# Diabetes and Ageing: Unique Considerations and Goals of Care

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# Disclosures

## Relevant relationships with commercial entities:

- None

## Potential for conflicts within this presentation:

- Discussing specific diabetes products and therapeutics

## Steps taken to review and mitigate potential bias:

- Will discuss all available products in Canada
- Not endorsing any specific product

# Objectives

1) To review blood glucose targets for older adults with diabetes
2) To highlight medication considerations unique to an older population
3) To discuss the use of technology in older adults with diabetes

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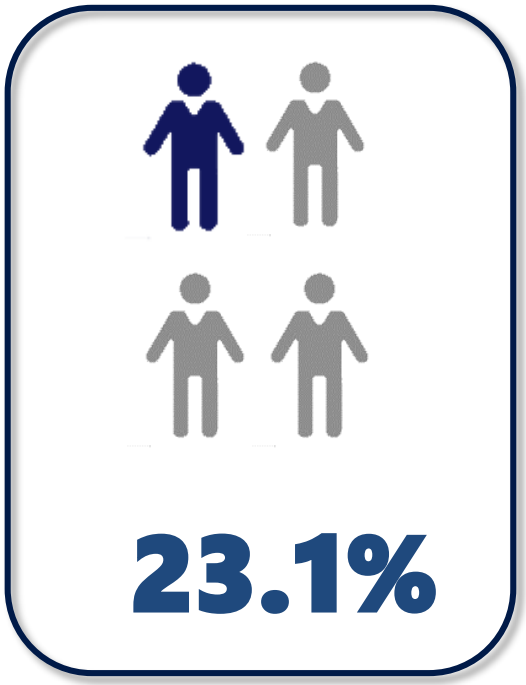
# Case

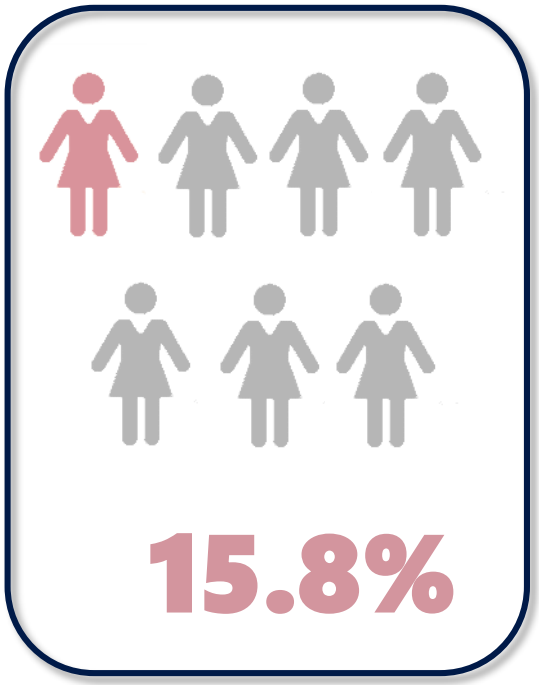
You are seeing a 70 year old male in diabetes clinic. He has a 20-year history of type 2 diabetes. He had a myocardial infarction at the age of 58, and he has mild to moderate chronic kidney disease (eGFR 55ml/min/1.73m$^2$).

Current Medications: Novomix 30/70, metformin, linagliptin, ramipril, atorvastatin.

His HbA1c is 7.4% and he has minimal hypoglycemia. He is not frail.

# 1 in 5 Canadians older than 65 have Diabetes



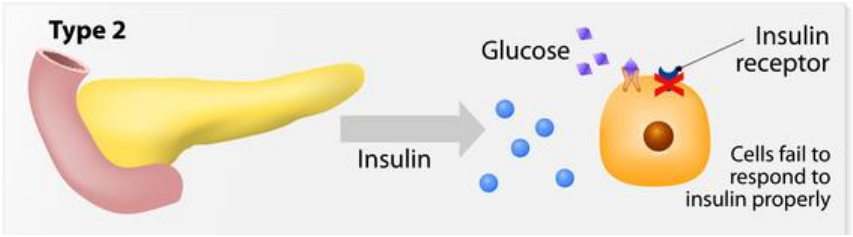




Statistics Canada, Diabetes by age group, 2019

# Type 1 vs. Type 2 Diabetes

## Type 2 Diabetes

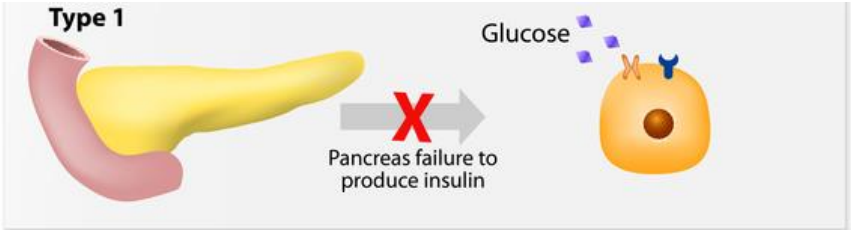
**90-95%**





## Type 1 Diabetes

**5-10%**





https://ghr.nlm.nih.gov/condition/type-2-diabetes

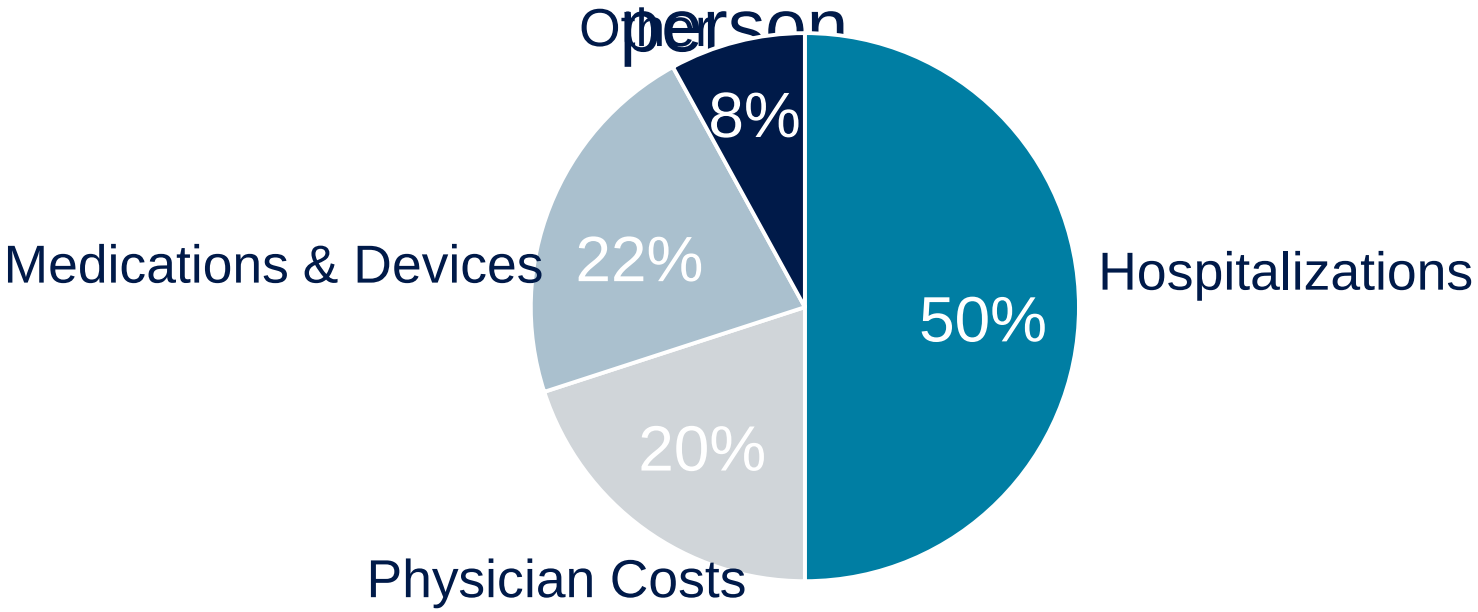
# Hemoglobin A1c

**Reflects average blood glucose control over the past 3 months**

| | |
|---|---|
| **>6.5%** | **Diabetes** |
| **6.0-6.5%** | **Prediabetes** |
| **<6.0%** | **Normal** |

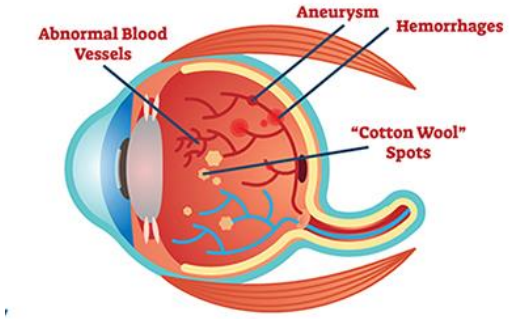
# Diabetes is Costly for the Health Care System

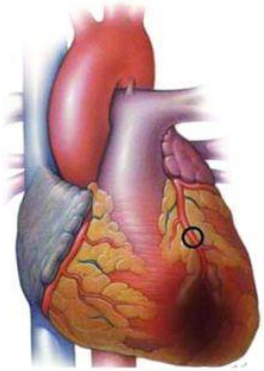
In the first 8 years after a new diabetes diagnosis, the excess costs of diabetes in Ontario are **$10,000** per person

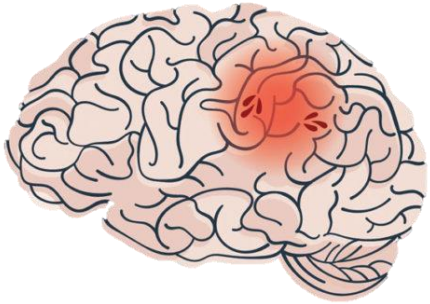


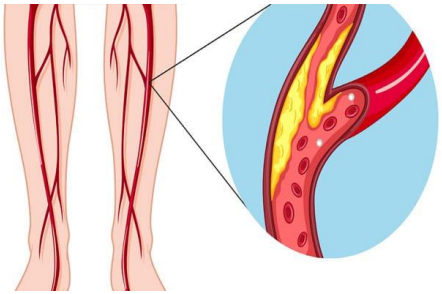

Rosella et al., Diabetic Medicine, 2015; 33(3): 395-403.

