



SGLT-2 Inhibitors in Practice: What Clinicians Need to Know

August 13, 2026

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Disclosures

In the past 24 months, I have **NOT** had any financial relationships with any ineligible companies.

Objectives

- Patient selection/Choice of therapy
- Clinical considerations
- Adverse effects

Case Scenario

Mr. Smith is a 68-year-old male who comes to the clinic as a new patient for T2DM.

He was diagnosed with T2DM 8 years ago. His current medications include metformin 1000 mg PO BID with excellent compliance. His BMI 28 kg/m², BP 144/84, PR 74. Point-of-care A1c in clinic today is 7.4%, and eGFR is 82 mL/min/1.73m²

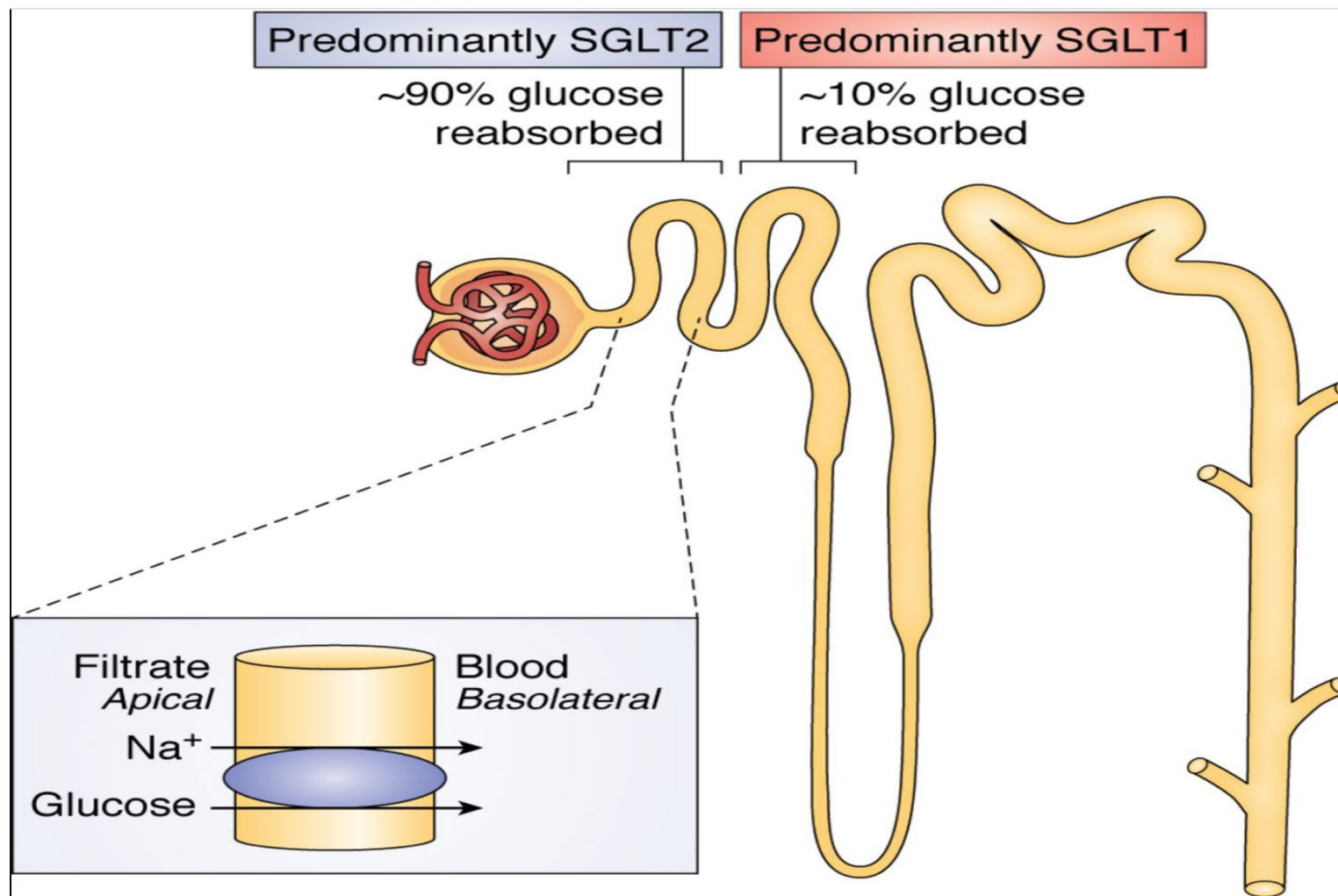
He has a history of myocardial infarction at the age of 61 years and subsequently developed HFrEF (EF 33%).

