Diabetes in Older Adults[1, 2, 3, 4, 5, 6, 7, 8, 9,10,11,12,13]

Note: This section of the Geri-RxFiles will focus on the medication management of type 2 diabetes in older adults and will not cover monitoring of glucose, nutrition, physical activity, nor screening for diabetes-related complications.

Key Messages When Managing Type 2 Diabetes (T2DM) in Older Adults

- The approach to diabetes management in older adults is distinctly different from that in the general population, particularly in those with multiple comorbidities, frailty (functional decline), cognitive impairment, or with limited life expectancy. **Medication therapy to achieve A1C values <7.0% in older adults with functional impairment is now considered overtreatment.**
- **Screen for geriatric syndromes** in older adults with diabetes, including cognitive impairment, depression, urinary incontinence, falls, chronic pain, and functional decline. These may impact diabetes self-management as well as quality of life.
- **Individualize blood glucose and A1c targets** for older adults based on cognitive and functional status, hypoglycemia risk, other comorbidities, and available supports.
  - For individuals with severe cognitive impairment, end-stage chronic illness, or residing in long-term care homes, the limited remaining life expectancy makes the benefit of glycemic control uncertain. HbA1c is a less important measure; focus treatment on avoiding hypoglycemia and symptomatic hyperglycemia.
- **Assess and avoid hypoglycemia.** If present, adjust medications and treat as needed.
- Consider the **goals of care** of the patient and family members/caregivers when considering de-intensifying medications to ↓ risk of hypoglycemia. **Education** may be required to reassure patients and caregivers who have been advised for many years to achieve "perfect" blood glucose and A1C values of <7.0%.
- Older adults with diabetic distal peripheral neuropathy are at **↑ risk of gait abnormalities and falls.** Minimize the use of other drugs that may increase fall-risk. Monitor for orthostatic hypotension and hypoglycemia. See Geri-RxFiles Preventing Falls in Community Dwelling Older Adults, page XXX.
- **Consider declining renal function** in older adults. Most glucose lowering medications, including insulin, require dosing reductions when eGFR is <30 ml/min.
- **Simplify complex medication regimens** as changes occur in a patient's cognitive function, ability to self-manage, and available nursing/caregiver support.
- **Cost** should be an important consideration for selecting medications as older adults tend to be on many medications and live on fixed incomes.

Remember: Healthy, functionally independent older adults with diabetes may be treated to achieve the same glycemic, blood pressure & lipid targets as younger adults with diabetes. **However, the *burden of treatment* should always be considered along with *burden of disease and time-to-benefit* for drug therapies.** For a strategy on how and when to deprescribe antihyperglycemic agents, see page XX and XX.

International diabetes guidelines recommend using **functional status, rather than age, to determine glycemic targets** in older adults with diabetes. These guidelines have similar recommendations for blood pressure and lipid lowering targets (see table with ***Summary of Guideline Recommendations*** on next page).

Considerations for Determining Glycemic Targets

❑ **Individualize targets & assess medications** (e.g. change in dose or frequency of administration, addition or discontinuation).

- Generally, optimal glycemic control (A1c < 7%) is recommended to prevent microvascular diabetic complications. However, it may take at least **5 years of tight glycemic control (A1C < 7%) to demonstrate microvascular benefits**. More stringent glycemic control (A1C <6.5%) has not been shown to ↓ macrovascular events in older adults with longer duration of diabetes and may ↑ morbidity and mortality. ACCORD, ADVANCE
- In individuals with multiple comorbidities, decreased functional status, cognitive impairment and/or limited life expectancy, avoidance of hypoglycemia is the priority.
  - Medication should aim to minimize hyperglycemia with associated glycosuria, risk of dehydration/electrolyte abnormalities, UTIs, and poor wound healing.

Table 1: Considerations for individualizing A1c targets

Consideration	Rationale
Shared-decision making	What are the patient's goals? What are the patient's preferences in terms of frequency or route of medication administration?
Burden of disease versus burden of treatment	Is the "impact on life" of the tx worth it? e.g. will using insulin and frequent blood glucose testing offer meaningful benefits?
Age/Health status, life expectancy, time to benefit	Will the patient live long enough to experience the benefits of tighter glycemic control? (≥ 5 years to reduce microvascular complications, 10+ to reduce CV risk).
Hypoglycemia risk	Does the patient have a history of hypoglycemia or hypoglycemia unawareness, warranting a more cautious approach to medications and glycemic targets? Do I need to 'back off' on the medications?
Diabetes duration	Have macrovascular complications already occurred? Has the patient had DM for a long time? If so, less stringent blood glucose targets may be warranted. The ACCORD trial found those with long durations of diabetes and a history of CV events were more likely to be harmed from intensive blood glucose control. Have microvascular complications already occurred? More intensive blood glucose control has been found to delay the onset of albuminuria, eye complications and neuropathy over a period of ~5 years. This may be of benefit for otherwise healthy older adults with microvascular complications.
Established vascular complications	
Other comorbid conditions	Do other health conditions affect the patient's ability to self-manage medications? Is cognition impaired and a complex medication regimen problematic? Does significant tremor or arthritis affect ability to administer injections?
Psycho-socioeconomic concerns, available support or resources, functional dependency,	Can the patient self-administer oral medications many times a day? Self-monitor glucose levels? Inject insulin? Is someone available to assist with medications if challenges exist?

See RxFiles Managing Type 2 Diabetes (T2DM) in Older Adults for more information.

Table 2: Summary of Guideline Recommendations for Key Clinical Criteria for Older Adults with Type 2 Diabetes

DC = Diabetes Canada 2018; ADA = American Diabetes Association 2024; IDF =International Diabetes Federation 2017

Patient Characteristics/ Health Status These categories are general concepts. Not every patient will clearly fall into a particular category. Consideration of patient & caregiver preferences is an important aspect of treatment individualization. Additionally, a patient's health status and preferences may change over time.	Frailty Index see page 5	Rationale	Reasonable A1C goal‡ ***	Target Fasting or PREprandial Glucose	DC: 2 hour POSTprandial Target ADA: Bedtime Glucose Target	Blood Pressure	Lipids
Functionally Independent **Healthy** (few coexisting chronic illnesses, intact cognitive & functional status)	1 to 3	- Longer remaining life expectancy	DC: ≤7.0% ADA: 7 - 7.5% IDF: <7%	DC: 4.0 to 7.0mmol/L ADA: 4.4 to 7.2mmol/L	DC: 5 to 10mmol/L ADA: 4.4 to 10mmol/L	DC: <130/80 mmHg if life expectancy >10 yrs ADA: <130/80mmHg IDF: 140-150/80 mmHg	DC, ADA: Statin unless contraindicated or not tolerated IDF: Statin if established CVD; statin if ≥ 40y and LDL-C > 2.6 mmol/L **LDL-C Targets** DC: <2.0 mmol/L or >50% reduction from baseline ADA: <1.8 mmol/L IDF: <1.8 mmol/L
Functionally Dependent **Complex/intermediate** (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	4 to 5	- Intermediate remaining life expectancy - High tx burden - Hypoglycemia vulnerability - Fall risk	DC: 7.1 to 8.0% ADA: <8.0% IDF: 7.5 - 8.0%	DC: 5.0 to 8.0mmol/L ADA: 5.0 to 8.3mmol/L	DC: <12.0mmol/L ADA: 5.6 to 10.0mmol/L	DC: individualize (also with orthostatic hypotension, or limited life expectancy) ADA: <130/80 mmHg	
Frail and/or with dementia **Very complex/poor health** (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	6 to 8	- Limited remaining life expectancy makes benefit uncertain	DC: 7.1 to 8.5% ADA: Avoid reliance on A1C; glucose control decisions based on avoiding hypoglycemia and symptomatic hyperglycemia IDF: 7.5 - 8%	DC: 6.0 to 9.0mmol/L ADA: 5.6 to 10.0mmol/L	DC: <14mmol/L ADA: 6.1 to 11.1mmol/L	ADA: <140/90 mmHg	ADA: Consider likelihood of benefit with statin; time to benefit ~2.5 years
End of Life	9		DC, ADA: A1C measurement not recommended. DC, ADA, IDF: Avoid symptomatic hyperglycemia or any hypoglycemia. Minimize burden of glycemic management.	DC: Individualized		ADA: Withdrawal of statin therapy may be appropriate.	

Abbreviations: **ADL** = activities of daily living

* Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, COPD, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. "Multiple" means at least three, but many patients may have five or more.

** The presence of a single end-stage chronic illness, such as stage 3 to 4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy.

*** Choosing Wisely Canada: ***Avoid*** *using medications known to cause hypoglycemia to achieve hemoglobin A1c <7.5% in many adults age 65 and older; moderate control is generally better.*

‡ A lower A1C goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden.

† A1C of 8.5% equates to an estimated average glucose of 11.1 mmol/L. Looser A1C targets above 8.5% are not recommended as they may expose patients to more frequent higher glucose values and the acute risks from glycosuria, dehydration, hyperglycemic hyperosmolar syndrome, and poor wound healing.

