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Module:

SGLT2 inhibitors/GLP-1 receptor agonists in patients with DM and CVD

Case Development & Disclosures

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- **Potential for conflict(s) of interest:**
  - None

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Mitigating Potential Bias

- Altering control over content: information and recommendations given in the program are evidence-based and sourced from multiple clinical practice guidelines/scientific professional associations.
- Program material is peer-reviewed by a committee with members representative of the target audience.

Outline of Today's Activity

- Introduction
- Case Presentation
- Key Learnings & Questions
- Wrap Up

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Case Module:
SGLT2i/GLP1 in Patients with DM and Cardiovascular Disease

Joe

A 63 yo man with a history of T2DM and CAD comes to your office for his annual check-up.

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Learning Objectives

1. Describe the patient who should be treated with an SGLT2i or GLP-1 agonist

2. Explain the rationale for this treatment and the potential benefits

3. Describe the steps for initiating and monitoring therapy for patients with diabetes

Sodium-glucose co-transporter 2 (SGLT2) inhibitors:

DIABETES CANADA

- Oral medication
- Mechanism of Action: eliminate glucose into the urine (by reducing glucose reabsorption in the proximal tubule, leading to urinary glucose excretion and osmotic diuresis)
- Side effects may include genital yeast infections, UTI, increased urination and low blood pressure
- Associated with weight loss (2-3kg) and a low risk of hypoglycemia

Examples:

Generic Name	Brand Name
Canagliflozin (100mg, 300mg)	Invokana
Dapagliflozin (5mg, 10mg)	Farxiga
Empagliflozin (10mg, 25 mg)	Jardiance

Glucagon-like peptide-1 (GLP-1) receptor agonists

DIABETES CANADA

- Subcutaneous injection (daily or weekly)
- Mechanism of Action:
  - act when blood glucose increases after eating (post-prandial)
  - increase insulin levels which helps lower blood glucose and lower glucagon levels
  - slow digestion and reduce appetite
- Possible side effect include nausea (usually goes away with time)
- Associated with weight loss (1.6-3kg) and low risk of hypoglycemia

Examples:

Generic Name	Brand Name
Dulaglutide (0.75mg, 1.5mg qweekly)	Trulicity
Exenatide/Exenatide ER (5mcg, 10mcg BID)/(2 mg qweekly)	Byetta
Lixisenatide (10mcg, 20mcg OD)	Adlyxin
Liraglutide (0.6mg, 1.2mg, 1.8mg OD)	Victoza
Semaglutide (0.25mg, 0.5mg, 1mg qweekly)	Ozempic

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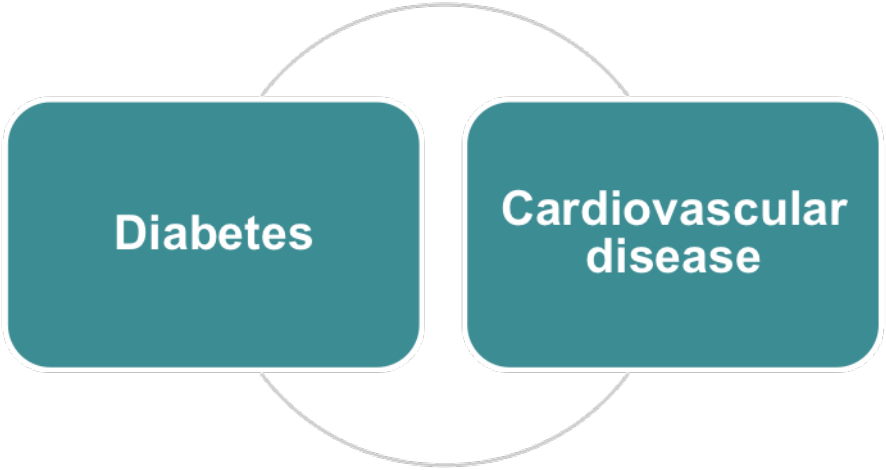
Diabetes and cardiovascular disease are intertwined



People with diabetes are **2-4x more likely** to develop cardiovascular disease than those without.

- Most **common** condition reported in Canadians with diabetes
- Most common cause of **death** in individuals with type 2 diabetes

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Public Health Agency of Canada. Diabetes in Canada: Facts and figures from a public health perspective. Ottawa. 2011; American Heart Association. Cardiovascular Disease & Diabetes. 2016. Available at: http://www.heart.org/HEARTORG/Conditions/Diabetes/WhyDiabetesMatters/Cardiovascular-Disease-Diabetes_UCM_313865_Article.jsp.

Type 2 diabetes is associated with an increased incidence of CVD

In a cohort of nearly 2 million people, there was a:

62% increase in **Stable angina**

53% increase in **Unstable angina**

54% increase in **Nonfatal MI**

43% increase in **Unheralded coronary death**

56% increase in **Heart failure**

72% increase in **Ischemic stroke**

in people with type 2 diabetes compared to the general population

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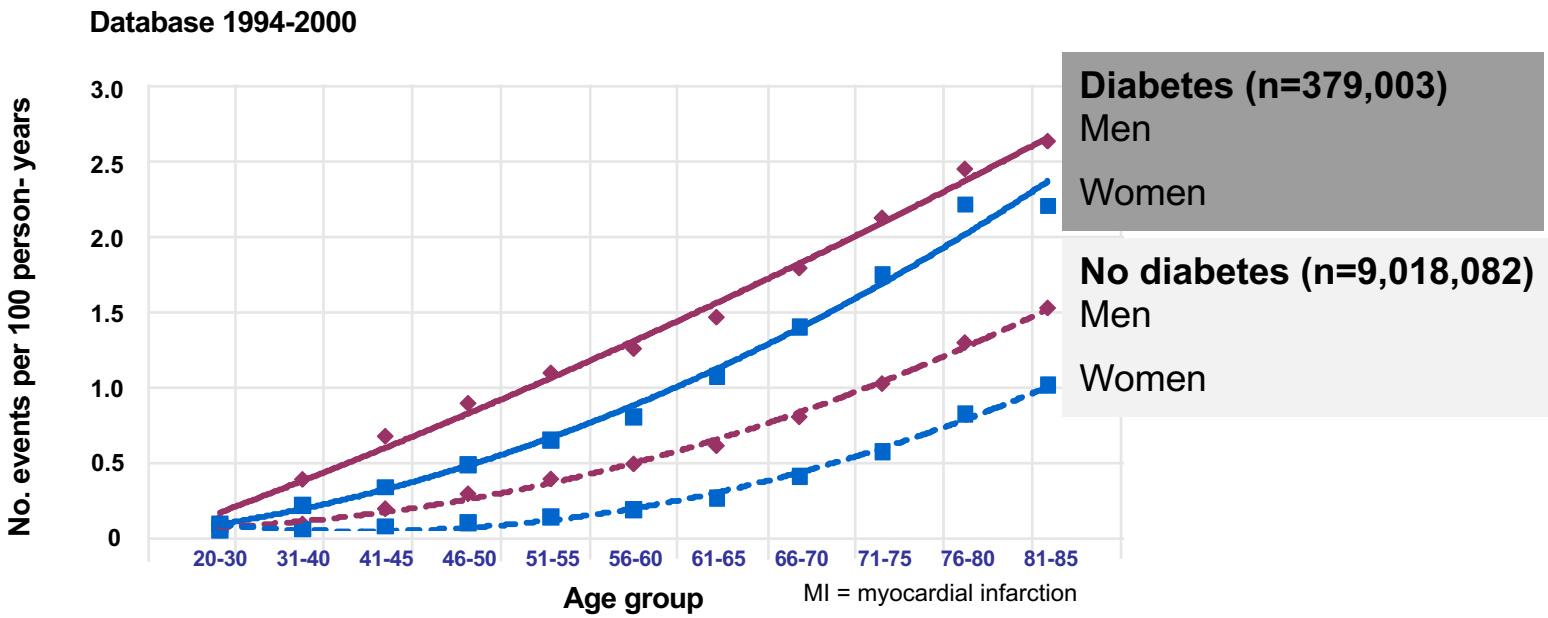
Unheralded coronary death=coronary death that was not previously expected/recognized.