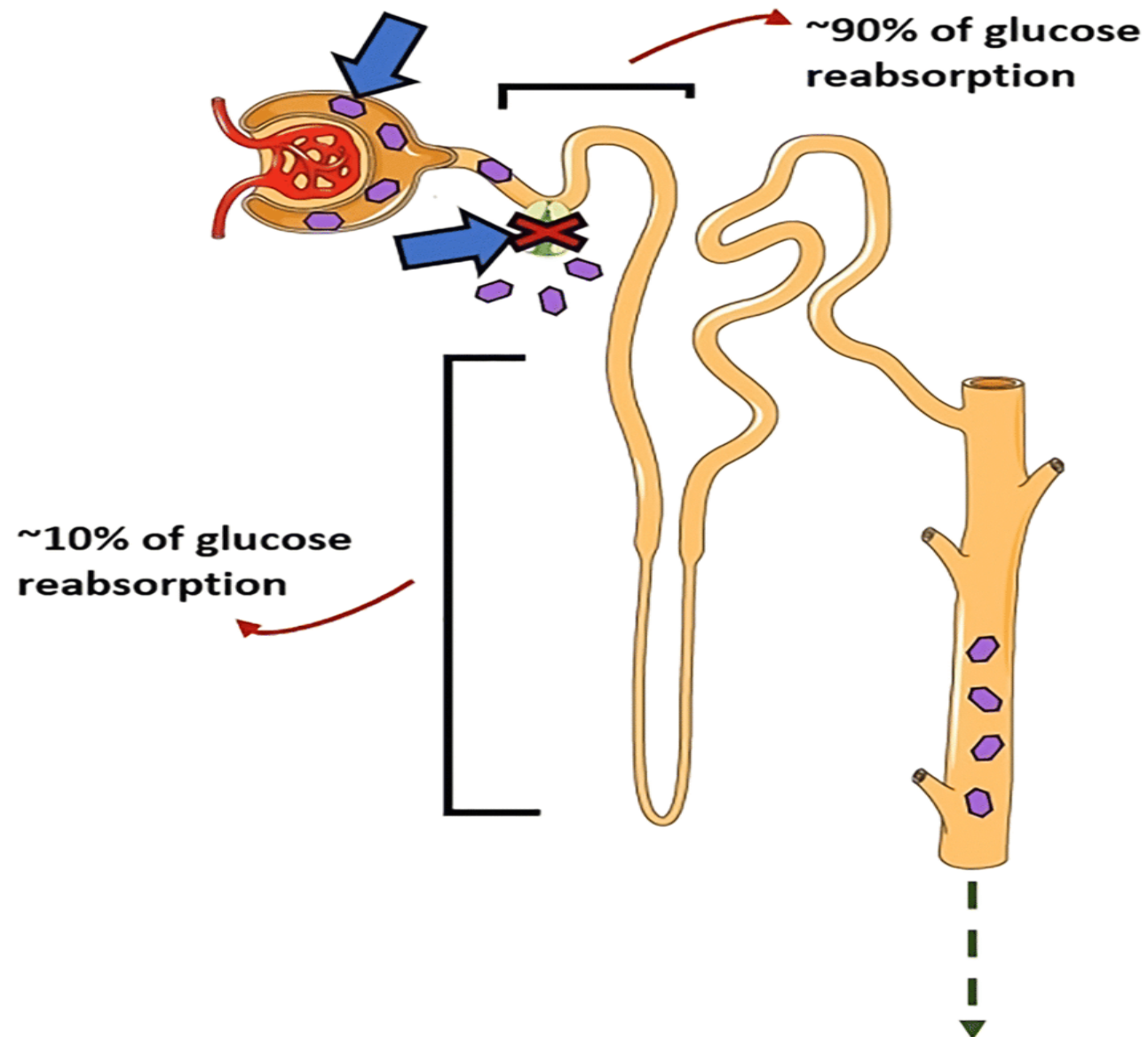
Of the following medications, which single medication would you recommend that he start, after discussing with him and assuming no contraindications?

