

Beyond Glycemic Control: The Hidden Talents of Diabetes Medications

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Conflict of Interest Disclosure

I have no actual or potential conflicts of interest in relation to this presentation.

Brand names of all products in this presentation are included for identification purposes only.

Learning Objectives (Pharmacists)



Evaluate current guideline-based pharmacologic treatment recommendations for patients with type 2 diabetes and associated comorbidities.



Differentiate the clinical benefits and appropriate use of GLP-1 receptor agonists and SGLT2 inhibitors for glycemic control, weight management, cardiovascular risk reduction, heart failure, and chronic kidney disease.



Apply evidence-based strategies to individualize diabetes medication regimens based on patient-specific cardiovascular, renal, and metabolic risk factors.



Develop comprehensive medication management plans that optimize therapeutic outcomes and support guideline-concordant diabetes care.

Learning Objectives (Technicians)



Identify common medication classes used in the treatment of type 2 diabetes, including GLP-1 receptor agonists and SGLT2 inhibitors.



Recognize the role of diabetes medications in managing glycemic control and supporting cardiovascular, renal, and weight-related health outcomes.



Describe key medication-use considerations, including dosage forms, administration requirements, storage, and patient access issues for newer diabetes therapies.



Support pharmacists and patients by facilitating accurate medication processing, adherence assistance, and coordination of care related to diabetes treatment plans.

Abbreviations

AACE = American Association of Clinical Endocrinologists

ADA = American Diabetes Association

Al/Cr = albumin to creatinine ratio

BMI = body mass index

CAD = coronary artery disease

CKD = chronic kidney disease

CV = cardiovascular

CVD = cardiovascular disease

CVOTs = cardiovascular outcomes trials

DKA = diabetic ketoacidosis

DPP-4 = dipeptidyl peptidase-4

eGFR = estimated glomerular filtration rate

GIP = glucose-dependent insulintropic peptide

GLP-1 = glucagon-like peptide-1

GLP-1 RA = glucagon-like peptide-1 receptor agonist

HF = heart failure

HF_rEF = heart failure with reduced ejection fraction

HF_pEF = heart failure with preserved ejection fraction

HHF = hospitalization for heart failure

HR = hazard ratio

KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire Clinical Summary Score

KDIGO = Kidney Disease: Improving Global Outcomes

MACE = major adverse cardiovascular events

MASH = metabolic dysfunction–associated steatohepatitis

MASLD = metabolic dysfunction–associated steatotic liver disease

MI = myocardial infarction

NYHA FC = New York Heart Association Functional Class

PMH = past medical history

SGLT2i = sodium-glucose cotransporter-2 inhibitors

OSA: Obstructive sleep apnea

T2DM = type 2 diabetes mellitus

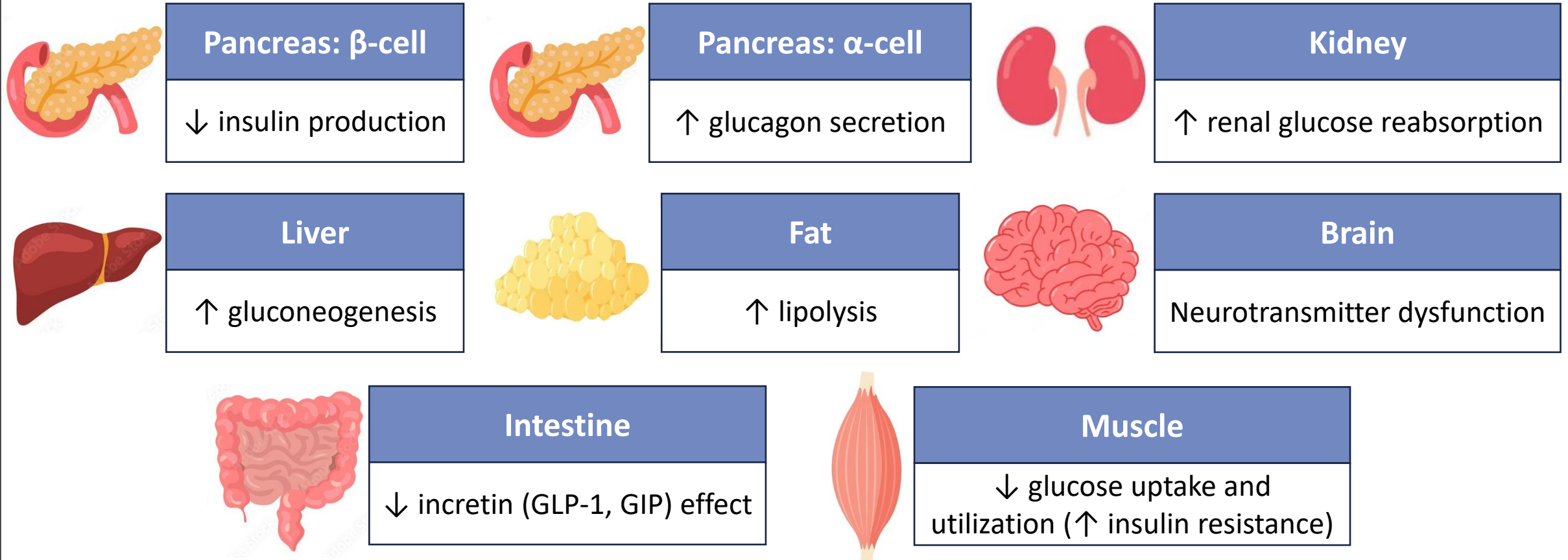
TZD = thiazolidinedione

6MW = 6-minute walk

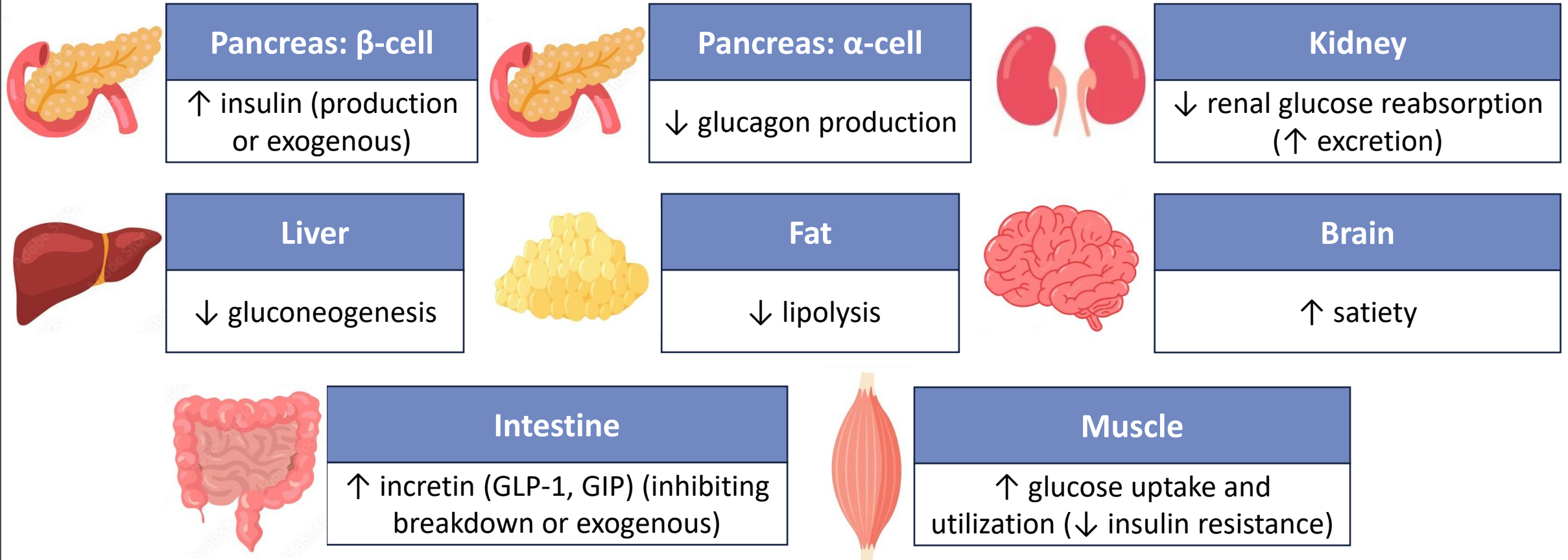
The Latest Diabetes Guidelines

- American Diabetes Association Standards of Care – 2026
 - Chapter 9: Pharmacological Approaches to Glycemic Treatment
- American Association of Clinical Endocrinologists Guideline
 - Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update
- Kidney Disease: Improving Global Outcomes Guidelines
 - Consensus Report by the ADA and KDIGO

