequently on multiple medications, many of which may be inappropriate in the setting of complex comorbidity and limited life expectancy (234). In selected populations, deprescribing should be considered to reduce complexity of therapy, side effects and adverse drug interactions (235). Drugs that can be considered first for deprescribing in these individuals include statins and sulfonylureas, because of lack of benefit in people with limited life expectancy and concerns about hypoglycemia, respectively.

## Diabetes in Long-Term Care

The prevalence of diabetes is high in institutions and individuals frequently have established microvascular and CV complications,

as well as substantial comorbidity (236–240). Canadian data shows over 25% of residents in long-term care facilities (LTC) have type 2 diabetes (241). Although the number of residents living in LTC with type 1 diabetes is unknown, a growing prevalence is noted as a result of advances of glucose management and adults being diagnosed with type 1 diabetes later in life, which requires the implementation of protocols specific for type 1 diabetes management (242). In observational studies, the degree of glycemic control varies widely between different centres (238,243), adherence to clinical practice guidelines is poor and insulin sliding scales (correction insulin only) are used frequently despite lack of evidence for their effectiveness (236,244). The complexity of antihyperglycemic medications is greater in LTC facilities than community-dwelling populations with most common patterns of therapy including insulin (245). Major problems faced by people with diabetes in LTC include: undernutrition (236), overly aggressive glycemic control with A1C levels below recommended target (<7.0%) (246) and polypharmacy. It has been shown that tight glycemic control with A1C <6.0% is associated with higher mortality in the aging population (35,36).

There are very few intervention studies on diabetes in LTC. The short-term substitution of a regular diet or a standard nutritional formula instead of a diabetic nutritional formula or “diabetic diet” did not modify the level of glycemic control (236,247–249). Available data about insulin therapy in people with diabetes in LTC settings are very scarce and great treatment variability of this population seems to prevail in current clinical practice (250). Substitution of regular insulin by lispro insulin at meal time may improve glycemic control with reduced number of hypoglycemic episodes in LTC patients (251). In a prospective randomized clinical trial in LTC, similar glycemic control was achieved with either basal insulin or with noninsulin antihyperglycemic agents in people with type 2 diabetes with no difference in the frequency of hypoglycemia, need for emergency room visits, hospital admission or mortality between treatment groups (252). The utilization of sliding scale insulin is prevalent in LTC and is associated with poorer glycemic control and higher frequency of capillary blood glucose (CBG) monitoring and hypoglycemia (244,250).

Frail older residents of LTC remain at high risk of hypoglycemia due to their advanced age, multiple comorbidities, polypharmacy, hypoglycemia unawareness and impaired renal function. To reduce risk of hypoglycemia, all antihyperglycemic agents have to be adjusted based on renal function (see Appendix 7. Therapeutic Considerations for Renal Impairment) at frequent intervals and higher glycemic targets are recommended for this high-risk population (see above). Deprescribing antihyperglycemic and other agents in high-risk people is recommended to achieve appropriate targets and reduce side effects of medication (235). Appropriate discontinuation of antihyperglycemic medication in older people who have tight glycemic control can potentially reduce risk of hypoglycemia and medication burden (253). Management of diabetes in LTC can be challenging as it requires an interprofessional team approach, collaboration with facility management, development of care protocols and acceptance of set treatment goals by the entire interprofessional team (254).

## RECOMMENDATIONS

1. Functionally independent older people with diabetes who have a life expectancy of greater than 10 years should be treated to achieve the same glycemic, BP and lipid targets as younger people with diabetes [Grade D, Consensus].
2. BP targets should be individualized for older adults who are functionally dependent, or who have orthostasis, or who have a limited life expectancy [Grade D, Consensus].

3. In the older person with diabetes and multiple comorbidities and/or frailty, strategies should be used to strictly prevent hypoglycemia, which include the choice of antihyperglycemic therapy and less stringent A1C target [Grade D, Consensus]. Antihyperglycemic agents that increase the risk of hypoglycemia or have other side effects should be discontinued in these people [Grade C, Level 3 (235,253)].
4. A higher A1C target may be considered in older people with diabetes taking antihyperglycemic agent(s) with risk of hypoglycemia, with any of the following: [Grade D, Consensus for all]
  - a. Functionally dependent: 7.1–8.0%
  - b. Frail and/or with dementia: 7.1–8.5%
  - c. End of life: A1C measurement not recommended. Avoid symptomatic hyperglycemia and any hypoglycemia.
5. The clock drawing test may be used to predict which older individuals will have difficulty learning to inject insulin [Grade C, Level 3 (164)].
6. Older people who are able should receive diabetes education with an emphasis on tailored care and psychological support [Grade A, Level 1A (24)].
7. If not contraindicated, older people with type 2 diabetes should perform aerobic exercise and/or resistance training to improve glycemic control as well as maintain functional status and reduce the risk of frailty [Grade B, Level 2 (73–77)].
8. In older people with type 2 diabetes, sulphonylureas should be used with caution because the risk of hypoglycemia increases substantially with age [Grade D, Level 4 (108)].
  - a. DPP-4 inhibitors should be used over sulphonylureas as second-line therapy to metformin because of a lower risk of hypoglycemia [Grade B, Level 2 (137)].
  - b. In general, initial doses of sulphonylureas in the older person should be half of those used for younger people, and doses should be increased more slowly [Grade D, Consensus].
  - c. Gliclazide and gliclazide MR [Grade B, Level 2 (113,115,119)] and glimepiride [Grade C, Level 3 (114)] should be used instead of glyburide, as they are associated with a reduced frequency of hypoglycemic events.
  - d. Meglitinides may be used instead of glyburide to reduce the risk of hypoglycemia [Grade C, Level 2 (121) for repaglinide; Grade C, Level 3 (122) for nateglinide], particularly in individuals with irregular eating habits [Grade D, Consensus].
9. In older people with type 2 diabetes with no other complex comorbidities but with clinical CVD and in whom glycemic targets are not achieved with existing antihyperglycemic medication(s) and with an eGFR >30 mL/min/1.73 m<sup>2</sup>, an antihyperglycemic agent with demonstrated CV outcome benefit could be added to reduce the risk of major CV events [Grade A, Level 1A (161) for empagliflozin; Grade A, Level 1A (150) for liraglutide; Grade C, Level 2 (162) for canagliflozin].
10. Detemir, glargine U-100 and U-300 and degludec may be used instead of NPH or human 30/70 insulin to lower the frequency of hypoglycemic events [Grade B, Level 2 (181) for glargine U-100; Grade B, Level 2 (182) for detemir; Grade D, Consensus for degludec and glargine U-300].
11. In older people, premixed insulins and prefilled insulin pens should be used to reduce dosing errors and to potentially improve glycemic control [Grade B, Level 2 (166,167)].
12. In older LTC residents, regular diets may be used instead of “diabetic diets” or nutritional formulas [Grade D, Level 4 (247–249)].
13. Sliding scale (reactive) and correction (supplemental) insulin protocols should be avoided in elderly LTC residents with diabetes to prevent worsening glycemic control [Grade C, Level 3 (244,250)].