- A. Glimepiride
- B. Semaglutide
- C. Empagliflozin
- D. Sitagliptin
- E. Basal insulin

Mechanism of Action

SGLT2i

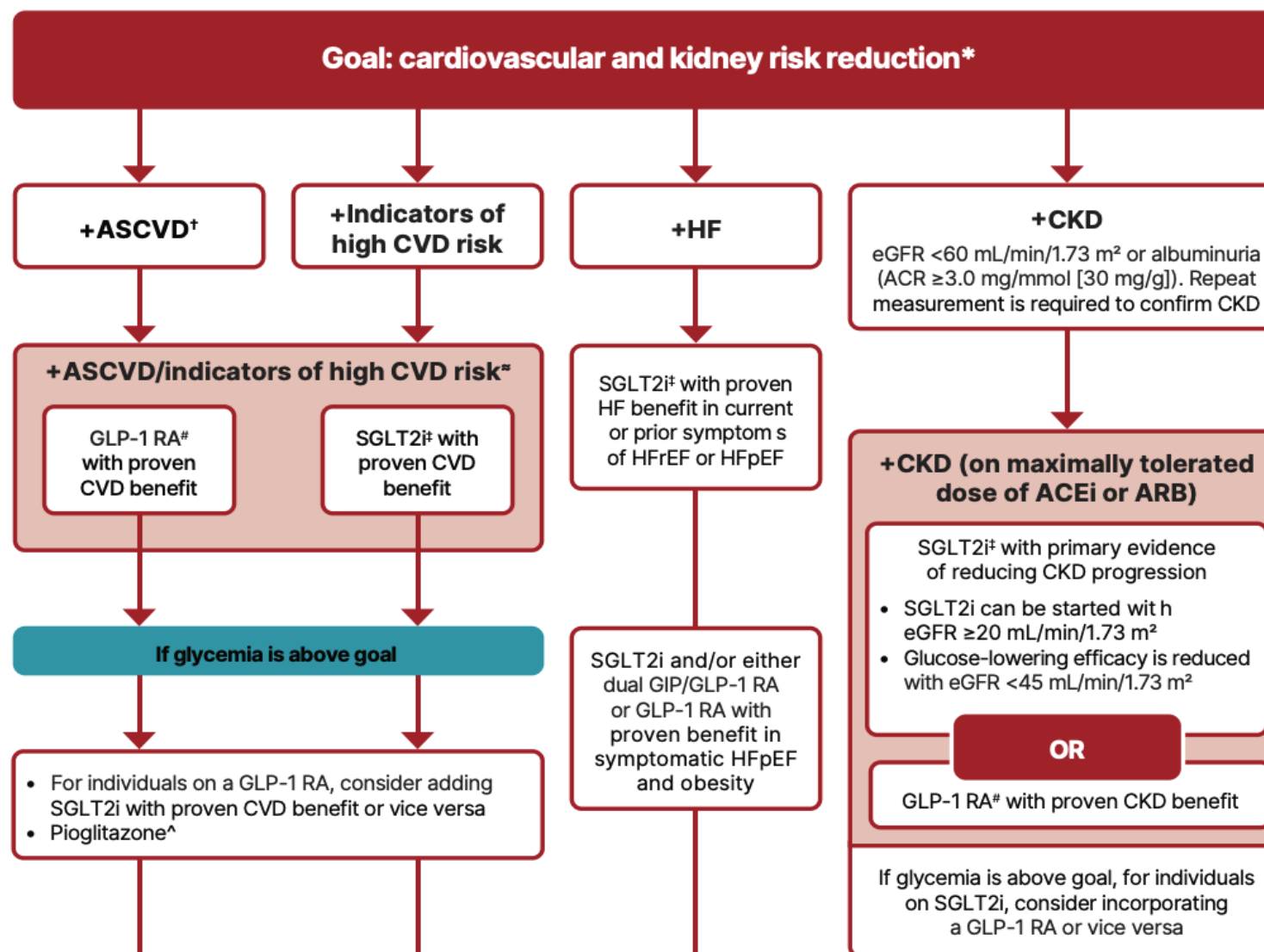