Type 2 Diabetes Pathophysiology



Type 2 Diabetes Therapeutic Targets



The **ABC's** of Diabetes

- **A**1C (and consider **A**SA)
 - < 7.0% ADA (< 6.5% AACE)
- **B**lood Pressure
 - < 130/80 mmHg
- **C**holesterol
 - LDL-C < 70 mg/dL (< 55 mg/dL for those with established ASCVD)
 - Statin therapy (moderate to high intensity doses)
 - HDL-C > 40 mg/dL (> 50 mg/dL in women)
 - TG's < 150 mg/dL (the addition of icosapent ethyl can be considered)
- **S**moking Cessation

Diabetes Treatment Options

Oral

- Alpha-glucosidase inhibitors
- Biguanide
- Bile acid sequestrant/resin binder
- Dopamine Agonist
- DPP-4i
- **GLP-1RA**
- Meglitinide*
- **SGLT2i**
- Sulfonylurea*
- TZDs

Injectable

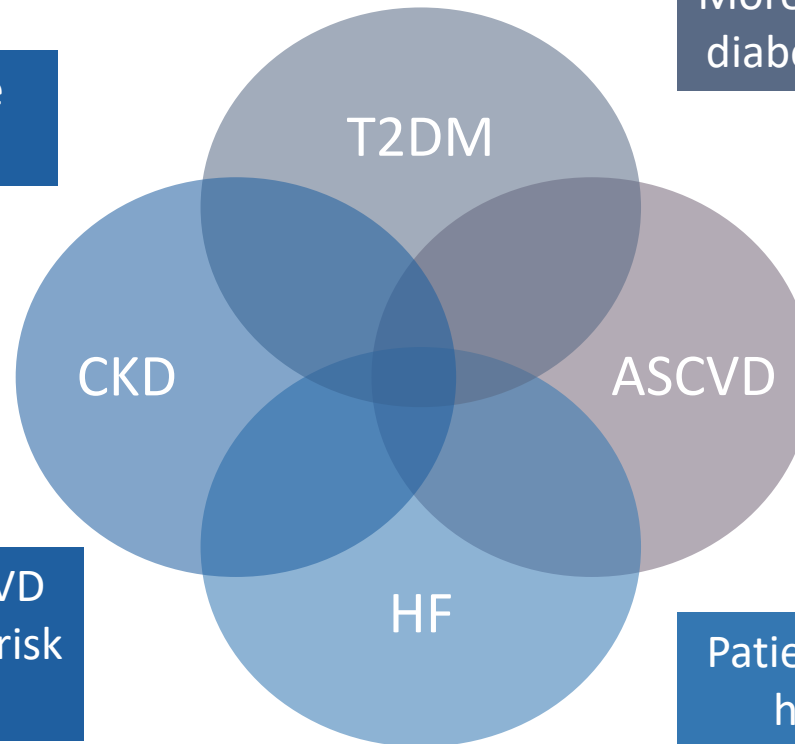
- Amylin analogue
- **Dual GLP-1/GIP RA**
- **GLP-1RA**
- Insulin*

*Hypoglycemia associated with use

Diabetes and Cardio-Renal Risk

Diabetes and CVD are the main causes of CKD

More than 37 million Americans have diabetes – 95% of whom have T2DM

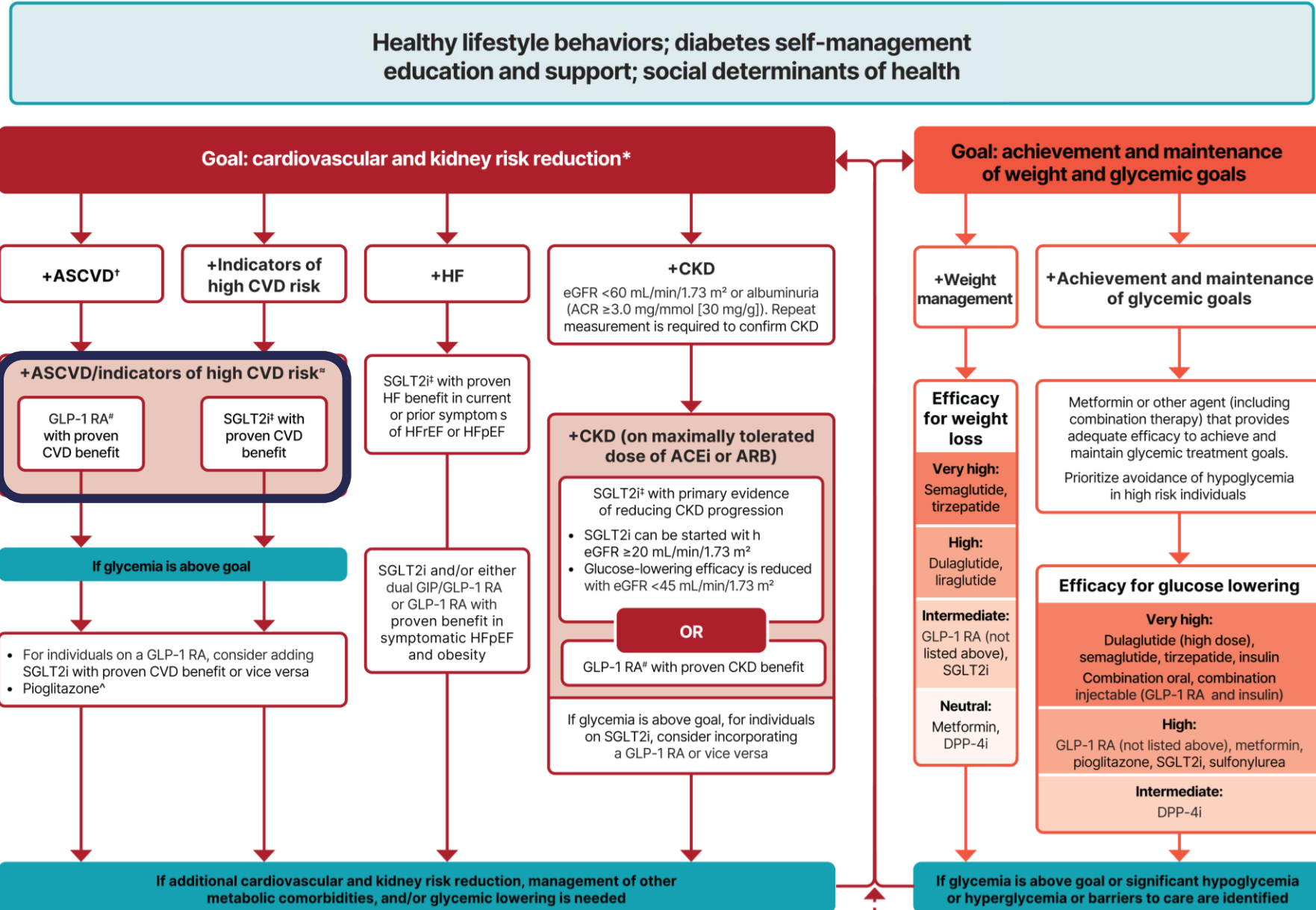


Adults with T2DM are twice as likely to have heart disease, a stroke, or heart failure

The presence of diabetes and CVD in adults with CKD increases the risk of morbidity and mortality