# Diabetes Complications



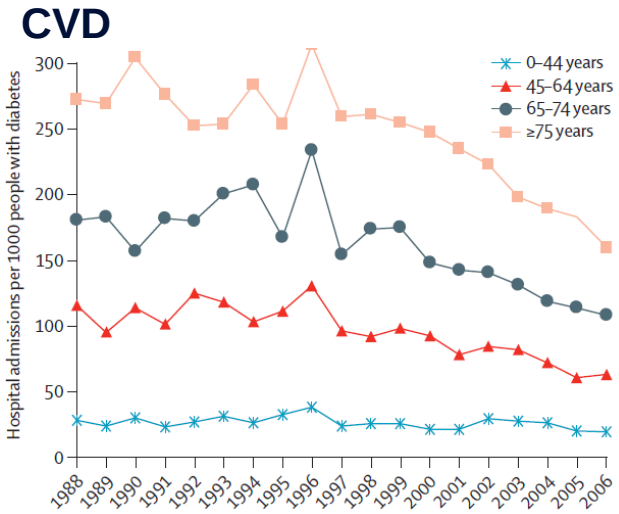



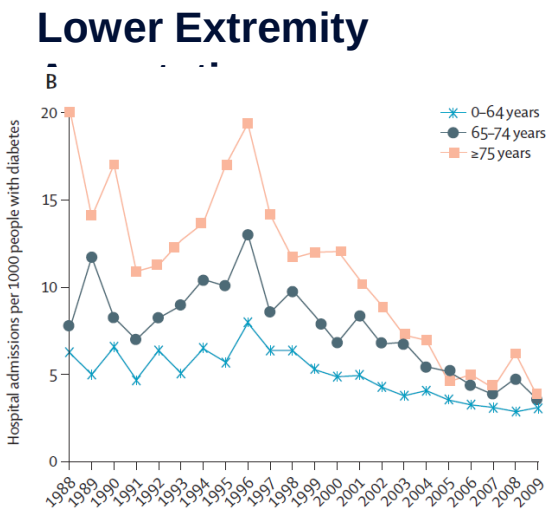


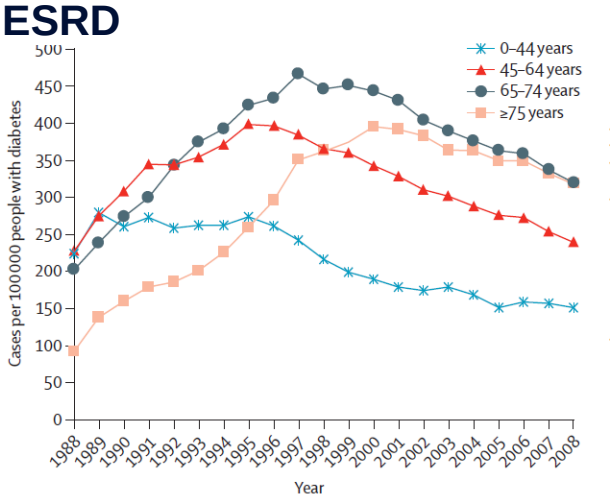


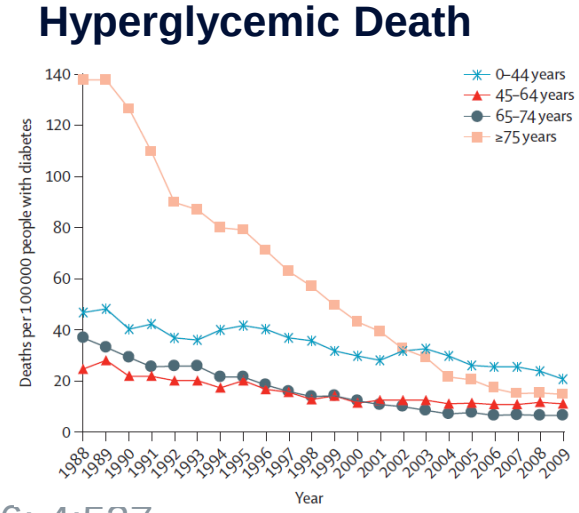
https://www.passionpodiatry.com/single-post/How-To-Manage-Foot-Ulcer
https://fmcna.com/products/home-dialysis-equipment/2008kathome/
https://www.aoa.org/healthy-eyes/eye-and-vision-conditions/diabetic-retinopathy?sso=y
https://www.ahajournals.org/doi/full/10.1161/CIR.0b013e31826e1058
https://health.clevelandclinic.org/how-to-prevent-a-second-stroke/
https://www.medgadget.com/2019/12/global-peripheral-artery-disease-market-2020-overview-size-estimation-share-growth-analysis-competitive-landscape-top-key-players-strategy-profiling-regional-outlook-by-2025.html

# Rates of Type 2 Diabetes Complications are Declining



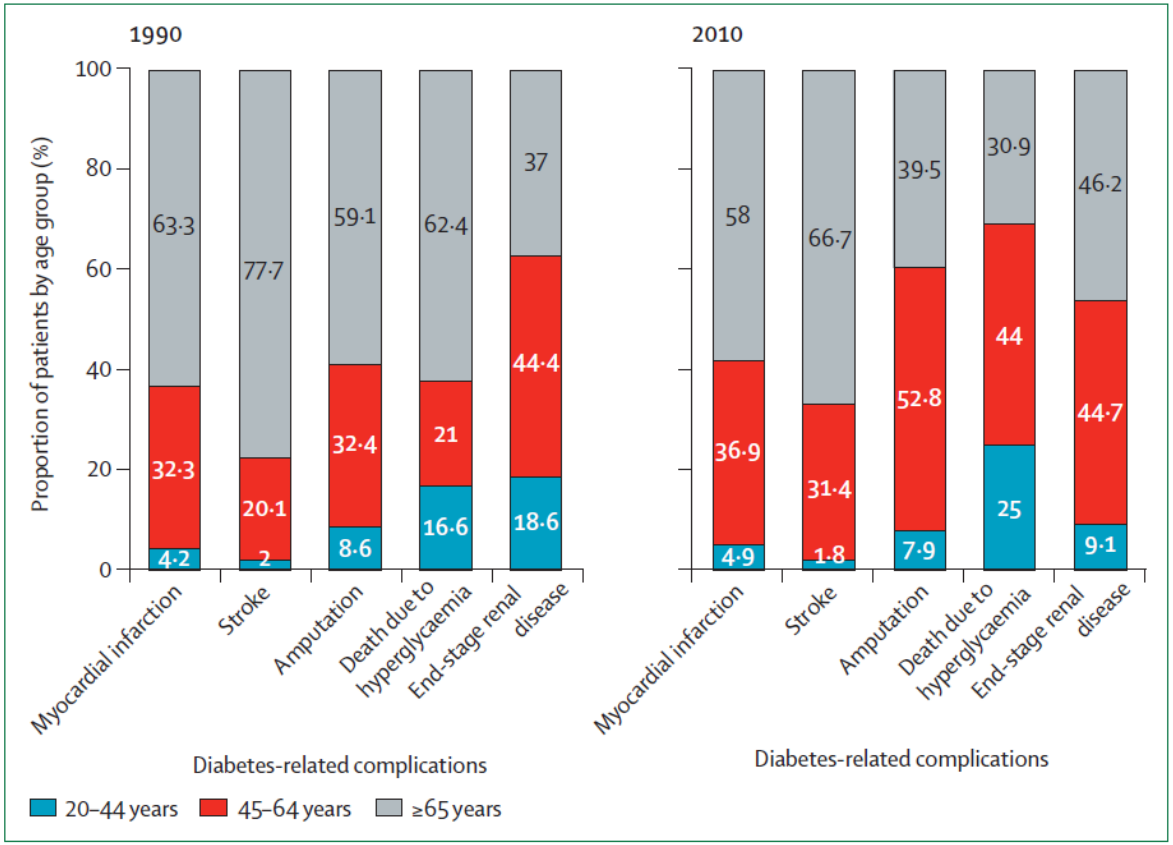




Gregg et al., Lancet Diabetes & Endocrinology, 2016; 4:537-547.