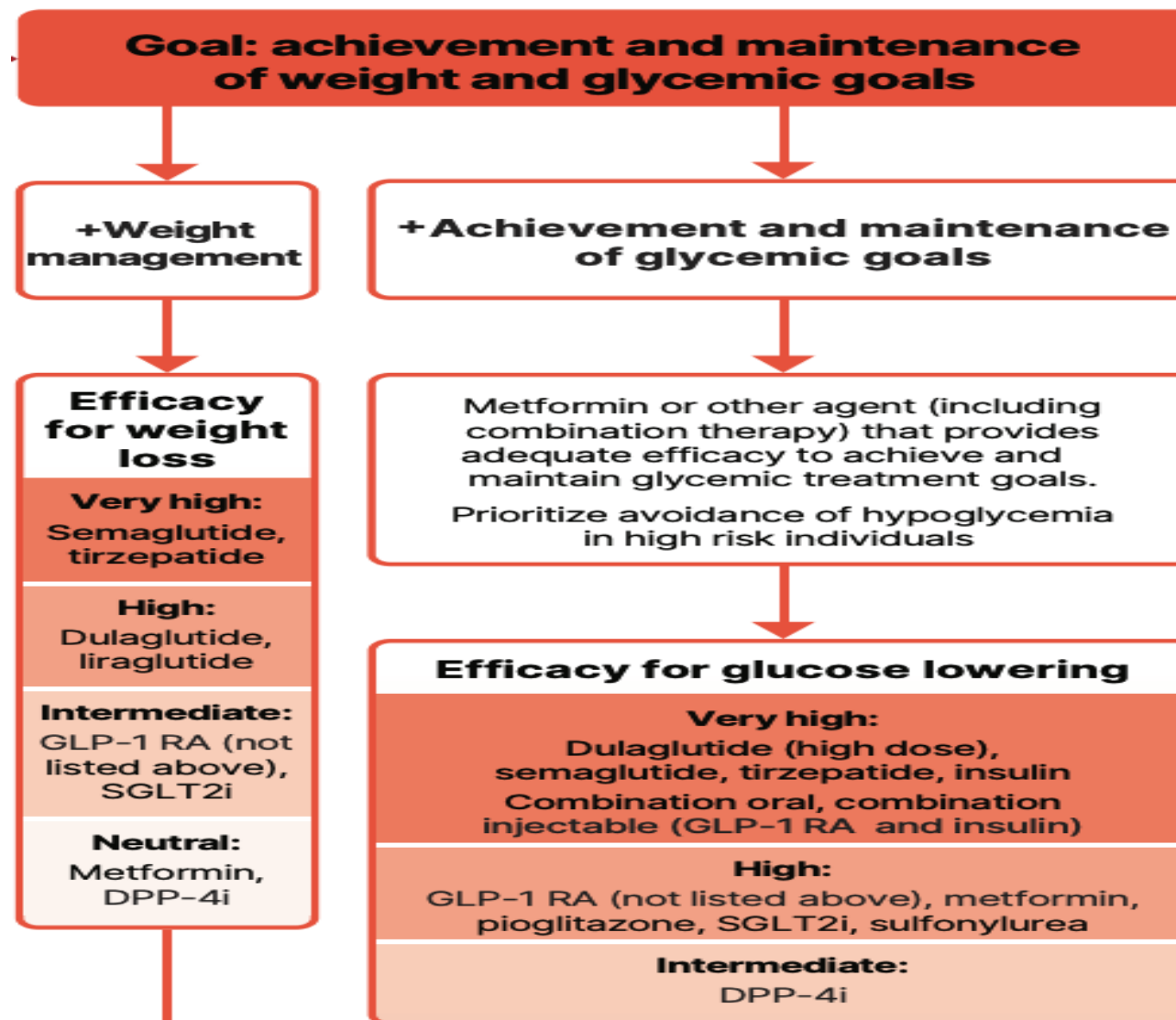
Scheen, A. J. (2014).. *Drugs*, 75(1), 33–59.
<https://doi.org/10.1007/s40265-014-0337-y>