Evidence to Support a Higher (Less Aggressive) A1C Target in Frail Older Adults

- Intensive A1C lowering in trials offers modest benefit, mostly microvascular, over 5+ years. There is some evidence for macrovascular benefit (e.g. ↓ myocardial infarction) over the long-term (>10 to 30 years).[UKPDS-80, EDIC] **{Metformin saw mortality benefits after 10 years [UKPDS-34] in obese T2DM with median age 53 years, A1C = 7.4%.}**
- Intensive A1C lowering (< 6.5%) ↑ risk of harms (e.g. hypoglycemia) [ADVANCE] and ↑ all-cause death.[ACCORD]
- In studies with A1Cs as high as 7.9% & 8.4%,[VADT] there were only marginal clinical outcome differences, but much less hypoglycemia in the less intensive tx arm.
- In cohort studies, best survival occurs in older adults with an A1C between 7.0% and 8.0%; values above or below this range are associated with ↑ mortality.[14, 15]
- A1C values <6.5% and >8.0% are associated with an ↑ risk of fractures.[16]

Hypoglycemia

- **Consider the risk of hypoglycemia when selecting antihyperglycemics and incorporate strategies to avoid it.**

In treating type 2 diabetes in older adults,
the first priority should be to **AVOID HYPOGLYCEMIA**.
hypoglycemia can kill

The severity of hypoglycemia is not strictly defined by glucose levels but is characterized by the severity of the associated symptoms of hypoglycemia and risks. An alert value of < 3.9mmol/L can be used as a cutoff to classify hypoglycemia, but as frailty increases, hypoglycemia can be experienced at higher blood glucose levels (< 5 mmol/L). The 3-tiered numbered classification system helps standardize the diagnosis and treatment response according to the severity of symptoms.[17]

Table 3: Classification of hypoglycemia and Treatment International Hypoglycaemia Study Group'17, DC'23

Characteristics	Level 1	Level 2	Level 3
Glucose level	Often between 3.0 – 3.9mmol/L	Often <3.0mmol/L	Below normal (regardless of glucose reading)
Autonomic symptoms^	✓	✓, ✗	✓, ✗
Neuroglycopenic symptoms*	✓, ✗	✓	✓
Altered mental or physical status	✗	✗	✓, significant
Requires assistance	✗	✗	✓
Treatment‡	Ingest **15g of carbohydrates**. Retest after 15 minutes and re-treat with another 15g of carbohydrates‡ if glucose levels remains < 3.9mmol/L.		If conscious, ingest **20g of carbohydrate** if capable of swallowing or 3mg of **glucagon** intranasal or **glucagon** 1mg SC/IM. Retreat after 15 minutes if glucose levels < 3.9mmol/L. If unconscious, treat with **glucagon** or 10-25g (20-50mL of D50W) of glucose IV. Retreat after 15 minutes if glucose levels < 3.9mmol/L.
After treatment of hypoglycemia	Consume usual meal or snack that is due at that time of the day. If a meal is > 1 hour away, consume a snack (including 15g of carbohydrate and a protein source).		
Comments	Use fingerprick to test glucose levels as it is more accurate than continuous glucose monitor (CGM). See patient handout Diabetes Canada - Lows and highs: blood sugar levels.		

✓= yes or present, ✗ = no or not present
^ Autonomic symptoms = trembling, palpitations, sweating, anxiety, hunger, nausea, tingling
* Neuroglycopenic symptoms = difficulty concentrating, confusion, weakness, drowsiness, vision changes, slurred speech, headache, dizziness
‡ Examples of 15g carbohydrates = 1 tbsp honey, 1bsp sugar in water, 2/3 cup (150mL) juice or regular soft drink, 6 Life Savers or 2 rolls Rocket Candy.

Hypoglycemia in older adults

- **Hypoglycemia is associated with ↑ morbidity and mortality in older adults with both type 1 and type 2 diabetes.** ACCORD, ADVANCE
- **Risk of severe hypoglycemia has been shown to increase by 2 to 3 times with tighter glycemic control (A1C <7.0%)**.
- **Hypoglycemia is more common in older adults with diabetes** for many reasons: ↓ renal function (↓ clearance of glucose-lowering medications and endogenous insulin); age-related reduction in glucagon production; autonomic neuropathy and ↓ stress hormone response to low blood sugars; cognitive impairment with ↓ awareness of and/or ability to respond to early symptoms of hypoglycemia; ± variable food intake.
- Frailty and hypoglycemia are reciprocal; tight glucose control and hypoglycemia increase risk of frailty and frailty increases risk of hypoglycemia.
- A1C <6.5% is associated with increased risk of fractures.
- Severe hypoglycemia has been linked to increased risk of dementia.[18]
- **Moderate to severe hypoglycemia may result in falls, confusion, seizures, cardiac arrhythmias, and cardiac ischemia.**
- If an individual with type 2 diabetes has established CVD **or** is at high risk for CVD, and has ≥1 episode of severe hypoglycemia, he/she is more likely to have a CV event and die in next 5 years.[19, 20]

***Remember**…glycemic targets in older adults will need to change along with changes in health or functional status. As functional status declines, glycemic targets should increase (corresponding to a less intensive diabetes treatment regimen).

Hypoglycemia prevention and assessment

- Assess diet, **skipping meals**, physical activity and/or inadvertently repeating doses of their medications (adherence).
- **Older adults may not experience typical early (neurogenic) symptoms of hypoglycemia** (tremor, sweating, palpitations, tachycardia, nausea) due to autonomic neuropathy and/or effect of medications such as **beta-blockers** s.
- **Continuous glucose monitoring** may assist in identifying asymptomatic hypoglycemia.[21]
- **Avoid** higher risk for hypoglycemia medications: insulin(s), sulfonylureas, meglitinides.
- **Consider** lower risk of hypoglycemia meds: metformin, DPP4i, SGLT2i, GLP-1 RAs
- **Prescribe Glucagon** to all older adults at high risk of severe hypoglycemia (e.g. insulin use, history of hypoglycemia), and provide caregiver education. A quality improvement project found that implementation of glucagon protocols and order sets for all LTC residents decreased severity of hypoglycemia as well as healthcare costs.[22]
  - **Intranasal glucagon BAQSIMI** may be easier to use than injectable glucagon
- Consider a **MedicAlert** bracelet or other diabetes identification.

s: STOPP non-selective beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms.

Medications in Type 2 Diabetes

Remember that it is important to **reassess medication regimens and goals of treatment on a regular basis**. The medication regimen may require simplification and therapeutic targets **may require de-intensification**. Key times to reassess include when:

- Recurrent or severe hypoglycemia
- Recent hospitalization
- Change in health status, cognitive or functional decline and/or change in level of care (e.g. is it practical/realistic for home care to administer insulin before meals 3 times a day for a community-dwelling patient? What is the risk of hypoglycemia with an intensive insulin regimen - is it still needed?).

When assessing a medication regimen, ensure to ask about how medications are being taken. Do not assume they are being taken as prescribed or being taken at all!

Considerations when Assessing T2DM Medications in Older Adults

- If an individual is experiencing hypoglycemia & is at or below glycemic target (low A1C), consider deprescribing one glucose-lowering medication at a time, starting with the one more likely to cause hypoglycemia (e.g. sulfonylureas). Remember to reassess.
- If an individual is experiencing hypoglycemia & is significantly above glycemic target (high A1C): Consider diet, skipping meals, physical activity, over-treatment of hypoglycemia, and medication adherence. Confirm if medication dosages are appropriate/optimized, the timing of medication administration, combination therapy, proportion of prandial:basal insulin, insulin administration, reusing pen needles, lipohypertrophy, etc. The target A1C and treatment goals may need to be re-evaluated.
- In lean older adults with T2DM, the principal metabolic defect is impairment of glucose-induced insulin secretion. Agents that stimulate insulin secretion without causing significant hypoglycemia may be considered (e.g. DPP-4 inhibitors, GLP-1 agonists).
- In obese older adults with T2DM, the principal metabolic defect is resistance to insulin-mediated glucose disposal, with insulin secretion being preserved in the initial stages of T2DM. Initial therapy for obese older adults with diabetes should involve healthy lifestyle, self-management education/support (e.g. physical activity, nutrition therapy) and/or agents that improve insulin resistance (e.g. metformin).

Remember: It may take at least **2 years for microvascular or macrovascular benefits.** Therefore, **individualize intensity of treatment** for patient priorities, treatment risks, and time to benefit.

For more details and information for each drug, see:

1. RxFiles Anti-Hyperglycemic Agents, page 42,
2. RxFiles Insulin Comparison Chart, pg 53,
3. RxFiles Insulin Initiation, Titration, & Follow up in T2DM, pg 54, and
4. T*he Long Story Short* for insulin injections tips: http://www.rxfiles.ca/rxfiles/uploads/documents/Insulin-Longer-Shorter-InfoGraphic-RxFiles.jpg

Pharmacologic Intervention for Diabetes

Metformin GLUCOPHAGE, GLUMETZA, GLYCON - *Commonly used as first line therapy*

- Almost always the first-line drug of choice in type 2 diabetes.
- There are no randomized trials of metformin with older adults specifically, but clinical experience suggests it is effective. It has been shown to ↓ all-cause mortality rates in adults with T2DM (not specifically older adults).
- Minimal risk of hypoglycemia, weight neutral, & inexpensive; also reduces weight gain from insulin and decreases insulin dose requirements by up to 20%.
- Initiate at a low dose & titrate up to minimize GI upset.
  - Starting with ½ or even ¼ of a 500mg scored tablet & increasing every 2 to 4 weeks as tolerated may minimize GI upset and improve adherence.
  - Consider renal function and reduce/adjust dose target accordingly (see below).
  - Nausea and diarrhea tend to be dose-dependent and may resolve within 1 to 2 weeks; if not, reduce dose.

