Diabetes – Which agent should I use for this patient?

Disclosures

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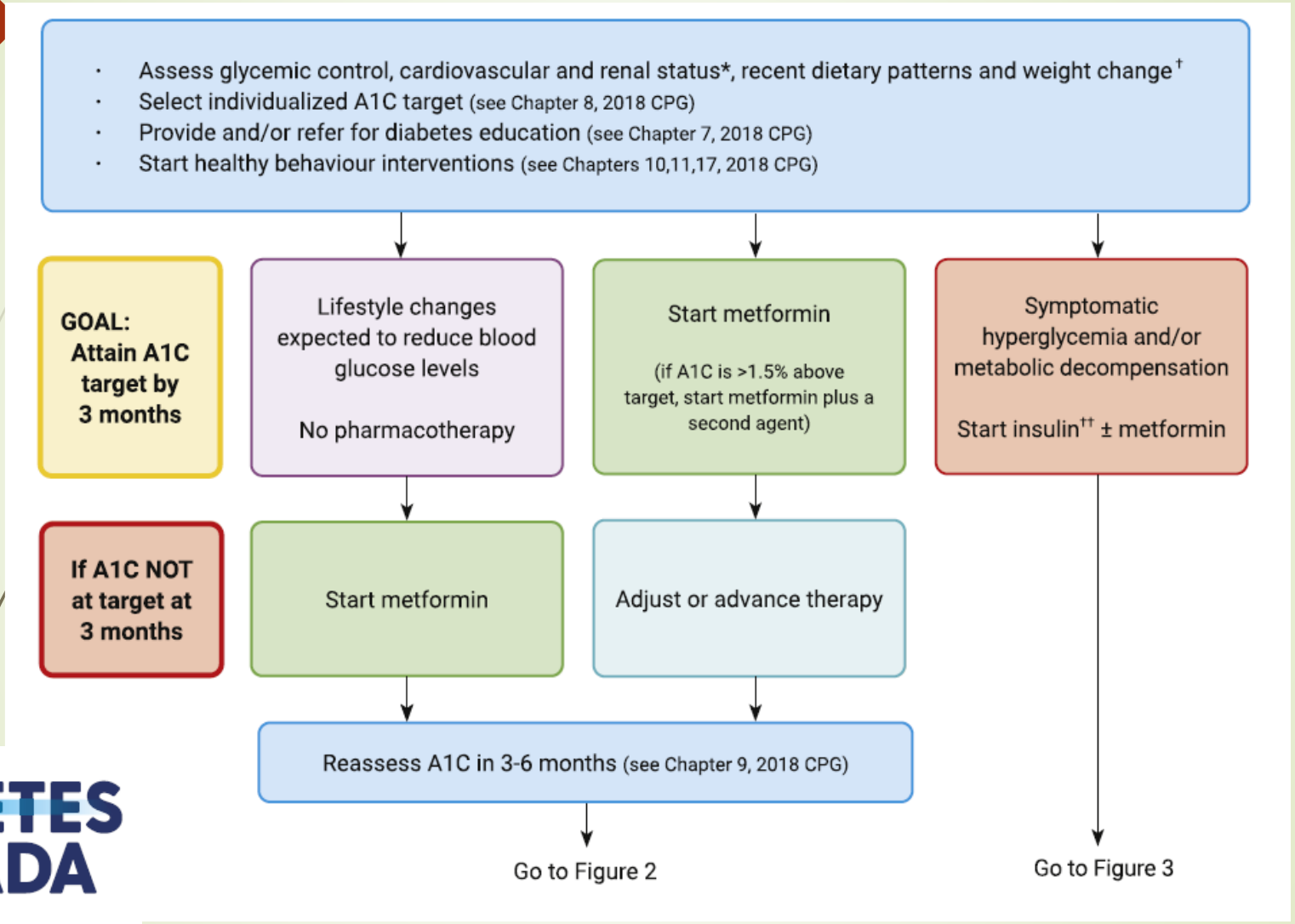
- Endocrinologist:
  - St-Jean-sur-Richelieu .
  - LMC Glen
  - Hôpital Chinois de Montréal
- Disclosures:
  - Advisory board/Conferences : Amgen, Astra Zeneca, Eli Lilly/Boehringer Ingelheim, Insulet, Janssen, Merck, Novo Nordisk, Sanofi-Aventis, Valeant
  - Research: Eli lilly, novo nordisk, sanofi-aventis
- My COI is not related to the topic I will be talking about
- Despite my COI my presentation will be strictly scientific and will not be influenced by any commercial interests. Slides were created by myself.