Triplitt, C., & Cornell, S. (2015). *Endocrinology and Diabetes*, 8, CMED–S31526. <https://doi.org/10.4137/cmed.s31526>

Patient Selection/Choice of Agent



American Diabetes Association Professional Practice Committee for Diabetes*; 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2026. *Diabetes Care* 1 January 2026; 49 (Supplement_1): S183–S215. <https://doi.org/10.2337/dc26-S009>



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Glucose lowering efficacy

- Intermediate to high

Hypoglycemia risk

- No
- Block reabsorption of filtered glucose -> Lower plasma glucose
- As plasma levels fall -> amount of filtered glucose falls.
- Therefore, they do not usually cause hypoglycemia in the absence of therapies that otherwise cause hypoglycemia.

Weight loss

- neutral/intermediate weight loss

Reduction in systolic blood pressure

- Prior to initiation – consider proactive modification of blood pressure medications

Clar C, et al BMJ Open. 2012 Oct 18;2(5):e001007. doi: 10.1136/bmjopen-2012-001007. PMID: 23087012; PMCID: PMC3488745.

Liu XY et al. J Diabetes Complications. 2015 Nov-Dec;29(8):1295-303. doi: 10.1016/j.jdiacomp.2015.07.011. Epub 2015 Jul 21. PMID: 26365905.

Agent	Empagliflozin	Dapagliflozin	Canagliflozin	Ertugliflozin
MACE	✓		✓	
Heart Failure	✓	✓	✓	✓
CKD	✓	✓	✓	

MACE - Major Adverse Cardiovascular Events
CKD – Chronic Kidney Disease

Zinman et al EMPA-REG. N Engl J Med. 2015 Nov 26;373(22):2117-28. doi: 10.1056/NEJMoa1504720. Epub 2015 Sep 17. PMID: 26378978.
 Neal B et al N Engl J Med. 2017 Aug 17;377(7):644-657. doi: 10.1056/NEJMoa1611925. Epub 2017 Jun 12. PMID: 28605608.
 Marilly E et al Diabetologia. 2022 Dec;65(12):2000-2010. doi: 10.1007/s00125-022-05773-8. Epub 2022 Aug 4. PMID: 35925319.

Diabetic Kidney Disease and SGLT2 inhibitors

- eGFR < 45mL/min/1.73 m² – Glucose lowering effect is minimal
- Continue to have significant CV and renal risk reduction at low eGFR.
- Okay to start/continue if eGFR >20mL/min/1.73 m²
- Continue until dialysis or transplantation
- SGLT2 inhibitors come in 2 dose levels.
- Glucose lowering effect is dose dependent
- Cardiorenal benefit is not dose dependent.

Low eGFR	High eGFR
CV/Renal benefit	CV/Renal benefit
	Glucose lowering benefit

Zelniker et al Lancet. 2019 Jan 5;393(10166):31-39. doi: 10.1016/S0140-6736(18)32590-X. Epub 2018 Nov 10
de Boer et al Diabetes Care. 2022 Dec 1;45(12):3075-3090. doi: 10.2337/dci22-0027. PMID: 36189689; PMCID: PMC9870667.

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In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT-2i with proven benefit should be made **irrespective of the A1c**.

SGLT-2i have demonstrated their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, Hospitalization for HF, and kidney outcomes in individuals with T2DM and established or high-risk CVD.