Remember: Monitor renal function, vitamin B12 levels (e.g. every 2 to 3 years[ADA])

Metformin & Renal Function[23]

Metformin may be used in individuals with ↓ but **STABLE** renal function, but at a ↓ dose.

Renal Function	Suggested Metformin dose	Monitor renal function
eGFR ≥60mL/min	≤2550 mg/day	Every 6 to 12 months
eGFR 45-59 mL/min	≤2000 mg/day	Every 3 to 6 months
eGFR 30-44 mL/min	≤1000 mg/day	Every 3 months
eGFR 15-29 mL/min S	500mg or Avoid**	N/A
eGFR <15 mL/min S	Avoid**	N/A
Peritoneal Dialysis	250mg/d	N/A
Hemodialysis	500mg after dialysis	N/A

Current American Guidelines suggest avoiding metformin if CrCl <30mL/min due to risk of lactic acidosis. However, it is reasonable to have **some flexibility with this cut-off.

See RxFiles Metformin – Precautions with renal impairment, hepatic disease and heart failure

- Given the outcome benefits seen with metformin, and the rare & controversial association with lactic acidosis, it is sometimes used cautiously in individuals with stable renal function between 15 to 30 mL/min. Alternative drugs carry risks as well (e.g. hypoglycemia with SUs; edema, weight gain) & often have less evidence of benefit/safety in older adults.

Lactic Acidosis & Metformin – How worried should we be?!

- Metformin-induced lactic acidosis is rare (9/100,000 patient years); causality uncertain.
- Consider holding metformin in individuals with lactic acidosis risk factors: **acute heart failure, acute renal injury** (e.g. use of contrast media), **acute hepatic dysfunction**, respiratory failure, sepsis, hypovolemia/dehydration.

S: STOPP metformin if eGFR < 30 mL/min/1.73m^2 (risk of lactic acidosis)

INCRETINS

DPP-4 inhibitors, GLP-1 RAs and GIP/GLP-1 RAs are in a drug class called **incretins** to lower blood glucose, suppress appetite, inhibit gastric emptying, promote insulin release, inhibit glucagon release and/or lose weight. Any combination of DPP-4 inhibitors, GLP-1 RAs or GIP/GLP-1 RAs is **NOT** recommended together due to similar mechanisms of action, lack of combination studies and cost.

Dipeptidyl peptidase-4 inhibitors (DPP-4i)[24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44]

- **DPP-4 inhibitors** are recommended as a **2nd line therapy to metformin** in older adults because of lower risk of hypoglycemia, effectiveness in reducing postprandial blood glucose, safety and weight neutral effect. Cost/drug coverage may be an issue.
- **When added to basal insulin, DPP-4 inhibitors may improve glycemic control without increasing the risk of hypoglycemia seen with prandial insulin.**
- DPP-4 inhibitors target prandial sugars in a glucose-dependent manner (i.e. if an individual does not eat, there is no glucose lowering), whereas sulfonylureas lower blood glucose in both the prandial and fasting state, causing hypoglycemia if there is inadequate or erratic food intake.
- DPP4-inhibitors are CV and renal neutral, they do not ↑ or ↓ risk of major adverse CV events, pancreatitis or pancreatic cancer; possible **↑ risk of heart failure** with **saxagliptin**[SAVOR-TIMI 53] and **alogliptin**.[EXAMINE] **Therefore, if cardiorenal benefits are desired, a SGLT2i or GLP-1RA would be more appropriate.**
  - **Linagliptin TRAJENTA**: 5mg daily (Max 5mg daily)
    - No dose adjustment for renal impairment; caution eGFR <15 mL/min.
    - Hepatically eliminated.
  - **Sitagliptin JANUVIA**: 50mg daily (Max: 100mg daily)
    - eGFR <50mL/min: 50mg daily, eGFR <30mL/min & ESRD: 25mg daily
  - **Saxagliptin ONGLYZA**: 2.5mg daily (Max: 5mg daily)
    - eGFR <50mL/min: 2.5mg daily, avoid if eGFR <15mL/min
  - **Alogliptin NESINA**: 12.5mg daily (Max 25mg daily)
    - eGFR <50mL/min: 12.5mg daily, eGFR <30mL/min: 6.25mg daily

Glucose-Dependent Insulinotropic Polypeptide (GIP) and Glucagon-like peptide-1 (GLP-1) receptor agonists (Double Incretin)[45]

- Tirzepatide **MOUNJARO** showed no overall differences in safety or efficacy in older adults ≥ 65 years compared to younger patients for treatment of type 2 diabetes.
- Tirzepatide significantly reduced A1c and weight compared to semaglutide 1mg SC weekly with more nausea, diarrhea and vomiting in 40 weeks.[46, SUSTAIN 2]
- An increased risk of hypoglycemia with concomitant use of a sulfonylurea or basal insulin. To reduce risk of hypoglycemia, a reduction in the dose of insulin secretagogue or insulin may be required.
- Evidence with respect to tirzepatide ↓ CV or renal outcomes is ongoing.
  - **Tirzepatide MOUNJARO**: 2.5mg SC once weekly x 4 weeks, then increase by 2.5mg increments after no less then 4 weeks on the current dose. (Max 15mg SC once weekly). No dosage adjustment required for renal/hepatic impairment.

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs)[47,48,49]

- GLP-1 RAs have maximal effect on lowering postprandial blood sugars, with some reduction in fasting glucose with longer acting agents (i.e. semaglutide, liraglutide, dulaglutide). Long-acting GLP-1 RAs provide steady exposure and relatively small fluctuations in plasma drug concentrations versus short acting agents (i.e. exenatide, lixisenatide).
- CV benefits (↓ major adverse cardiovascular events, CV deaths, stroke, MI) appear similar in those ≥ 65y as in the general population
- Similar tolerability in older adults as in general adult population:
  - Most common side effects of concern are GI-related, such as abdominal pain, constipation, diarrhea, nausea, and vomiting; slowly titrate dose to mitigate effects.
  - Serious adverse reactions to consider include gallstones, pancreatitis, and a possible link to thyroid cancer with liraglutide.
- Caution with use if frail, decreased appetite, unexplained weight loss, gastroparesis, or impaired cognition or vision which could complicate injectable administration.
- Low risk of hypoglycemia, but may occur if added to insulin (consider ↓ basal insulin).
- Greater reduction in A1c, minimal hypoglycemia and decreased weight gain seen when GLP-1 RA is added to basal insulin compared to prandial insulin.
- Liraglutide & semaglutide SC ↓ major adverse cardiovascular events (MACE) in older people with diabetes & pre-existing CVD. [LEADER 50, SUSTAIN-6 51] Lixisenatide & exenatide do not ↑ or ↓ risk of MACE in older adults with CVD. [ELIXA 52, EXSCEL 53]
- In patients with T2DM and CKD (eGFR 50-75mL/min), **semaglutide 1.0mg SC weekly** significantly ↓ MACE (**NNT=45**), ↓ all-cause mortality (**NNT=39**) and ↓ the risk of clinically important kidney outcomes (**NNT=20**) vs placebo over 3 years.[54, FLOW]
- Oral semaglutide **RYBELSUS** is non-inferior to placebo for CV outcomes.[55 PIONEER 6]
- GLP-1 RAs are injectable agents (with exception of oral semaglutide) which require visual, motor, and cognitive skills for appropriate administration.

  - **Semaglutide OZEMPIC**: 0.25mg SC once weekly (Max: 2mg SC once weekly)
    - No dose adjustment for renal impairment, but caution at eGFR <15 mL/min
  - **Semaglutide RYBELSUS**: 3mg PO once daily x 30 days, then 7mg PO once daily x 30 days, then 14mg PO once daily if needed or as tolerated. (max 14mg/d).
    Take on an empty stomach, at least 30 minutes before first food, with no more than 120mL water.
    - No dose adjustment for renal/hepatic impairment
  - **Dulaglutide TRULICITY**: 0.75mg SC once weekly (Max: 1.5mg SC once weekly)
    - eGFR <15 mL/min: caution / avoid due to lack of efficacy & safety data
  - **Liraglutide VICTOZA**: 0.6mg SC daily (Max: 1.8mg SC daily)
    - Avoid if eGFR <15 mL/min
  - **Exenatide BYETTA**: 5mcg SC BID ac (Max: 10mcg SC BID); **BYDUREON**: 2mg SC once weekly
    - eGFR 30 to 50 mL/min: caution, consider dose reduction; avoid if eGFR <30 mL/min
  - **Lixisenatide ADLYXINE**: 10mcg SC daily ac (Max: 20mcg SC daily)
    - eGFR <30 mL/min: caution / avoid due to lack of efficacy & safety data

Sodium-glucose co-transporter-2 inhibitors (SGLT-2i)[56,57,58,59,60,61,62] S B

- Overall, SGLT-2i provides slight reduction of A1C (0.5-0.8%), significant cardiovascular (CV) and renal protection, ↓ all-cause mortality in heart failure (HF), ↓ HF hospitalisation, slight weight loss with potential adverse effects including increased urinary frequency/ volume, nausea, dizziness, genital mycotic infection and/or diabetes ketoacidosis (DKA=rare). In older adults, other adverse effects include: volume depletion, orthostatic hypotension, dehydration and urinary tract infections.