Shah AD. *Lancet Diabetes Endocrinol.* 2015;3:105–113.

Absolute Risk of MI is Higher in Patients with Diabetes



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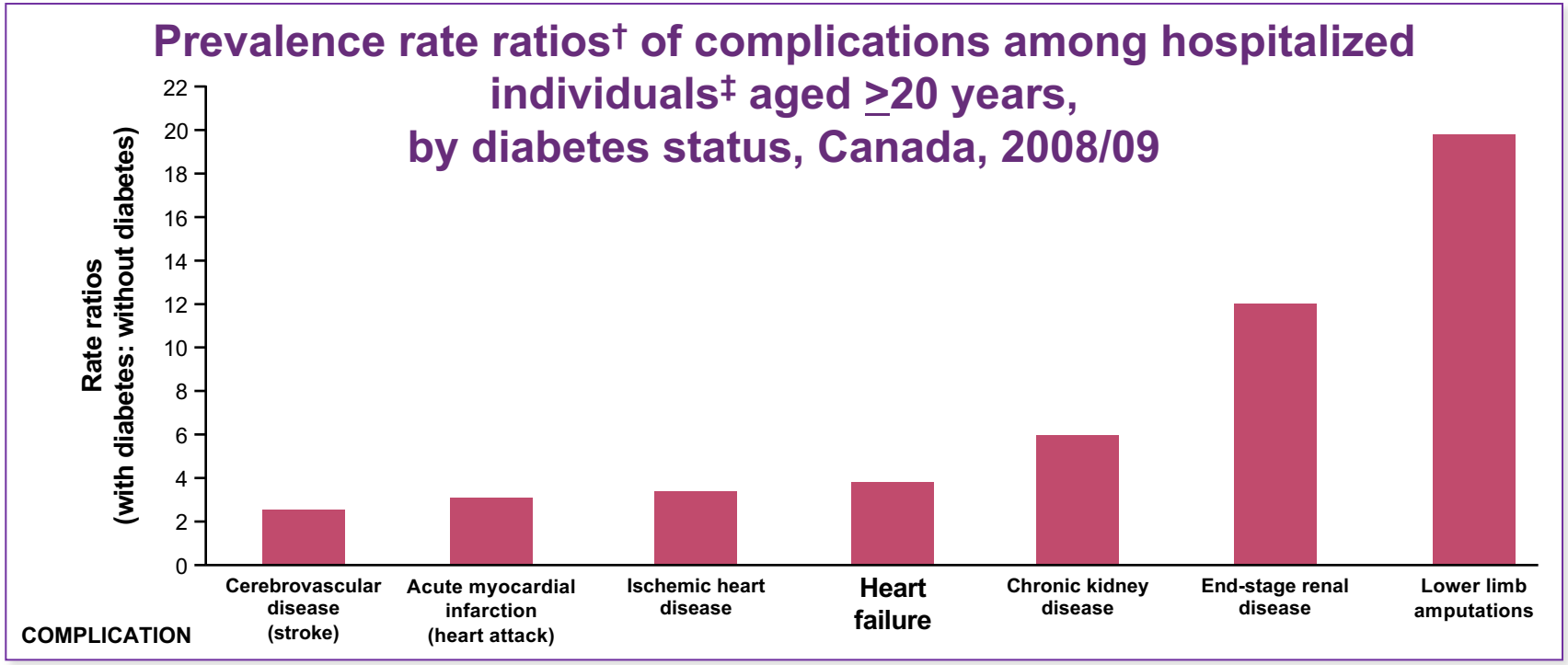
Booth GL, et al. *Lancet* 2006;368:29-36.

Patients with Diabetes are More Likely to be Hospitalized for Many Conditions



† Rate ratios based on rates age-standardized to the 1991 Canadian population.
‡ A person with diabetes hospitalized with more than one complication was counted once in each category, except for cases of acute myocardial infarction, where regardless of multiple counts in the acute myocardial infarction category, the individual was counted only once under the broader ischemic heart disease category.

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Source: Public Health Agency of Canada (August 2011); using 2008/09 data from the Canadian Chronic Disease Surveillance System (Public Health Agency of Canada).

Optimal Medical Therapy

- Blood glucose control
- Blood pressure control
- Lipid control
- Use of RAAS blockers
- Smoking cessation
- Diet
- Exercise

- Multiplicative rather than additive CV protection due to modulation of:
  - Pro-inflammatory
  - Pro-thrombotic
  - Proliferative factors

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Steno 2, Stone JA, Can J DM 42(2018) S162-169

Statement of Need

"My greatest challenge as a health care professional in the cardiovascular management of patients with ***diabetes and CVD*** *is _____"*

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History of Present Illness

- Joe is a 63 year old male with T2DM for 10 years and a history of CVD
- He presents to your office for his diabetes f/u visit, and you note he hasn’t seen you for a year

Past History

- Joe has T2DM x 10 years
- CAD: MI (with stent x 2) 3 years ago
- Hypertension
- He is an ex-smoker with social alcohol use
- Married with 2 children

Family History

- Father: Died age 48 in MVA
- Mother: Died age 80 breast cancer and had Type 2 diabetes (was on oral meds)
- Siblings: Brother age 67 with Hypertension

Current Medications

- Perindopril 8 mg po od
- Atorvastatin 40 mg po od
- ASA 81 mg po od
- Metformin-Sitagliptin XR 1000-50 mg po bid

Physical Examination

- Height: 175 cm
- Weight: 88 kg
- BMI: 29 kg/m^2
- BP (left arm, seated): 136/77 mmHg using an automated device while the patient is unattended

- No stroke or TIA
- No CHF
- No MAU
- Normal LV function

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Lab Results

Test	Results	Normal Values
Fasting Glucose	8.9	4.0-8.0 mmol/L
HbA1c	8.0%	0.045 - 0.057 mmol/L
Creatinine	98	44-106 µmol/L
eGFR	70	> 60 ml/min
Na	140	135-145 mmol/l
K	4.0	3.5-5.0 mmol/L

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Lab Results

Test	Results	Target values
LDL	2.2	<2.0 mmol/L
Total chol	4.2	<5.20 mmol/L
TG	1.2	<1.70 mmol/L
HDL	1.1	>0.99 mmol/L
Urinalysis	Neg	Neg
Alb/creat	1.9	< 2.0 mg/mmol

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Discussion Question 1

You wonder what can be done to help Joe better manage his diabetes.

What is the 2018 Diabetes Canada Guideline for starting an SGLT2i or GLP1 in People with Type 2 Diabetes and CVD with eGFR>30 ml/min?