Contraindications/Precautions/Adverse Effects

SGLT2i

- SGLT2 inhibitors should not be used specifically for the treatment of hyperglycemia in patients with:
- Type 1 diabetes
- Prior diabetic ketoacidosis (DKA)

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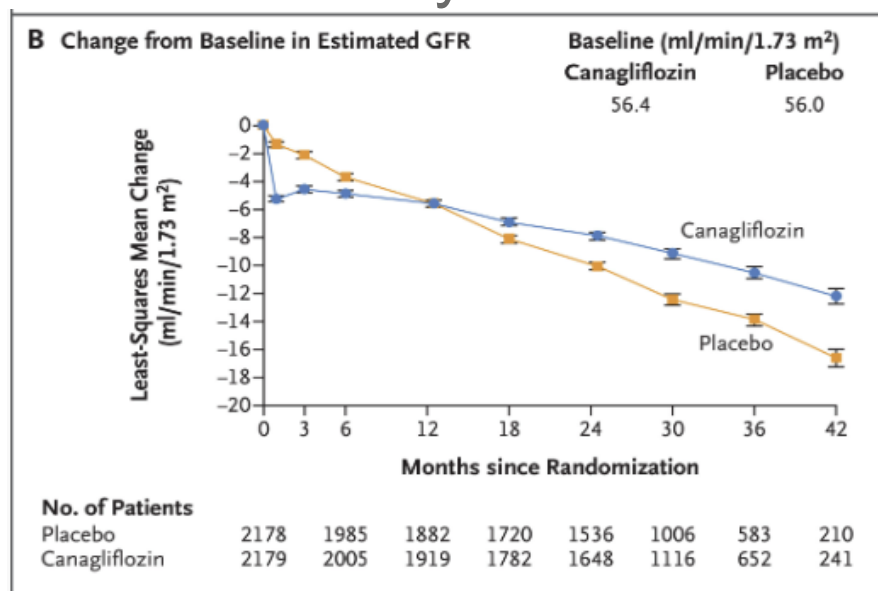
- Genitourinary infections
 - Genital mycotic infections
 - Urinary tract infections
 - More common in women and uncircumcised men
 - Fournier gangrene
 - Necrotizing soft tissue infection of the perineum:
 - 1/10,000, not statistically significantly increased from non-SGLT-2i users.

- Mild volume loss

- Monitor blood pressure and volume status
- Patient education – monitor orthostatic symptoms related to volume loss (lightheadedness, dizziness, nausea etc.) and blood pressure
- Proactive modification of blood pressure medications prior to initiation especially diuretic therapy.

- Acute kidney injury

- An initial decline in eGFR can occur
- This initial reduction stabilizes over time
- Overall, renal protective effect.
- Monitor kidney function at the initiation and during treatment

