Navigating GLP1-RA and SGLT2i Use in Your Patients with Diabetes and Obesity – Incorporating the ADA, AACE and AHA CKM Perspectives

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Disclosure

Consultant: Genentech/Roche

Independent Data Monitoring Committee: Genentech/Roche

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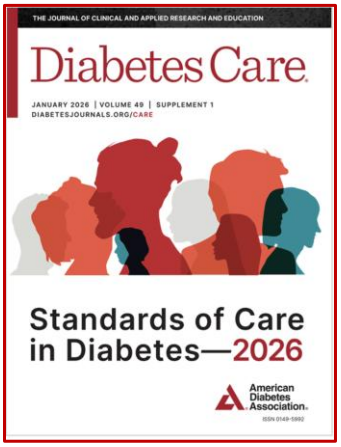
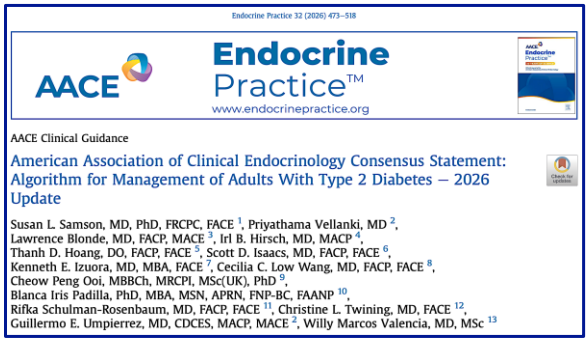
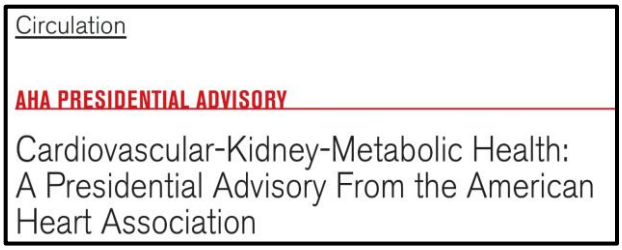


American Diabetes Association



American Association of Clinical Endocrinology



American Heart Association

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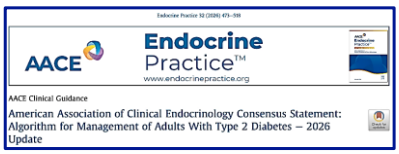
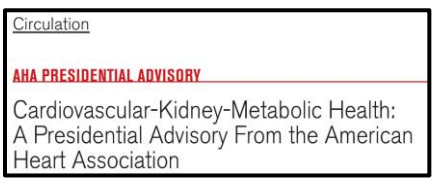
Outline

- Obesity tracks with Type 2 Diabetes (T2D)
- Pathophysiology of T2D: insulin resistance, beta-cell deficiency, and blunted incretin response
- Obesity drives metabolic risk
- CKM Syndrome – what is it and why is it important?
- How to choose between SGLT2i and GLP1RA in T2D
- Adjunctive use of GLP1RA in T1D





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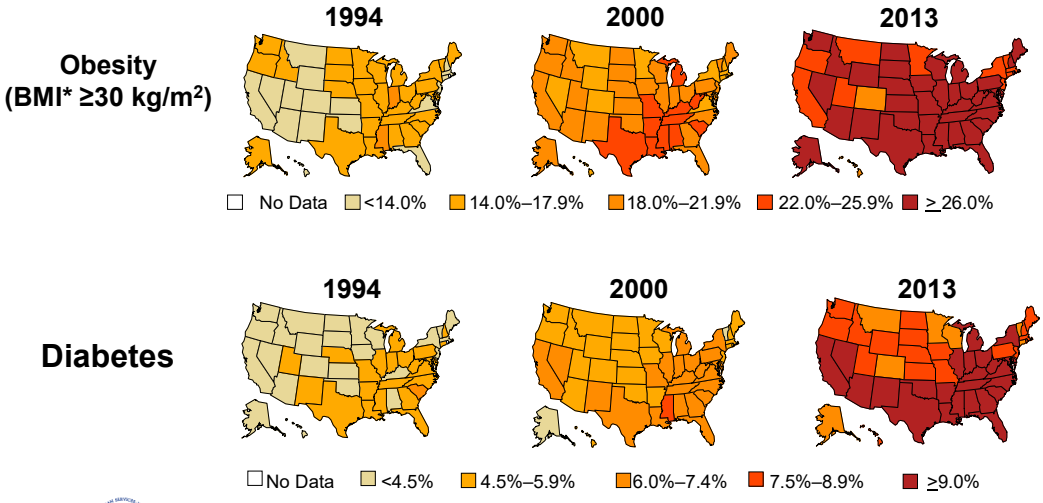
Diagnosed Diabetes and Obesity Track Together in Parallel Epidemics



Age-adjusted Prevalence in US adults

*BMI: body mass index; weight in kg/height in meters, squared)

CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

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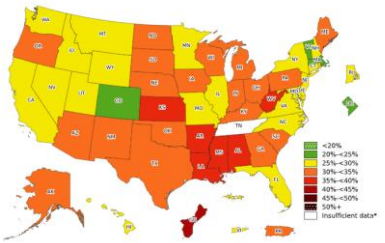
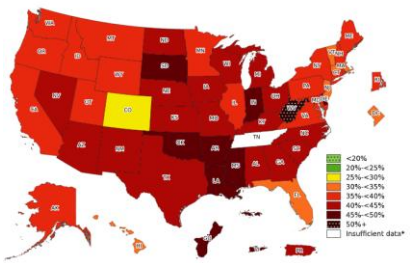
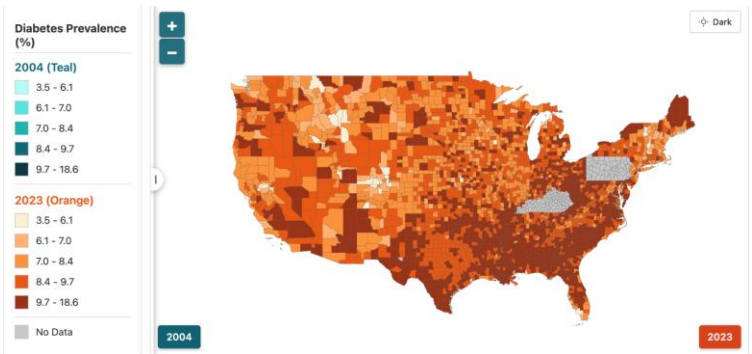
Prevalence of Obesity Among Adults Aged 18–39 Years, BRFSS, 2024



Prevalence of Obesity Among Adults Aged 40–59 Years, BRFSS, 2024



Diagnosed Diabetes Prevalence Among Adults, BRFSS, 2023



*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

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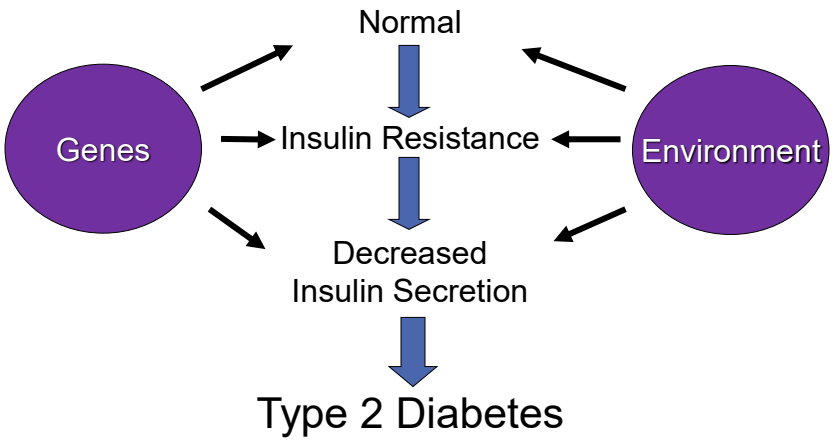
Pathogenesis of Type 2 Diabetes (T2D)



CR Kahn. *Diabetes* 43:1066-1084, 1994

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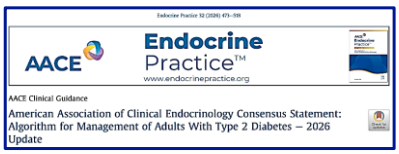

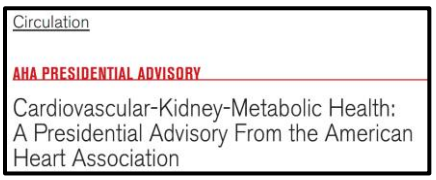

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The Link Between Obesity and T2D

- Accumulation of an excessive amount of body fat can cause type 2 diabetes, and the risk of type 2 diabetes increases linearly with an increase in body mass index.
- The worldwide increase in the prevalence of obesity has led to a concomitant increase in the prevalence of type 2 diabetes.
- The cellular and physiological mechanisms responsible for the link between obesity and type 2 diabetes are complex and involve adiposity-induced alterations in beta-cell function, adipose tissue biology, and multi-organ insulin resistance, which are often ameliorated and can even be normalized with adequate weight loss.