Benefits

Consider **time to benefit** for desired outcome:
↓ Risk of CV events: ~2 years,
↓Progression of CKD: ~2.5 years
↓ HF hospitalizations: ~3-6 months

- SGLT-2i significantly reduced risk of all-cause mortality, cardiac death and hospitalization for heart failure in frail older adults (age >65) with T2DM and HF but did not substantially improve HbA1C—main advantage for use in this population is the reduction in cardio-renal events and improved HF outcomes rather than improved glycemic control.
- CV and renal benefits appear to be maintained even as renal function declines.
- In frail patients with heart failure, dapagliflozin showed improvement in health-related quality of life compared to placebo.[DELIVER]
- **Empagliflozin** [EMPA-REG] and **canagliflozin** [CANVAS] CVD outcome trials demonstrated ↓MACE (death from CV causes, nonfatal MI or nonfatal stroke) **in adults with established CVD**; **dapagliflozin** [DECLARE-TIMI 58] did not ↑ or ↓ risk of MACE (only 40% had established CVD).
- Empagliflozin, canagliflozin and dapagliflozin all ↓ HF hospitalizations and CKD progression.
- **CVD-REAL:** multinational, retrospective, observational study found that treatment with SGLT-2i vs other glucose-lowering drugs was **associated with a ↓ risk of hospitalization for heart failure and death.** This suggests that the benefits seen in **EMPA-REG**, **CANVAS** and **DECLARE-TIMI 58** trials may be a class effect applicable to a broad population of patients with type 2 diabetes mellitus in real-world practice.

Potential Harms

- Older adults are more prone to volume depletion, orthostatic hypotension, dehydration and urinary tract infections. These adverse events (AEs) increase risk for falls and fractures, [which] are already of particular high concern in this population
- Other potential AEs to consider include increased urinary frequency/ volume, nausea, dizziness, genital mycotic infection, DKA (rare)
- **Canagliflozin** associated with ↓ bone mineral density at hip, ↑ arm and leg fractures, ↑ foot amputations.
- Low risk (≤0.1%) of diabetic ketoacidosis (euglycemic).[Health Canada, 63] In most cases, associated with known contributing factor (e.g. insulin dose reduction/omission, bariatric surgery, alcohol, exercise, low carbohydrate/food intake).[DC 2018]
- SGLT2is should not be started in those with a history of DKA

Practical considerations for the use of SGLT-2 inhibitors in Older Adults:

- Monitor renal function and electrolytes 2-4 weeks after initiation & after dose increases.
- Consider reduced dose/holding diuretic therapy when initiating an SLGT-2i to ↓ risk of orthostatic hypotension (particularly with loop diuretics).
- When used with insulin, SGLT2-Is can improve glycemic control, limit weight gain, and can ↓ daily insulin requirements.
- May contribute to **hypoglycemia** when used with insulin or sulfonylurea.

Renal dosing considerations:

- **Canagliflozin INVOKANA**: 100mg po daily in the AM (Max: 300mg/d)
  - eGFR >60 ml/min: No dosage adjustment necessary
  - eGFR 30 to <60 ml/min: Reduce dose to 100mg once daily
  - eGFR <30 ml/min: Use should not be initiated but may continue therapy in patients already established on canaglifozin
- **Dapagliflozin FORXIGA**: 5mg po daily in the AM (Max: 10 mg/d)
  - eGFR >45 mL/min: No dosage adjustment necessary
  - eGFR 25-45 ml/min take into consideration comorbid conditions:
    - **CKD** maintain on therapy if already established, but do not initiate if eGFR <25 mL/min
    - **T2DM** not recommended glycemic control, but may continue for HF and CKD benefits
    - **HF** do not initiate, but may continue established therapy
- **Empagliflozin JARDIANCE**: 10mg po daily in the AM (Max: 25mg/d)
  - eGFR >30 mL/min: No dosage adjustment necessary
  - eGFR <30 ml/min consider comorbid conditions:
    - **CKD** do not adjust dose if eGFR >20 mL/min, do not initiate therapy if eGFR <20 mL/min
    - **T2DM** not recommended for glycemic control, however can continue treatment if eGFR >20 mL/min for renal and CV benefits
    - **HF** benefits shown in patients with eGFR >20mL/min
- **Ertugliflozin STEGLATRO**: 5mg po daily in the AM (Max: 15mg/d)
  - eGFR > 45 mL/min: No dosage adjustment necessary
  - eGFR <45 mL/min: Avoid

S: **STOPP SGLT-2 inhibitors** (e.g. canagliflozin, dapagliflozin, empagliflozin, ertugliflozin) with **symptomatic hypotension** (risk of exacerbation of hypotension).

B: Use SGLT-2 inhibitors with caution. Monitor patients for urogenital infections and ketoacidosis. Older adults may be at increased risk of urogenital infections, particularly women in the first month of treatment. An increased risk of euglycemic diabetic ketoacidosis has also been seen in older adults.

Sulfonylureas (SU) S B

- SUs stimulate pancreatic release of insulin irrespective of blood glucose levels; this is why they are associated with a higher risk of hypoglycemia, particularly in patients with unpredictable eating patterns.
- Sulfonylureas are **not** a good choice if there is irregular/unreliable food intake, or if there are functional concerns (e.g. functional decline, difficulty with ADLs, no access to support).
- Current EDS criteria for many other antihyperglycemic agents in SK requires trial and intolerance to SUs to qualify for coverage.

B: **Avoid all sulfonylureas** as first- or second-line monotherapy or add-on therapy unless there are substantial barriers to the use of safer and more effective agents. **Sulfonylureas have a higher risk of cardiovascular events, all-cause mortality, and hypoglycemia** than alternative agents. Sulfonylureas may increase the risk of cardiovascular death and ischemic stroke.

B: If a sulfonylurea is used, **choose short-acting agents** (e.g. glipizide, gliclazide IR) over long-acting agents (e.g. glyburide, glimepiride). Among sulfonylureas, long-acting agents (e.g. glyburide, glimepiride) confer a higher risk of prolonged hypoglycemia than short-acting agents (e.g. glipizide, gliclazide).

S: STOPP sulfonylureas with a long half-life (e.g. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).

Other Oral Agents/Classes[64]

- **Meglitinides** (**repaglinide GLUCONORM**) are associated with a lower frequency of hypoglycemia in older adults compared to sulfonylureas & may be preferred in individuals with irregular eating habits. Skip dose if meal is missed to decrease risk for hypoglycemia. On the flip side, multiple daily doses for meglitinides could be a barrier to adherence. May be used in individuals with impaired renal function.

- **Thiazolidinediones** S B (**pioglitazone ACTOS** & **rosiglitazone AVANDIA**) are effective glucose lowering agents but are associated with edema & heart failure in older adults, & ↑ risk of fractures in women.
  - Rosiglitazone may ↑ risk of CV events.
  - Pioglitazone associated with ↓ risk of CV events.
  - Pioglitazone may ↑ risk of bladder cancer (rare).
  - **Contraindicated in heart failure (at any stage).**
  - Avoid use in older adults on insulin as well as in those with osteoporosis, falls or fractures, and/or macular edema.

S: STOPP thiazolidinediones (e.g. rosiglitazone, pioglitazone) with heart failure (risk of exacerbation of heart failure).

B: Avoid thiazolidinediones in heart failure due to the potential to promote fluid retention and/or exacerbate heart failure.

Insulin Therapy[65]

- Optimize non-insulin therapy (e.g. metformin, GLP-1RA, GIP/GLP-1 RA double incretin, DPP-4 inhibitor or SGLT2i) before initiating basal and/or prandial insulin.
- If adding non-insulin therapy to existing insulin regimen, may need to lower insulin dose (depending on baseline blood glucose, A1c and individualized glycemic targets).
- A once-daily long-acting insulin may be added to achieve glycemic control. Over time, adding prandial insulin may be required when all other options optimized/tried.
- In older adults, the risk of hypoglycemia with insulin therapy ↑ with complex insulin regimens, use of intermediate (NPH), regular insulin & tight glycemic control (A1C <7.0%).
- If hypoglycemia is present, consider modification of glycemic target &/or medication.
- Consider **continuous glucose monitoring (CGM)** for older adults on insulin to improve glucose control and reduce hypoglycemia.
  - In adults > 60 yrs with DM using multiple daily injections, CGM was associated with improved A1C/glycemic outcomes and reduced glycemic variability.[66,DIAMOND]
- Insulin adjustment/administration requires cognitive, visual, and motor skills. The **clock-drawing test** is a useful tool to assess the ability of insulin self-management.
- If required, scheduled basal (long-acting) insulin with bolus/prandial insulin ± correction insulin (rapid-acting insulin used in addition to scheduled doses) is recommended over sliding scale insulin (administration of short- or rapid-acting insulin in response to high blood sugars only – no scheduled or basal insulin).
  - Scheduled basal-bolus insulin prevents hyperglycemia, allows for more flexibility of insulin dosing, & ↓ hypoglycemia risk compared with sliding scale insulin.B

Dosing of insulin for basal-bolus insulin therapy:

- Basal insulin should be 40 to 50% of total daily insulin dose, & prandial insulin the remaining 50 to 60% of the total daily dose, divided and given before each meal. If not eating, hold prandial insulin to avoid hypoglycemia.
- Total daily dose is based on weight & insulin sensitivity and should be titrated up slowly.
- If basal insulin dose > total prandial insulin dose → ↑risk of hypoglycemia at night & between meals.
- In older adults with progressive frailty, **simplifying the insulin regimen** by switching multiple-dose insulin regimens to a once-daily long-acting insulin analogue, with or without non-insulin agents, may result in reasonable glycemic control and less hypoglycemia.[67] Alternatively, use basal insulin plus prandial insulin with largest meal.