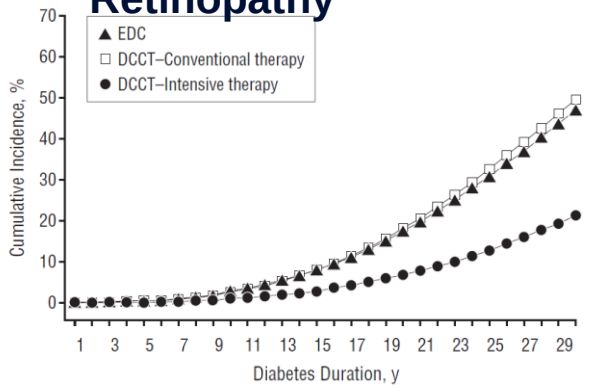
# A Large Proportion of Diabetes Complications Occur in Older Adults



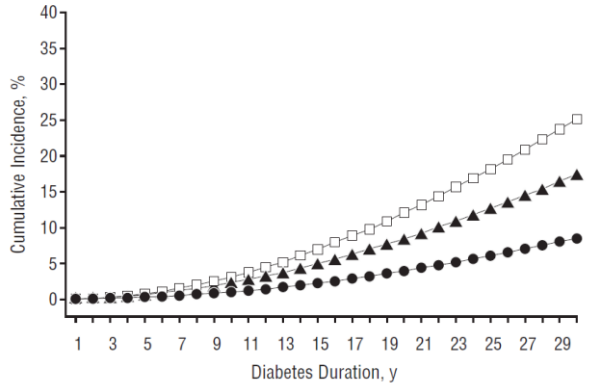

Gregg et al., Lancet Diabetes & Endocrinology, 2016; 4:537-547.

# The Burden of Complications in Type 1 Diabetes is High

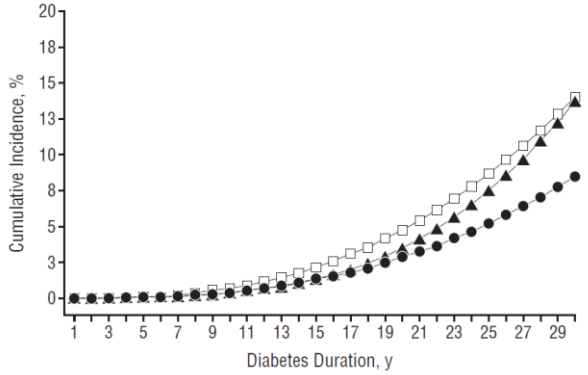
**Proliferative Retinopathy**




**Nephropathy**

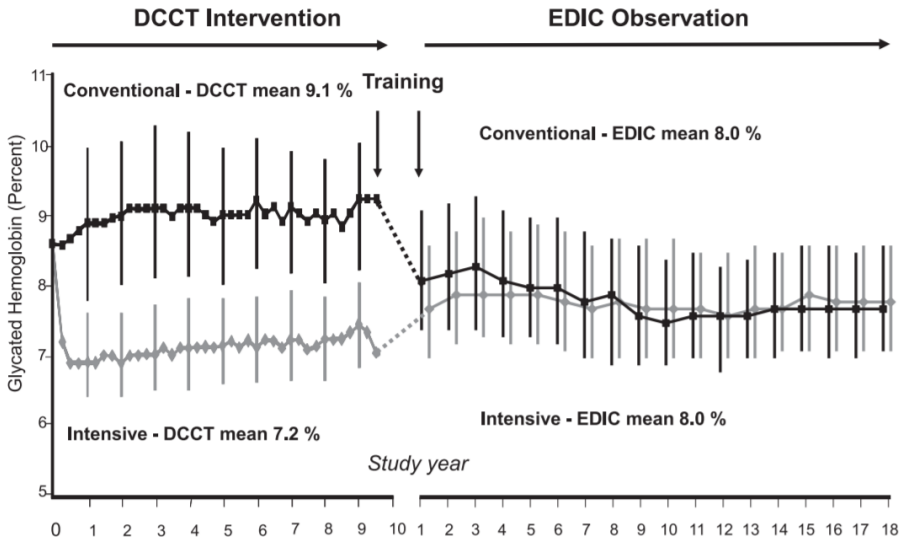



**CVD**




Nathan et al., Arch Intern Med, 2009; 169(14): 1307- 1316.

# The Importance of Blood Glucose Control for Reducing Complications (DCCT)

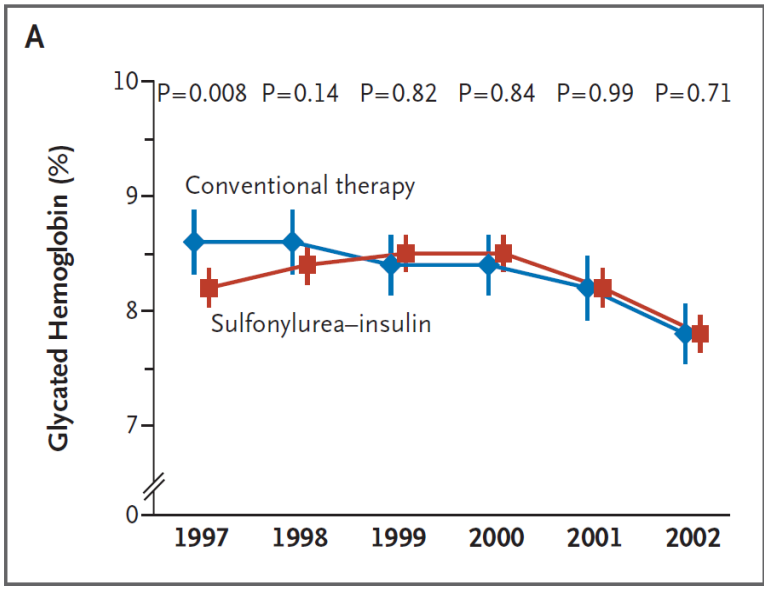


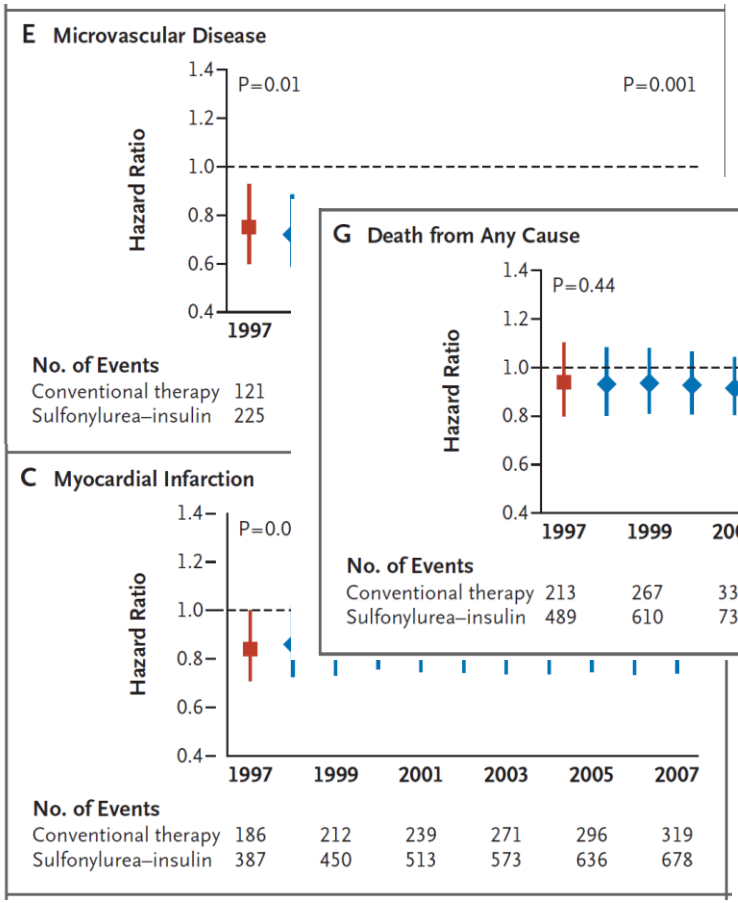

| | % Reduction | |
|---|---|---|
| | During DCCT (n=1441) | During EDIC (n=1357) |
| **Retinopathy (3-step change)** | 63 | 72 |
| **Microalbuminuria** | 39 | 53 |
| **Macroalbuminuria** | 51 | 77 |
| **Neuropathy** | 60 | - |
| **Cardiovascular Disease** | - | 42 |

Summary of the DCCT/EDIC Study: https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/GetPdf.cgi?id=phd000390

DCCT/EDIC Study Research Group, NEJM, 2005; 353(25): 2643-2653. Nathan et al., Diabetes Care, 2014; 37: 9-16.