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Discussion Question 1. What is the 2018 Diabetes Canada Guideline for starting an SGLT2i or GLP1 in People with Type 2 Diabetes and CVD with eGFR>30 ml/min?

a) All patients <u>at risk</u> for CVD with uncontrolled diabetes despite therapy?
b) All patients <u>with</u> clinical CVD regardless of A1c?
c) All patients <u>with</u> clinical CVD with uncontrolled diabetes despite therapy?
d) All patients with Type 2 diabetes <u>regardless</u> of presence of CVD?

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Discussion Question 1. What is the 2018 Diabetes Canada Guideline for starting an SGLT2i or GLP1 in People with Type 2 Diabetes and CVD with eGFR>30 ml/min?

Secondary Prevention (established CVD)

In adults with type 2 diabetes with clinical CVD in whom glycemic targets are not achieved with existing antihyperglycemic medication(s)and with an eGFR > 30 mL/min/1.73m2, an antihyperglycemic agent with demonstrated CV outcome benefit should be added added to reduce the risk of major CV events.

Discussion Question 1. What is the Diabetes Canada Guideline for starting an SGLT2i or GLP1 in People with Type 2 Diabetes and CVD with eGFR>30 ml/min?

- Patient must have clinical CVD and uncontrolled diabetes and already be on therapy, ex. metformin.

Therefore **c) is correct:**

c) All patients with clinical CVD with uncontrolled diabetes despite therapy

Not only do many SGLTi and GLP-1 agonists reduce blood sugar, although they also have been shown to reduce secondary CV events!

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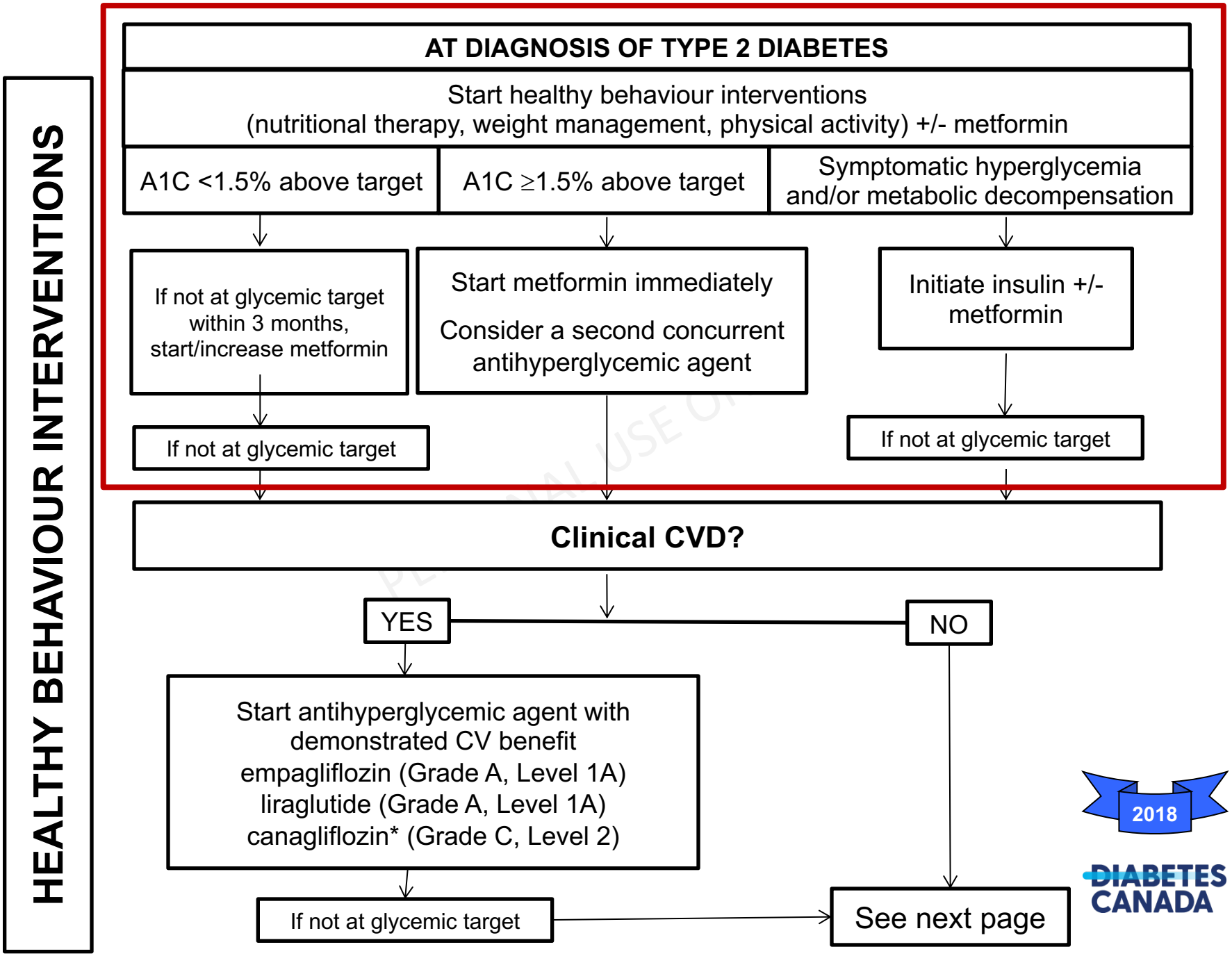
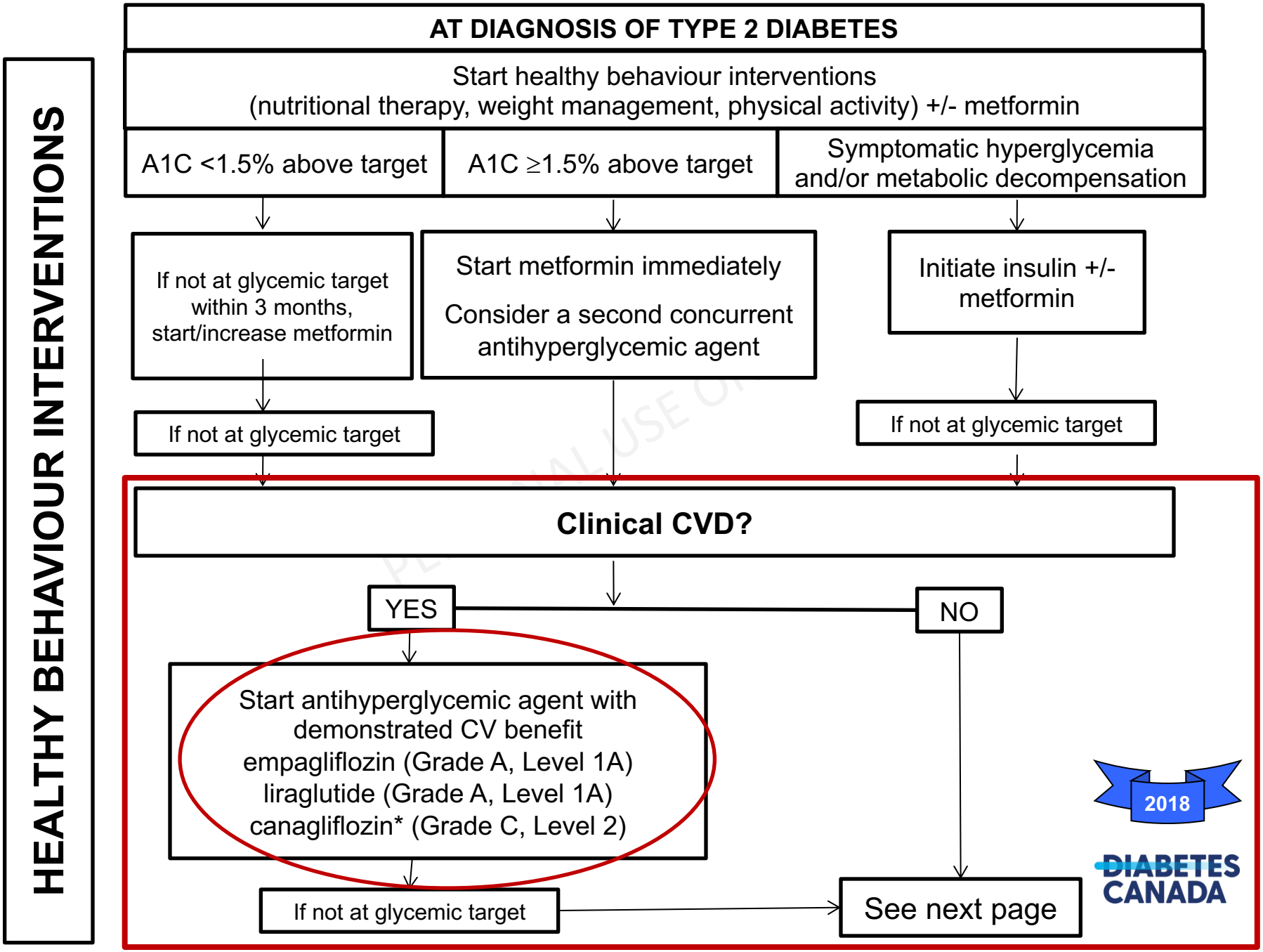