Choice of Basal Insulin

- Long-acting insulin analogues (**degludec**, **detemir**, **glargine U-100**, **glargine U-300**) may cause less hypoglycemia (especially nocturnal) & less weight gain than NPH or premixed. Most are dosed once daily; BID dosing may be required with **glargine** > 80 units daily.
- Insulin **degludec** and insulin **glargine U-300 TOUJEO** may be considered over insulin **glargine U-100** to reduce overall/nocturnal hypoglycemia.[DC 2018]

B: Avoid insulin sliding scale (insulin regimens containing only short- or rapid-acting insulin dosed according to current blood glucose levels without concurrent use of basal or long-acting insulin). Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting. This recommendation does not apply to regimens that contain basal insulin or long-acting insulin.

Insulin in Long-Term Care (LTC)

- Premixed insulin may be useful due to the predictable mealtimes & activity levels in LTC, as well as more lenient BG targets. If the resident is ill or not eating, it is important to switch to basal long-acting insulin with no prandial insulin to decrease hypoglycemia risk until back to baseline.
- Rapid-acting insulin may be injected right after a meal if uncertain how much food a resident may consume.
- Basal-bolus (multiple daily injection) insulin regimens increase risk of hypoglycemia and require more frequent blood glucose monitoring, thus require ↑ staff resources.
  - Consider benefit/risk ratio of this approach – often these regimens may be simplified as more lenient blood glucose targets are required
- **Over-treatment** of type 2 diabetes **is common in LTC**, leading to ↑ hypoglycemia, falls, fractures, and hospitalizations.[68]
- Consider **de-intensification** of insulin regimens as health status declines
  - e.g. change basal-bolus → basal insulin with rapid-acting insulin with largest meal only, or basal insulin + non-insulin tx.
- Avoid sliding scale insulin protocols.[69] B

Insulin is a 'high-alert' medication, and caution must be exercised with its use in older adults. It is a common cause of adverse events; insulin-treated individuals ≥80 years have been shown to be **>2X more likely to visit an emergency department** (rate ratio 2.5; 95% CI 1.5 to 4.3) and **~5X as likely to be hospitalized** (rate ratio 4.9; 95% CI 2.6 to 9.1) for insulin-related hypoglycemia and medication errors, than individuals age 45 to 64 years. The most commonly identified precipitants for insulin-related adverse events were:

1. Reduced food intake and
2. Administration of the wrong insulin product. [70]

Medications to Hold in the Event of Illness (to minimize kidney damage & avoid adverse events)

If an individual becomes acutely ill (e.g. sepsis, acute GI illness, acute heart failure) and is unable to maintain adequate fluid intake, medications that ↑ risk for acute renal injury or have reduced clearance in renal impairment should be held until the individual recovers.

Medications/Medication classes to hold in acute GI illness/dehydration/intravascular volume depletion		Examples
S	**Sulfonylureas, other Secretagogues**	gliclazide **DIAMICRON**, glimepiride **AMARY**[L], glyburide **DIABETA**, repaglinide **GLUCONORM**
A	**ACE-inhibitors**	lisinopril **ZESTRIL, PRINIVIL**, perindopril **COVERSYL**, ramipril **ALTACE**
D	**Diuretics** **Direct renin inhibitors**	hydrochlorothiazide, indapamide, furosemide aliskiren **RASILEZ**
M	**Metformin**	metformin **GLUCOPHAGE, GLUMETZA , GLYCON**, combination products
A	**Angiotensin receptor blockers**	candesartan **ATACAND**, telmisartan **MICARDIS**
N	**NSAIDs & COXIBs**	ibuprofen **ADVIL**, naproxen **ALEVE**, celecoxib **CELEBREX**
S	**SGLT-2 inhibitors**	canagliflozin **INVOKANA**, dapagliflozin **FORXIGA**, empagliflozin **JARDIANCE**, ertugliflozin **STEGLATRO**

Patient Handouts available at: https://www.diabetes.ca/DiabetesCanadaWebsite/media/Health-care-providers/2018%20Clinical%20Practice%20Guidelines/Appendix-8-sick-day-medication-list.pdf?ext=.pdf or
RxFiles Type 2 Diabetes and sick days medications to pause – SADMANS.

Assessing Cardiovascular Risk & the Role of Evidence-Based Risk Reduction Strategies in Older Adults with Type 2 Diabetes[71]

- Diabetes significantly accelerates the development of cardiovascular (CV) disease.
- The requirement for pharmacological cardiovascular protection therapies (statins, angiotensin-converting enzyme inhibitors or aldosterone receptor blockers, and anti-platelets) should consider the individual's approximate and lifetime CV event risk.

Should I start my patient on a STATIN? *It all depends!*

YES. Diabetes Canada (DC) recommends that all individuals >40 years of age with T2DM be started on a statin for cardiovascular protection.

- DC recommends a statin unless contraindicated or not tolerated in individuals who have a long to intermediate life expectancy, with a LDL target of <2.0 mmol/L or >50% reduction from baseline.
- However, for very frail individuals with limited life expectancy, consider the likelihood of benefit with statin therapy (e.g. more benefit for secondary prevention than primary). See GeriRxFiles Dyslipidemia in Older Adults, page XX.

Should I start my patient on an ACEI or ARB? *It all depends!*

LIKELY. DC recommends anyone >55 years of age with additional CV risk factors receive and ACEI/ARB. An ACEI/ARB is also recommended if microvascular disease is present (e.g. retinopathy, kidney disease, neuropathy), or if there is any end organ damage (e.g. albuminuria, retinopathy, LVH). An ACEI/ARB is an attractive first-line option for older adults with diabetes also requiring antihypertensive therapy. However, be cautious to avoid hypotension and orthostatic hypotension when adding an ACEI/ARB, particularly in normotensive older adults.

Should I start my patient on ASA? *It all depends!*[72]

ONLY IF your patient has cardiovascular disease. If there is a history of heart attack or stroke/TIA, cardiac ischemia (silent or overt), symptomatic peripheral artery disease, or cerebrovascular/carotid disease, ASA is recommended. If intolerant/allergic to ASA, consider **clopidogrel PLAVIX**.

Keep in mind that there is limited evidence to support the use of ACEI/ARBs and statins for primary prevention of cardiovascular events in adults >84 years of age.

Abbreviations:

ACEI=Angiotensin converting enzyme inhibitor **ADA**=American Diabetes Association **AE(s)**=adverse effects **AKI**=acute kidney injury **ARB**=angiotensin II receptor blocker **ASA**=acetylsalicylic acid **B**=BEERS criteria **CGM**=continuous glucose monitor **CI**=confidence interval **CKD**=chronic kidney disease **CV**=cardiovascular **DPP-4i**=dipeptidyl peptidase-4 inhibitor **DC**=Diabetes Canada **DM**=Diabetes Mellitus **GIP**=glucose dependent insulinotropic polypeptide **GLP-1 RA(s)**=glucagon-like peptide-1 receptor agonist(s) **HbA1C**=hemoglobin A1C **HF**=heart failure **LDL**=low density lipoprotein **LTC**=long-term care **LVH**=left ventricular hypertrophy **S**=STOPP/START criteria **SC**=subcutaneous **SGLT-2i** = sodium-glucose co-transporter-2 inhibitor **STOPP**=Screening Tool of Older Persons' Prescriptions **T2DM**=Type 2 Diabetes Mellitus **tx**=treatment **yr(s)**=year(s)

Search Terms

A1c	45
Antihyperglycemic	45
Diabetes	45
Glucose	45
Hypoglycemia	**45**
Type 2 Diabetes Mellitus	45
A1c	46
ACCORD	46
ADVANCE	46
Diabetes	46
UKPDS	46
BAQSIMI	47
Diabetes	47
Glucagon	47
Hypoglycemia	47
MedicAlert	47
Diabetes	48
GLUCOPHAGE	48
GLUMETZA	48
GLYCON	48
Metformin	**48**
ADLYXINE	49
Alogliptin	49
BYDRUEON	49
BYETTA	49
Diabetes	49
DPP-4 inhibitors	49
Dulaglutide	49
Exenatide	49
GLP1 Agonist	49
Incretins	49
JANUVIA	49
Linagliptin	49
Liraglutide	**49**
Lixisenatide	**49**
MOUNJARO	49
NESINA	49
ONGLYZA	49
OZEMPIC	49
RYBELSUS	49
Saxagliptin	49
Semaglutide	**49**
Sitagliptin	**49**
Tirzepatide	49
TRIJARDY	49
TRULICITY	49
VICTOZA	**49**
Canagliflozin	**50**
Dapagliflozin	**50**
Diabetes	50
Empagliflozin	**50**
Ertugliflozin	50
FORXIGA	**50**
INVOKANA	50
JARDIANCE	**50**
SGLT2 Inhibitors	50
STEGLATRO	50
ACTOS	51

AVANDIA	51
CGM	51
Diabetes	51
GLUCONORM	51
Glyburide	51
Insulin	51
Pioglitazone	51
Repaglinide	51
Rosiglitazone	51
Sulfonylureas	51
TOUJEO	51
ASA	52
Diabetes	52
Insulin	52
SADMANS	52
Statin	52

Acknowledgements: Erin Yakiwchuk, Shayla McKee, Margaret Jin (2024 update)
Thanks to our reviewers:
Disclosures: No conflicts of interest are reported by the authors.