# The Importance of Blood Glucose Control for Reducing Complications (UKPDS)



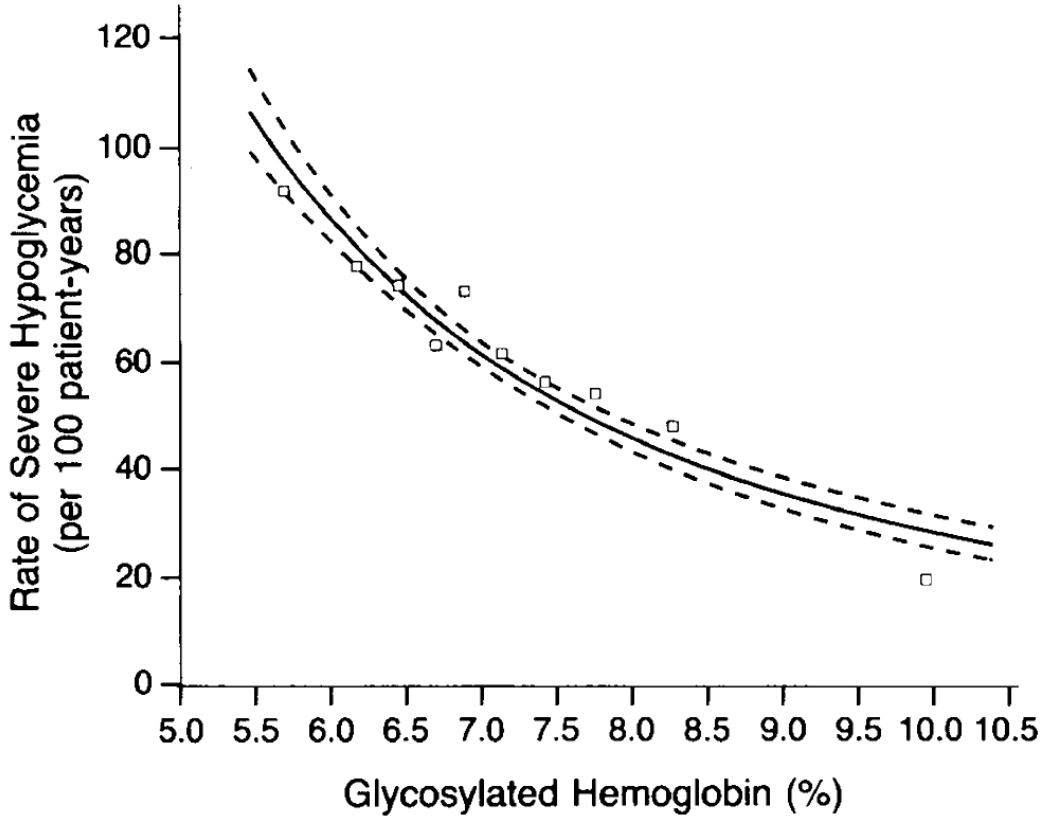

Holman et al., NEJM, 2008; 359: 1577-1589.

# Blood Glucose Control and Diabetes Complications

**Summary:**

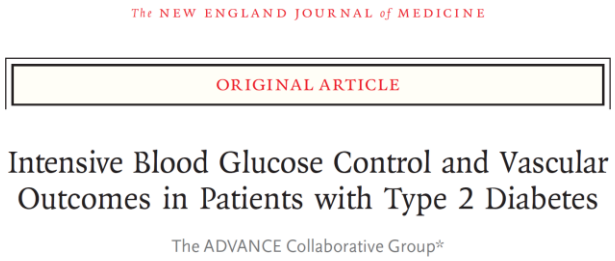
- Both type 1 and type 2 diabetes are associated with a high burden of complications in older adults, though rates are declining over time
- Complications result in morbidity, mortality, and costs to the health care system
- Lowering blood glucose levels is the dominant strategy for reducing complications

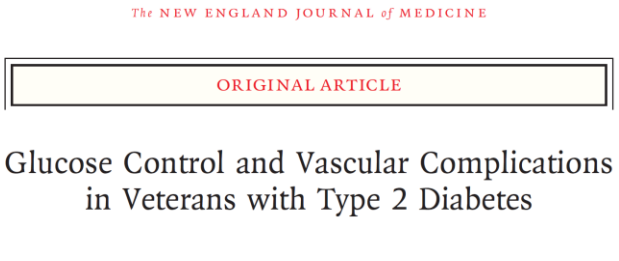
# The Risk of Hypoglycemia Increases as Blood Glucose Levels Decrease

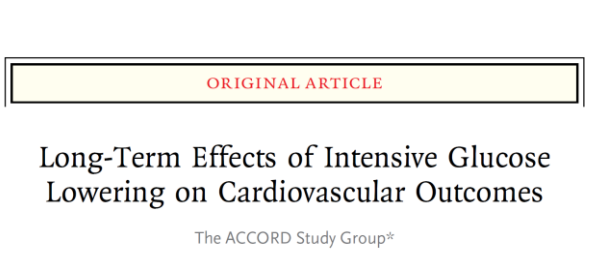



DCCT Research Group, NEJM, 1993; 329(14): 977-986.

# Glycemic Control




↔ **MACE**

↔ **MACE**

↑ **deaths**

↓ **nephropathy**

↓ **albuminuria**

ADVANCE group, NEJM, 2008; 358: 2560-72.
Duckworth et al., NEJM, 2009; 360(2): 129-139.
ACCORD group, NEJM, 2011; 364: 818-828.

# A Balancing Act

**Hyperglycemia**

**Hypoglycemia**

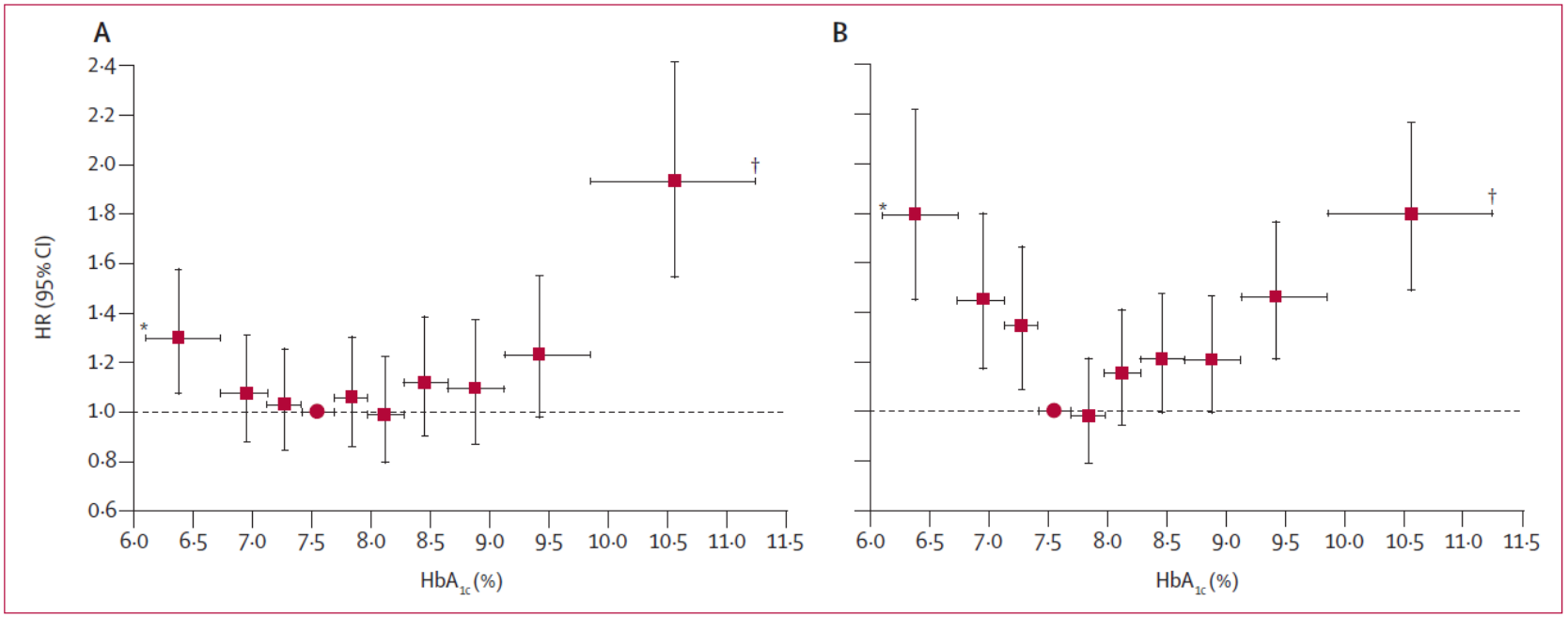
**Chronic:**
- Micro- and macrovascular complications

**Acute:**
- Infections
- Dehydration
- Vision impairment
- Urinary incontinence

**Chronic:**
- Dementia
- Cardiovascular mortality

**Acute:**
- Falls
- Seizure
- Death

# U-Shaped Association between HbA1c and Mortality in Older Adults




Metformin + SU regimen

Insulin regimen

Currie et al, Lancet, 2010; 375: 481-489.