Kelin S, et al. Why does obesity cause diabetes? *Cell Metab* 2022;34:11-20..

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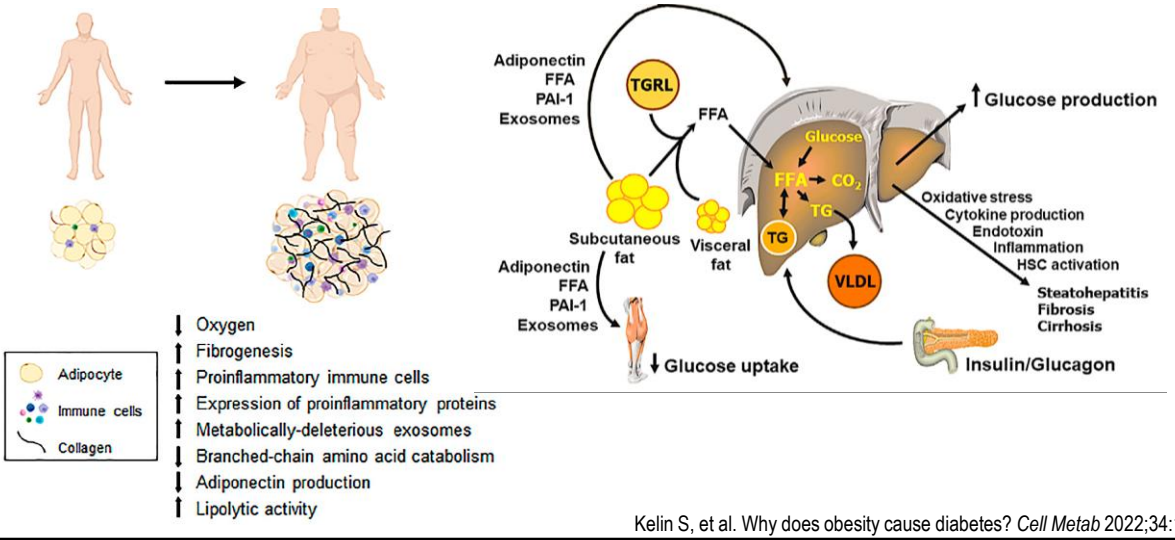
Pathophysiology of Obesity → T2D



Kelin S, et al. Why does obesity cause diabetes? *Cell Metab* 2022;34:11-20..

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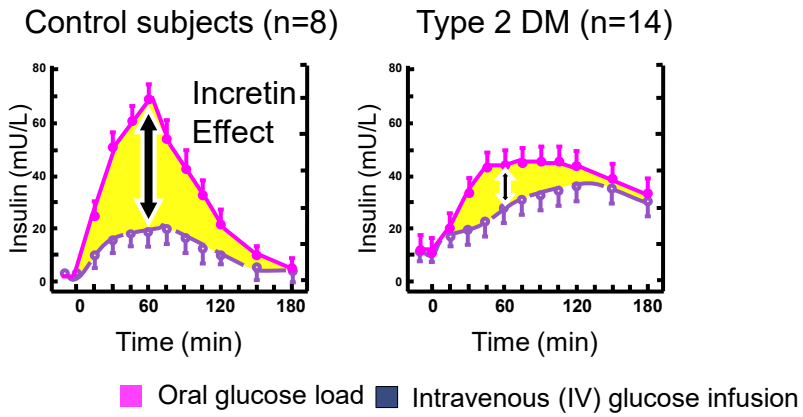
Type 2 Diabetes Is Associated with Blunting of Incretin (GLP1, GIP) Response to Oral Ingestion



Adapted from Nauck M, et al. *Diabetologia* 1986;29(1):46.

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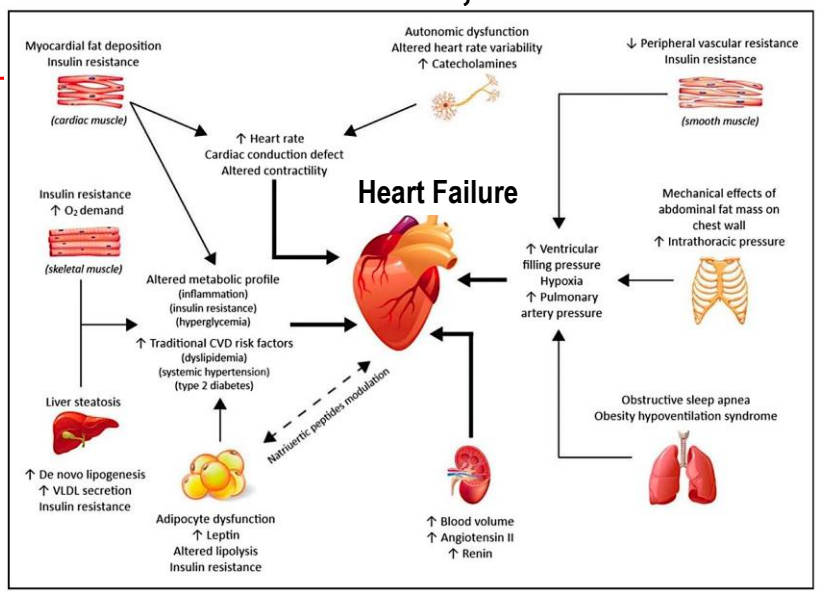
Obesity Also Independently Increases CV Risk – HF, Sudden Cardiac Death, and Atrial Fibrillation



Powell-Wiley TM, et al. Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation* 143:e984–e1010.

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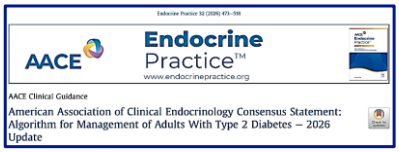

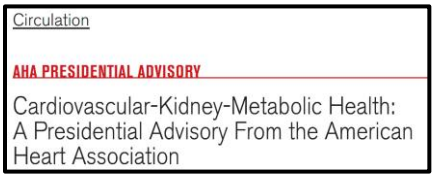

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CKM Syndrome and Dysfunctional Adiposity

- In 2023, the American Heart Association proposed a comprehensive care model, “Cardiovascular-Kidney-Metabolic Syndrome”
  - Highlighted need for holistic approach to cardiovascular disease (CVD), metabolic syndrome, T2D, and chronic kidney disease (CKD)
  - Encompasses obesity and components of the metabolic syndrome, but also clinical and laboratory elements of kidney function, CVD, and “dysfunctional adiposity”
- Dysfunctional adiposity: excess visceral fat, ectopic fat deposition, inflammatory/adipokine dysregulation, insulin resistance.
  - Key factor for development of T2D in those with obesity

Low Wang

Stefanakis K, et al, . The impact of weight loss on fat-free mass, muscle, bone and hematopoiesis health: Implications for emerging pharmacotherapies aiming at fat reduction and lean mass preservation. *Metabolism* 2024;161:156057.