Objectives

- As a result of attending this session, participants will be able to:
  - Explore the different modalities of treatment in type 2 diabetes and help patients attain their treatment goal, with respect to the new Diabetes Canada guidelines
  - Discuss the effects of the choices of the treatment in type 2 diabetes
  - Reflect on the current practice and identify opportunities to help optimise the care to patients



DIABETES CANADA

Case 1: Mr M

- 55M DM2 x 2015
- PMH: HTN, Hypercholesterolemia
- Meds:
  - Metformin 1000mg po bid
  - Perindopril 4mg po qd
  - Atorvastatin 40mg po qd
- Physical exam:
  - BMI 29.5
  - BP 132/75
- Labs:
  - A1c 7.5%
  - Creat 70, eGFR over 60
  - LDL 1.8
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Mr M – What would you do next?

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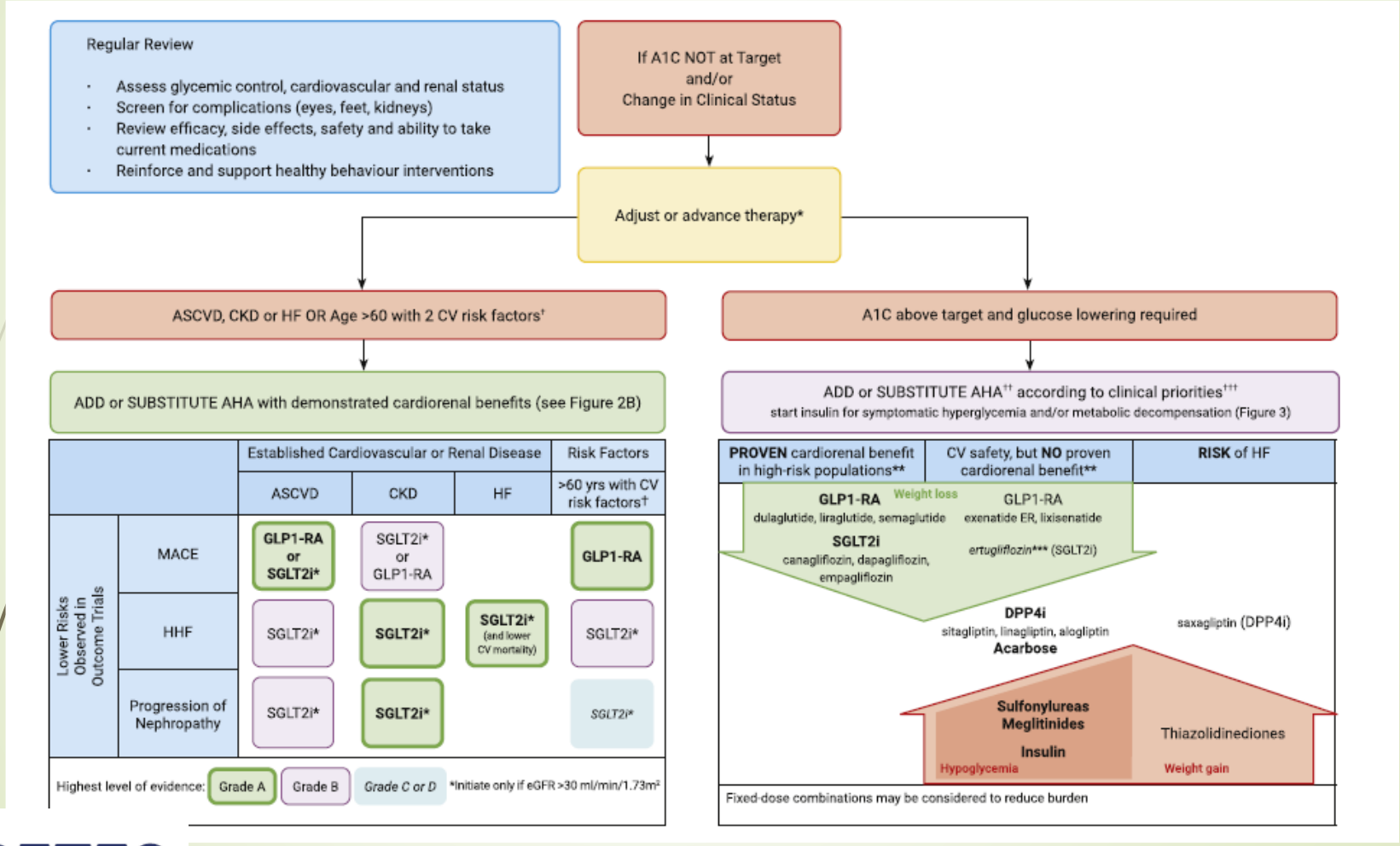
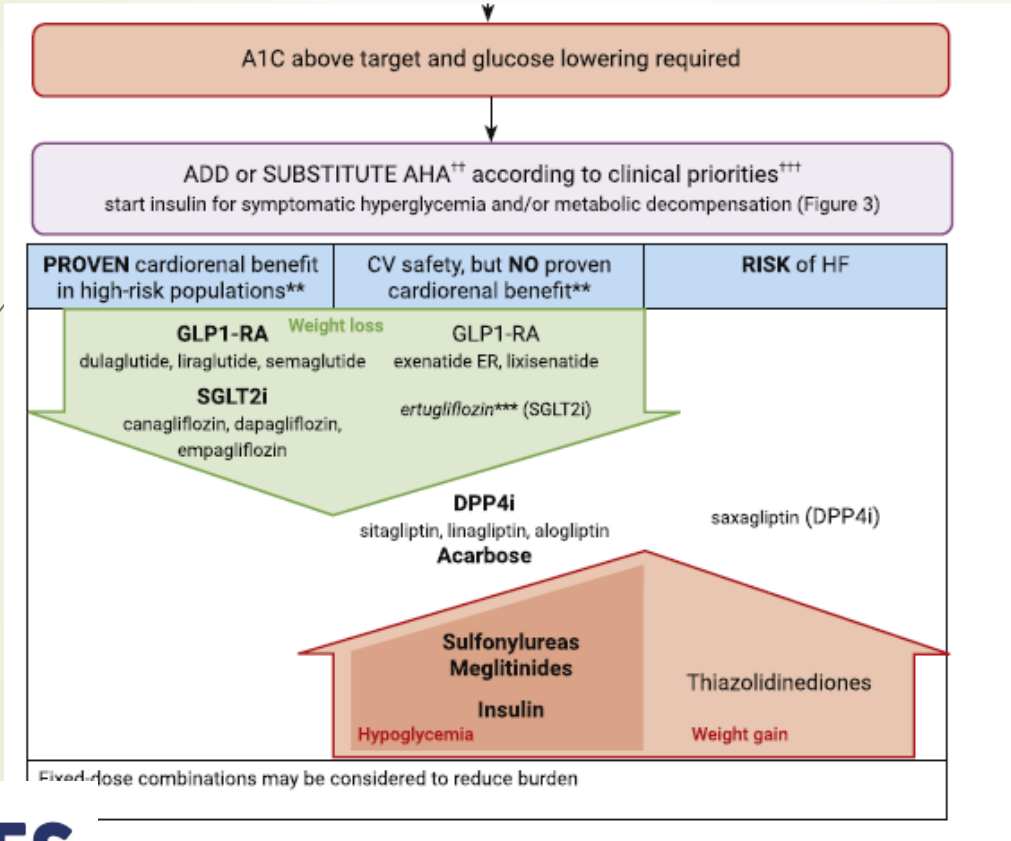