* Avoid in people with prior lower extremity amputation



* Avoid in people with prior lower extremity amputation

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DIABETES CANADA

Clinical CVD?

NO

Add additional antihyperglycemic agent best suited to the individual based on the following

CLINICAL CONSIDERATIONS	CHOICE OF AGENT
Avoidance of hypoglycemia and/or weight gain with adequate glycemic efficacy	DPP-4 inhibitor, GLP-1 receptor agonist or SGLT2 inhibitor
Other considerations: Reduced eGFR and/or albuminuria Clinical CVD or CV risk factors Degree of hyperglycemia Other comorbidities (CHF, hepatic disease) Planning pregnancy Cost/coverage Patient preference	see Renal Impairment Appendix See Table Below

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DIABETES CANADA

Add additional antihyperglycemic agent best suited to the individual by prioritizing patient characteristics (*agents listed in alphabetical order by CV outcome data*):

Class	Effect on CVD Outcomes	Hypo-glycemia	Weight	Relative A1C Lowering when added to metformin	Other therapeutic considerations	Cost
GLP-1R agonists	lira: Superiority in T2DM with clinical CVD exenatide LAR & lixi: Neutral	Rare	↓↓	↓↓ to ↓↓↓	GI side-effects, Gallstone disease Contraindicated with personal / family history of medullary thyroid cancer or MEN 2 Requires subcutaneous injection	$$$$
SGLT2 inhibitors	Cana & empa: Superiority in T2DM patients with clinical CVD	Rare	↓↓	↓↓ to ↓↓↓	Genital infections, UTI, hypotension, dose-related changes in LDL-C. Caution with renal dysfunction, loop diuretics, in the elderly. Dapagliflozin not to be used if bladder cancer. Rare diabetic ketoacidosis (may occur with no hyperglycemia). Increased risk of fractures and amputations with canagliflozin. Reduced progression of nephropathy & CHF hospitalizations with empagliflozin and canagliflozin in those with clinical CVD	$$$
DPP-4 Inhibitors	alo, saxa, sita: Neutral	Rare	Neutral	↓↓	Caution with saxagliptin in heart failure Rare joint pain	$$$
Insulin	glar: Neutral degludec: noninferior to glar	Yes	↑↑	↓↓↓↓	No dose ceiling, flexible regimens Requires subcutaneous injection	$- $$$$
Thiazolidinediones	Neutral	Rare	↑↑	↓↓	CHF, edema, fractures, rare bladder cancer (pioglitazone), cardiovascular controversy (rosiglitazone), 6-12 weeks for maximal effect	$$
α-glucosidase inhibitor (acarbose)		Rare	Neutral	↓	GI side-effects common Requires 3 times daily dosing	$$
Insulin secretagogue: **Meglitinide** **Sulfonylurea**		 Yes Yes	 ↑ ↑	 ↓↓ ↓↓	More rapid BG-lowering response Reduced postprandial glycemia with meglitinides but usually requires 3 to 4 times daily dosing. Gliclazide and glimepiride associated with less hypoglycemia than glyburide. Poor durability	 $$ $
Weight loss agent (orlistat)		None	↓	↓	GI side effects Requires 3 times daily dosing	$$$