Patients with diabetes and heart failure have a 50% 5-year mortality rate

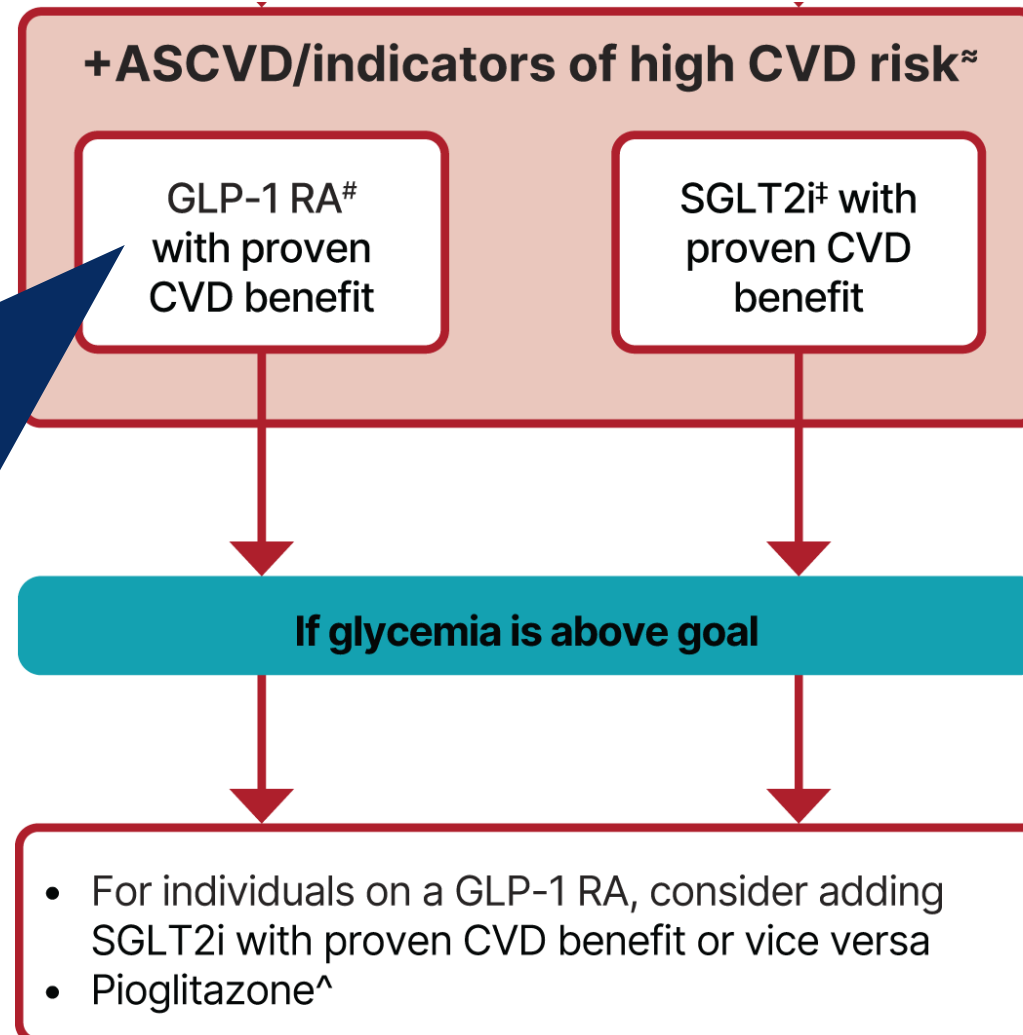
2026 ADA Glycemic Management



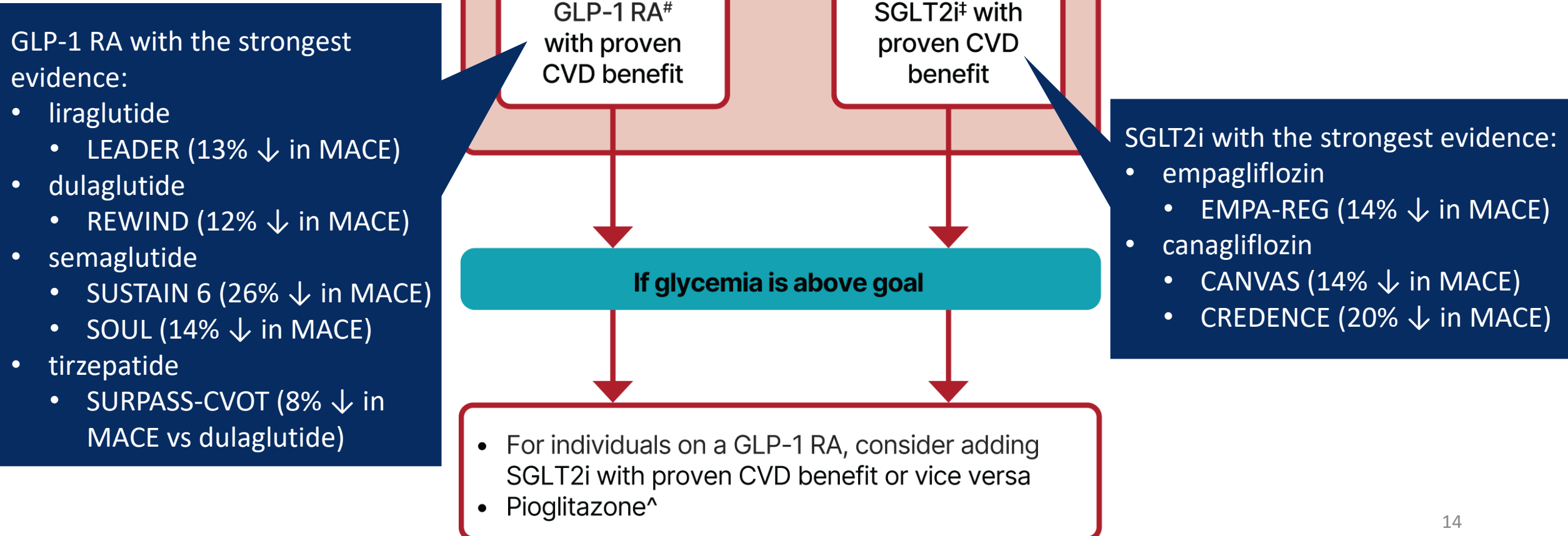
ASCVD or Indicators of High CV Risk

GLP-1 RA with the strongest evidence:

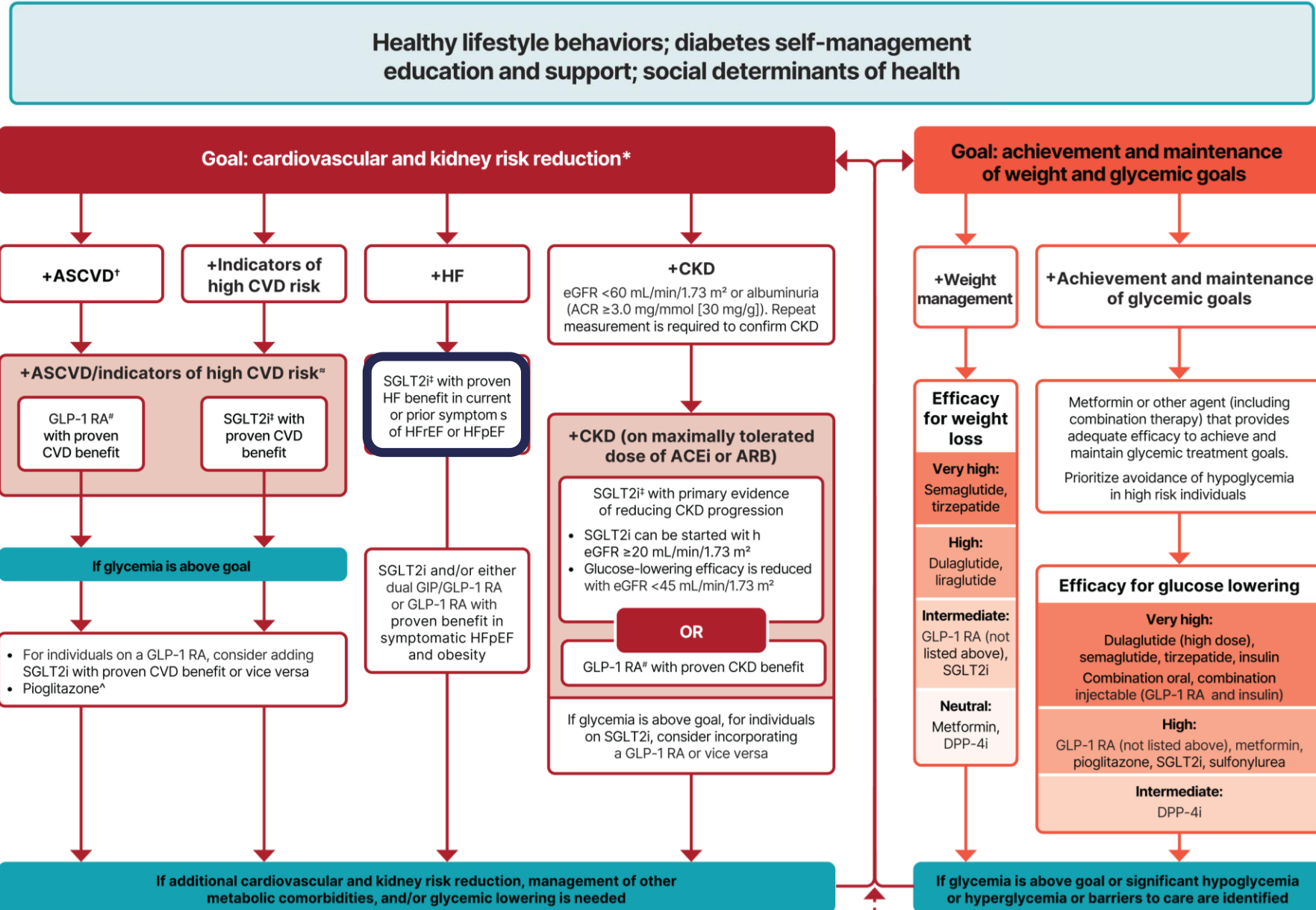
- liraglutide
 - LEADER (13% ↓ in MACE)
- dulaglutide
 - REWIND (12% ↓ in MACE)
- semaglutide
 - SUSTAIN 6 (26% ↓ in MACE)
 - SOUL (14% ↓ in MACE)
- tirzepatide
 - SURPASS-CVOT (8% ↓ in MACE vs dulaglutide)