EXTRA:

CADTH Canadian Drug Expert Committee Recommendations (May 2017)[73]

1. For patients with type 2 diabetes and without established cardiovascular disease, CDEC recommends that a sulfonylurea be added to metformin for adults inadequately controlled on metformin alone.
2. For adults with type 2 diabetes and established cardiovascular disease, CDEC recommends that therapy be considered in accordance with CDEC recommendations for individual drugs that have been reviewed specifically for this indication.

Diabetes Canada Renal Dosing Chart (https://guidelines.diabetes.ca/GuideLines/media/Docs/Key%20Messages/Renal_Dosing_Chart.pdf)

Antihyperglycemic Agents and Kidney Function

eGFR (mL/min/1.73m²)	DRUG CLASS						
	Metformin (max daily dose)	**SGLT2i** (Recommended daily dose*)	**GLP1-RA**	**DPP4i** (max daily dose)	**All Insulins**	**Secretagogues**	
						Glyburide	**Others**
45 – 59	2 g	No dose change	No dose change	No dose change	No dose change	Avoid Glyburide	No dose change
30 – 44	1 g	Canagliflozin 100 mg Dapagliflozin 10 mg Empagliflozin 10 or 25 mg		Linagliptin 5 mg Sitagliptin 50 mg (Saxagliptin 2.5 mg**)			Gliclazide or Repaglinide preferred Dose reduction may be needed
15 – 29	500 mg			Linagliptin 5 mg Sitagliptin 25 mg	Dose reduction may be needed		
<15 or on dialysis	Avoid	Stop on dialysis	Limited data available				
Risk related to low GFR	Lactic acidosis	Cardiorenal protection preserved but less reduction in A1C with low GFR		Accumulation***	Accumulation and hypoglycemia	Prolonged and severe hypoglycemia	Hypoglycemia

*listed alphabetically, **increased risk for heart failure, ***except linagliptin

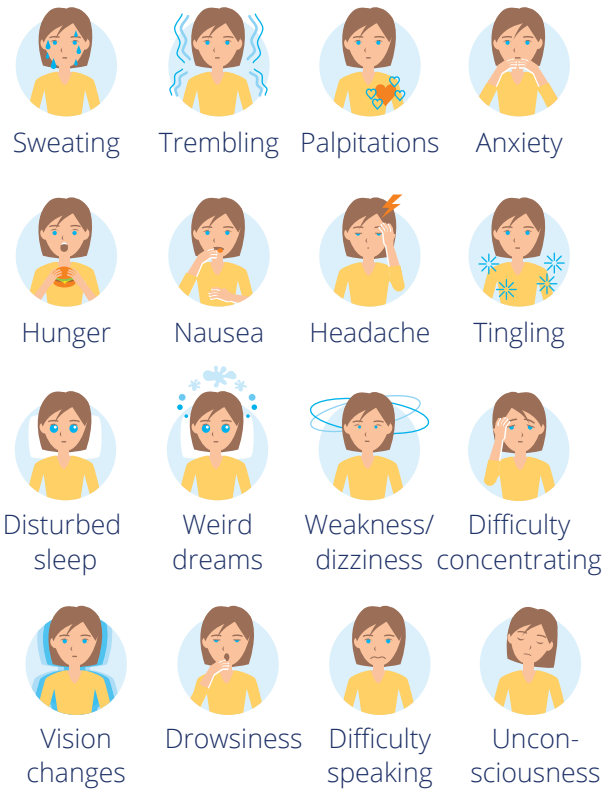
Hypoglycemia low blood sugar in adults

What are the signs?

Each person will have their own way of recognizing low blood sugar.

Some of the signs include:

Severity



Why does low blood sugar happen?

Have you:

- Eaten less than planned?
- Eaten later than normal?
- Taken more medication than planned?
- Been more active than planned?
- Drunk any alcohol within the past 24 hours?

Fear of lows is common and may cause excess anxiety, stress, reducing the ability to function and quality of life. If you are having lows, speak with your diabetes health-care team:

- Doctor • Nurse practitioner • Pharmacist
- Nurse • Dietitian

How to take action

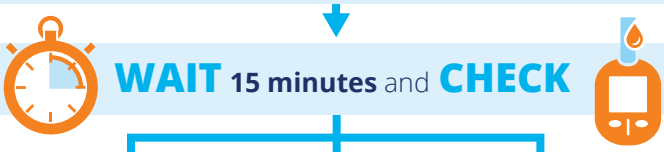
If able to swallow, EAT fast-acting sugar

- 15 g of glucose in the form of glucose tablets
- 1 tablespoon (15 mL) of honey
- 1 tablespoon (15 mL) sugar in water
- 2/3 cup (150 mL) of juice or regular soft drink
- 15 g fast-acting sugar (e.g. 6 Life Savers® or 2 rolls Rocket Candy)

With more severe signs (affecting mental/physical ability):

- If able to swallow → EAT 20g fast-acting sugar
- If unable to swallow → GIVE 3 mg glucagon intranasal or 1 mg SC/IM

WAIT 15 minutes and CHECK



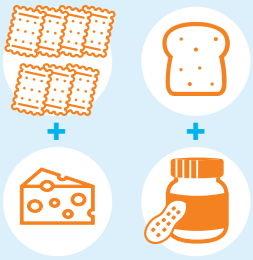
If blood sugar is 3.9 mmol/L or **ABOVE AND next meal is in the hour** ✔	If blood sugar is 3.9 mmol/L or **ABOVE AND next meal is LONGER than 1 hour away**	If blood sugar is **BELOW** 3.9 mmol/L **REPEAT steps above** ✘

Eat ONE of:

Starch:
ex. 7 crackers OR 1 slice of bread

AND

Protein:
ex. 1 piece of cheese OR
2 tablespoons of peanut butter



Are you Driving?

After treating a low, **Wait** until your blood sugar is above 5 mmol/L to start driving. Your brain might need up to 40 minutes to recover before you can safely drive again.

diabetes.ca
1-800-BANTING (226-8464) | info@diabetes.ca
DIABETES CANADA

02/24 112025

GERI-RXFILES DIABETES REFERENCES

[1] ADA 2019 standards of medical care in diabetes: older adults; Diabetes Canada 2018 CPG

[2] Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline, 2019

[3] Diabetes Canada Clinical Practice Guideline Expert Committee. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes. 2018;42(Suppl 1):S1-S325.

[4] American Diabetes Association. 11. Older adults: Standards of Medical Care in Diabetes – 2018. Diabetes Care 2018;41(Suppl. 1):S119-S125.

[5] International Diabetes Federation. Managing older people with type 2 diabetes global guideline. Brussels, Belgium: International Diabetes Federation (IDF), 2013 http://www.idf.org/sites/default/files/IDF-Guideline-for-older-people-T2D.pdf.

[6] Nuha A. ElSayed, Grazia Aleppo, Vanita R. Aroda, Raveendhara R. Bannuru, Florence M. Brown, Dennis Bruemmer, Billy S. Collins, Marisa E. Hilliard, Diana Isaacs, Eric L. Johnson, Scott Kahan, Kamlesh Khunti, Jose Leon, Sarah K. Lyons, Mary Lou Perry, Priya Prahalad, Richard E. Pratley, Jane Jeffrie Seley, Robert C. Stanton, Robert A. Gabbay; on behalf of the American Diabetes Association, 13. Older Adults: *Standards of Care in Diabetes—2023*. *Diabetes Care* 1 January 2023; 46 (Supplement_1): S216–S229. https://doi.org/10.2337/dc23-S013

[7] Idrees T, Castro-Revoredo IA, Migdal AL*, et al,* Update on the management of diabetes in long-term care facilities. *BMJ Open Diabetes Research and Care* 2022;**10:**e002705. doi: 10.1136/bmjdrc-2021-002705.

[8] International Diabetes Foundation. Recommendations for Managing Type 2 Diabetes in Primary Care, 2017. www.idf.org/managing-type2-diabetes. https://idf.org/media/uploads/2023/05/attachments-63.pdf, accessed July 1, 2024.

[9] Diabetes Canada Clinical Practice Guidelines Expert Committee. *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*. Can J Diabetes. 2018;42(Suppl 1):S1-S325. Chapter 37 of guideline

[10] Wilson E. Person-centered medication therapy for diabetes in older adults: A practical review. J Gerontological Nursing. 2021;47(10):7-13. https://doi.org/10.3928/00989134-20210908-02

[11] American Diabetes Association Professional Practice Committee; 13. Older Adults: *Standards of Care in Diabetes—2024*. *Diabetes Care* 1 January 2024; 47 (Supplement_1): S244–S257. https://doi.org/10.2337/dc24-S013

[12] By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023 Jul;71(7):2052-2081. doi: 10.1111/jgs.18372. Epub 2023 May 4. PMID: 37139824.

[13] O'Mahony D, Cherubini A, Guiteras AR, Denkinger M, Beuscart JB, Onder G, Gudmundsson A, Cruz-Jentoft AJ, Knol W, Bahat G, van der Velde N, Petrovic M, Curtin D. STOPP/START criteria for potentially inappropriate prescribing in older people: version 3. Eur Geriatr Med. 2023 Aug;14(4):625-632. doi: 10.1007/s41999-023-00777-y. Epub 2023 May 31. Erratum in: Eur Geriatr Med. 2023 Aug;14(4):633. doi: 10.1007/s41999-023-00812-y. PMID: 37256475; PMCID: PMC10447584.