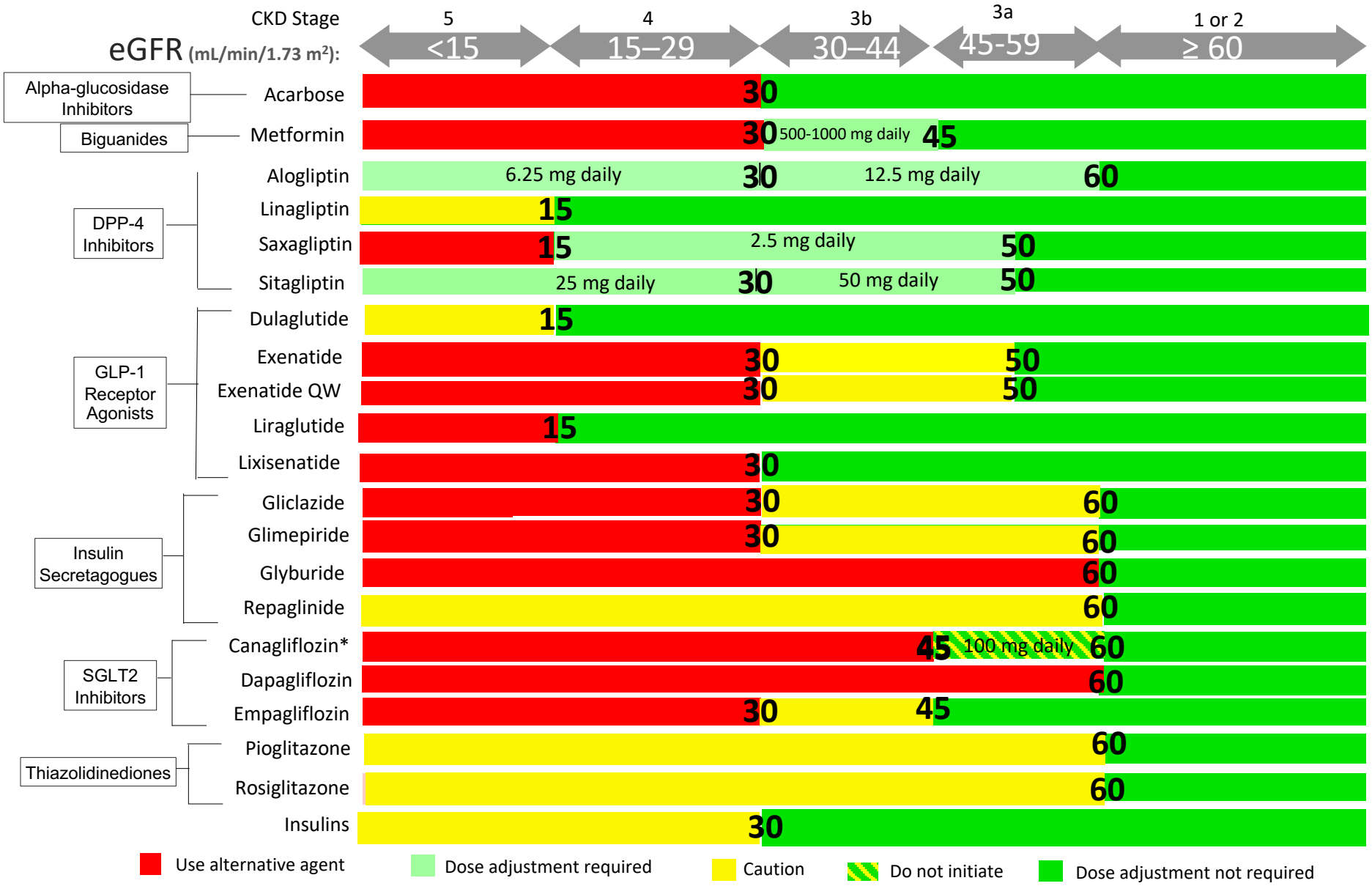
↓

If not at glycemic targets

↓

Add another antihyperglycemic agent from a different class and/or add/intensify insulin regimen
Make timely adjustments to attain target A1C within 3-6 months

Antihyperglycemic Agents and Renal Function

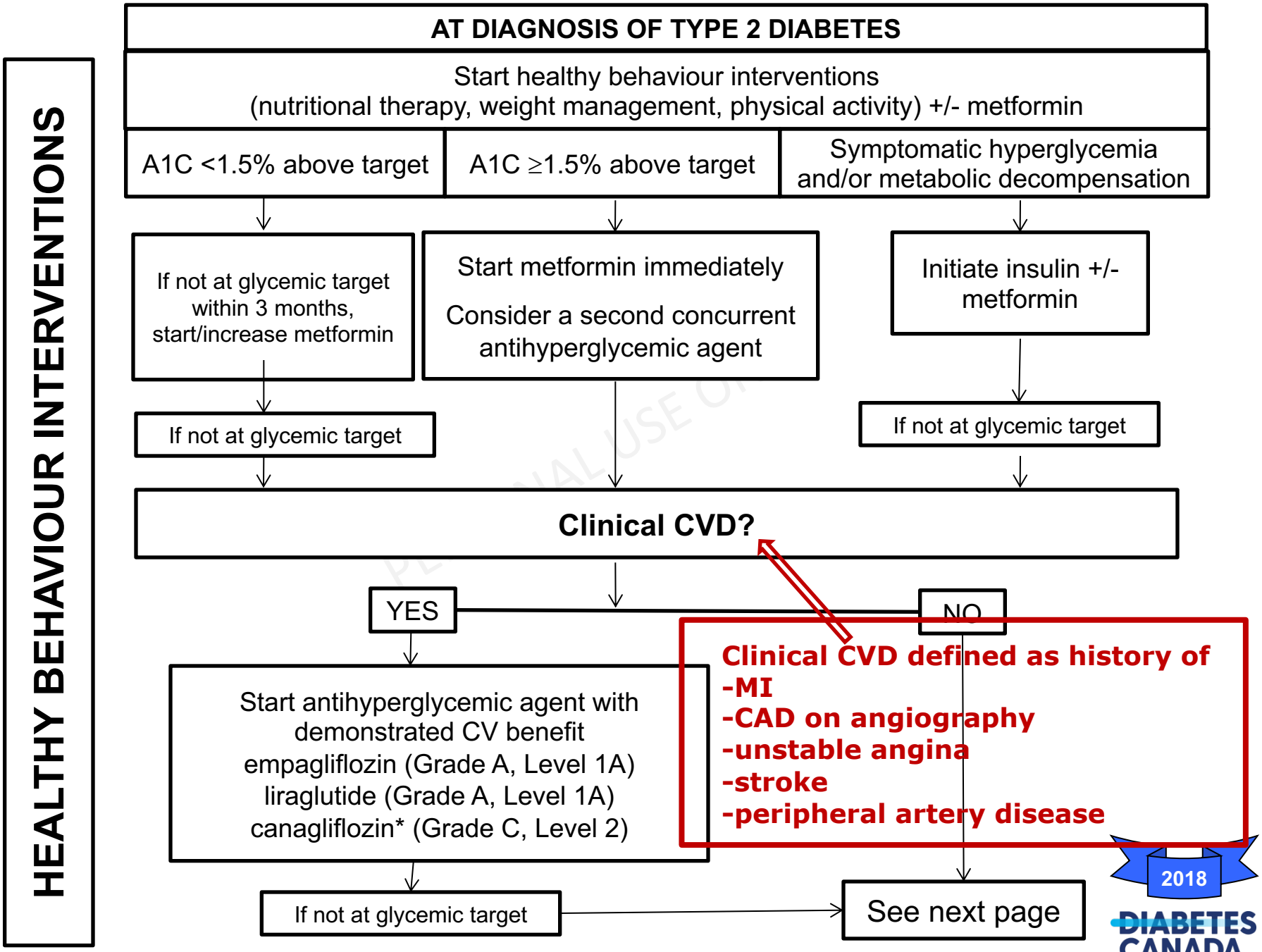


** May be used for cardiorenal benefits in those with clinical CVD, A1C above target and eGFR >30 mL/min/1.73m²*

Discussion Question 2

You begin to assess whether or not Joe has clinical CVD.

What is the definition of clinical CVD?



* Avoid in people with prior lower extremity amputation

Discussion Question 2.
What is the definition of clinical CVD in the CVOTs?

Inclusion Criteria:

EMPAREG

One or more of:

- MI >2 months prior
- multivessel CAD
- single vessel CAD with positive stress test or unstable angina hospitalization in prior year
- unstable angina >2 months prior and evidence of CAD
- stroke >2 months prior
- occlusive peripheral artery disease

CANVAS:

•Symptomatic coronary, cerebrovascular or peripheral vascular disease

•50 years or older with at least 2 CV risk factors

- duration of diabetes ≥10 years
- SBP >140 mmHg on Tx
- current smoker
- Micro or macro albuminuria
- HDL <1 mmol/L)

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Discussion Question 2.
What is the definition of clinical CVD?