DIABETES CANADA

Mr M



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DIABETES CANADA

Class	Effect on CVD Outcomes	Hypo-glycemia	BW	Relative A1C Lowering when added to metformin	Other therapeutic considerations	Cost
GLP-1RA	Lira: Superiority Sema OW: Superiority* Dula: Superiority 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.	$$$$
SGLT2i	Empa: Superiority Cana: Superiority	Rare	↓↓	↓↓ to ↓↓↓	Genital infections, UTI, hypotension. Rare diabetic ketoacidosis (may occur with no hyperglycemia). Canagliflozin showed increased risk of amputations in one study.	$$$
DPP-4i	Neutral	Rare	Neutral	↓↓	Caution with saxagliptin in heart failure Rare joint pain.	$$$
Insulin	IGlar: Neutral Degludec: Neutral	Yes	↑↑	↓↓↓↓	No dose ceiling, flexible regimens. Requires subcutaneous injection.	$- $$$$
SUs		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	$

DIABETES CANADA

*Test for superiority not a pre-specified endpoint. BG, blood glucose; BW, body weight; CVD, cardiovascular disease; GI, gastrointestinal; GLP-1RA, glucagon-like peptide-1 receptor agonist; LAR, long-acting release; MEN 2, multiple endocrine neoplasia type **2;** SGLT2i, sodium-glucose cotransporter 2 inhibitor; SU, sulfonylurea; UTI, urinary tract infection. Lipscombe L et al. *Can J Diabetes* 2008;42:S88–103.

What if Mr M had a history of MI?

- 55M DM2 x 2015
- PMH: HTN, Hypercholesterolemia
- Hx of MI 3 years ago, stent x 1
- Meds:
  - Metformin 1000mg po bid
  - Perindopril 4mg po qd
  - Atorvastatin 40mg po qd
  - ASA 80mg po qd
  - Bisoprolol 5mg
- Physical exam:
  - BMI 29.5
  - BP 132/75
- Labs:
  - A1c 7.5%
  - Creat 70, eGFR over 60
  - LDL 1.8
  - Alb/creat 1.0

Mr M – What would you do next?