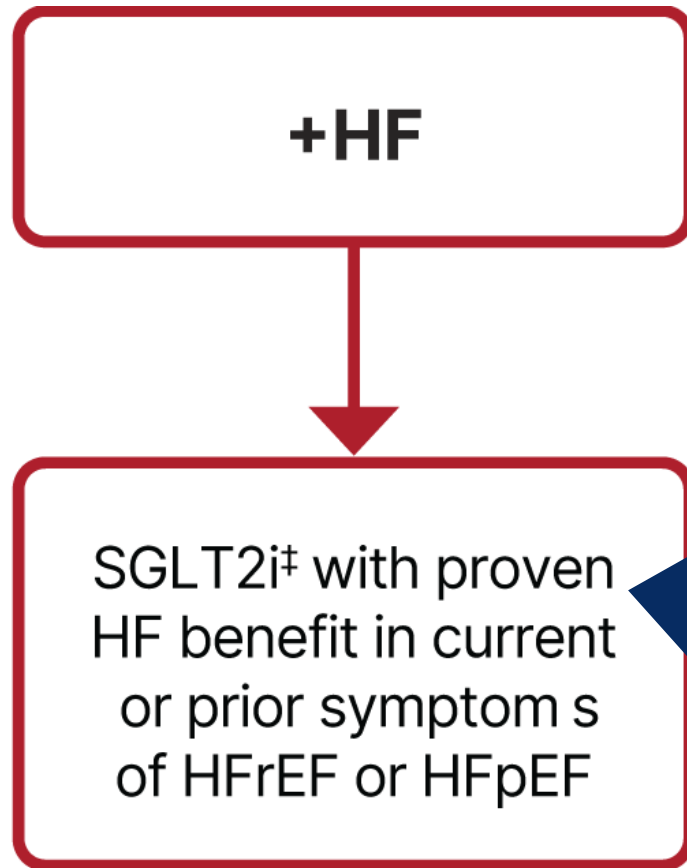
ASCVD or Indicators of High CV Risk



2026 ADA Glycemic Management



Heart Failure



empagliflozin

- EMPA-REG (35% ↓ in HHF)
- EMPEROR-REDUCED (31% ↓ in HHF)
- EMPEROR-PRESERVED (29% ↓ in HHF)

canagliflozin

- CANVAS (33% ↓ in HHF)
- CREDENCE (39% ↓ in HHF)

dapagliflozin

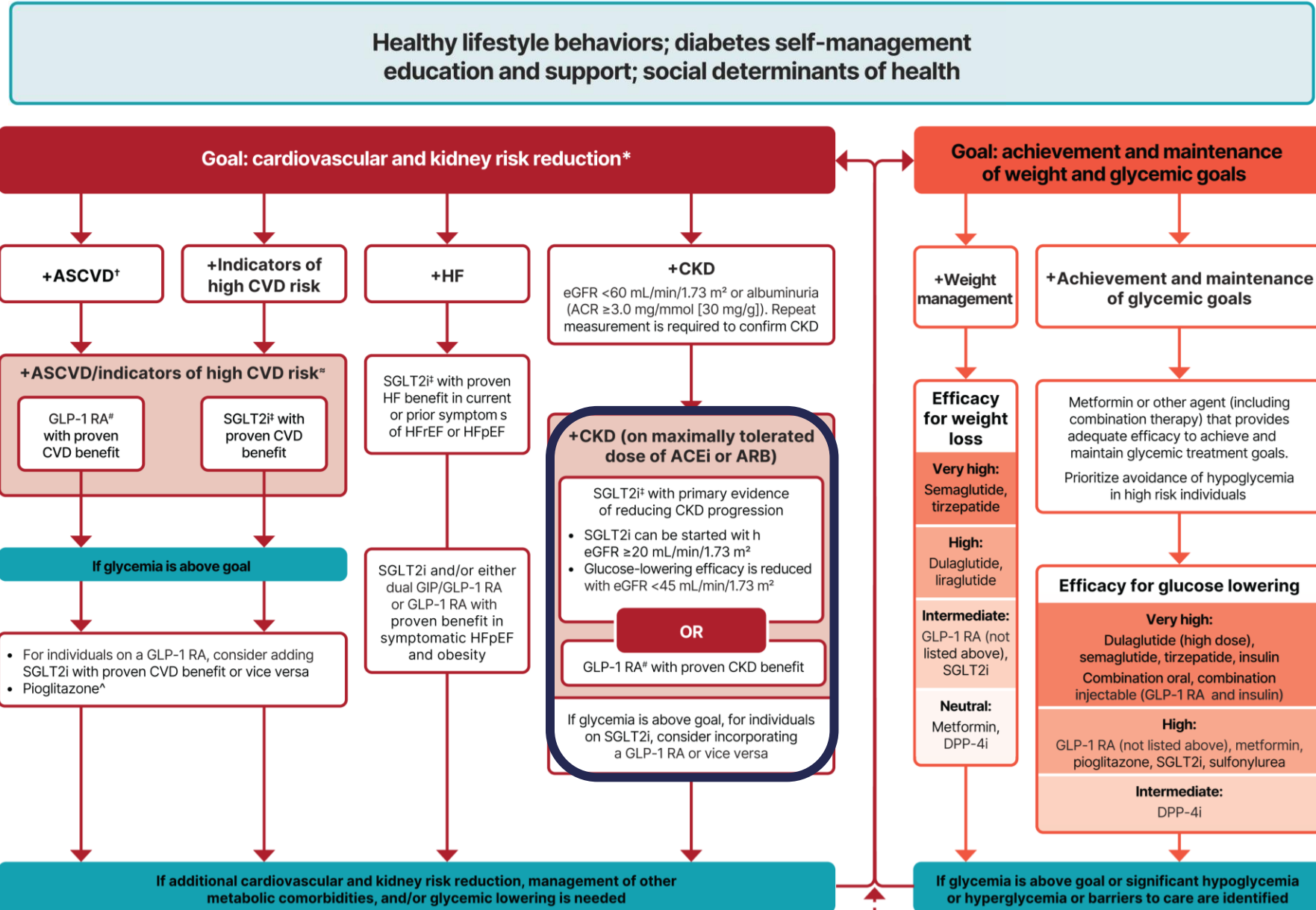
- DECLARE-TIMI (27% ↓ in HHF)
- DAPA-HF (30% ↓ in HHF)
- DELIVER (23% ↓ in HHF)

ertugliflozin

- VERTIS-CV (30% ↓ in HHF)