[14] Huang ES, Liu JY, Moffet HH, et al. Glycemic control, complications, and death in older diabetic patients: The diabetes and aging study. Diabetes Care 2011;34:1329–36.

[15] Hamada S, Gulliford MC. Mortality in individuals aged 80 and older with type 2 diabetes mellitus in relation to glycosylated hemoglobin, blood pressure, and total cholesterol. J Am Geriatr Soc 2016;64:1425–31.

[16] Conway BN, Long DM, Figaro MK, et al. Glycemic control and fracture risk in elderly patients with diabetes. Diabetes Res Clin Pract 2016;115:47–53.

[17] International Hypoglycaemia Study Group. Glucose concentrations of less than 3.0 mmol/L (54 mg/dL) should be reported in clinical trials: A joint position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2017;40:155-157.

[18] Feinkohl I, Aung PP, Keller M, Robertson CM, Morling JR, McLachlan S, Deary IJ, Frier BM, Strachan MW, Price JF; Edinburgh Type 2 Diabetes Study (ET2DS) Investigators. Severe hypoglycemia and cognitive decline in older people with type 2 diabetes: the Edinburgh type 2 diabetes study. Diabetes Care. 2014 Feb;37(2):507-15. doi: 10.2337/dc13-1384. Epub 2013 Oct 8. PMID: 24103900.

[19] Cha SA, Yun JS, Lim TS, Hwang S, Yim EJ, Song KH, Yoo KD, Park YM, Ahn YB, Ko SH. Severe Hypoglycemia and Cardiovascular or All-Cause Mortality in Patients with Type 2 Diabetes. Diabetes Metab J. 2016 Jun;40(3):202-10. doi: 10.4093/dmj.2016.40.3.202. Epub 2016 Apr 21. PMID: 27098504; PMCID: PMC4929224.

[20] Zinman B, Marso SP, Christiansen E, Calanna S, Rasmussen S, Buse JB; LEADER Publication Committee on behalf of the LEADER Trial Investigators. Hypoglycemia, Cardiovascular Outcomes, and Death: The LEADER Experience. Diabetes Care. 2018 Aug;41(8):1783-1791. doi: 10.2337/dc17-2677. Epub 2018 Jun 14. PMID: 29903847.

[21] Munshi MN, Segal AR, Suhl e et al. Frequent hypoglycemia among elderly patients with poor glycemic control. Arch Intern Med 2011; 171:362-4

[22] Idrees T, Castro-Revoredo IA, Migdal AL, Moreno EM, Umpierrez GE. Update on the management of diabetes in long-term care facilities. BMJ Open Diabetes Res Care. 2022 Jul;10(4):e002705. doi: 10.1136/bmjdrc-2021-002705. PMID: 35858714; PMCID: PMC9305812.

[23] Flory JH, Hennessy S. Metformin use reduction in mild to moderate renal impairment: possible inappropriate curbing of use based on food and drug administration contraindications. JAMA Intern Med. 2015 Mar;175(3):458-9. doi: 10.1001/jamainternmed.2014.6936. PubMed PMID: 25561419.

[24] Nuha A. ElSayed, Grazia Aleppo, Vanita R. Aroda, Raveendhara R. Bannuru, Florence M. Brown, Dennis Bruemmer, Billy S. Collins, Marisa E. Hilliard, Diana Isaacs, Eric L. Johnson, Scott Kahan, Kamlesh Khunti, Jose Leon, Sarah K. Lyons, Mary Lou Perry, Priya Prahalad, Richard E. Pratley, Jane Jeffrie Seley, Robert C. Stanton, Robert A. Gabbay; on behalf of the American Diabetes Association, 13. Older Adults: *Standards of Care in Diabetes—2023*. *Diabetes Care* 1 January 2023; 46 (Supplement_1): S216–S229. https://doi.org/10.2337/dc23-S013

[25] Umezawa S, Kubota A, Maeda H, et al. Two-year assessment of the efficacy and safety of sitagliptin in elderly patients with type 2 diabetes: Post hoc analysis of the ASSET-K study. BMC Endocr Disord 2015;15:34.

[26] Lajara R, Aguilar R, Hehnke U, et al. Efficacy and safety of linagliptin in subjects with long-standing type 2 diabetes mellitus (>10 years): Evidence from pooled data of randomized, double-blind, placebo-controlled, phase III trials. Clin Ther 2014;36:1595–605.

[27] Schernthaner G, Barnett AH, Patel S, et al. Safety and efficacy of the dipeptidyl peptidase-4 inhibitor linagliptin in elderly patients with type 2 diabetes: A comprehensive analysis of data from 1331 individuals aged ≥ 65 years. Diabetes Obes Metab 2014;16:1078–86.

[28] Round EM, Engel SS, Golm GT, et al. Safety of sitagliptin in elderly patients with type 2 diabetes: A pooled analysis of 25 clinical studies. Drugs Aging 2014;31:203–14.
[29] Barnett AH, Huisman H, Jones R, et al. Linagliptin for patients aged 70 years or older with type 2 diabetes inadequately controlledwith common antidiabetes treatments: A randomised, double-blind, placebo-controlled trial. Lancet 2013;382:1413–23.
[30] Karyekar CS, Ravichandran S, Allen E, et al. Tolerability and efficacy of glycemic control with saxagliptin in older patients (aged ≥ 65 years) with inadequately controlled type 2 diabetes mellitus. Clin Interv Aging 2013;8:419–30.
[31] Schwartz SL. Treatment of elderly patients with type 2 diabetes mellitus: A systematic review of the benefits and risks of dipeptidyl peptidase-4 inhibitors. Am J Geriatr Pharmacother 2010;8:405–18.
[32] Doucet J, Chacra A, Maheux P, et al. Efficacy and safety of saxagliptin in older patients with type 2 diabetes mellitus. Curr Med Res Opin 2011;27:863–9.
[33] Barzilai N, Guo H, Mahoney EM, et al. Efficacy and tolerability of sitagliptin monotherapy in elderly patients with type 2 diabetes: A randomized, doubleblind, placebo-controlled trial. Curr Med Res Opin 2011;27:1049–58.
[34] Chien M-N, Lee C-C, ChenW-C, et al. Effect of sitagliptin as add-on therapy in elderly type 2 diabetes patients with inadequate glycemic control in taiwan. Int J Gerontol 2011;5:103–6. http://www.sciencedirect.com/science/article/pii/S1873959811000469.
[35] Shankar RR, Xu L, Golm GT, et al. A comparison of glycaemic effects of sitagliptin and sulfonylureas in elderly patients with type 2 diabetes mellitus. Int J Clin Pract 2015;69:626–31.
[36] Bron M, Wilson C, Fleck P. A post hoc analysis of HbA1c, hypoglycemia, and weight change outcomes with alogliptin vs glipizide in older patients with type 2 diabetes. Diabetes Ther 2014;5:521–34.
[37] Schernthaner G, Duran-Garcia S, Hanefeld M, et al. Efficacy and tolerability of saxagliptin compared with glimepiride in elderly patients with type 2 diabetes: A randomized, controlled study (GENERATION). Diabetes Obes Metab 2015;17:630–8.
[38] Hartley P, Shentu Y, Betz-Schiff P, et al. Efficacy and tolerability of sitagliptin compared with glimepiride in elderly patients with type 2 diabetes mellitus and inadequate glycemic control: A randomized, double-blind, non-inferiority trial. Drugs Aging 2015;32:469–76.
[39] Rosenstock J, Wilson C, Fleck P. Alogliptin versus glipizide monotherapy in elderly type 2 diabetes mellitus patients with mild hyperglycaemia: A prospective, double-blind, randomized, 1-year study. Diabetes Obes Metab 2013;15:906–14.
[40] Inzucchi SE, Nauck MA, Hehnke U, et al. Improved glucose control with reduced hypoglycaemic risk when linagliptin is added to basal insulin in elderly patients with type 2 diabetes. Diabetes Obes Metab 2015;17:868–77.
[41] Leiter LA, Teoh H, Braunwald E, et al. Efficacy and safety of saxagliptin in older participants in the SAVOR-TIMI 53 trial. Diabetes Care 2015;38:1145–53.
[42] DC 2018 CPG
[43] Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, Josse R, Kaufman KD, Koglin J, Korn S, Lachin JM, McGuire DK, Pencina MJ, Standl E, Stein PP, Suryawanshi S, Van de Werf F, Peterson ED, Holman RR; TECOS Study Group. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015 Jul 16;373(3):232-42. doi: 10.1056/NEJMoa1501352. Epub 2015 Jun 8. Erratum in: N Engl J Med. 2015 Aug 6;373(6):586. PubMed PMID: 26052984.
[44] Barnett AH, Huisman H, Jones R, von Eynatten M, Patel S, Woerle HJ. Linagliptin for patients aged 70 years or older with type 2 diabetes inadequately controlled with common antidiabetes treatments: a randomised, double-blind, placebo-controlled trial. Lancet. 2013 Oct 26;382(9902):1413-23. doi:10.1016/S0140-6736(13)61500-7. Epub 2013 Aug 13. PubMed PMID: 23948125.
[45] Bilal A, Pratley RE. Newer Glucose-Lowering Therapies in Older Adults with Type 2 Diabetes. Endocrinol Metab Clin North Am. 2023 Jun;52(2):355-375. doi: 10.1016/j.ecl.2022.10.010. Epub 2023 Feb 20. PMID: 36948784.
[46] Frías JP, Davies MJ, Rosenstock J, Pérez Manghi FC, Fernández Landó L, Bergman BK, Liu B, Cui X, Brown K; SURPASS-2 Investigators. Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes. N Engl J Med. 2021 Aug 5;385(6):503-515. doi: 10.1056/NEJMoa2107519. Epub 2021 Jun 25. PMID: 34170647.
[47] Jessica A. Huthmacher, Juris J. Meier, Michael A. Nauck; Efficacy and Safety of Short- and Long-Acting Glucagon-Like Peptide 1 Receptor Agonists on a Background of Basal Insulin in Type 2 Diabetes: A Meta-analysis. *Diabetes Care* 1 September 2020; 43 (9): 2303–2312. https://doi.org/10.2337/dc20-0498
[48] Karagiannis T, Tsapas A, Athanasiadou E, et al. GLP-1 receptor agonists and SGLT2 inhibitors for older people with type 2 diabetes: a systematic review and meta-analysis. Diabetes Res Clin Pract 2021;174:108737
[49] Vemulapalli HS, Vajje J, Rehman W, Virk GS, Shah K, Chaudhari SS, Mian IU, Saleem F. Safety and Efficacy of Liraglutide on Cardiovascular Outcomes in Patients With Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials. Cureus. 2023 Sep 17;15(9):e45421. doi: 10.7759/cureus.45421. PMID: 37854744; PMCID: PMC10581595.
[50] Marso S, Danels G, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016;374:311-22.
[51] Marso S, Bain S, console A, et al. Semaglutide and cardiovascular outcomes in pateints with type 2 diabetes. N Engl J Med 2016;375:1834-44.
[52] Pfeffer M, Claggett B, Diaz R, et al. Lixisenatide in patients with type 2 diabetes and acute coronary syndrome. N Eng J Med. 2015;373:2247-57.
[53] Holman RR, Bethel MA, Mentz RJ, et al. Effects of Once-Weekly Exenatide on Cardiovascular Outcomes in Type 2 Diabetes. (EXSCEL) N Engl J Med. 2017 Sep 14.
[54] Perkovic V, Tuttle KR, Rossing P, Mahaffey KW, Mann JFE, Bakris G, Baeres FMM, Idorn T, Bosch-Traberg H, Lausvig NL, Pratley R; FLOW Trial Committees and Investigators. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. N Engl J Med. 2024 May 24. doi: 10.1056/NEJMoa2403347. Epub ahead of print. PMID: 38785209.
[55] Husain M, Birkenfeld AL, Donsmark M, Dungan K, Eliaschewitz FG, Franco DR, Jeppesen OK, Lingvay I, Mosenzon O, Pedersen SD, Tack CJ, Thomsen M, Vilsbøll T, Warren ML, Bain SC; PIONEER 6 Investigators. Oral Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2019 Aug 29;381(9):841-851. doi: 10.1056/NEJMoa1901118. Epub 2019 Jun 11. PMID: 31185157.
[56] Aldafas R, Crabtree T, Alkharaiji M, Vinogradova Y, Idris I. Sodium-glucose cotransporter-2 inhibitors (SGLT2) in frail or older people with type 2 diabetes and heart failure: a systematic review and meta-analysis. Age Ageing. 2024 Jan 2;53(1):afad254. doi: 10.1093/ageing/afad254. PMID: 38287703; PMCID: PMC10825241.
[57] Kluger AY, Tecson KM, Lee AY, Lerma EV, Rangaswami J, Lepor NE, Cobble ME, McCullough PA. Class effects of SGLT2 inhibitors on cardiorenal outcomes. Cardiovasc Diabetol. 2019 Aug 5;18(1):99. doi: 10.1186/s12933-019-0903-4. PMID: 31382965; PMCID: PMC6683461.