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55M DM2 x 2015
Hx of MI x 2018
BMI 29.5
BP 132/75

A1c 7.5%
Creat 70, eGFR over 60
LDL 1.8
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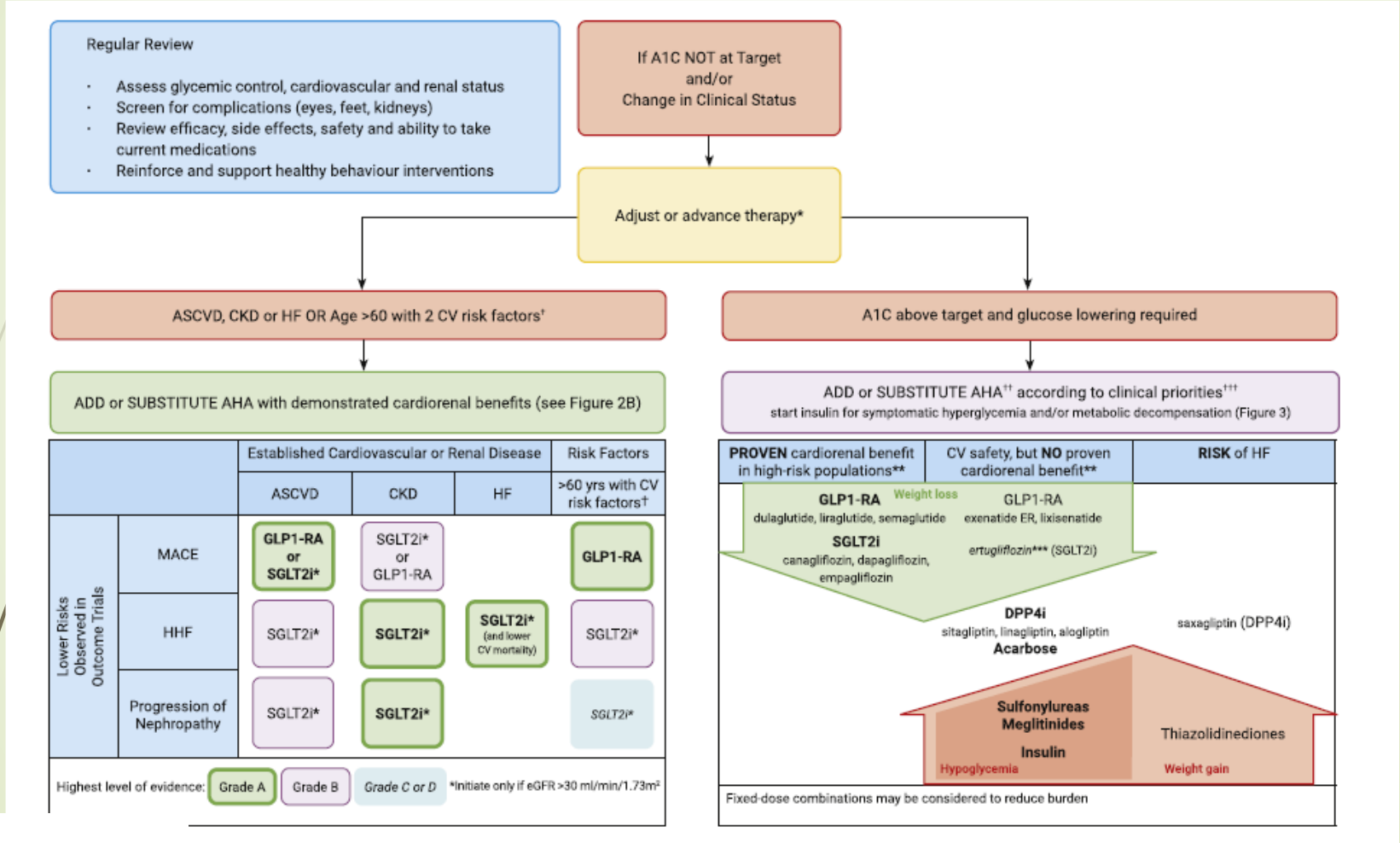
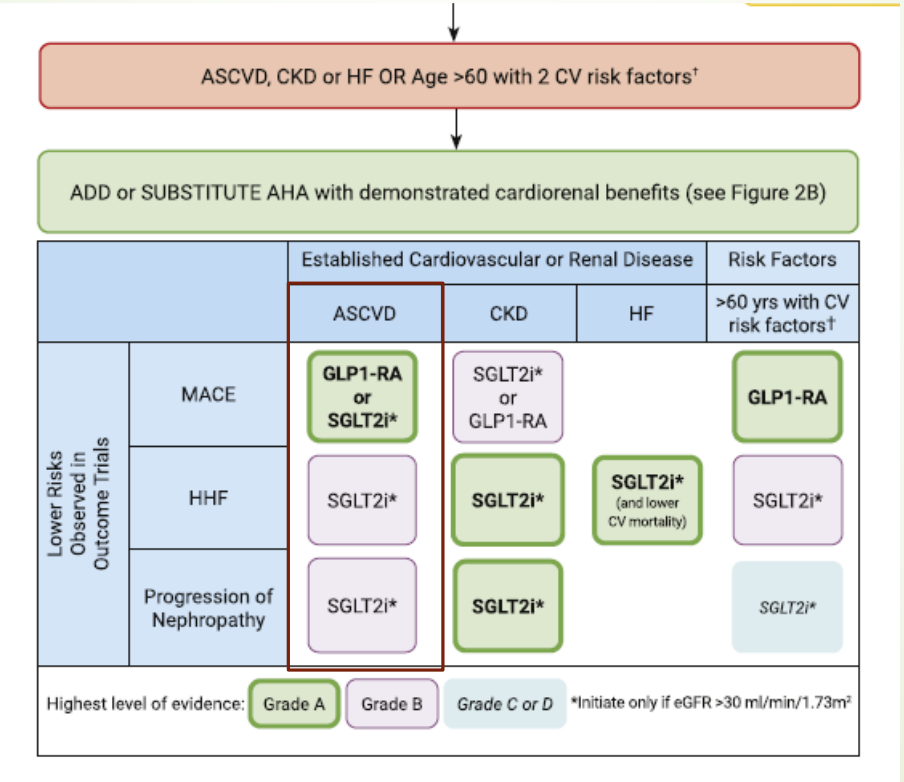