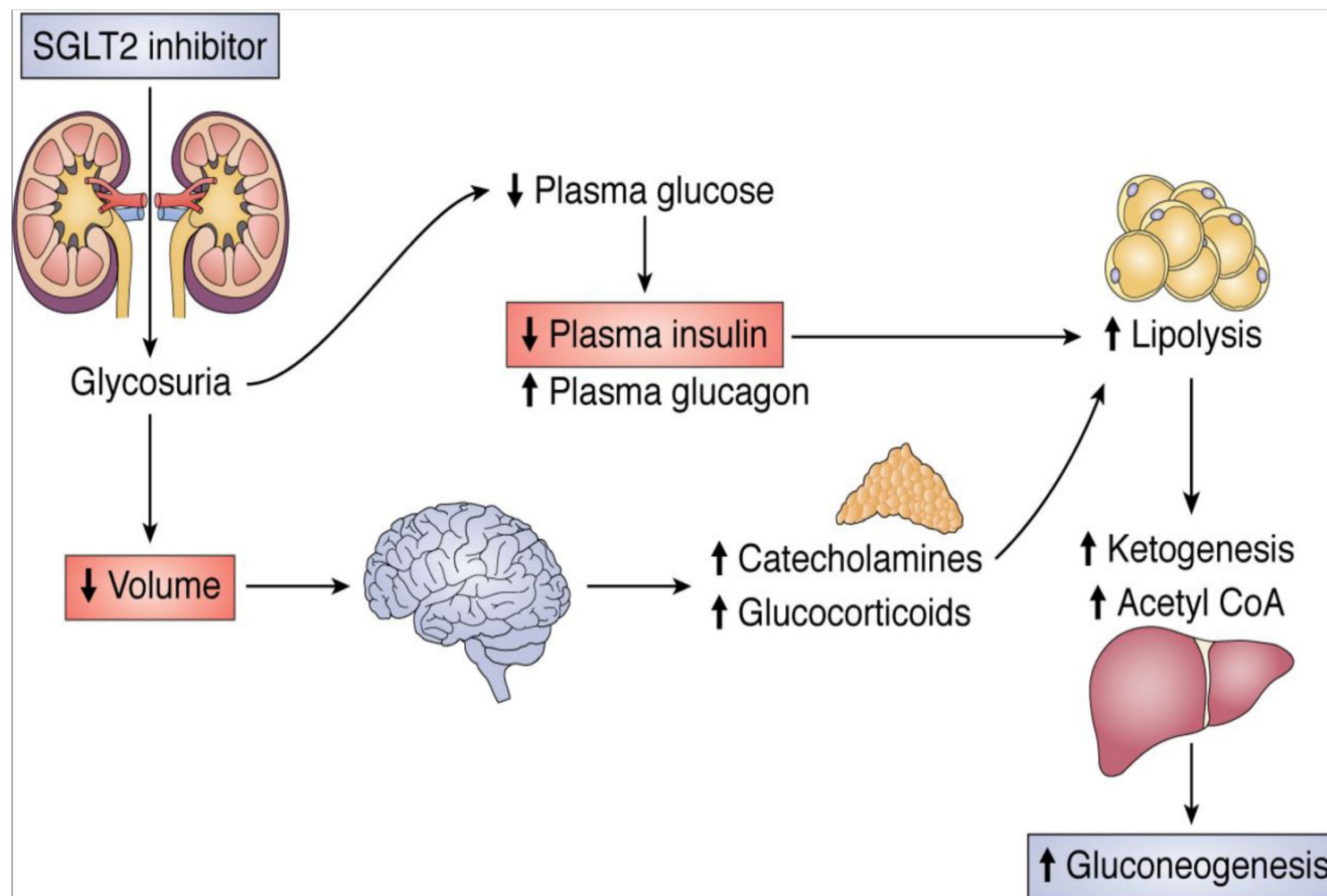


CREDENCE Trial. N Engl J Med. 2019 Jun 13;380(24):2295-2306. doi: 10.1056/NEJMoa1811744. Epub 2019 Apr 14. PMID: 30990260.

- Lower extremity amputation

- SGLT2 inhibitors, particularly [canagliflozin](#), are associated with an increased risk of amputation.
- Used with caution in patients with history of severe neuropathy (loss of protective sensation), foot deformity, vascular disease, and history of previous foot ulceration or prior amputation.
- Patients' education - perform daily foot examination
- Regular examination by the provider.

DKA with SGLT2i



Diabetic Ketoacidosis

- Euglycemic - plasma glucose <250 mg/dL
- Absence of substantial hyperglycemia delays the diagnosis
- Off-label use in type 1 diabetes is NOT recommended.
- Counsel about symptoms (e.g., fatigue, myalgias, nausea, and emesis) -> perform urine ketone monitoring.
- SGLT2 inhibitors should be withheld during times of increased DKA risk (e.g., infection, hospitalization, or surgery).

Clinical Pearls

Patient education

- Maintain good hydration status
- Genital mycotic infections - Diminish the risk with genital hygiene
- Risk of euglycemic DKA
 - Discontinue before scheduled surgery (3-4 days), during critical illness, and during prolonged fasting
- Foot care
 - Monitor kidney function and blood pressure
 - Not FDA approved for T1DM



Questions?