Consider adding a GLP-1 RA or dual GIP/GLP-1 RA if symptomatic HFpEF and obesity

2026 ADA Glycemic Management



Chronic Kidney Disease

empagliflozin

- EMPA-KIDNEY (28% ↓ in composite progression of CKD)

canagliflozin

- CREDENCE (30% ↓ in composite progression of CKD)

dapagliflozin

- DAPA-CKD (39% ↓ in composite progression of CKD)

+CKD (on maximally tolerated dose of ACEi or ARB)

SGLT2i[†] with primary evidence of reducing CKD progression

- SGLT2i can be started with eGFR ≥ 20 mL/min/1.73 m²
- Glucose-lowering efficacy is reduced with eGFR < 45 mL/min/1.73 m²

OR

GLP-1 RA[#] with proven CKD benefit

If glycemia is above goal, for individuals on SGLT2i, consider incorporating a GLP-1 RA or vice versa

Chronic Kidney Disease

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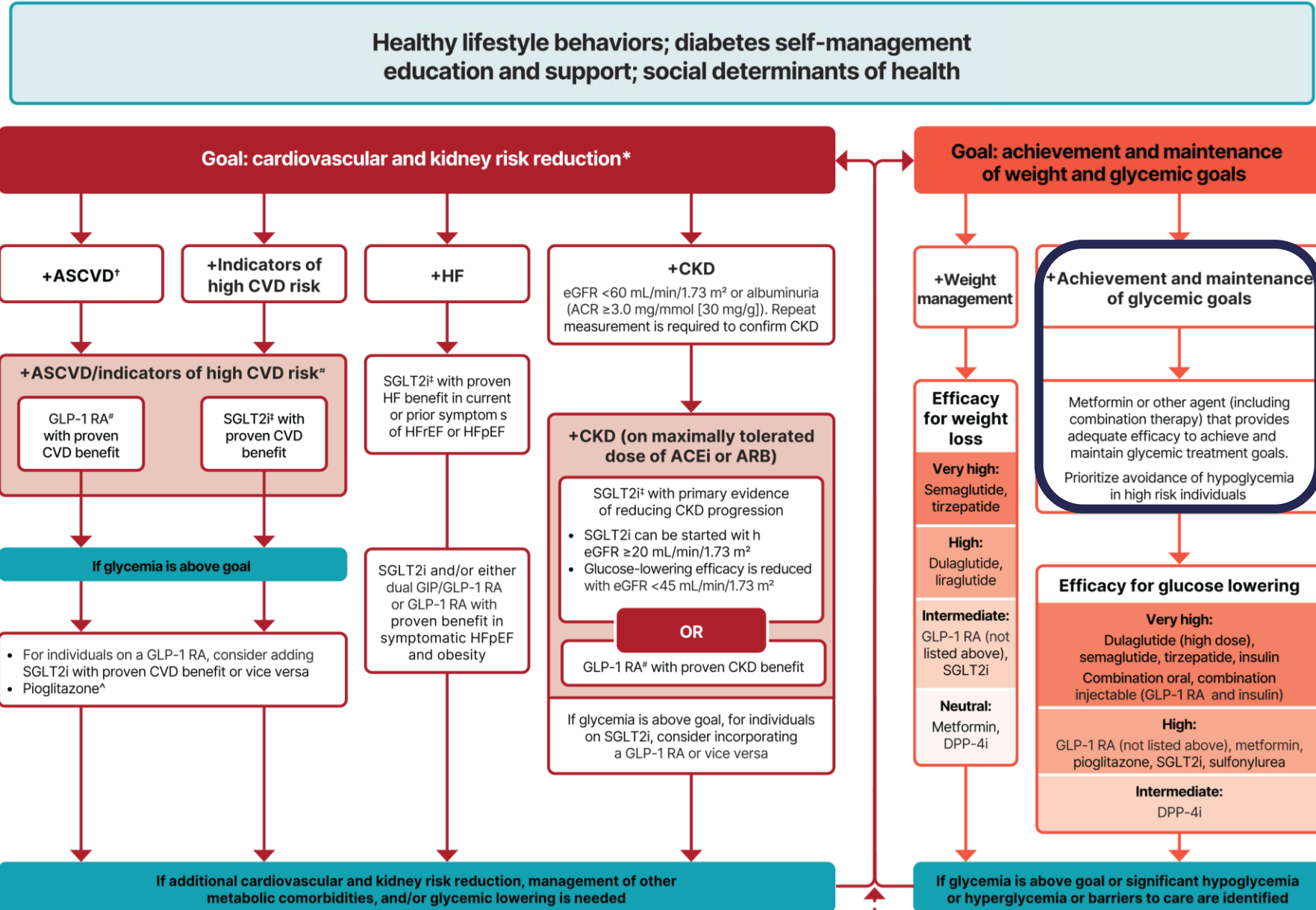
GLP-1 RA[#] with proven CKD benefit

If glycemia is above goal, for individuals on SGLT2i, consider incorporating a GLP-1 RA or vice versa

semaglutide

- FLOW (24% ↓ in composite progression of CKD)

2026 ADA Glycemic Management





Glycemic Management

Efficacy for glucose lowering

Very high:

Dulaglutide (high dose),
semaglutide, tirzepatide, insulin
Combination oral, combination
injectable (GLP-1 RA and insulin)

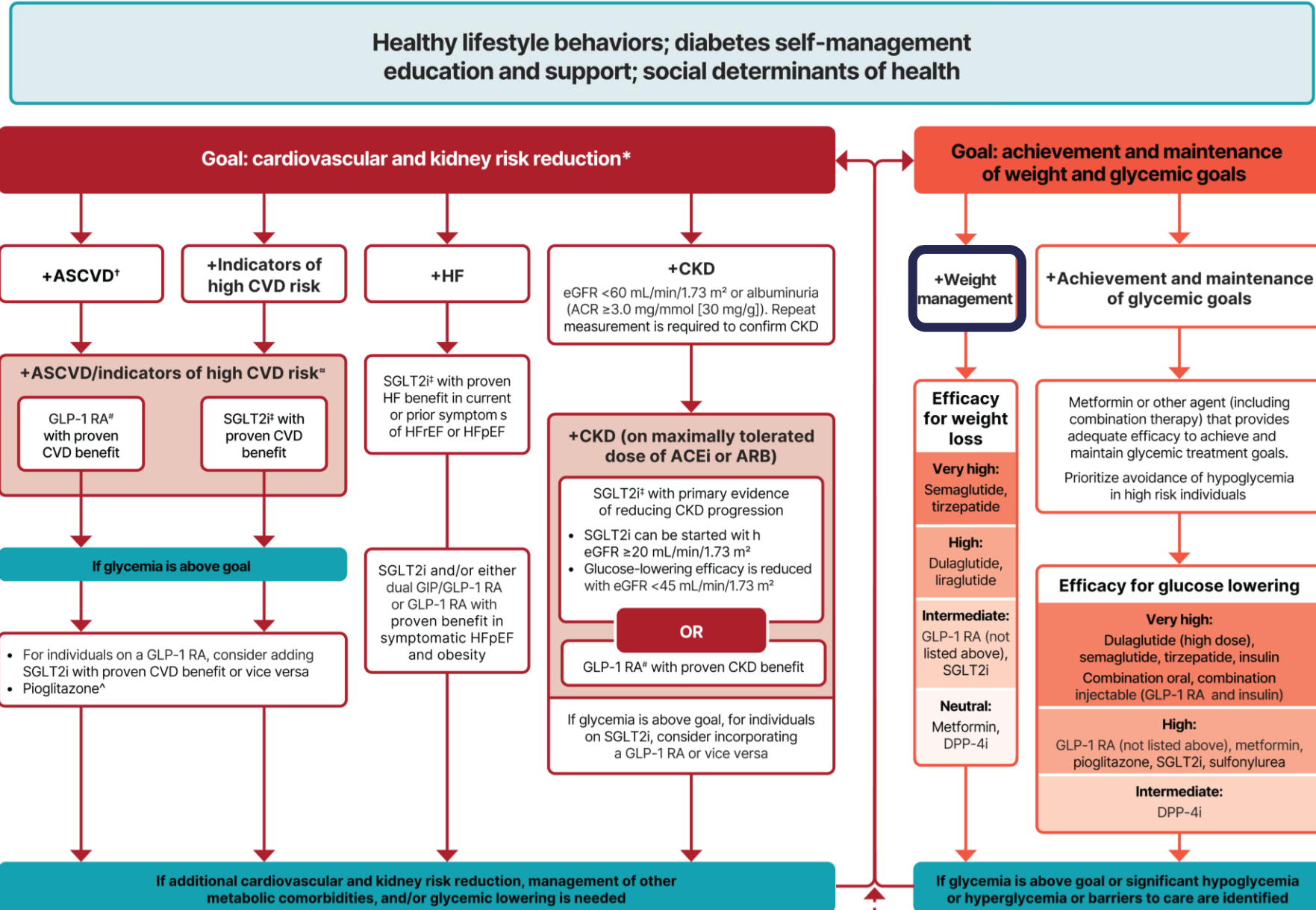
High:

GLP-1 RA (not listed above), metformin,
pioglitazone, SGLT2i, sulfonylurea

Intermediate:

DPP-4i

2026 ADA Glycemic Management





Weight Management

**Efficacy
for weight
loss**

Very high:
Semaglutide,
tirzepatide

High:
Dulaglutide,
liraglutide

Intermediate:
GLP-1 RA (not
listed above),
SGLT2i

Neutral:
Metformin,
DPP-4i

Metabolic Dysfunction-Associated Steatohepatitis

+Mitigating risk of MASLD or MASH



Agents with potential benefit in MASLD or MASH

GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, or combination of GLP-1 RA with pioglitazone

Use insulin in the setting of decompensated cirrhosis

Metabolic Dysfunction-Associated Steatohepatitis

Previous Terminology

NAFLD

A group of conditions characterized by liver fat accumulation without secondary causes such as excessive alcohol consumption, viral hepatitis, or other known causes.

NASH

The most severe form of NAFLD involves inflammation and hepatocyte injury with hepatic steatosis, leading to progressive liver fibrosis, cirrhosis, and HCC.

Updated Terminology

MASLD

Characterized by hepatic steatosis without secondary causes and the presence of 1 or more cardiometabolic risk factors. Patients may have steatosis with or without inflammation and fibrosis

MASH

Type of MASLD characterized by inflammation and cellular injury, often indicated by elevated aminotransferases. The hepatic inflammation may be histologically similar to ASH.

Metabolic Dysfunction-Associated Steatohepatitis

+Mitigating risk of MASLD or MASH



Agents with potential benefit in MASLD or MASH

GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, or combination of GLP-1 RA with pioglitazone

Use insulin in the setting of decompensated cirrhosis

Semaglutide gained approval for MASH with moderate to advanced liver fibrosis in people with obesity in August 2025

Incretin Trials for MASLD/MASH

Drug	Study design	Population	Arms	Outcomes	
				Resolution of MASH	Improvement of fibrosis
Liraglutide ⁴⁹	Phase 2 RDBPC 48w	52 patients with MASLD	1:1 liraglutide QW SQ 1.8 mg/placebo	39%:9% (RR = 4.3 [1.0–17.7])	Significantly less progression of fibrosis; Decrease in fibrosis score with no statistical difference
Semaglutide ^{50,51}	Phase 2 RDBPC 72w	320 patients with MASH and F1-3 fibrosis	1:1:1:1 semaglutide QD SQ 0.1 mg/0.2 mg/0.4 mg/placebo	40%:36%:59%:17% (0.4 mg RR = 6.87 [2.6–17.6])	49%:32%:43%:33% No statistical difference
	Phase 2 RDBPC 48w	71 patients with MASH and cirrhosis	2:1 semaglutide QW SQ 2.4 mg/placebo	34%:21% No statistical difference	11%:29% No statistical difference
Tirzepatide ⁵²	Phase 2 RDBPC 52w	190 patients with MASH and F2-3 fibrosis	1:1:1:1 tirzepatide QW SQ 5 mg/10 mg/15 mg/placebo	44%:56%:62%:10% (15 mg RD = 53 [37–69])	55%:51%:51%:30% (15 mg RD = 21 [1–42])
Survodutide ⁵³	Phase 2 RDBPC 48w	293 patients with MASH and F2-3 fibrosis	1:1:1:1 Survodutide QW SQ 2.4 mg/4.8 mg/6.0 mg/placebo	47%:62%:43%:14%	34%:36%:32%:18% No statistical difference

Obstructive Sleep Apnea

- OSA is a chronic sleep-related breathing disorder characterized by repeated upper airway obstructions during sleep, resulting in reduced or absent airflow, typically accompanied by reduced oxygen saturation
- Approximately 80.6 million individuals in the U.S. are estimated to be living with OSA in 2024, with a prevalence of 32.2% among adults aged 20 years and older
- Apnea-Hypopnea Index (AHI) quantifies OSA severity, calculated as the average number of apneas and hypopneas per hour of sleep. Severity is classified as mild (5–15 events/hour), moderate (15–30 events/hour), and severe (>30 events/hour)
- OSA is a major risk factor for cardiovascular disease, metabolic dysfunction, and impaired daytime functioning

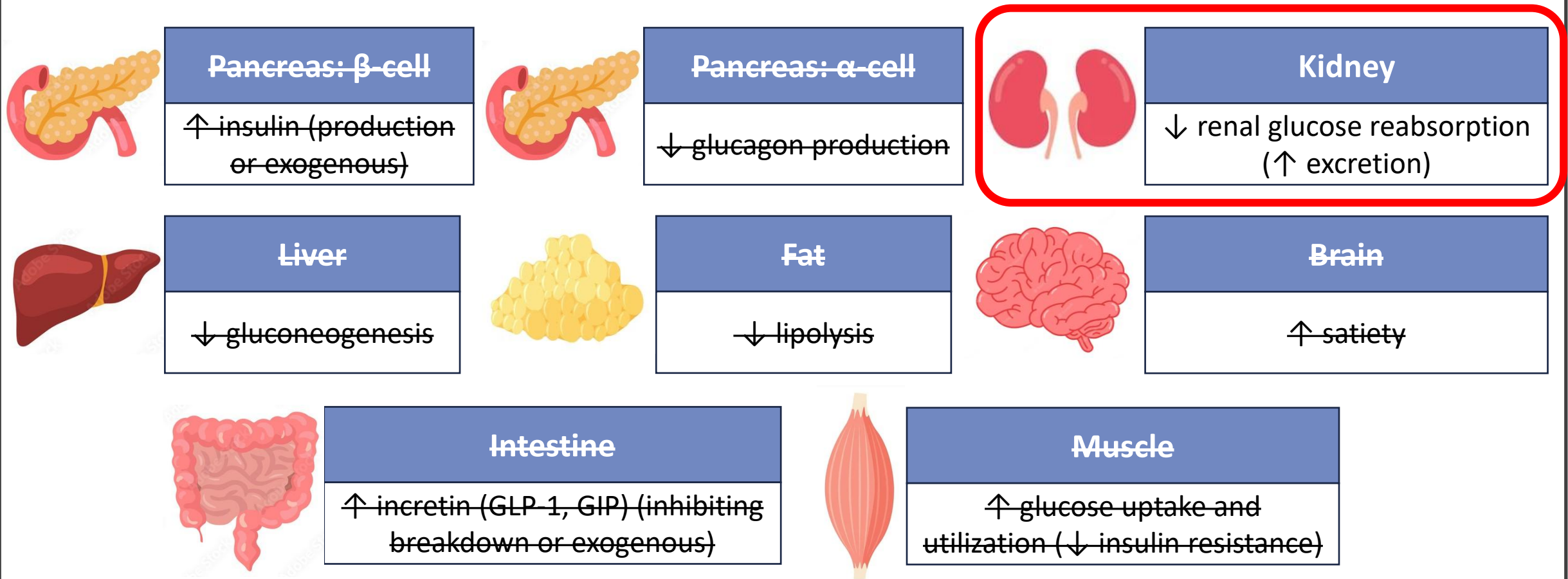
Obstructive Sleep Apnea

Trial	GLP-1 RA Studied	Population	Baseline Risk	Primary Outcome	Key Findings
SURMOUNT-OSA	Tirzepatide	Moderate-to-severe OSA and obesity (n=469)	49.9% unable or unwilling for CPAP; 50.1% on CPAP	Change in AHI	↓ 20 events per hour ($P < 0.001$) for trial 1; ↓ 23.8 events per hour for trial 2 ($P < 0.001$); significant reductions in patient reported outcome measurements