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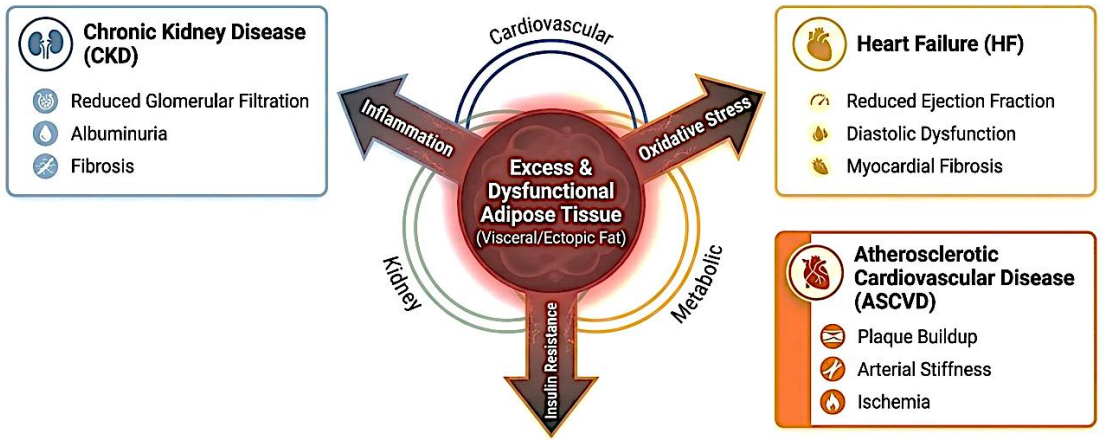
Defining Cardio-Kidney-Metabolic (CKM) Syndrome



A systemic disorder characterized by pathophysiological interactions among metabolic risk factors, CKD, and the cardiovascular system leading to multiorgan dysfunction and a high rate of adverse cardiovascular outcomes.

Ndumele CE, et al. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circ* 2023;148:1606-1635

Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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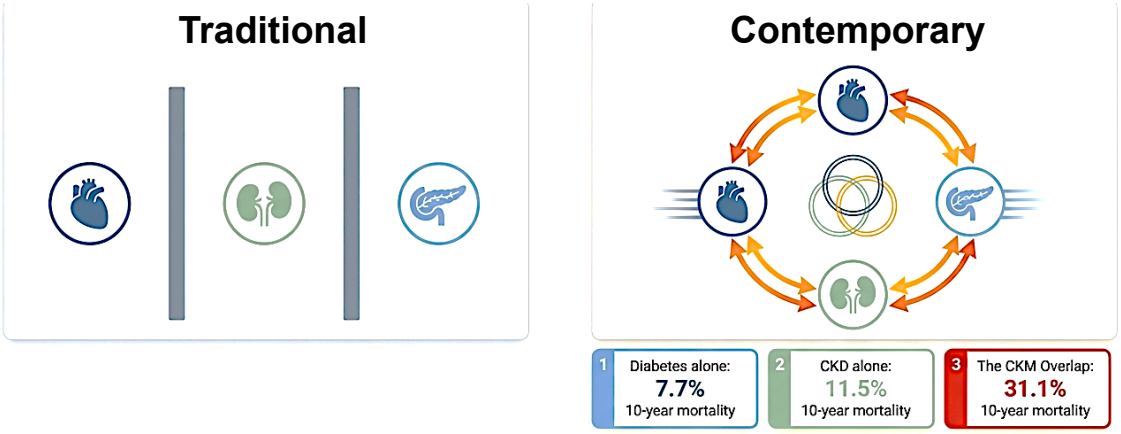
Breaking Down Siloed Care



Organ dysfunction in one system actively drives destruction in the others.
We must treat the system, not the symptom.

Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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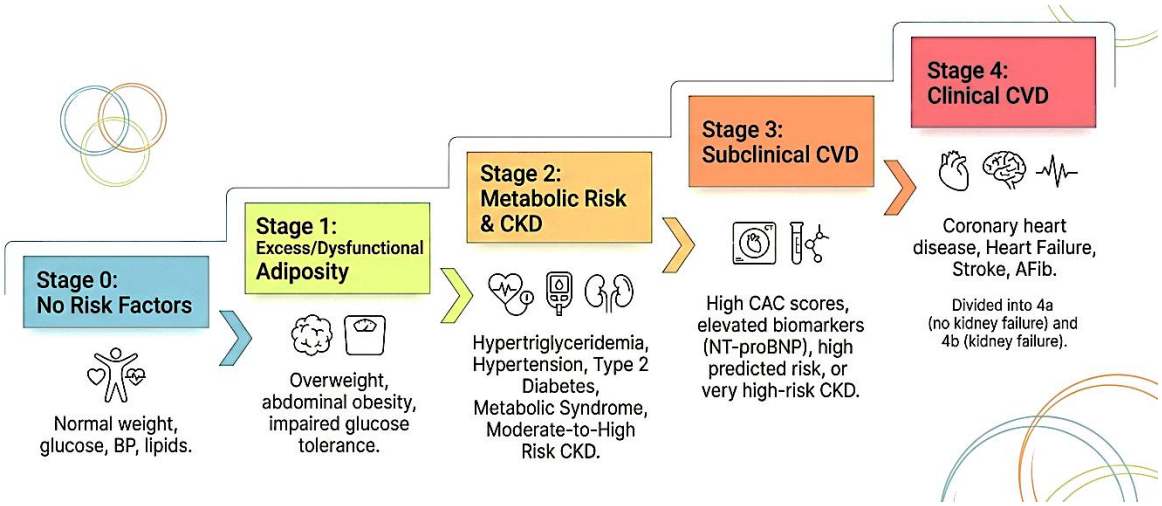
Stages of CKM Syndrome



Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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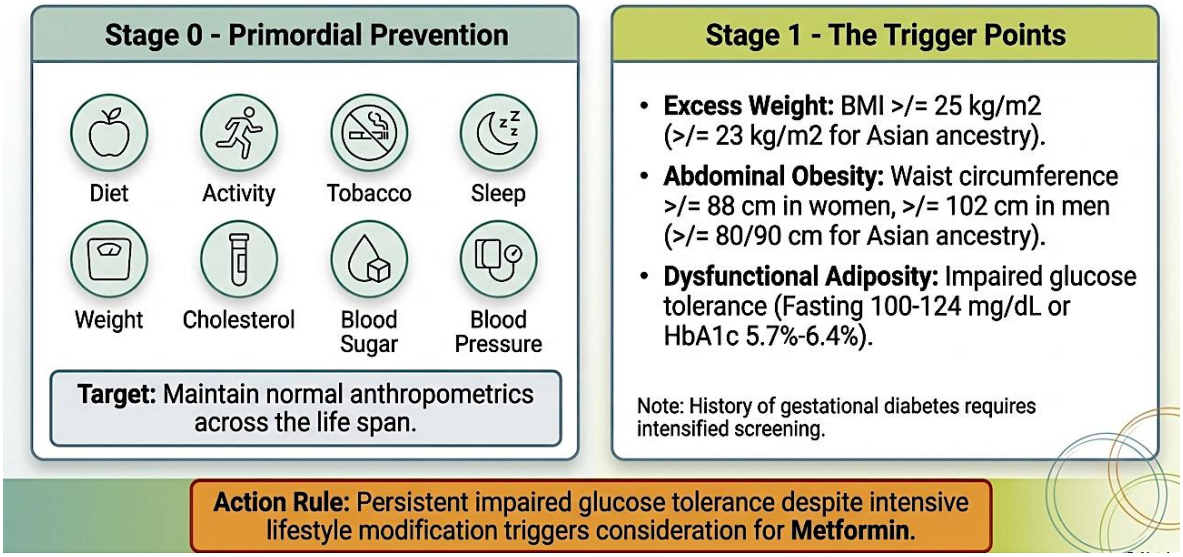
CKM Stages 0 and 1: Prevention and the Adiposity Trigger



Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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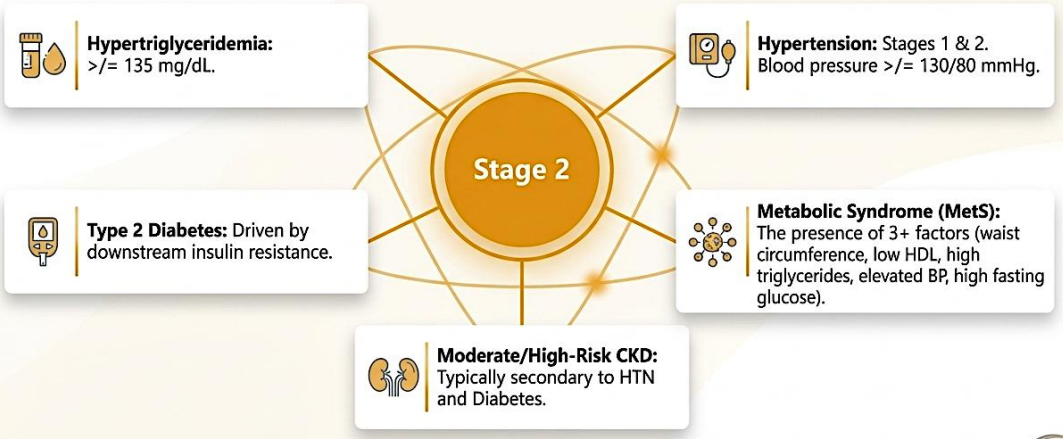
CKM Stage 2: Advancing to Metabolic Risk



MetS is not just a cluster of symptoms; it represents active endothelial dysfunction, systemic inflammation, and a prothrombotic state. The presence of MetS must trigger intensified lifestyle interventions targeting multifactorial risk control.

Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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Lifestyle and Behavior Change Are Foundational

Graphic prepared with help of Notebook LM AI using AACE statement as reference document.

Samson SL, et al. *Endocr Pract* 2026;32:473-518.

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Choosing Between SGLT2i vs GLP-1RA

Clinical Profile	Priority	Clinical Rationale
Patient has CKD (eGFR >/= 20)	SGLT2i	Reduces HF hospitalizations, slows kidney decline.
Patient has Heart Failure	SGLT2i	Cornerstone of GDMT regardless of diabetes status.
Patient has Severe Obesity (BMI >/= 35)	GLP-1RA	Induces >10% intentional weight loss.
Patient has HbA1c >/= 9% or high insulin dose	GLP-1RA	Superior glycemic control.
Patient has ASCVD / Multiple Comorbidities	Synergy: Combine SGLT2i + GLP-1RA	Maximum absolute risk reduction.

Rule: Co-utilize Metformin with either agent if HbA1c >/= 7.5% to achieve targets with minimal side effects.

Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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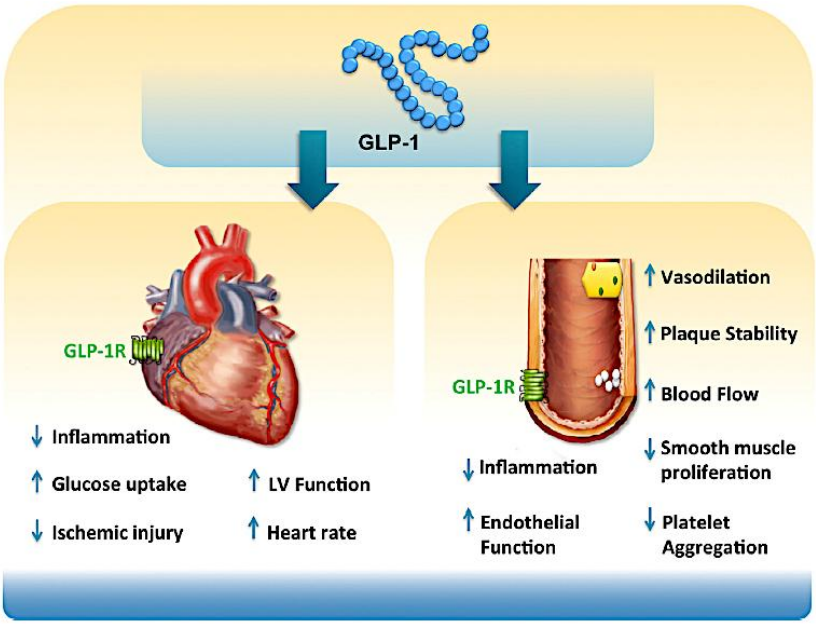
GLP1 Has Direct and Indirect Effects in the Heart and Blood Vessels



Drucker D. The Cardiovascular Biology of Glucagon-like Peptide-1. Cell Metab 2016;24:15-30.

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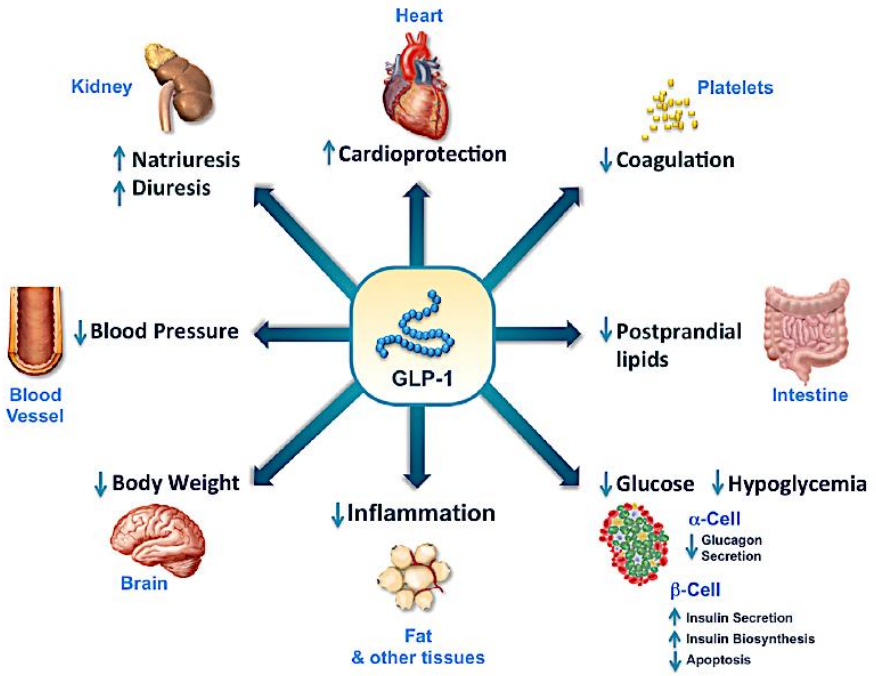
GLP1 Modifies CV Risk Through Direct and Indirect Actions in Multiple Organs



Drucker D. The Cardiovascular Biology of Glucagon-like Peptide-1. Cell Metab 2016;24:15-30.

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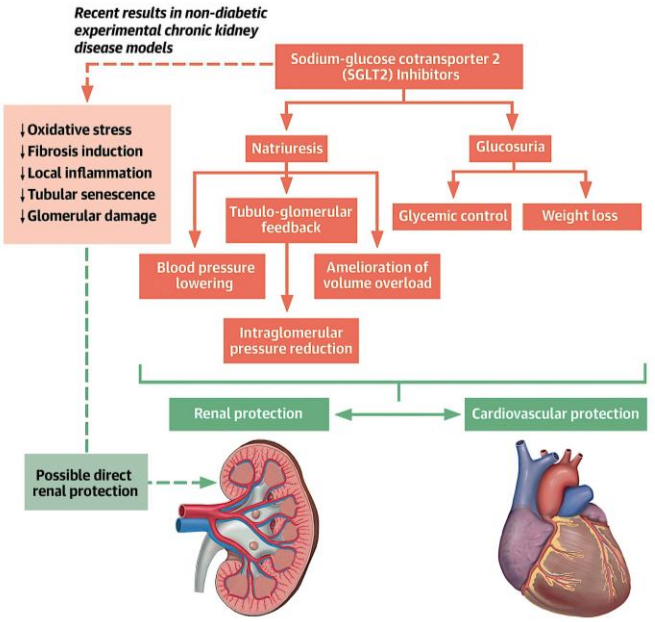
Mechanisms of Cardiorenal Protection by SGLT2i



Zelniker TA, Braunwald E. Mechanisms of Cardiorenal Effects of Sodium-Glucose Cotransporter 2 Inhibitors: JACC State-of-the-Art Review. *JACC* 2020;75(4):422-434.