# Recommended Glycemic Targets 2018 Diabetes Canada Clinical Practice Guidelines

| | |
|---|---|
| ≤ 6.5 | Adults with type 2 diabetes to reduce the risk of CKD and retinopathy if at low risk of hypoglycemia* |
| ≤ 7.0 | **MOST ADULTS WITH TYPE 1 OR TYPE 2 DIABETES** |
| 7.1 ↓ 8.5 | Functionally dependent*: **7.1-8.0%**<br>Recurrent severe hypoglycemia and/or hypoglycemia unawareness: **7.1-8.5%**<br>Limited life expectancy: **7.1-8.5%**<br>Frail elderly and/or with dementia†: **7.1-8.5%** |
| | Avoid higher A1C to minimize risk of symptomatic hyperglycemia and acute and chronic complications |

End of life: A1C measurement not recommended. Avoid symptomatic hyperglycemia and any hypoglycemia.
* based on class of antihyperglycemic medication(s) utilized and the person's characteristics
† see Diabetes in Older People chapter, p. S283

# Recommended Glycemic Targets 2018 Diabetes Canada Clinical Practice Guidelines




| | Functionally Independent | Functionally Dependent | Frail and/or with dementia | End of life |
|---|---|---|---|---|
| Clinical Frailty Index | 1-3 | 4-5 | 6-8 | 9 |
| **HbA1c Target** | | | | |
| Low-risk for hypoglycemia | ≤7.0% | <8.0% | <8.5% | Not measured |
| High-risk for hypoglycemia | | 7.1-8.0% | 7.1-8.5% | Not measured |
| **Capillary Blood Glucose** | | | | |
| Preprandial | 4-7mmol/L | 5-8mmol/L | 6-9mmol/L | Individualized |
| Postprandial | 5-10mmol/L | <12mmol/L | <14mmol/L | Individualized |

# Risk Factor Modification by Life Expectancy

**Table 2** Median remaining life expectancy (25th, 75th percentiles) by modified ADA Framework and age categories

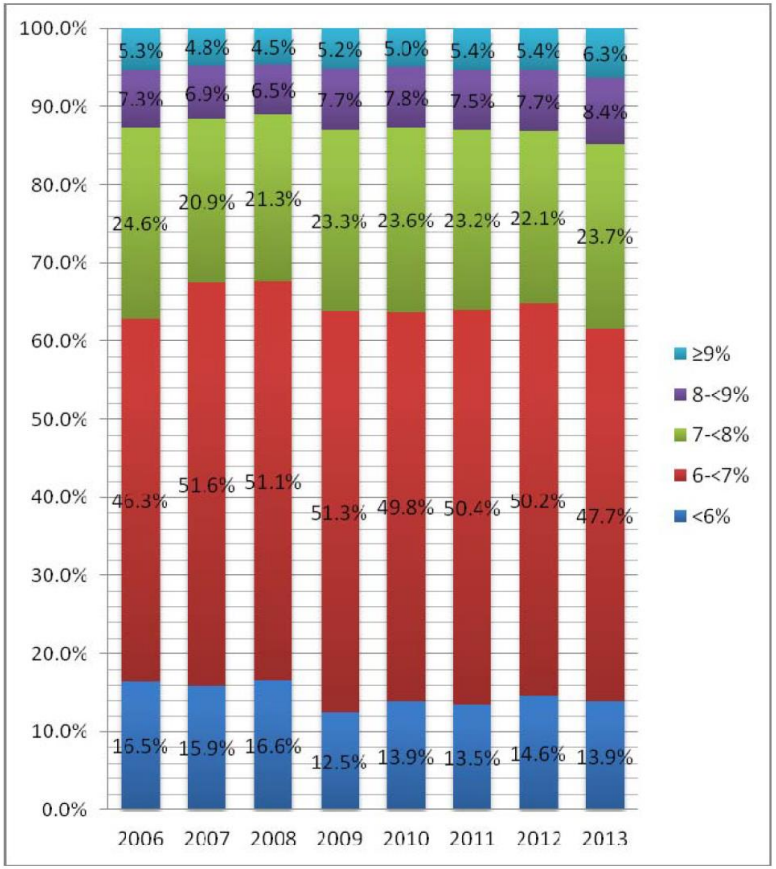
| Age | Healthy | Intermediate Health | Poor Health |
|---|---|---|---|
| 65–69 | 16.3 [10.2, 21.9] | 10.5 [5.5, 16.0] | 6.4 [2.7, 12.0] |
| 70–74 | 12.5 [7.2, 17.6] | 8.9 [4.5, 14.0] | 4.5 [1.9, 8.6] |
| 75–79 | 10.1 [5.5, 14.8] | 8.4 [4.2, 13.2] | 3.9 [1.6, 7.5] |
| 80+ | 7.6 [3.9, 11.7] | 5.9 [2.8, 9.8] | 2.6 [1.1, 5.1] |

ADA, American Diabetes Association.

***8 years for glycemic control***
***2-3 years for blood pressure and lipid control***

Lee et al., BMJ Open Diab Res Care, 2008; 8: e001624.
Kirkman et al., Diabetes Care, 2012; 35: 2650-2664,

# Over Half of Adults >75 in the U.S. have HbA1c <7.0%



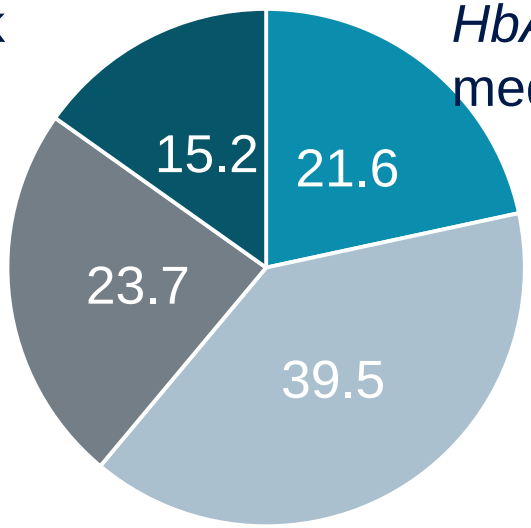

Lipska et al., Diabetes Care, 2017;40:468-475.