Tirzepatide gained approval for moderate to severe OSA in people with obesity in January 2025

Sodium glucose co-transporter 2 inhibitors (SGLT2i)

empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, bexagliflozin



SGLT2 Inhibitors

	empagliflozin	dapagliflozin	canagliflozin	ertugliflozin	bexagliflozin
Doses available	10 mg, 25 mg	5 mg, 10 mg	100 mg, 300 mg	5 mg, 15 mg	20 mg
Max dose	25 mg once daily	10 mg once daily	300 mg once daily	15 mg once daily	20 mg once daily
Renal dosing	Not recommended for GFR <30 for DM*	Initiation not recommended for GFR <25 Can continue 10mg dose without adjustment*	GFR 30-60: adjust dose to 100mg daily GFR <30: Initiation not recommended*	Not recommended for GFR <45	Not recommended for GFR <30
ASCVD	Yes (EMPA-REG)	No (DECLARE-TIMI)	Yes (CANVAS + CREDENCE)	No (VERTIS CV)	No
Heart Failure	Yes (EMPEROR PRESERVED + REDUCED)	Yes (DAPA-HF + DELIVER)	Yes in T2DM (CANVAS + CREDENCE)	Yes in T2DM (VERTIS CV)	No
CKD	Yes (EMPA-KIDNEY)	Yes (DAPA-CKD)	Yes in T2DM (CREDENCE)	No (VERTIS CV)	No

*Renal dosing is for initiation, can be continued

SGLT-2 Inhibitors

Advantages

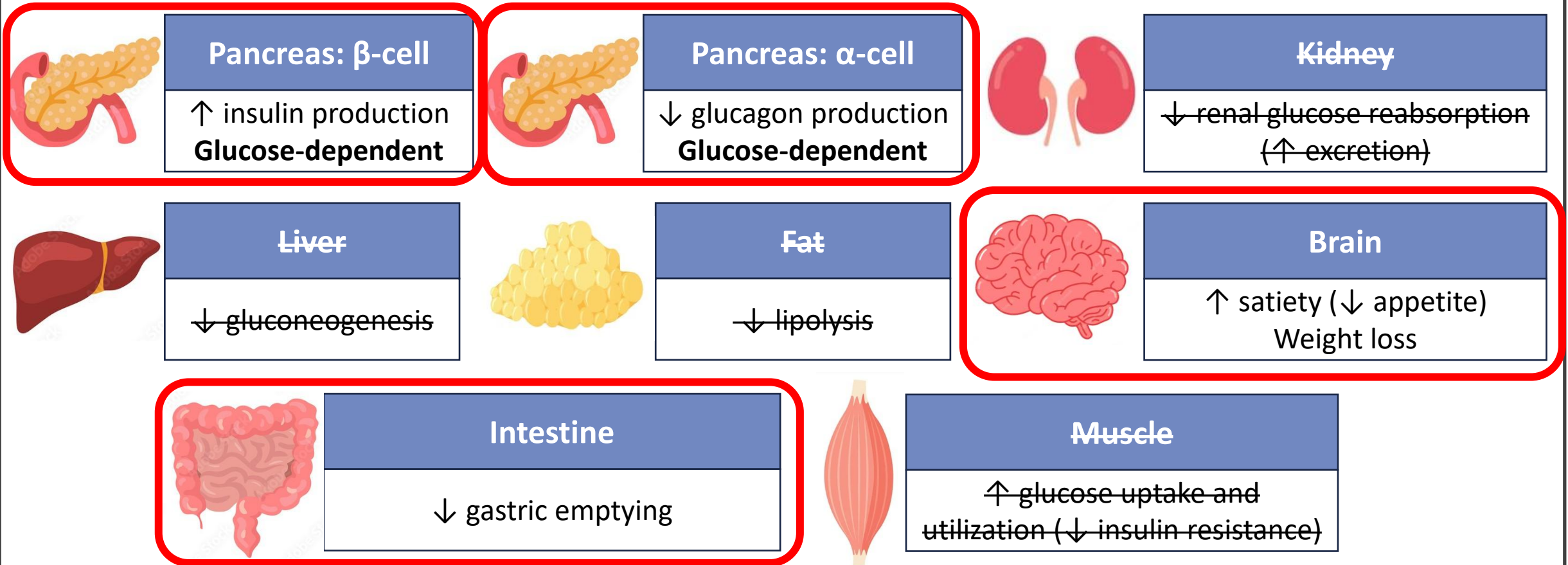
- A1c ↓0.7–1.1%
- **ASCVD risk reduction (Em, C)**
- **Decrease in HF hospitalizations (Em, D, C, Er)**
- **Renal protection (Em, D, C)**
- Weight loss (2-4 kg)
- BP reduction (5-6/1-2 mmHg)
- No hypoglycemia as monotherapy (placebo-like risk)
- Uric acid reduction

Disadvantages

- Genital mycotic infections
- Volume depletion/Hypotension
- Acute Kidney Injury
- Euglycemic ketoacidosis (not DKA)
- Bone loss/fractures (C)
- Cost

Incretin Mimetics (GLP-1 RA's)

exenatide, liraglutide, dulaglutide, lixisenatide, semaglutide



GLP-1 RA's

	exenatide	liraglutide	exenatide ER	semaglutide	dulaglutide
Doses available	5 mcg, 10 mcg	0.6 mg, 1.2 mg, 1.8 mg	2 mg	0.25 mg, 0.5 mg, 1 mg, 2 mg	0.75 mg, 1.5 mg, 3 mg, 4.5 mg
Max dose	10 mcg	1.8 mg	2 mg	2 mg	4.5 mg
Frequency	Twice Daily	Daily		Weekly	
Renal dose	CrCl <30: not recommended	None	eGFR <45: not recommended	None	None
Autoinjector?	No	No	Yes	No	Yes
MACE benefits	No	Yes (LEADER)	No	Yes (SUSTAIN-6)	Yes (REWIND)
CI in MTC or MEN2	No	Yes	Yes	Yes	Yes

Oral semaglutide

- 1.5, 4 and 9 mg daily doses; increases after 30 days at lower doses
- Take at least 30 minutes before the first food, beverage or other oral medication of the day, with no more than 4 ounces of plain water.
- Slows digestion, potential impact on other medications absorption including oral contraception
- Received ASCVD risk reduction indication in patients with T2DM on October 17, 2025 with data from the SOUL trial

GLP-1 RA's

Advantages

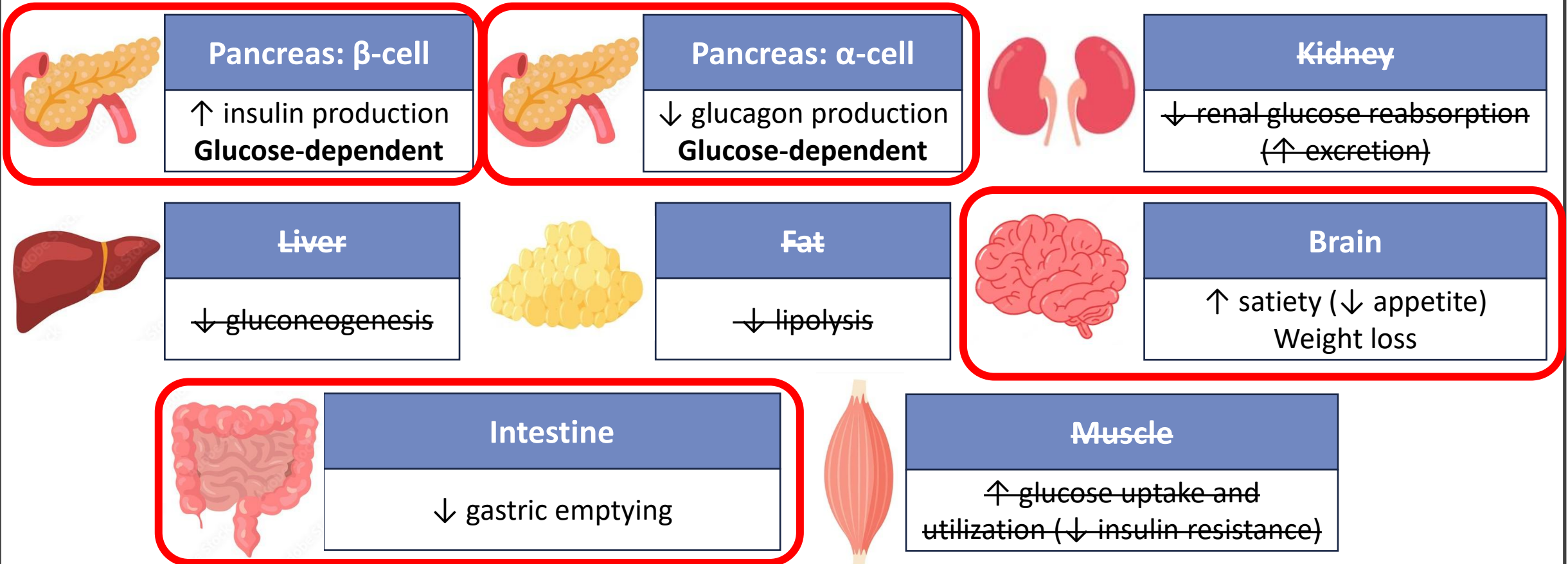
- A1c ↓0.8–2.1%
- **CV benefit** (L,D,S)
- **Renal benefit** (L,D,S)
- No hypoglycemia as monotherapy (placebo-like risk)
- Weight loss
- Convenient dosing
- B-cell sparing effect?