LEADER

Age >50 and one or more of:

- Prior MI, Stroke/TIA
- Prior coronary, carotid or peripheral arterial revascularization
- single vessel CAD w/ positive stress test or unstable angina hospitalization in prior year
- unstable angina >2 months prior & evidence of CAD
- stroke >2 months prior
- occlusive peripheral artery disease
- >50% stenosis of coronary, carotid, or lower extremity arteries
- History of symptomatic CHD documented by positive exercise stress test or any cardiac imaging or unstable angina with ECG changes
- Asymptomatic cardiac ischemia documented by positive nuclear imaging test, exercise test or dobutamine stress echo
- Chronic heart failure NYHA class II-III
- Chronic renal failure: eGFR <60 mL/min/1.73m2 (MDRD and Cockcroft-Gault formula)

No Prior cardiovascular disease group: Age ≥60 y and ≥1 of the following criteria:

- Microalbuminuria or proteinuria
- Hypertension and left ventricular hypertrophy by ECG or imaging
- Left ventricular systolic or diastolic dysfunction by imaging
- ABI<0.9

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Discussion Question 3

What would be the beneficial effects of starting Joe on a SGLT2i and/or GLP-1 Agonist?

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Discussion Question 3. All of the following are known benefits of SGLT2i and GLP-1 Agonists <u>except</u> for?

a) Blood glucose lowering?
b) Blood pressure lowering?
c) Weight loss?
d) Bone protection?
e) Renal protection?
f) Positive CV outcomes?

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Known Benefits of SGLT2i and GLP-1:

d) Bone Health?

- Meta-analyses suggest only a neutral effect
- SGLT2i
  - Changes in bone density likely weight loss related
  - Fracture risk in elderly likely related to falls associated with volume depletion events
- **Therefore Bone protection is <u>not</u> a benefit**

Egger A, Current Osteoporosis Reports 2016
Tang HL, Diabetes, Obesity, Metabolism 2016

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Known Benefits of SGLT2i and GLP-1:
a) **Blood Glucose Lowering as Monotherapy?**

Medication Class	Approx A1c lowering (%)
Biguanide	1.0
DPP-4 inhibitor	0.5-0.7
GLP-1 receptor agonist	**1.0**
SGLT-2 inhibitor	**0.4-0.7**
Alpha-glucosidase inhibitor	0.7-0.8
Insulin	0.9-1.2+
Sulfonylureas	0.7-1.3
Meglitinides	0.7-1.1
Thiazolidinedione	0.8-0.9
Weight loss agent (Orlistat)	0.2-0.4

Therefore blood glucose lowering is a benefit

Known Benefits of SGLT2i and GLP-1: b) **BP Lowering?**

Systolic BP Lowering compared to Placebo in mmHg	
Canagliflozin 300 mg	5.6
Canagliflozin 100 mg	4.2
Empagliflozin 25 mg	3.4
Empagliflozin 10	2.6
Dapagliflozin 10	2.7
GLP-1 Agonists	2.0

Therefore blood pressure lowering is a benefit

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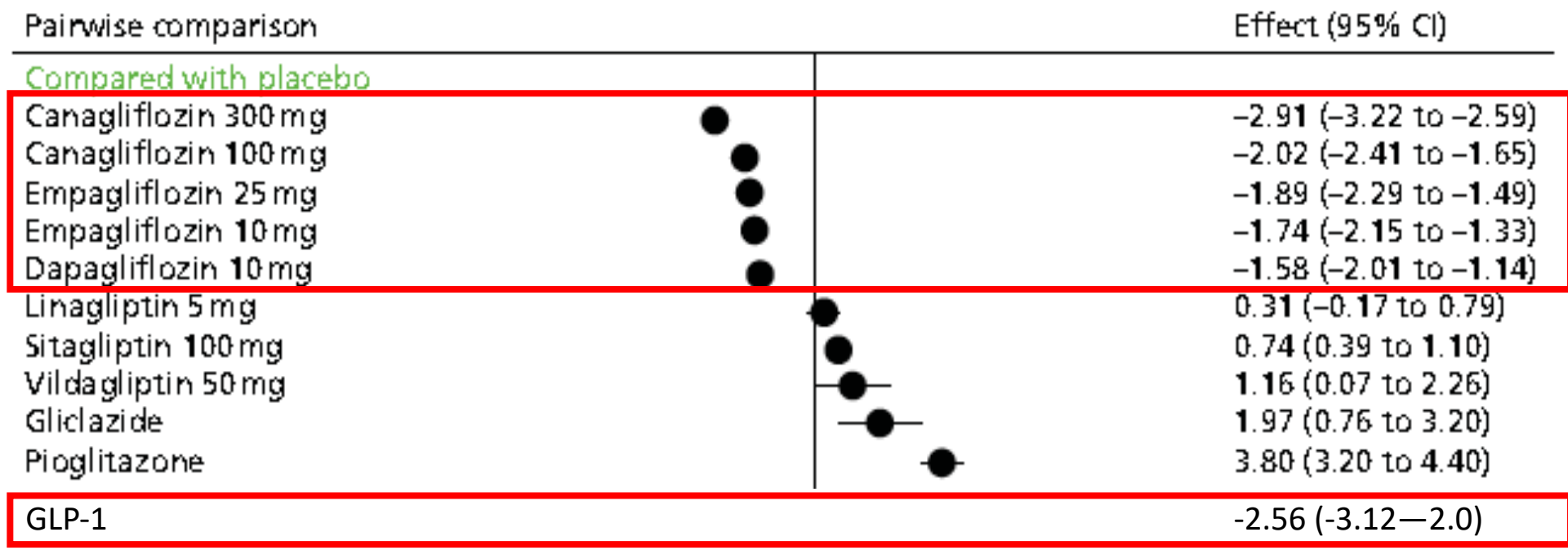
Johnston R. Health Technology Assessment 2017. Cana, Dapa, Empa Network Meta-analysis Goud A, Curr Hypertension Reports, 2016. GLP-1 Agonists and BP effects

Known Benefits of SGLT2i and GLP-1:
c) **Weight Loss?**



Therefore weight loss is a benefit

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Johnston R. Health Technology Assessment 2017. Cana, Dapa, Empa Network Meta-analysis
Katout M, American J Hypertension 2015. GLP-1 Effects on weight loss and BP

Known Benefits of SGLT2i and GLP-1:
e) **Renal Outcomes?**

CVOT Trials in Type 2 Diabetes with GLP-1 or SGLT2i Treatment: Renal Outcomes						
	LEADER	SUSTAIN-6	EXSCEL	EMPA-REG	CANVAS Program	DECLARE
Tx	Lira vs P	Sema v P	Exena v P	Empa v P	Cana v P	Dapa vs P
F/up yrs	3.8	2.1	3.2	3.1	5.7	4.2
eGFR	30+	30+	30+	30+	60+	60+
Outcome	New Alb, 2xCreat, RRT, renal death	New Alb, 2xCreat, RRT, renal death	New Alb, 40% ↓ in eGFR, RRT, renal death	New Alb, 2xCreat, RRT, renal death	2xCreat, RRT, renal death	40% ↓ in eGFR, RRT, renal/CV death
HR (± 95% CI)	**0.78** **(.67-.92)**	**0.52** **(.33-.80)**	**0.85** **(.73-.98)**	**0.61** **(.53-.70)**	**0.53** **(.33-.84)**	**0.76** **(0.67-0.87)**

Therefore renal outcomes are a benefit

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American Diabetes Association. 9. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes. 2018. Diabetes Care 2018;41(Suppl. 1):S86–S104