DIABETES CANADA

Mr M – hx of MI 3 years ago



DIABETES CANADA

Summary of outcome trials of drugs with cardiorenal benefits							
Agent (outcome trial)	Population	Clinical outcomes (HR [95% CI] vs placebo)					
		MACE	CV mortality	All-cause mortality	Fatal/ nonfatal MI	Fatal/ nonfatal stroke	Hosp HF
GLP1-RA							
Exenatide (EXSCEL)	**CVD (73%) or CV risk factors**	0.91* (0.83-1.00)	0.88 (0.76–1.02)	**0.86 (0.77-0.97)**	0.97 (0.85–1.10)	0.85 (0.70–1.03)	–
Liraglutide (LEADER)	**CVD (72%) or CV risk factors**	**0.87* (0.78-0.97)**	**0.78 (0.66–0.93)**	**0.85 (0.74-0.97)**	0.86 (0.73–1.00)	0.86 (0.71–1.06)	–
Semaglutide SC (SUSTAIN 6)	**CVD (59%) or CV risk factors**	**0.74* (0.58-0.95)**	0.98 (0.65–1.48)	1.05 (0.74-1.50)	0.74 (0.51-1.08)†	**0.61 (0.38-0.99)†**	–
Semaglutide Oral (PIONEER 6)	**CVD (85%) or CV risk factors**	0.79* (0.57-1.11)	**0.49 (0.27–0.92)**	**0.50 (0.31-0.84)**	1.18 (0.73-1.90)†	0.74 (0.35-1.57)†	–
Dulaglutide (REWIND)	**CVD (31.5%) or CV risk factors**	**0.88* (0.79-0.99)**	0.91 (0.78–1.06)	0.90 (0.80-1.01)	0.96 (0.79-1.16)†	**0.76 (0.61-0.95)†**	–
Albiglutide (HARMONY) (withdrawn from market)	**CVD or PVD**	**0.78* (0.68-0.90)**	0·93 (0·73–1·19)	0.95 (0.79-1.16)	0.96 (0.79–1.15)	**0.76 (0.62–0.94)**	–
SGLT2i							
Empagliflozin (EMPA-REG)	**CVD**	**0.86* (0.74-0.99)**	**0.62 (0.49-0.77)**	**0.68 (0.57-0.82)**	0.87 (0.70–1.09)	1.18 (0.89–1.56)	**0.65 (0.50-0.85)**
Canagliflozin (CANVAS PROGRAM)	**CVD (66%) or CV risk factors**	**0.86* (0.75-0.97)**	0.87 (0.72-1.06)	0.87 (0.74-1.01)	0.89 (0.73–1.09)	0.87 (0.69–1.09)	**0.67 (0.52-0.87)**
Canagliflozin (CREDENCE)	**CKD (eGFR 30–90 + proteinuria)**	**0.80 (0.67-0.95)**	0.78 (0.61-1.00)	0.83 (0.68-1.02)	–	–	**0.61 (0.47-0.80)**
Dapagliflozin (DECLARE-TIMI)	**CVD (41%) or CV risk factors**	0.93* (0.84-1.03)	0.98 (0.82-1.17)	0.93 (0.82-1.04)	0.89 (0.77–1.01)	1.01 (0.84–1.21)	**0.73 (0.61-0.88)**
Dapagliflozin (DAPA-HF)	**CHF (reduced EF) ± DM (42%)**	–[1]	**0.82 (0.69-0.98)**	**0.83 (0.71-0.97)**	–	–	**0.70 (0.59-0.83)**

DIABETES CANADA

What if Mr M has CKD?

- 55M DM2 x 2015
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- Meds:
  - Metformin 1000mg po bid
  - Perindopril 4mg po qd
  - Atorvastatin 40mg po qd
- Physical exam:
  - BMI 29.5
  - BP 132/75
- Labs:
  - A1c 7.5%
  - Creat 120, eGFR 50
  - LDL 1.8
  - Alb/creat 3.5

Mr M – What would you do next?