## Abbreviations:

A1C, glycated hemoglobin; ACE, angiotensin-converting enzyme; ARC, angiotensin receptor blocker; BP, blood pressure; CBG, capillary blood glucose; CGM, continuous glucose monitoring; CHF, congestive heart failure; CSII, continuous subcutaneous insulin infusion; CV, cardiovascular; CVD, cardiovascular disease; DHC, diabetes health care; DPP-4, dipeptidyl peptidase-4; ESRD, end stage renal disease; GFR, glomerular filtration rate; GLP, glucagon-like peptide; HDL-C, high-density lipoprotein cholesterol; LTC, long-term care; MI, myocardial infarct; NPH, neutral protamine Hagedorn; SGLT, sodium glucose co-transporter; SMBG, self-monitoring of blood glucose; TZD, thiazolidinedione.

## Other Relevant Guidelines

Screening for Diabetes in Adults, p. S16  
 Reducing the Risk of Developing Diabetes, p. S20  
 Organization of Diabetes Care, p. S27  
 Self-Management Education and Support, p. S36  
 Targets for Glycemic Control, p. S42  
 Glycemic Management in Adults With Type 1 Diabetes, p. S80  
 Pharmacologic Glycemic Management of Type 2 Diabetes in Adults, p. S88  
 Hypoglycemia, p. S104  
 Screening for the Presence of Cardiovascular Disease, p. S170  
 Dyslipidemia, p. S178  
 Treatment of Hypertension, p. S186  
 Sexual Dysfunction and Hypogonadism in Men With Diabetes, p. S228

## Relevant Appendix

Appendix 7. Therapeutic Considerations for Renal Impairment

## Author Disclosures

Dr. Meneilly reports personal fees from Merck, Novo Nordisk, and grants from Sanofi, outside the submitted work. Dr. Miller reports personal fees from AstraZeneca, Eli Lilly, Novo Nordisk, and Sanofi; grants and personal fees from Boehringer Ingelheim, Janssen, and Merck, outside the submitted work. Dr. Sherifali reports investigator-initiated funding from AstraZeneca. Dr. Tessier has received honoraria from Merck, AstraZeneca, Boehringer Ingelheim, and Eli Lilly. Dr. Zahedi has received honorarium for CME programs and Advisory Boards from the following companies: Eli Lilly, Merck, Novo Nordisk, and Sanofi. No other authors have anything to disclose.

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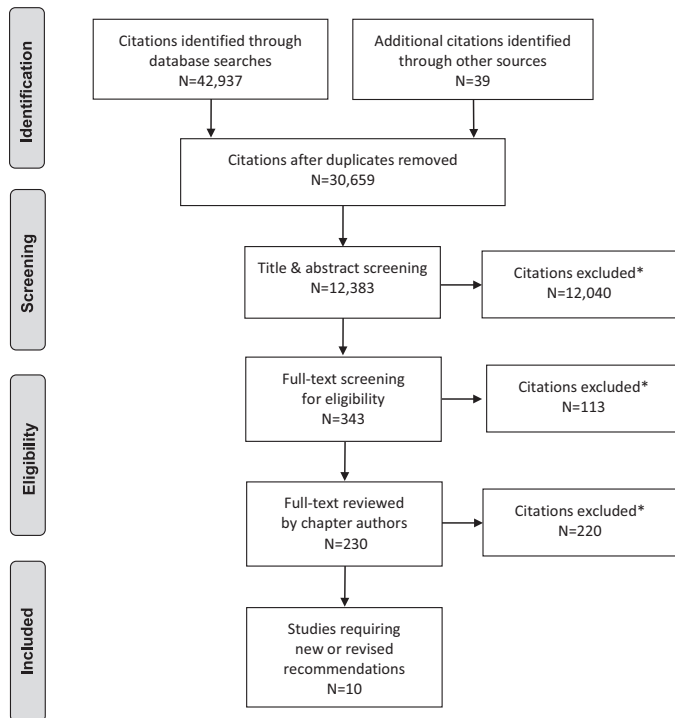
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## Literature Review Flow Diagram for Chapter 37: Diabetes in Older People



\*Excluded based on: population, intervention/exposure, comparator/control or study design.

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