CVOT Trials in T2DM: GLP-1, SGLT2i
f) **CV Outcomes?**

CVOT Trials in Type 2 Diabetes with GLP-1 or SGLT2i Treatment: CV Outcomes					
	LEADER	**SUSTAIN-6**	**EMPA-REG**	**CANVAS Program**	**DECLARE**
Tx	Lira vs P	Sema v P	Empa v P	Cana v P	Dapa v P
F/up yrs	3.8	2.1	3.1	5.7	4.2
Prior CVD %	81	60	99	65.6	41
Outcome	3-point MACE	3-point MACE	3-point MACE	3-point MACE	CV Death HHF
HR (± 95% CI)	**0.87 (.78-.97)**	**0.74 (.58-.95)**	**0.86 (.74-.99)**	**0.86 (.75-.97)**	**0.83 (0.73-0.95)**

Therefore CV protection is a benefit

Major Adverse Cardiac Events (MACE) = CV death, non-fatal MI, or non-fatal stroke

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American Diabetes Association. 9. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes. 2018. Diabetes Care 2018;41(Suppl. 1):S86–S104

Summary of CV Protection with SGLT2i and GLP-1 Agonists

- **EMPA-REG Outcome study** (7,020 w/ T2DM and CVD) - empagliflozin
  - NNT of 63 to prevent 1 CV event (CV death, nonfatal MI, nonfatal stroke) and 71 to prevent 1 CHF admission over 3 years
- **CANVAS program** (10,142 w/ T2DM and most w/ CVD) – canagliflozin
  - NNT of 44 to prevent 1 CV event and 63 to prevent 1 CHF admission over 5 years
- **LEADER study** (9,340 w/ T2DM and most w/ CVD) - liraglutide
  - NNT of 53 to prevent 1 CV event over 3 years

Note: Although CANVAS and LEADER study had a small proportion of pts without CVD (primary prevention), a significant decrease in the primary endpoint (MACE) was only found in those with CVD (secondary prevention) → thus, recommendation for SGLTi/GLP1 use in pts with 'clinical CVD' for CV benefit (i.e. secondary prevention)

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Lipscombe L et al, Cdn J Diabetes, 2018, Pharmacologic Glycemic Management of T2DM in Adults

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Recommendation

In adults with type 2 diabetes with **clinical CVD** in whom glycemic targets are not achieved with existing antihyperglycemic medication(s) and with **eGFR >30** mL/min/1.73m^2, an antihyperglycemic agent with demonstrated **CV outcome benefit should be added** to reduce the risk of:

a) major CV events [Grade A, Level 1A for empagliflozin; Grade A, Level 1A for liraglutide; Grade C, Level 2 for canagliflozin]

b) heart failure hospitalization [Grade B, Level 2 for empagliflozin; Grade C, Level 2 for canagliflozin],

c) progression of nephropathy [Grade B, Level 2 for empagliflozin; Grade C, Level 3 for canagliflozin]

CV, cardiovascular; *CVD*, cardiovascular disease; *eGFR*, estimated glomerular filtration rate

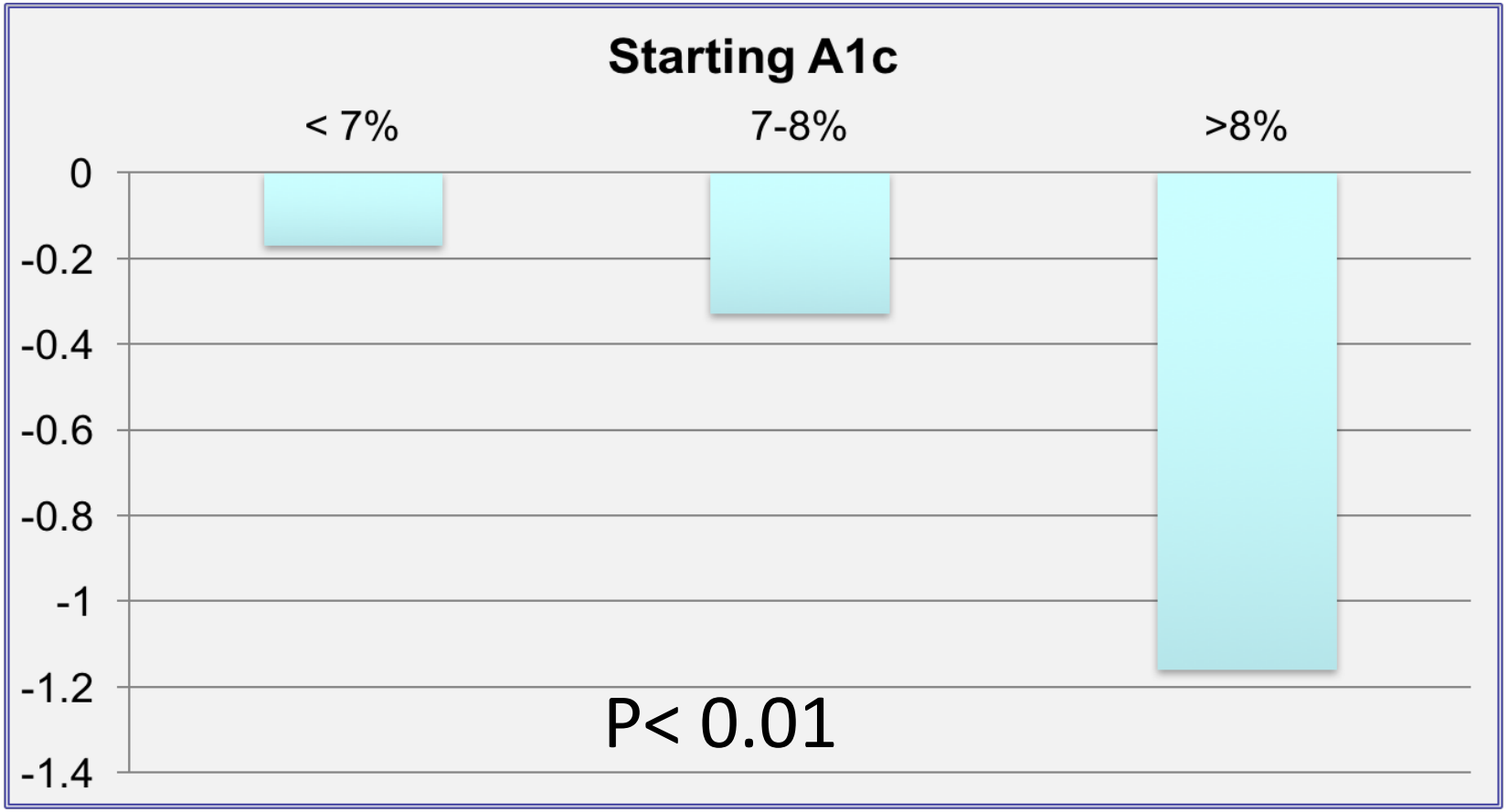
Discussion Question 4

What are considerations when starting patients like Joe on a SGLT2i and GLP1?

Discussion Question 4.
What are considerations when starting a SGLT2i and GLP1?

a) A1c: The higher the start, the bigger the fall?
b) CKD?
c) Hypotensive and volume events?
d) Amputations?
e) Risk of hypoglycemia?

a) SGLTi Reduction in A1c Depends on Starting A1c



b) SGLT2i and eGFR?