- 1. Add DPP4i
- 2. Add GLP1-RA
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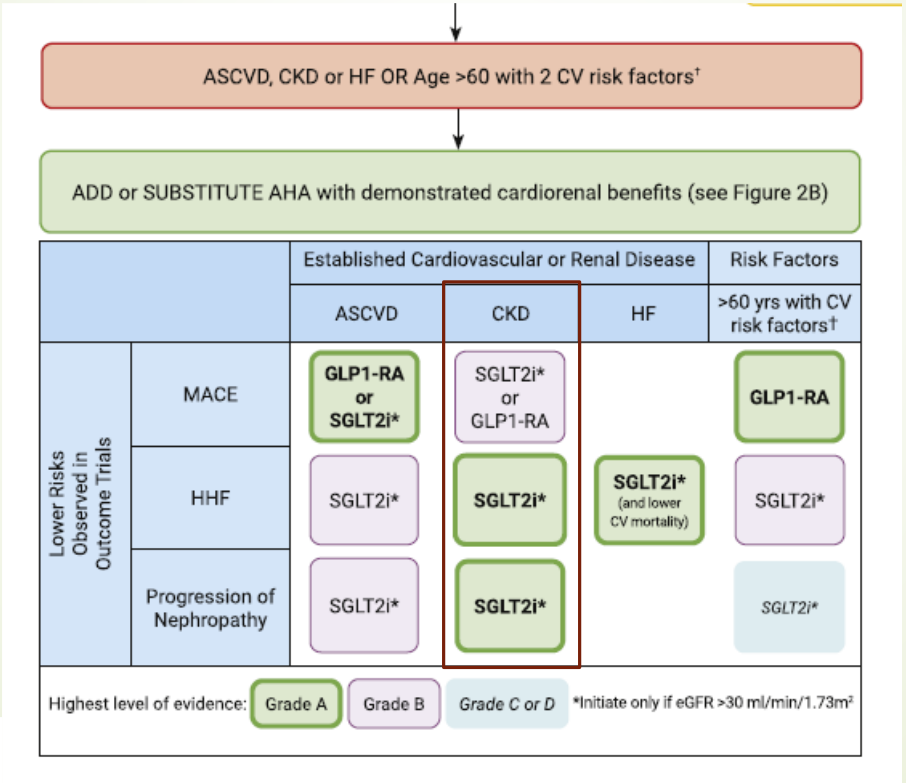
Mr M – eGFR 50, alb/cr 3.5