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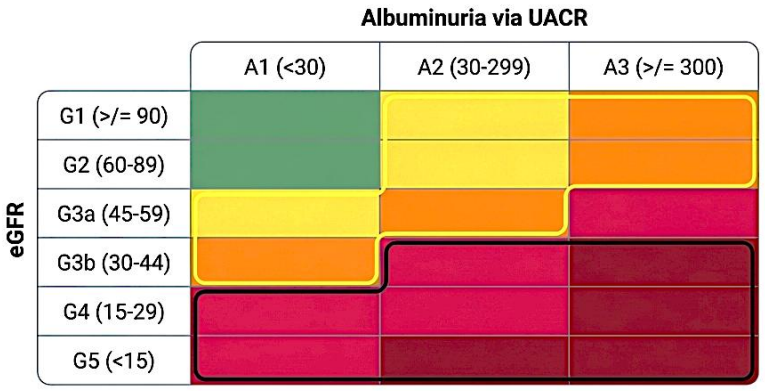
Using the KDIGO Risk Matrix



Moderate-to-High Risk CKD
→ Triggers CKM Stage 2

Very High-Risk CKD
→ Triggers CKM Stage 3
(Risk Equivalent to Subclinical CVD)

Clinical Imperative: Routine eGFR testing is insufficient. Annual Urine Albumin-Creatinine Ratio (UACR) measurement is mandatory for all Stage 2+ adults to accurately predict HF risk and kidney failure.

Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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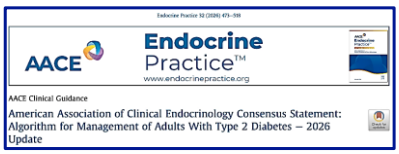

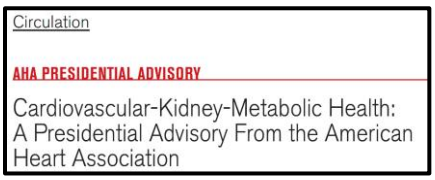

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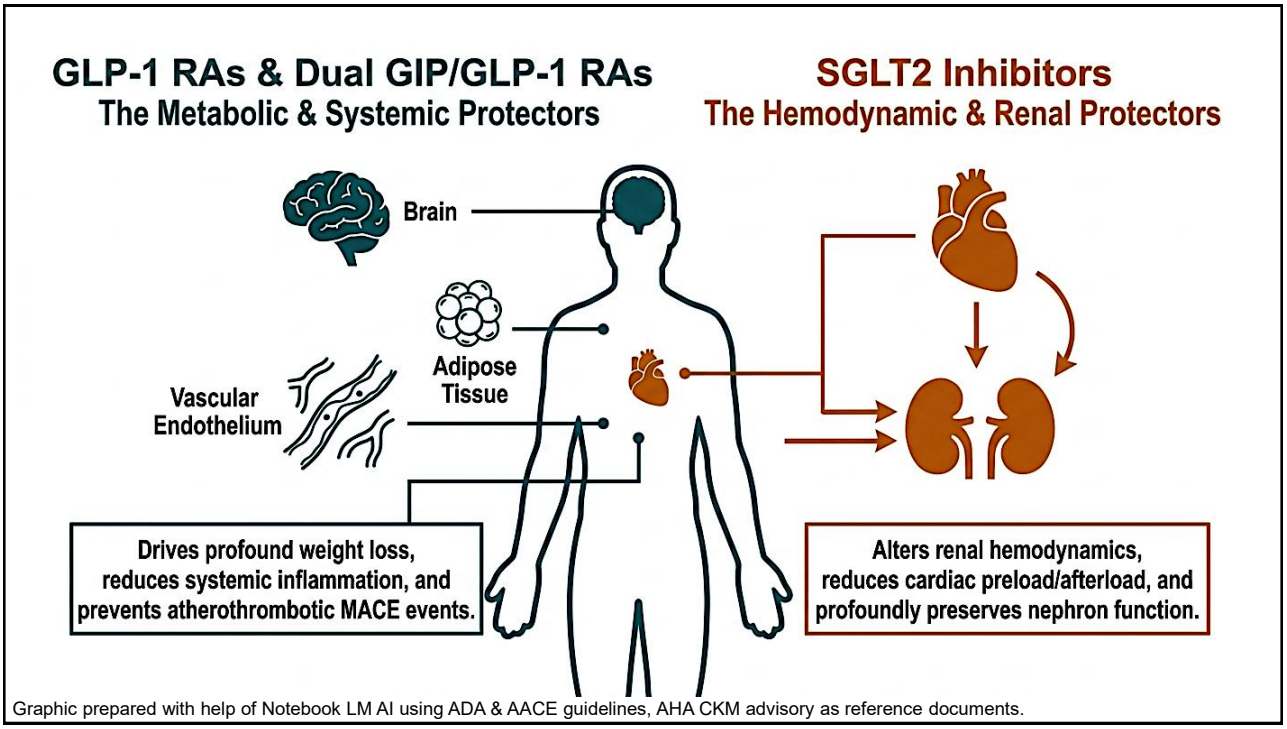

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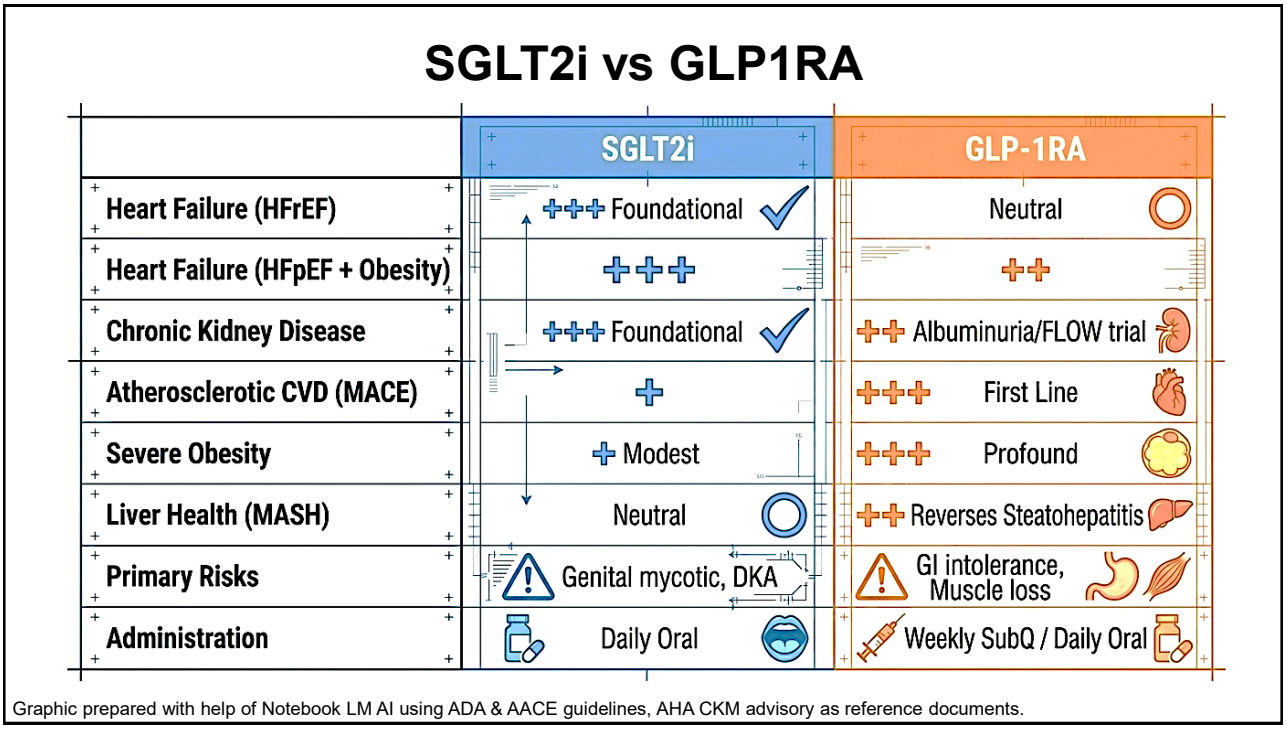