- Lower eGFR associated with less improvement in A1c
- However, the effect of SGLT2i on weight, BP, and urine ACR was independent of eGFR
- CANVAS, EMPA-REG and DECLARE showed improved renal outcomes

CVOT Trials in Type 2 Diabetes with SGLT2i Treatment: Renal Outcomes

	EMPA-REG	CANVAS Program	DECLARE
Tx	Empa v P	Cana v P	Dapa vs P
F/up yrs	3.1	5.7	4.2
eGFR	30+	60+	60+
Outcome	New Alb, 2xCreat, RRT, renal death	2xCreat, RRT, renal death	40% ↓ in eGFR, RRT, renal/CV death
HR (± 95% CI)	**0.61** **(.53-.70)**	**0.53** **(.33-.84)**	**0.76** **(0.67-0.87)**

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Perkovic V, CJSAN 2017 Are SGLT2i ready for prime time for CKD?

Antihyperglycemic Agents and Renal Function

Medication	CKD 3A (eGFR 45-59mL/min)	CKD 3B (eGFR 30–44 mL/min)	CKD 4 (eGFR 15–29 mL/min)	CKD 5 (eGFR <15 mL/min or dialysis)
Metformin‡	Dose adjustment not required	Reduce dose (500–1,000 mg/day) Do not initiate, can maintain	Use alternative agent due to risk of accumulation	
GLP-1 receptor agonists				
Dulaglutide	Dose adjustment not required			Caution as safety not established
Exenatide/ Exenatide ER	Dose adjustment not required (>50 mL/min)	Caution (30–50 mL/min)	Use alternative agent due to risk of accumulation	
Lixisenatide	Dose adjustment not required		Use alternative agent as safety not established	
Liraglutide	Dose adjustment not required			Use alternative agent as safety not established
SGLT2 inhibitors				
Canagliflozin‡	Can maintain at 100 mg daily, do not initiate for glycemic control. May be initiated when indicated for CV and renal protection*	Use alternative agent because of limited glycemic efficacy. May be considered when indicated for CV and renal protection*	Use alternative agent due to lack of glycemic efficacy	
Dapagliflozin‡	Use alternative agent due to lack of glycemic efficacy			
Empagliflozin‡	Can maintain, do not initiate for glycemic control. May be initiated when indicated for CV and renal protection*	Use alternative agent because of limited glycemic efficacy. May be considered when indicated for CV and renal protection*	Use alternative agent due to lack of glycemic efficacy	

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Therapeutic Considerations for Renal Impairment, Appendix 7
Canadian Journal of Diabetes March 2018 42, S314

b) SGLT2i and the Kidney?

- No nephrotoxicity
- Good evidence for renal protection from diabetic nephropathy
- Potential for volume depletion (osmotic diuresis)

c) Volume Events and SGLT2i?

Data from Dapagliflozin 12 week Studies

Events are uncommon but more likely with diuretics and ACEi/ARB

	DAPA 10 mg/d (% with volume event)	Placebo (% with volume event)
No antihypertensive	0.2	0.2
Any antihypertensive	1.5	0.9
Non loop diuretic	1.7	1.0
Loop diuretic	2.5	1.5
ACEi/ARB	2.5	1.5
Baseline orthostatic hypotension	4.2	4.2
Cumulative over 12 weeks	13.1	11.3

Volume Depletion defined: hypotension, dehydration, hypovolemia

Orthostatic Hypotension: 20/10 mmHg change from seated to standing

Johnsson K, Postgraduate Medicine, 2016. Osmotic diuresis from Dapa Studies

Sick Day Medication List

- **S** sulfonylureas
- **A** ACE inhibitors
- **D** diuretics

- **M** metformin
- **A** angiotensin receptor blockers
- **N** NSAIDs
- **S** SGLT2 inhibitors

- Diabetes Canada CPGs Cdn J Diabetes, 2018, Appendix 7

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d) Amputations and SGLT2i's?

- Data from CANVAS study
- Doubling of lower extremity amputation
- In participants with prior amputation
  - NNT to prevent 1 CV event was 7 over 5 years
  - NNH for amputation was 5 over 5 years
- Therefore, for now, avoid SGLT2i in people with prior amputation

Lipscombe L et al, Cdn J Diabetes, 2018, Pharmacologic Glycemic Management of T2DM in Adults

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e) Risk of Hypoglycemia with SGLT2i (and GLP-1 Agonists)?

- Negligible risk as monotherapy
- Increased risk as add-on therapy with insulin or sulfonylureas

Yale JF_Cdn J Diabetes, 2018. Hypoglycemia

Discussion Question 5.

How do you introduce and monitor SGLT2i and GLP1 in clinical practice?

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Discussion Question 5.

How do you introduce and monitor SGLT2i in clinical practice?

SGLT2i

- Introduce if eGFR >60
  - *Note: empagliflozin and canagliflozin may be considered with GFR >45 mL/min when indicated for CV and renal protection (although limited glycemic efficacy). Based on post-hoc analysis of EMPA-REG trial, Empagliflozin may be considered for GFR>30 for CV and renal benefits.*
- Monitor eGFR 2-4 months later
  - See initial eGFR decline, but it comes back (not to baseline)
- Careful with BP if patient on diuretic and BP is low (consider stopping or decreasing diuretic dose)

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Discussion Question 5.

How do you introduce and monitor GLP1 in clinical practice?

GLP-1 agonist

- Initiate in office, if possible.
  - Improves adherence and patient fear (subcut inj)
  - Start low dose to help with nausea which is usually self-limited

Discussion Question 5.
How do you introduce and monitor SGLT2i or GLP1 in clinical practice?

a) What to monitor?

- Blood glucose
- Blood pressure
- Volume status
- Concomitant meds (ex. BS, BP)
- Renal function

Discussion Question 5.
How do you introduce and monitor SGLT2i or GLP1 in clinical practice?

b) Reduce risk of ketoacidosis – euglycemic DKA

SGLT2 inhibitors should be **temporarily withheld prior to major surgical procedures**, and during **acute infections** and **serious illness** to reduce the risk of ketoacidosis [Grade D, Consensus]

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Case Wrap-up

- Joe is started on an SGLT2i
- Over the next 3 months he loses 2 kg, new weight is 86 kg
- BP falls from 136/77 to 124/72
- A1c falls from 8.0% to 7.4%
- He feels better and is motivated to increase his physical activity

Discussion & Reflection

1. Do you need to change your current practice to implement any of these recommendations?
2. How do you engage patients and their families in therapy and manage expectations?
3. What are some other adherence strategies that were discussed or not discussed that could work for your practice?
4. Who are some agents of change who can help you implement the recs?

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The C-Change Collaborative

Founding Partners

- Institute of Circulatory and Respiratory Health (ICRH) and the Public Health Agency of Canada (PHAC)

Partner Organizations

- Canadian Association of Cardiovascular Prevention and Rehabilitation (CACPR)
- Canadian Action Network for the Advancement, Dissemination and Adoption of Practice-informed Tobacco Treatment (CAN ADAPTT)
- Canadian Cardiovascular Society (CCS) – Lipids
- Canadian Cardiovascular Society (CCS) - Heart Failure
- Diabetes Canada
- Hypertension Canada
- Canadian Society for Exercise Physiology (CSEP)
- Heart and Stroke Foundation of Canada
- Obesity Canada

Learning Objectives

Upon completion of this activity, participants should be able to:

- ✓Describe the patient who should be treated with an SGLT2i or GLP1 agonist
- ✓Explain the rationale for this treatment and the potential benefits
- ✓Describe the steps for initiating and monitoring therapy for patients with diabetes