# Potential Overtreatment in Older Adults with Diabetes

***In 108,620 Ontarians > age 75 with diabetes:***

*HbA1c 7.0-8.5%,* low-risk meds

*HbA1c <7.0%,* high-risk meds

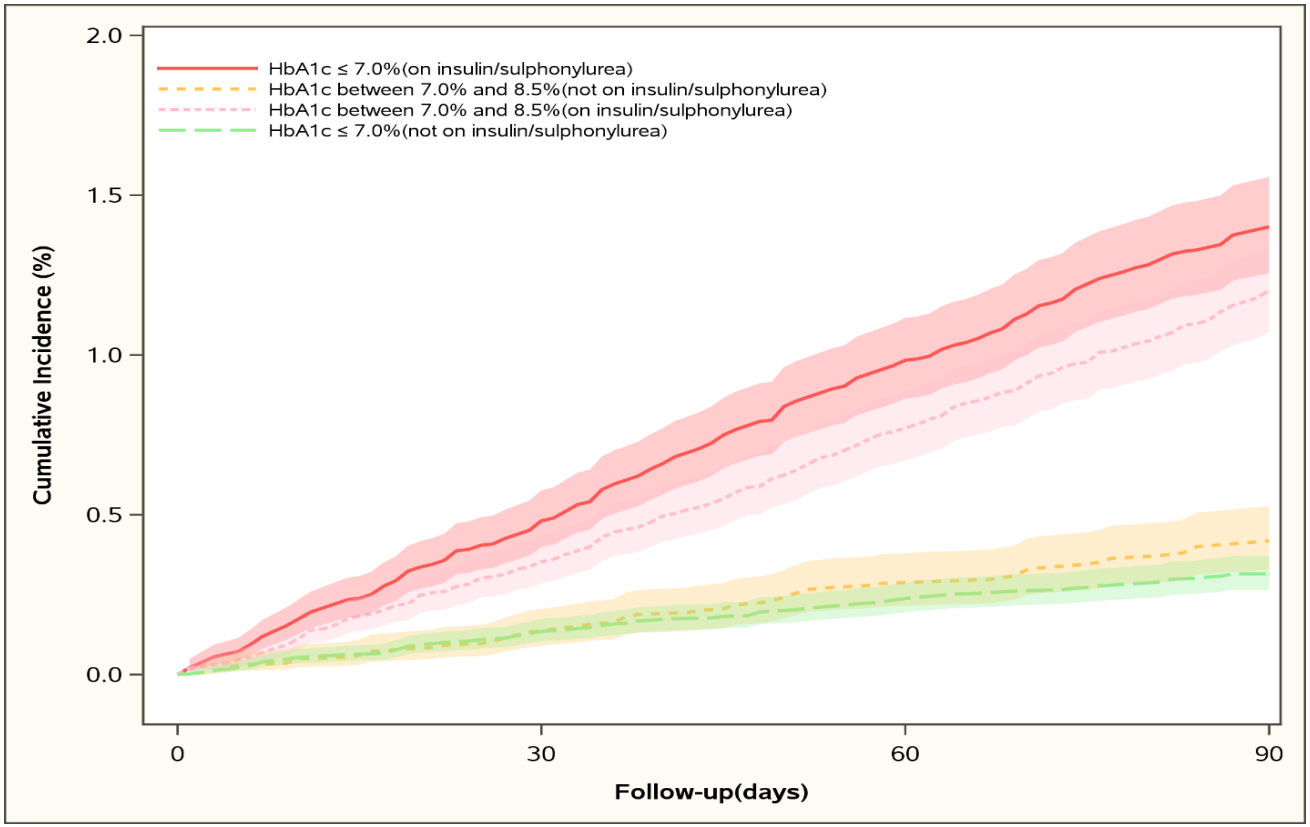



*HbA1c 7.0-8.5%*, high-risk meds

*HbA1c <7.0%*, low-risk med

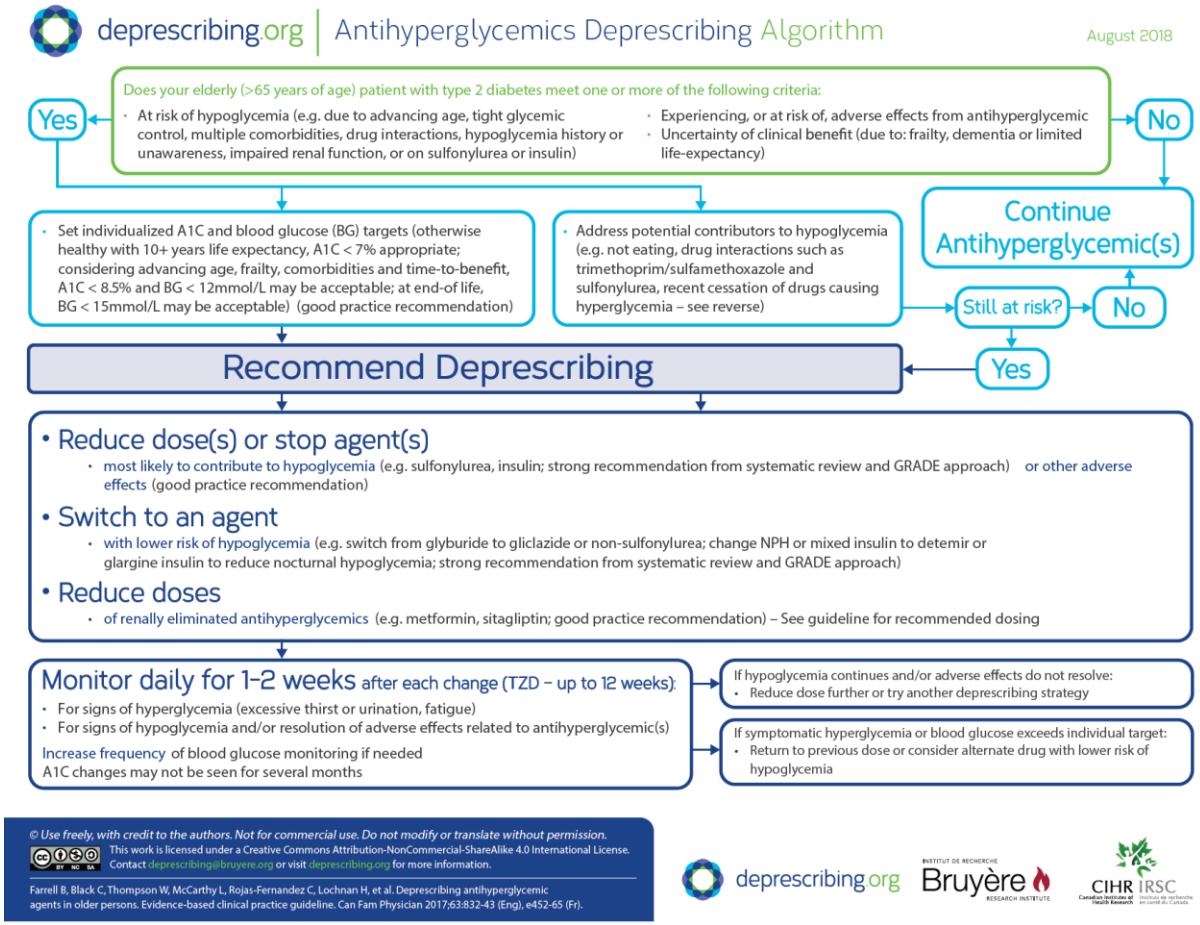
Lega et al, Diabetologia, 2020, in press.

# Cumulative Incidence of Adverse Events in 108,000 Ontarians > Age 75 with Diabetes




Lega et al, Diabetologia, 2020, in press.

# Deprescribing Antihyperglycemic Medications




Barbara Farrell & Cara Tanenbaum, www.deprescribing.org

# Comprehensive Risk Factor Reduction

- Smoking cessation
- Blood pressure lowering
- Lipid lowering
- Aspirin for secondary prevention
- Exercise
- Avoid complex nutrition plans

Zahedi et al., Diabetes Canada 2018 Guidelines, Chapter 37

# Summary

- The use of high-risk medications in older adults is still common and associated with harm
- Consider frailty and life expectancy when choosing glycemic targets for older adults
- Consider deprescribing, with high-risk medications (insulin, SU) the first to be discontinued
  - Choose lower risk within the high-risk category

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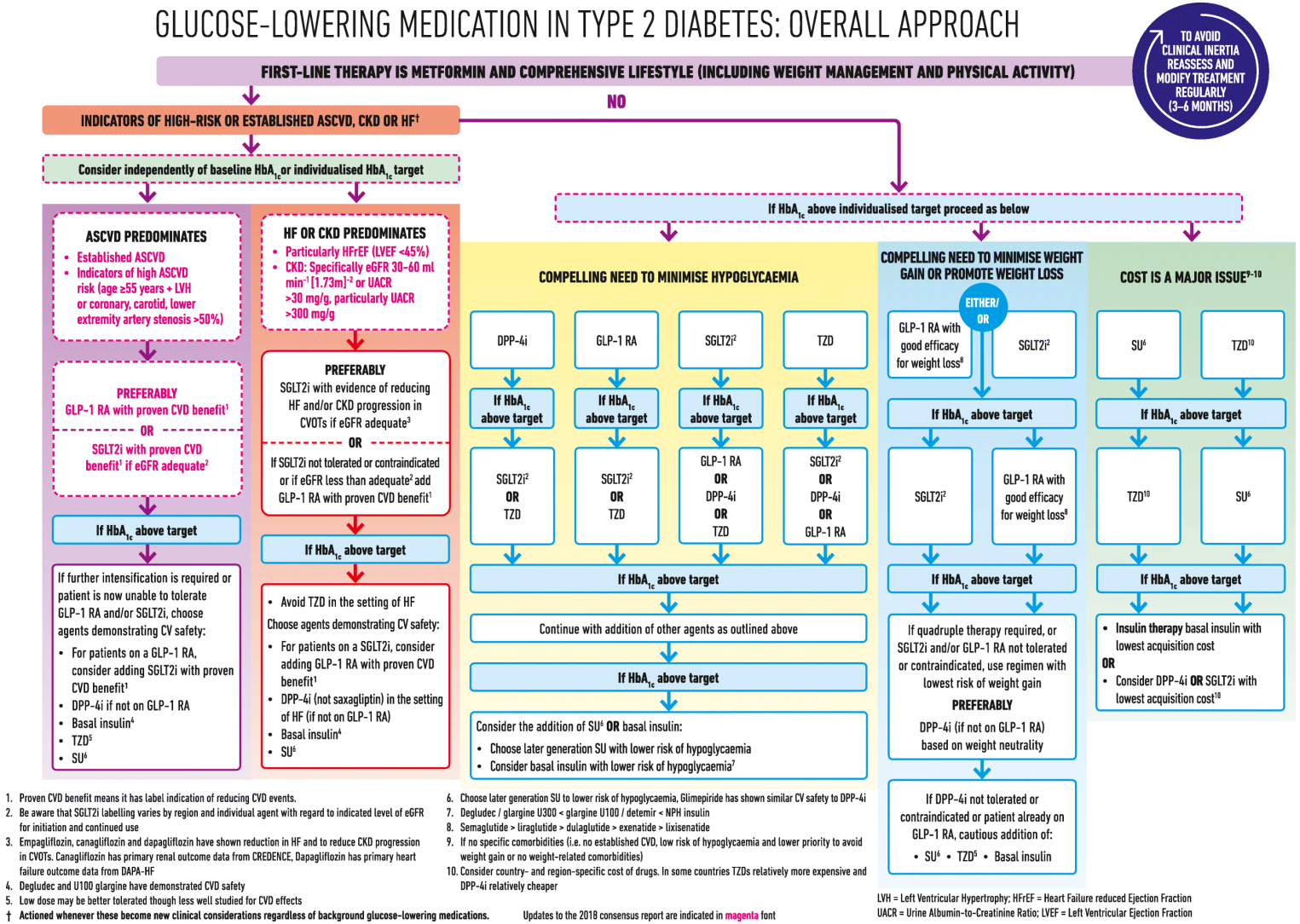
# GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH




1. Proven CVD benefit means it has label indication of reducing CVD events.
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE, Dapagliflozin has primary heart failure outcome data from DAPA-HF
4. Degludec and U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU to lower risk of hypoglycaemia, Glimepiride has shown similar CV safety to DPP-4i
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