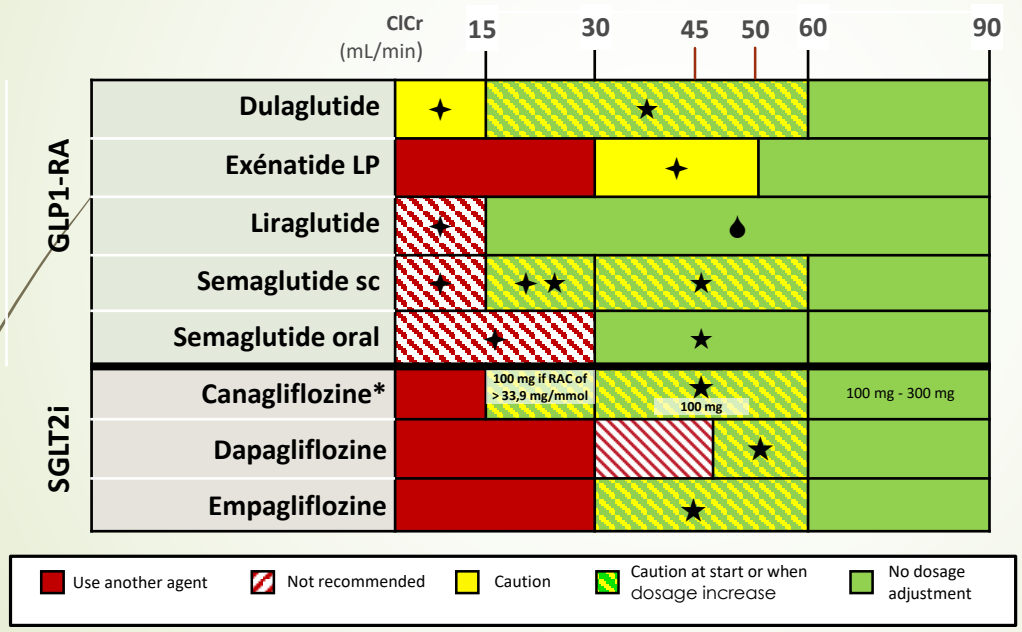
DIABETES CANADA

Summary of outcome trials of drugs with cardiorenal benefits

Agent (outcome trial)	Population	Progression of CKD
GLP1-RA		
Exenatide (EXSCEL)	**CVD (73%) or CV risk factors**	–
Liraglutide (LEADER)	**CVD (72%) or CV risk factors**	–
Semaglutide SC (SUSTAIN 6)	**CVD (59%) or CV risk factors**	–
Semaglutide Oral (PIONEER 6)	**CVD (85%) or CV risk factors**	–
Dulaglutide (REWIND)	**CVD (31.5%) or CV risk factors**	–
Albiglutide (HARMONY) (withdrawn from market)	**CVD or PVD**	–
SGLT2i		
Empagliflozin (EMPA-REG)	**CVD**	**0.61 (0.53–0.70)**
Canagliflozin (CANVAS PROGRAM)	**CVD (66%) or CV risk factors**	**0.73 (0.67–0.79)**
Canagliflozin (CREDENCE)	**CKD (eGFR 30–90 + proteinuria)**	**0.70*[2] (0.59–0.82)**
Dapagliflozin (DECLARE–TIMI)	**CVD (41%) or CV risk factors**	**0.76 (0.67–0.87)**
Dapagliflozin (DAPA-HF)	**CHF (reduced EF) ± DM (42%)**	0.71 (0.44-1.16)

DIABETES CANADA

Adjustment of the dosage in renal failure



Legend :

✦	Limited clinical experience
★	Follow renal funtion, esp if GI symptoms
💧	Caution in patients with dehydration

Warning:

- **Canagliflozine :** insufficient data to start when eGFR < 30 mL/min/1,73 m²
- **Empagliflozine** stop treatment if eGFR drops < 30 mL/min/1,73 m²
- **Dapagliflozine :**not recommended if eGFR < 45 mL/min/1,73 m²

* Peut être utilisé pour ses bienfaits cardiorénaux chez les patients présentant une MCV clinique, un taux d'HbA_{1c} supérieur à la cible et un DFGe > 30 mL/min/1,73 m²
1 f.p.j., une fois par jour; 1 f.p.s., une fois par semaine; ClCr, clairance de la créatinine; DFG, débit de filtration glomérulaire; iDPP-4, inhibiteur de la dipeptidyl peptidase-4; iSGLT2, inhibiteur de cotransporteur sodium-glucose de type 2; LP, libération prolongée; RAC, ratio albumine/créatinine.
Monographie de la canagliflozine, Janssen Inc., 2020; monographie de la dapagliflozine, AstraZeneca Canada Inc., 2020; comité d'experts des Lignes directrices de pratique clinique de Diabète Canada. Can J Diabetes. 2018;42 Suppl 1:S88-103; monographie de la dulaglutide, Eli Lilly Canada Inc., 2019; monographie de l'empagliflozine, Boehringer Ingelheim (Canada) Ltd., 2019; monographie de l'exenatide LP, AstraZeneca Canada Inc., 2019; monographie du liraglutide, Novo Nordisk Canada Inc., 2020; monographie du sémaglutide oral, Novo Nordisk Canada Inc., 2020; monographie du sémaglutide 1 f.p.s., Novo Nordisk Canada Inc., 2018. Comité d'experts des Lignes directrices de pratique clinique de Diabète Canada. Can J Diabetes. 2018;42 Suppl 1:S47-53.

What if Mr M is 65 year old

- 65M DM2 x 2015
- PMH: HTN, Hypercholesterolemia
- Meds:
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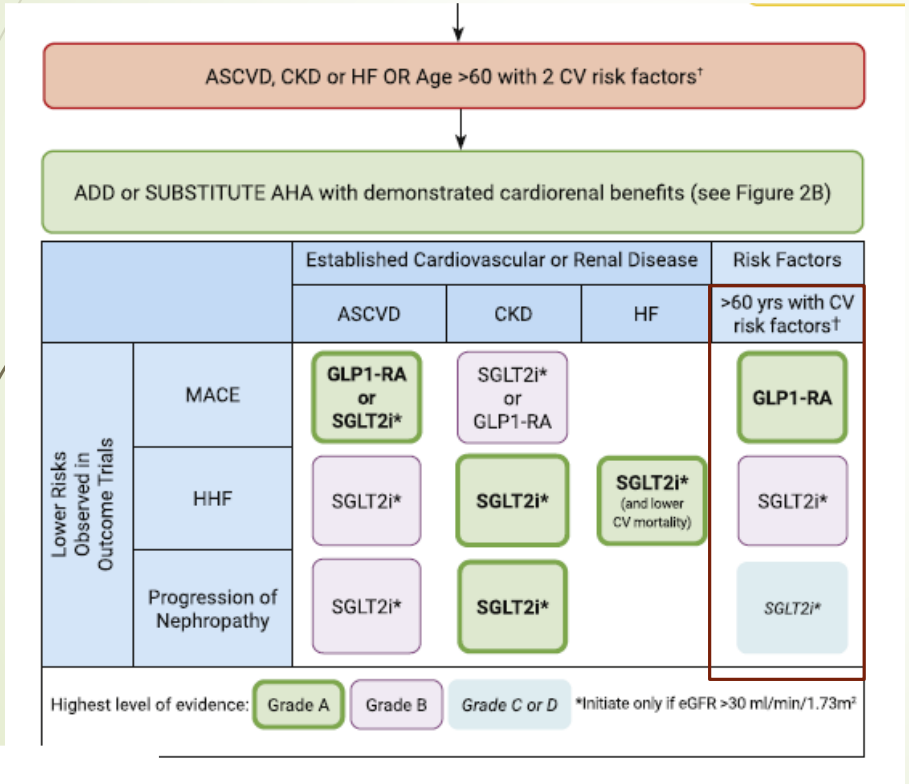