Disadvantages

- Gastrointestinal adverse effects
- Pancreatitis risk
- Caution for use with gastroparesis
- Most require an injection
- Aspiration risk with surgery
- Impact on oral contraception
- Cost

Dual Incretin Mimetics (GLP-1/GIP RA)

tirzepatide



Dual GLP-1/GIP RA's

Drug	Average Δ HbA1C (%) from Baseline	Confidence Interval	Difference in Average Δ HbA1C (%) Relative to Semaglutide 1 mg	P-Value
Tirzepatide 5 mg	-2.01%	(-0.28 to -0.03)	-0.15%	0.02
Tirzepatide 10 mg	-2.25%	(-0.51 to -0.26)	-0.39%	P < 0.001
Tirzepatide 15 mg	-2.30%	(-0.57 to -0.32)	-0.45%	P < 0.001
Semaglutide 1 mg	-1.86%		0 %	-

Drug	Average Δ in Body Weight (kg)	P-Value
Tirzepatide 5 mg	-7.6	P < 0.001
Tirzepatide 10 mg	-9.3	P < 0.001
Tirzepatide 15 mg	-11.2	P < 0.001
Semaglutide 1 mg	-5.7	-

Dual GLP-1/GIP RA's

Advantages

- Superior efficacy
- A1c ↓ 2–2.3%
- **CV benefit** as of August 28th 2026
- Post-hoc decreased albuminuria and total eGFR decline
- No hypoglycemia as monotherapy (placebo-like risk)
- Significant weight loss
- Convenient dosing

Disadvantages

- Gastrointestinal adverse effects
- Pancreatitis risk
- Caution for use with gastroparesis
- Injectable agent
- Aspiration risk with surgery
- Impact on oral contraception
- Cost

Incretin Agonist Summary: Indications

Drug	Glucose Lowering	Cardiovascular Effects		Kidney Effects	Liver Disease
		MACE Effect To reduce the risk of death in T2D and established CV	HF	Slow progression of DKD	MASH
Semaglutide (injectable)	✓	✓	⌚	✓	✓
Liraglutide	✓	✓			
Tirzepatide	✓	⌚	⌚	⌚	⌚
Exenatide	✓				
Dulaglutide	✓	✓			
Semaglutide (oral)	✓	✓			

SGLT2i Summary: Indications

SGLT2 Inhibitor	Glucose Lowering	Cardiovascular Effects		Kidney Effects
		MACE effect To reduce the risk of death in T2D and established CV	HF	Slow progression of DKD
Canagliflozin	✓	✓	✓	✓
Dapagliflozin	✓		✓	✓
Empagliflozin	✓	✓	✓	✓
Ertugliflozin	✓		✓	
Bexagliflozin	✓			
Sotagliflozin			✓	

Pipeline

Completed Trials

- Osteoarthritis
- Peripheral Artery Disease
- Alzheimer's Disease
- Parkinson's Disease

Ongoing Trials

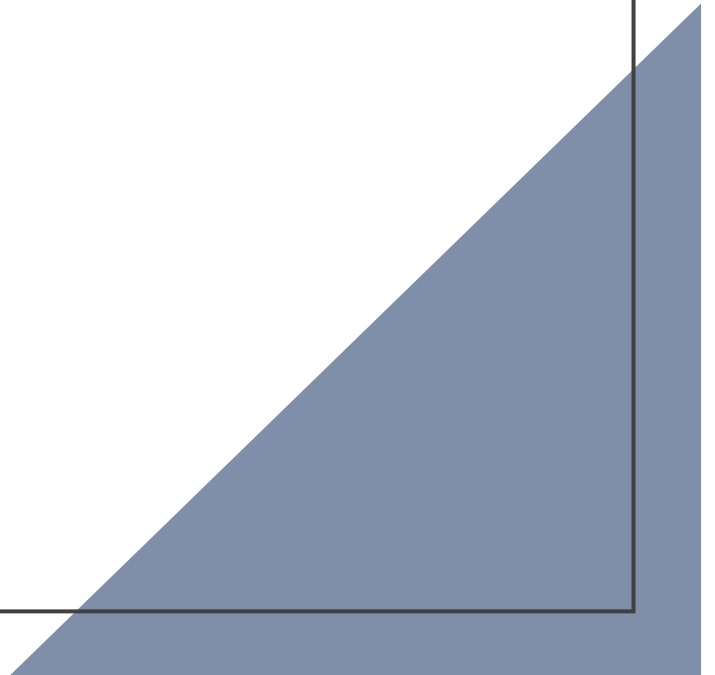
- Substance Use Disorders
- Polyendocrine metabolic ovarian syndrome (formerly known as PCOS)
- Psoriasis
- Depression
- Antipsychotic-associated weight gain

Bottom Line ...

- T2DM is associated with multiple complications
- SGLT2i's decrease CV events, hospitalizations for heart failure and are renal protective
- GLP-1 RA's decrease CV events and are renal protective
- Consider these therapies for appropriate patients, including CKD and HF patients, with or without diabetes

2026 Approach to the Pharmacotherapy of Diabetes

- Emphasis on Cardio-Renal protection
- No longer glucose (A1C) centric
- Individualization of therapy
- Hypoglycemia avoidance
- Weight stable or weight loss
- Use of SGLT-2 inhibitors and GLP-1 receptor agonists early



Initial Patient Case

RP is a 54-year-old male with newly diagnosed T2DM presenting for initial management.

- Past Medical History: HTN, MI in 2019, hyperlipidemia, obesity
- Current Medications: rosuvastatin 20mg daily, aspirin 81mg daily, losartan 100mg daily, amlodipine 5mg daily
- Labs: A1C 7.42%, Al/Cr 15 mg/g, eGFR 98, LDL 50 mg/dL
- Vitals: BP 128/74 mmHg, BMI 31.2

In addition to lifestyle changes, what would be an appropriate initial regimen?

- a) DPP-4i
- b) SGLT2i
- c) GLP-1 RA
- d) Metformin

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- a) DPP-4i
- b) SGLT2i (with ASCVD benefit)
- c) GLP-1 RA (with ASCVD benefit)
- d) Metformin

Initial Patient Case

SL is a 62-year-old women diagnosed one year ago with T2DM. She is very concerned about taking medication that may cause hypoglycemia or weight gain.

- Past medical history: T2DM, HTN, CKD stage 3a, hyperlipidemia
- Medications: metformin 1000mg twice daily, aspirin 81mg daily, atorvastatin 40mg daily, lisinopril 10mg daily
- Labs: A1C 7.6%, Al/Cr 320 mg/g, eGFR 56
- Vitals: 122/74 mmHg, BMI 24

What approach would you take to this patient's follow up management?

- a) Pioglitazone
- b) Ertugliflozin
- c) Semaglutide
- d) Glipizide

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