† **Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.**

Updates to the 2018 consensus report are indicated in magenta font

LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction
UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

2019 update to: Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

# SGLT-2 Inhibitors

Reduce major adverse cardiovascular events in people with established atherosclerotic cardiovascular disease or at high risk (empagliflozin, dapagliflozin, canagliflozin)

Reduce worsening of heart failure and cardiovascular death in people with heart failure with reduced ejection fraction with or without diabetes (empa, dapa)

Reduce progression of diabetic kidney disease in those with reduced GFR and macroalbuminuria (cana, dapa)

- initiate above eGFR >30ml/min/1.73m$^2$)

# SGLT-2 Inhibitors

**Side Effects:**

- Genitourinary infections
- Volume contraction
- Acute Kidney Injury
- Diabetic Ketoacidosis
- Amputations (cana)

# GLP-1 Receptor Agonists

Reduce major adverse cardiovascular events in people with established atherosclerotic cardiovascular disease or at high risk (not oral semaglutide)

May reduce progression of diabetic kidney disease

- Generally renal dosing not required

# GLP-1 Receptor Agonists

**Side Effects:**

- Nausea
- Vomiting
- Weight loss
- Progression of retinopathy (semaglutide)

# Age-Related Effects of SGLT2 Inhibitors and GLP-1 Receptor Agonists

| | Semaglutide Empagliflozin | Dapagliflozin | |
|---|---|---|---|
| Age <65 | 57% | 54% | 56% |
| 65-75 | 43% | 40% | 35% |
| >75 | | 6% | 9% |

***Efficacy and safety consistent across age groups***

Leiter et al., Cardiovasc Diabtol, 2019; 18: 73.
Cahn et al., Diabetes Care, 2020: 43; 468-475.
Monteiro et al., Age and Ageing, 2019; 48: 859-866.

# Other Antihyperglycemic Medications

| Medication | Concerns in the Elderly |
|---|---|
| Metformin | Renal dosing |
| DPP-4 Inhibitor | Renal dosing |
| TZD | Rarely used |
| Acarbose | Rarely used |
| Sulfonylurea | Hypoglycemia, renal dosing |
| Meglitinides | Hypoglycemia, limited financial coverage |
| Insulin | Hypoglycemia |

# Summary

- SGLT-2 inhibitors and GLP-1 receptor agonists are newer agents with benefits beyond glycemic control
- There is good efficacy and safety data for GLP-1 receptor agonists and SGLT-2 Inhibitors in those < age 75, but more limited for older people
- Metformin and DPP-4 inhibitors have excellent safety profiles in older people

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# Glucose Monitoring Devices

Capillary Glucose Meter

Flash Glucose Monitor

Continuous Glucose Monitor

# Flash Glucose Monitoring


$200/month

Covered by ODB for those using insulin

# Flash Glucose Monitoring



# Flash Glucose Monitoring

## AGP Report

LibreView

### GLUCOSE STATISTICS AND TARGETS

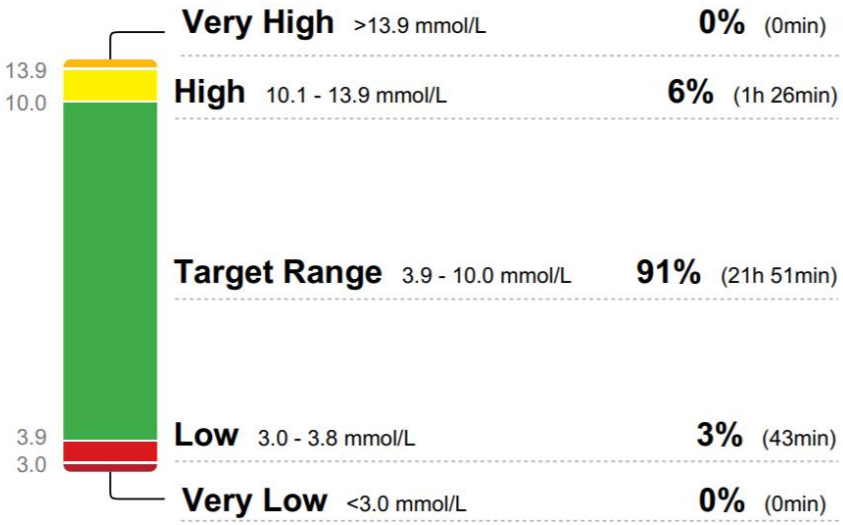
| | 14 Days |
|---|---|
| **% Time Sensor is Active** | **96%** |

| Ranges And Targets For | Type 1 or Type 2 Diabetes |
|---|---|
| **Glucose Ranges** | **Targets** % of Readings (Time/Day) |
| Target Range 3.9-10.0 mmol/L | Greater than 70% (16h 48min) |
| Below 3.9 mmol/L | Less than 4% (58min) |
| Below 3.0 mmol/L | Less than 1% (14min) |
| Above 10.0 mmol/L | Less than 25% (6h) |
| Above 13.9 mmol/L | Less than 5% (1h 12min) |
| Each 5% increase in time in range (3.9-10.0 mmol/L) is clinically beneficial. | |

| | |
|---|---|
| **Average Glucose** | **6.7** mmol/L |
| **Glucose Management Indicator (GMI)** | **6.2% or 44 mmol/mol** |
| **Glucose Variability** | **28.3%** |

**Defined as percent coefficient of variation (%CV); target ≤36%**

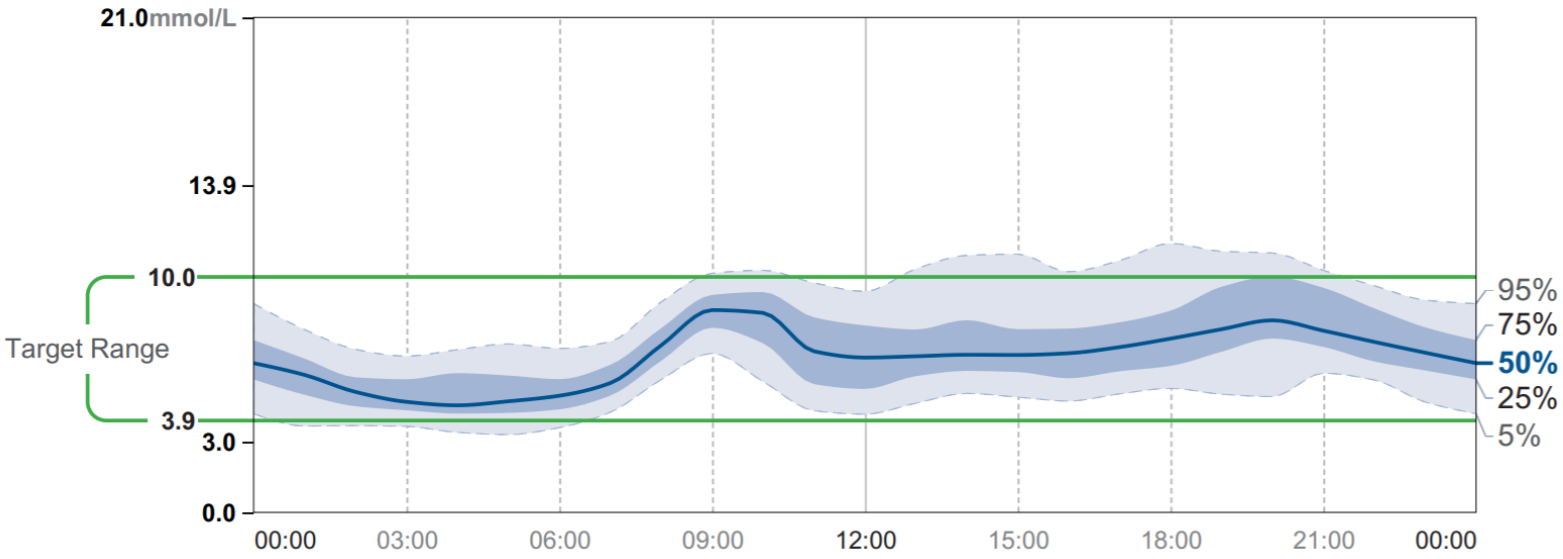
### TIME IN RANGES



# Flash Glucose Monitoring

**AMBULATORY GLUCOSE PROFILE (AGP)**

*AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.*



# Flash Glucose Monitoring

## AGP Report

LibreView

### GLUCOSE STATISTICS AND TARGETS

| | 14 Days |
|---|---|
| **% Time Sensor is Active** | **88%** |

| Ranges And Targets For | Type 1 or Type 2 Diabetes |
|---|---|
| **Glucose Ranges** | **Targets** % of Readings (Time/Day) |
| Target Range 3.9-10.0 mmol/L | Greater than 70% (16h 48min) |
| Below 3.9 mmol/L | Less than 4% (58min) |
| Below 3.0 mmol/L | Less than 1% (14min) |
| Above 10.0 mmol/L | Less than 25% (6h) |
| Above 13.9 mmol/L | Less than 5% (1h 12min) |
| Each 5% increase in time in range (3.9-10.0 mmol/L) is clinically beneficial. | |