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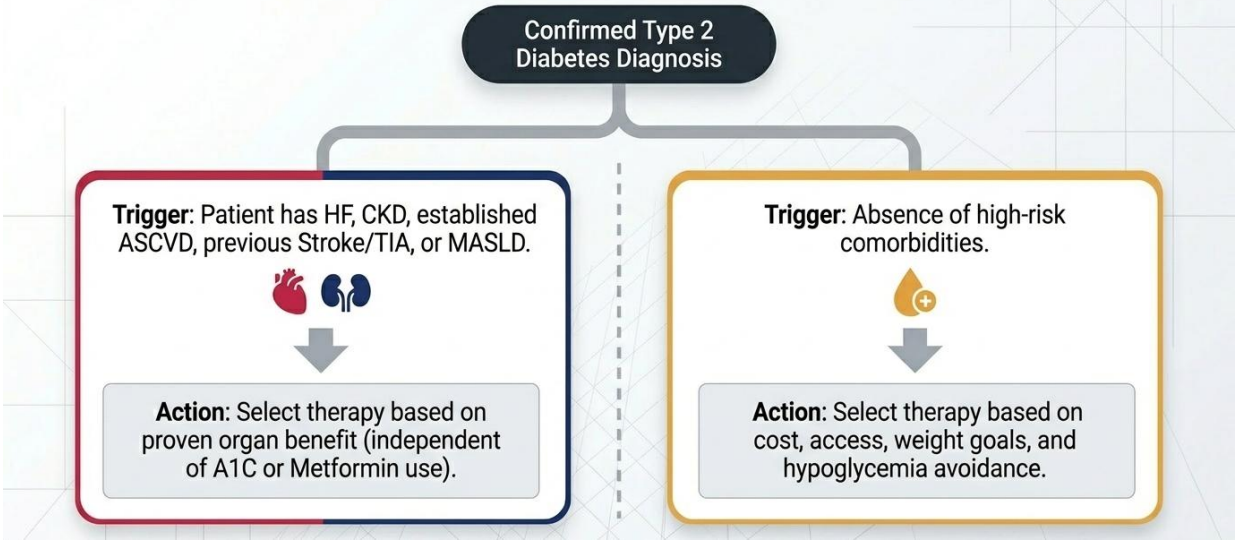
The First Decision Point



Graphic prepared with help of Notebook LM AI using AACE statement as reference document. Samson SL, et al. *Endocr Pract* 2026;32:473-518.

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#1: Does the Patient Have Heart Failure?

Primary Pathway: SGLT2i

The Rule: First-line foundational therapy (Class 1 guideline recommendation) regardless of baseline A1C.

The Impact: Reduces heart failure hospitalizations by 20–25% and improves clinical stability across HFrEF and HFpEF.

Emerging Pathway: GLP-1 RAs

The HFpEF + Obesity Phenotype: Demonstrated by the STEP-HFpEF DM trial data.

The Impact: Semaglutide 2.4mg yields a 13.7-point improvement in KCCQ-CSS symptoms, significant 6-minute walk distance gains, and 9.8% weight loss over 1 year.

Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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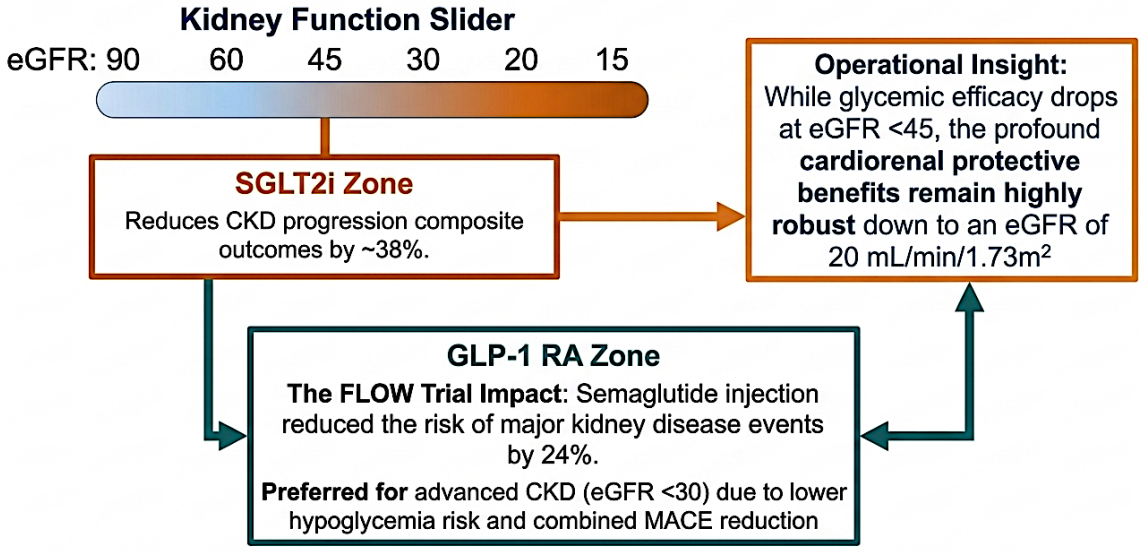
#2: Does the Patient Have CKD (eGFR, UACR)?



Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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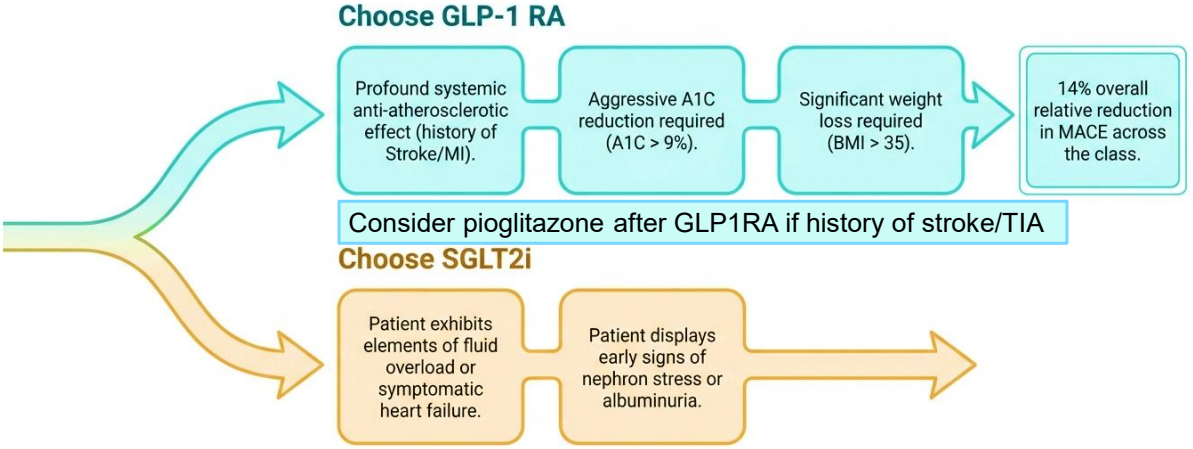
#3: Does the Patient Have ASCVD or Are They at High Risk? Have They Had a Stroke or TIA?