[58] Zannad F, Ferreira JP, Pocock SJ, Anker SD, Butler J, Filippatos G, Brueckmann M, Ofstad AP, Pfarr E, Jamal W, Packer M. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. Lancet. 2020 Sep 19;396(10254):819-829. doi: 10.1016/S0140-6736(20)31824-9. Epub 2020 Aug 30. PMID: 32877652.

[59] Ingelfinger JR, Rosen CJ. Clinical Credence - SGLT2 Inhibitors, Diabetes, and Chronic Kidney Disease. N Engl J Med. 2019 Jun 13;380(24):2371-2373. doi: 10.1056/NEJMe1904740. Epub 2019 Apr 14. PMID: 30990261.

[60] Jongs N, Greene T, Chertow GM, McMurray JJV, Langkilde AM, Correa-Rotter R, Rossing P, Sjöström CD, Stefansson BV, Toto RD, Wheeler DC, Heerspink HJL; DAPA-CKD Trial Committees and Investigators. Effect of dapagliflozin on urinary albumin excretion in patients with chronic kidney disease with and without type 2 diabetes: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol. 2021 Nov;9(11):755-766. doi: 10.1016/S2213-8587(21)00243-6. Epub 2021 Oct 4. PMID: 34619106.

[61] The EMPA-KIDNEY Collaborative Group; Herrington WG, Staplin N, Wanner C, Green JB, Hauske SJ, Emberson JR, Preiss D, Judge P, Mayne KJ, Ng SYA, Sammons E, Zhu D, Hill M, Stevens W, Wallendszus K, Brenner S, Cheung AK, Liu ZH, Li J, Hooi LS, Liu W, Kadowaki T, Nangaku M, Levin A, Cherney D, Maggioni AP, Pontremoli R, Deo R, Goto S, Rossello X, Tuttle KR, Steubl D, Petrini M, Massey D, Eilbracht J, Brueckmann M, Landray MJ, Baigent C, Haynes R. Empagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2023 Jan 12;388(2):117-127. doi: 10.1056/NEJMoa2204233. Epub 2022 Nov 4. PMID: 36331190; PMCID: PMC7614055.

[62] Hawker K, Akter R, Molnar F, Frank C. Management of type 2 diabetes in patients with frailty. Can Fam Physician. 2024 Jan;70(1):30-32. doi: 10.46747/cfp.700130. PMID: 38262761; PMCID: PMC11126279.

[63] Government of Canada. Summary Safety Review – SGLT2 Inhibitors (canagliflozin, dapagliflozin, empagliflozin) – Assessing the risk of the body producing high levels of acids in the blood (diabetic ketoacidosis. May 16, 2016. https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/summary-safety-review-sglt2-inhibitors-canagliflozin-dapagliflozin-empagliflozin.html, accessed June 14, 2018

[64] Bellary S, Kyrou I, Brown JE, Bailey CJ. Type 2 diabetes mellitus in older adults: clinical considerations and management. Nat Rev Endocrinol. 2021 Sep;17(9):534-548. doi: 10.1038/s41574-021-00512-2. Epub 2021 Jun 25. PMID: 34172940.

[65] Idrees T, Castro-Revoredo IA, Migdal AL, Moreno EM, Umpierrez GE. Update on the management of diabetes in long-term care facilities. BMJ Open Diabetes Res Care. 2022 Jul;10(4):e002705. doi: 10.1136/bmjdrc-2021-002705. PMID: 35858714; PMCID: PMC9305812.

[66] Beck RW, Riddlesworth T, Ruedy K, Ahmann A, Bergenstal R, Haller S, Kollman C, Kruger D, McGill JB, Polonsky W, Toschi E, Wolpert H, Price D; DIAMOND Study Group. Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections: The DIAMOND Randomized Clinical Trial. JAMA. 2017 Jan 24;317(4):371-378. doi: 10.1001/jama.2016.19975. PMID: 28118453.

[67] Munshi M, Slyne C, Segal A, et al. Simplification of insulin regimen in older adults and risk of hypoglycemia. JAMA Intern Med 2016;176:1023-6.

[68] Lederle LI, Steinman MA, Jing B, Nguyen B, Lee SJ. Glycemic treatment deintensification practices in nursing home residents with type 2 diabetes. J Am Geriatr Soc. 2022 Jul;70(7):2019-2028. doi: 10.1111/jgs.17735. Epub 2022 Mar 23. PMID: 35318647; PMCID: PMC9283249.

[69] DC 2018 CPG

[70] Geller AI, Shehab N, Lovegrove MC, Kegler SR, Weidenbach KN, Ryan GJ, Budnitz DS. National estimates of insulin-related hypoglycemia and errors leading to emergency department visits and hospitalizations. JAMA Intern Med. 2014 May;174(5):678-86. doi: 10.1001/jamainternmed.2014.136. PubMed PMID: 24615164.

[71] Stone J, Houlden R, Lin P, Udell J, Verma S. . *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*: Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Can J Diabetes 2018;42(Suppl 1):S162-S169.

[72] Peripheral Arterial Disease. Thrombosis Canada, 2021. https://thrombosiscanada.ca/wp-content/uploads/2021/09/32.-Peripheral-Arterial-Disease_17September2021.pdf, accessed July 5, 2024.

[73] CADTH. New Drugs for Type 2 Diabetes: Second-Line Therapy – Recommendations Report. May 2017. https://www.cadth.ca/dv/new-drugs-type-2-diabetes-second-line-therapy-recommendations-report