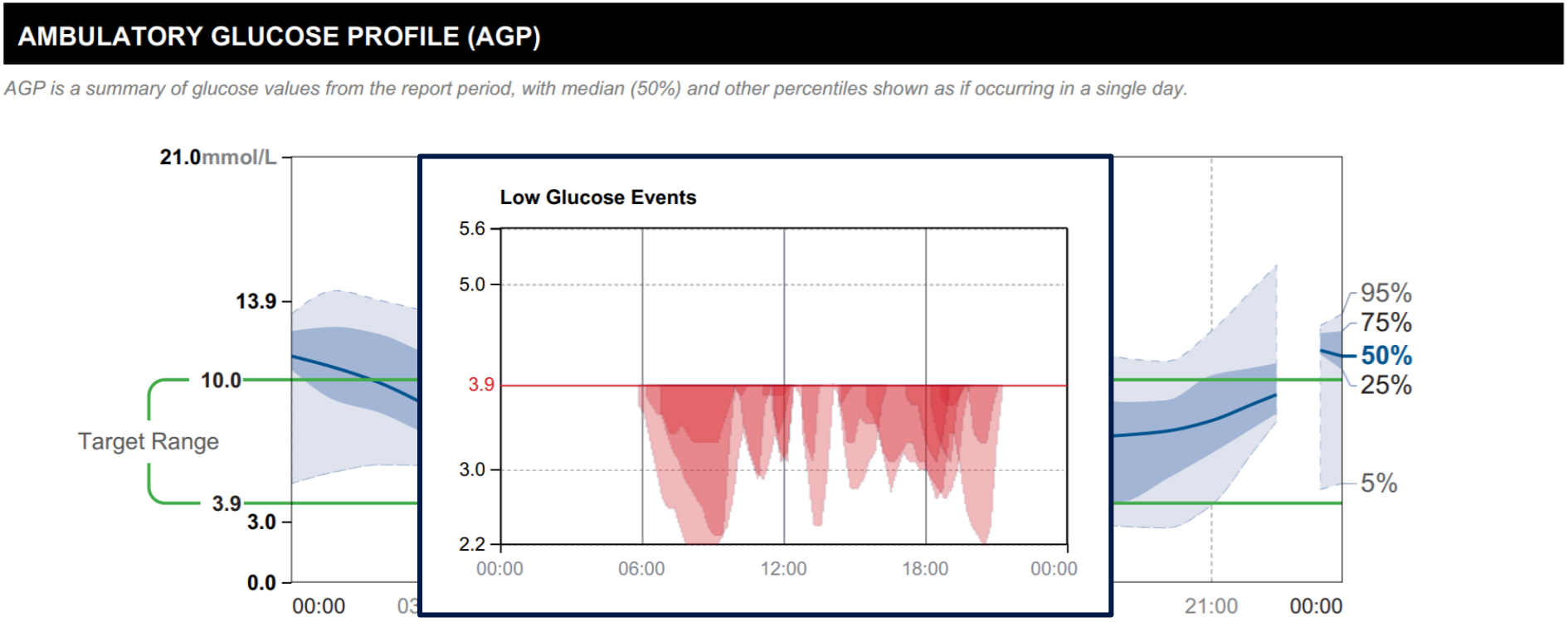
| | |
|---|---|
| **Average Glucose** | **7.0** mmol/L |
| **Glucose Management Indicator (GMI)** | **6.3% or 46 mmol/mol** |
| **Glucose Variability** | **40.8%** |

**Defined as percent coefficient of variation (%CV); target ≤36%**

### TIME IN RANGES


| | | |
|---|---|---|
| **Very High** | >13.9 mmol/L | **1%** (14min) |
| **High** | 10.1 - 13.9 mmol/L | **16%** (3h 50min) |
| **Target Range** | 3.9 - 10.0 mmol/L | **69%** (16h 34min) |
| **Low** | 3.0 - 3.8 mmol/L | **10%** (2h 24min) |
| **Very Low** | <3.0 mmol/L | **4%** (58min) |

# Flash Glucose Monitoring



# Canadian Study of Longevity in Diabetes

**305 participants with type 1 diabetes**

Median age: 65

45% male

Median diabetes duration: 54 years

Mean HbA1c: 7.5%

**44% insulin pump use**

**13% CGM use**


Boulet, Weisman et al., Diabetes Technology & Therapeutics, 2016; 18(5): 298-307.

# Summary

- Many older adults are willing and capable of using flash glucose monitors
- Flash glucose monitors provide very helpful data beyond capillary glucose monitoring
- Covered by ODB for those on insulin

# Case

You are seeing a 70 year old male in diabetes clinic. He has a 20-year history of type 2 diabetes. He had a myocardial infarction at the age of 58, and he has mild to moderate chronic kidney disease (eGFR 55ml/min/1.73m$^2$).

Current Medications: Novomix 30/70, metformin, linagliptin, ramipril, atorvastatin.

His HbA1c is 7.4% and he has minimal hypoglycemia. He is not frail.

# Helpful Resources

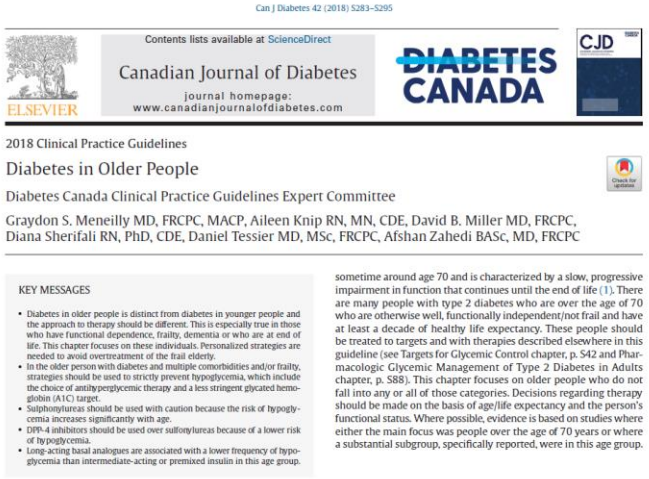
2018 Diabetes Canada Clinical Practice Guidelines

Chapter 37: Diabetes in Older People

http://guidelines.diabetes.ca/cpg

Diabetes Resource Manual

http://guidelines.diabetes.ca/financial-support-and-services



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2018 Clinical Practice Guidelines

Diabetes in Older People

Diabetes Canada Clinical Practice Guidelines Expert Committee

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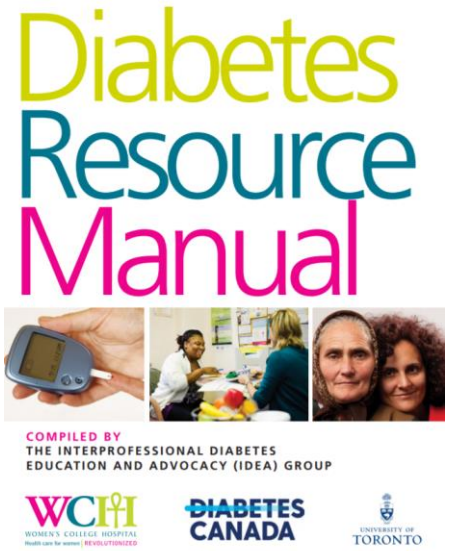
KEY MESSAGES

- 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 sulfonylureas 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.

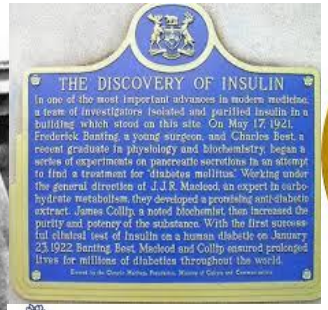
sometime around age 70 and is characterized by a slow, progressive impairment in function that continues until the end of life (1). There are many people with type 2 diabetes who are over the age of 70 who are otherwise well, functionally independent/not frail and have at least a decade of healthy life 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.



UNIVERSITY OF TORONTO

INSULIN 100

**Lectures starting January 2021** **Faculty Discussions APRIL 15-16 2021**





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**Insulin100.com**

# Questions/Discussion

Department of Medicine: deptmedicine.utoronto.ca

# Thank You.

# Impact of intensive glycemic control and high-risk agents on risk of ED visits/hospitalization or death

| | Events N (%) (ED visits/hospitalizations or death) | Univariate RR (95% CI) | Weighted RR* |
|---|---|---|---|
| **30 days** | | | |
| **Intensive control, high risk agent vs.** | 217 (0.92%) | 2.24 (1.71-2.94) | **1.49 (1.08-2.05)** |
| **Conservative control, low-risk agent** | 68 (0.41%) | Ref | Ref |
| Intensive control, high risk agent vs. | 217 (0.92%) | 1.37 (1.12-1.67) | 1.25 (1.02-1.52) |
| Conservative control, high-risk agent | 174 (0.67%) | Ref | Ref |
| Intensive control, high risk agent vs. | 217 (0.92%) | 2.22 (1.82-2.71) | 1.48 (1.18-1.85) |
| Intensive control, low-risk agent | 178 (0.42%) | Ref | Ref |

* Inverse probability treatment weighting (IPTW) using a propensity score

Lega et al, Diabetologia, 2020, in press.