CV Risk factors:

- Smoking (tobacco use)
- Hypertension
  - Untreated BP ≥140/90, or
  - Current antihypertensive therapy
- Dyslipidemia
  - Untreated LDL>3.4 mmol/L OR HDL-C <1.0 mmol/L (men) <1.3 mmol/L (women) OR triglyceride >2.3 mmol/L, or
  - Current lipid-lowering therapy
- Central obesity

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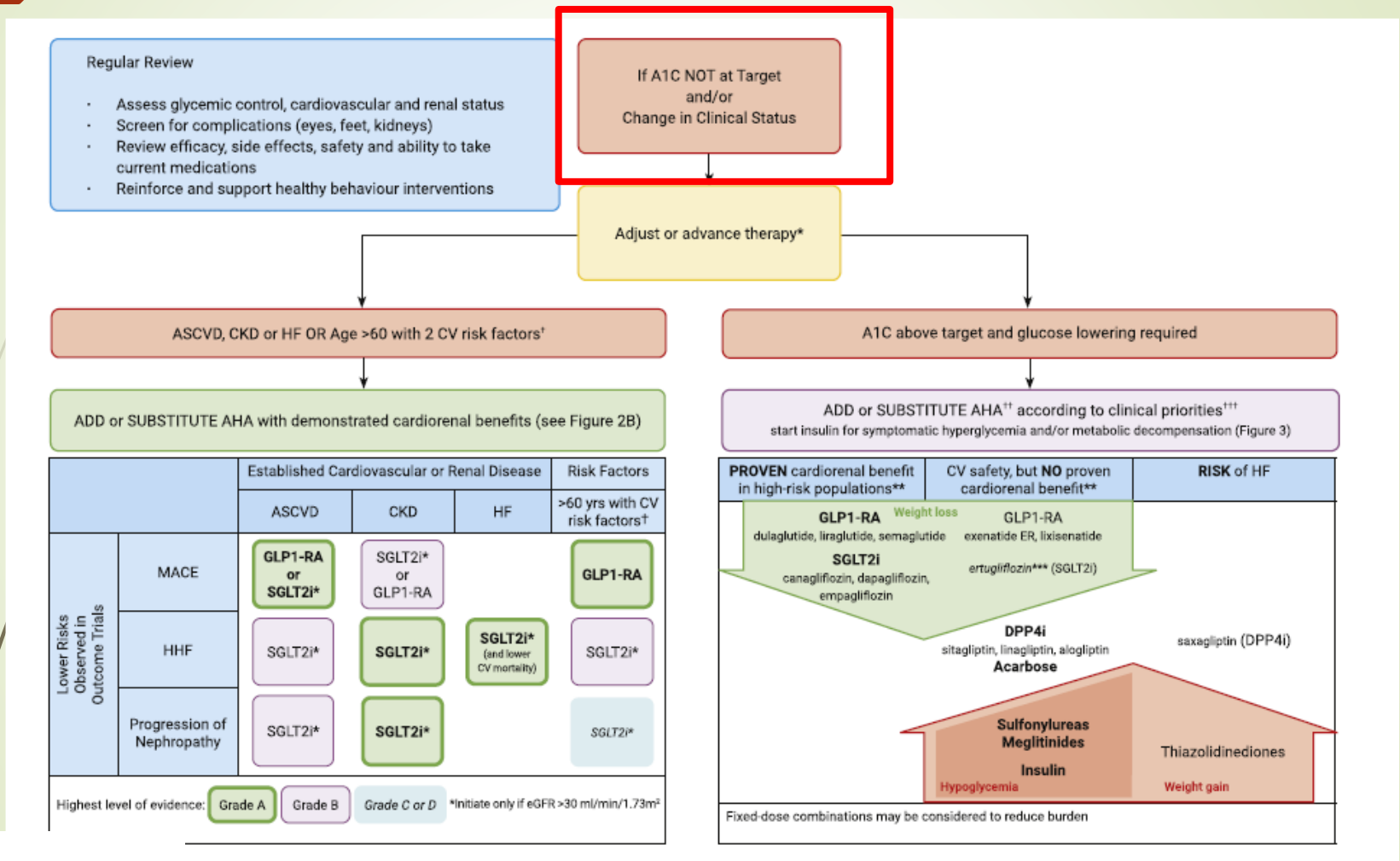

DIABETES CANADA

Questions?