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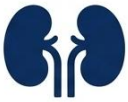
The Comorbidity Pathway: Heart, Kidney, and Vascular Risk

Heart Failure (HFrEF or HFpEF)

First-Line: SGLT2 inhibitor (regardless of background therapy or A1C).

Benefit: Reduces risk of HF hospitalization.



Chronic Kidney Disease (CKD)

First-Line: SGLT2 inhibitor (preferred) **OR** GLP-1 RA (proven benefit).

Note: Essential for elevated UACR (>30 mg/g).

ASCVD & Stroke/TIA Risk

First-Line: GLP-1 RA (proven MACE benefit) **OR** SGLT2i.

Details: Semaglutide, Liraglutide, or Dulaglutide significantly lower 3-point MACE and nonfatal stroke risk. Can be added even if the patient is already on an SGLT2i.

Graphic prepared with help of Notebook LM AI using AACE statement as reference document.

Samson SL, et al. *Endocr Pract* 2026;32:473-518.

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#4: Does the Patient have MASLD?

The Clinical Reality

Up to **70%** of patients with T2D have metabolic dysfunction-associated steatotic liver disease (MASLD).

Primary Choice: GLP-1 RAs (Semaglutide) & Dual GIP/GLP-1 RAs (Tirzepatide)

Preferred agents based on proven biopsy-level benefits for MASH resolution and fibrosis prevention (e.g., SYNERGY-NASH trial).

Alternative/Adjunct: SGLT2is & Pioglitazone

SGLT2is show potential MRI-based fat reduction but currently lack direct histological proof compared to GLP-1s. **Pioglitazone** can be considered for glycemic management with potential MASH benefits.

Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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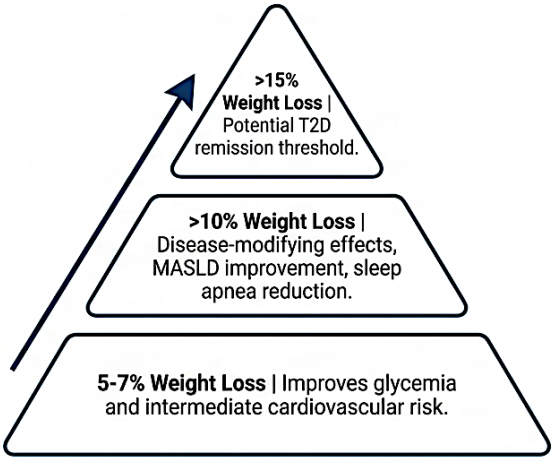
#5: Is Weight Loss a Primary Goal?



The Clear Winners: GLP-1 RAs & Dual GIP/GLP-1 RAs

SURMOUNT-2 Data: Tirzepatide yields 9.6% - 11.6% weight loss over placebo.

To treat the insulin resistance, you must directly treat the adipose tissue.

The Contrast: SGLT2 Inhibitors

SGLT2is provide only modest weight loss, typically 1-2 kg. They do not act as primary anti-obesity agents.

Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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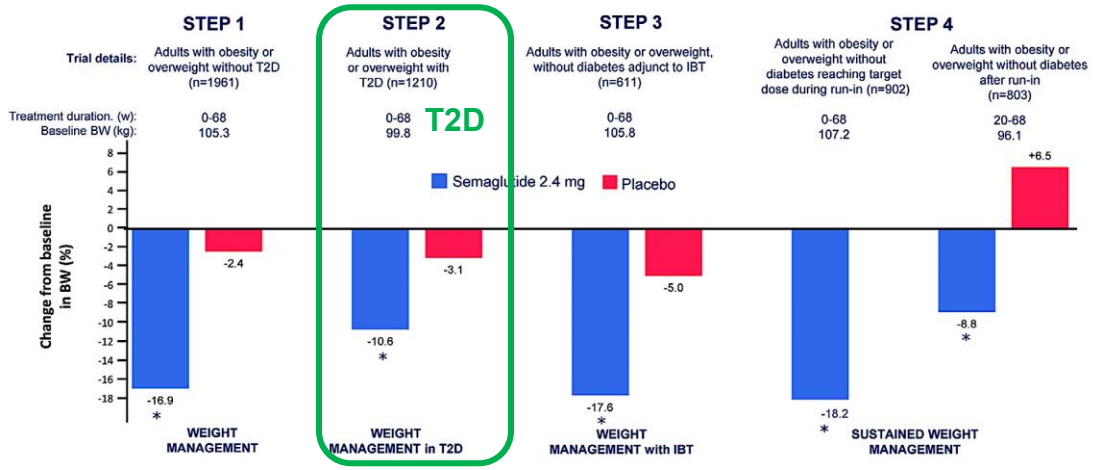
There Is Less Weight Loss with GLP1RA in Individuals with T2D



Drucker DJ. GLP-1 physiology informs the pharmacotherapy of obesity. Molec Metab 2022;57:101351.

36

When Should Insulin Be Started Instead?

Initiate Basal Insulin immediately if:

- A1C >10%
- **OR** Blood Glucose >300 mg/dL **AND** patient exhibits catabolic symptoms (weight loss, polyuria, polydipsia).

⚠ **Note:** Avoid starting GLP-1 RAs alone in this state; acute glucose toxicity requires immediate reduction.

Step 1
Goal: Fasting Blood Glucose <110 mg/dL (without hypoglycemia).

→

Step 2
Adjustment: Titrate Glargine every 2-3 days, Degludec every 3-5 days.

→

Step 3
Safety Check: Reduce dose by 10-20% if FBG drops below 70 mg/dL.

Samson SL, et al. *Endocr Pract* 2026;32:473-518.

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Monitor for Adverse Effects

GLP-1 RA Guardrails

- Manage GI side effects via slow, flexible titration rules.
- Monitor for nutritional gaps: Up to 13.6% of patients develop Vitamin D deficiency at 12 months.
- Require resistance training/protein intake to prevent lean muscle mass loss.

SGLT2i Guardrails

- Counsel strictly on genital mycotic infection hygiene.
- Hold medication before surgery/fasting to mitigate the risk of euglycemic DKA.

Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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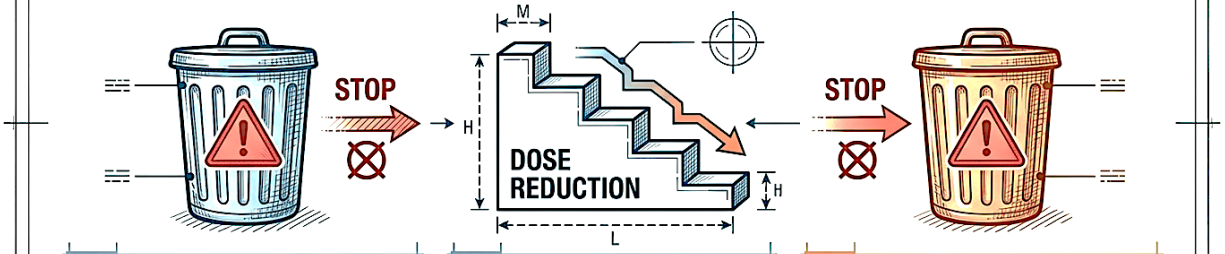
Don't Forget to Deprescribe

The Hypoglycemia Imperative: Introducing SGLT2is or GLP-1RAs into an outdated regimen can trigger dangerous hypoglycemia. You must deprescribe proactively.



Sulfonylureas & Meglitinides

- Stop entirely, or drastically reduce the dose. These insulin secretagogues are incompatible with the safety profile of modern CKM care.

Basal Insulin

- When adding a GLP-1RA or Dual GIP, preemptively reduce the basal insulin dose by 10-20% (especially if baseline A1C is <7.5%).

DPP-4 Inhibitors

- Discontinue immediately when starting a GLP-1RA. They target the same pathway; combining them adds cost without additional glucose-lowering benefit.

Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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Use the PREVENT Equations to Estimate Risk

The Legacy Paradigm

- **Tool:** Pooled Cohort Equations.
- **Horizon:** 10-Year Risk.
- **Blind Spots:** Only calculates ASCVD.
  - Ignores Heart Failure entirely.
  - Ignores kidney markers (eGFR/UACR).
  - Excludes adults under 40.

The New CKM Paradigm

- **Horizon:** Starts at age 30, projects 30-year lifetime risk.
- **Breadth:** Calculates absolute risk for BOTH ASCVD and Heart Failure.
- **Integrates:** Direct kidney function markers and SDOH variables.

Why it matters: Guides Specific Therapy

If HF risk outweighs ASCVD risk, **SGLT2i** is prioritized.
If ASCVD risk is paramount, **GLP-1RA** is prioritized.

Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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PREVENT Risk Equations

Derived from Individual-Level Participant Data from 25 Data Sets, n=3,281,919; Validated in 21 Add'l Data Sets, n=3,330,085

- Broadens outcome to heart failure (HF)
- Removes race from risk prediction – acknowledges race as a social construct, not a biological predictor
- Lowers age for risk prediction to 30 (age range 30-79)
- Predicts risk of total or global CVD (composite of ASCVD and HF) as well as each separately
- Risk estimates provided for 10-yr and 30-yr time span
- Optional models incorporating measures of kidney and metabolic health
- Includes a measure of place-based social disadvantage (social deprivation index) to acknowledge role of SDOC in CVD risk

Khan SS, et al. Development and validation of the American Heart Association's PREVENT Equations *Circulation* 2024;149:430-449.

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The American Heart Association PREVENT™ Online Calculator

https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

CVD | ASCVD | Heart Failure

Sex*
Male Female

Current Smoking
Any cigarette use within the last 30 days
No Yes

Lipid-lowering medication
Current use of statin medication to lower cholesterol
No Yes

Age (years)*
30-79

HDL Cholesterol (mg/dL)*
20-100

BMI (kg/m²)*
18.5-39.9

Total Cholesterol (mg/dL)*
130-320

SBP (mmHg)*
90-200

eGFR (mL/min/1.73m²)*
15-140

Diabetes
Any history of diabetes.
No Yes

Anti-hypertensive medication
Current use of any medication for hypertension
No Yes

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available,
If available or indicated, select "Yes" and enter the value.

UACR (mg/g)
UACR is clinically indicated for individuals with chronic kidney disease, diabetes, or hypertension
No Yes

HbA1C
HbA1c is clinically indicated for individuals with diabetes, prediabetes, overweight, or obesity, or those with history of gestational diabetes
No Yes

Zip Code
valid 5-digit zip code is needed to estimate social deprivation index [SDI]
No Yes

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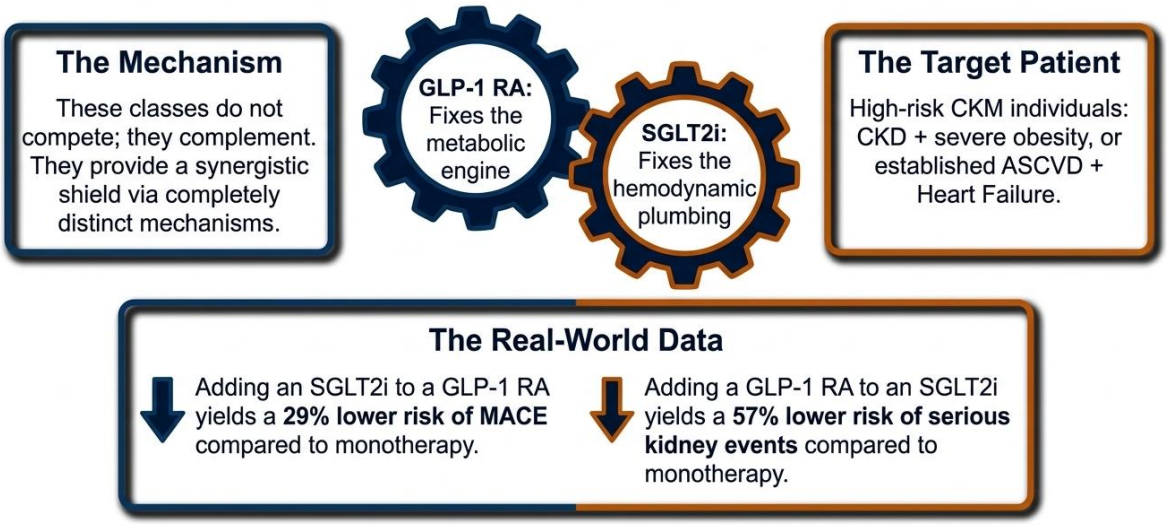
The Synergistic Approach: Combination Therapy



Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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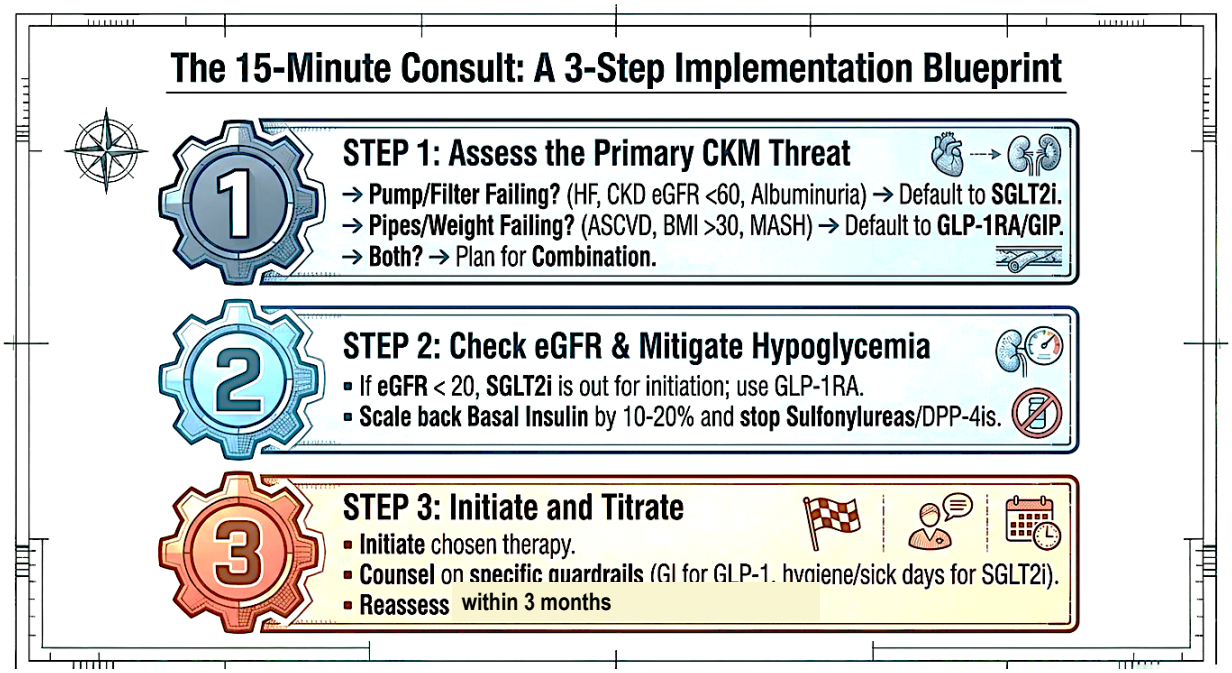
Combining GLP1RA and SGLT2i

- **10.40d** In people with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD, combined therapy with an SGLT2 inhibitor with demonstrated cardiovascular benefit and a GLP-1 RA with demonstrated cardiovascular benefit may be considered for additive reduction of the risk of adverse cardiovascular and kidney events. **B**
- If A1c is ≥1.5% above goal in a high risk patient, initiate both to address CKM risks including glycemia

(1) ADA PPC. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes—2026. *Diabetes Care* 2026;49(Suppl. 1):S216-S245. (2) Samson SL, et al. *Endocr Pract* 2026;32:473-518.

44



Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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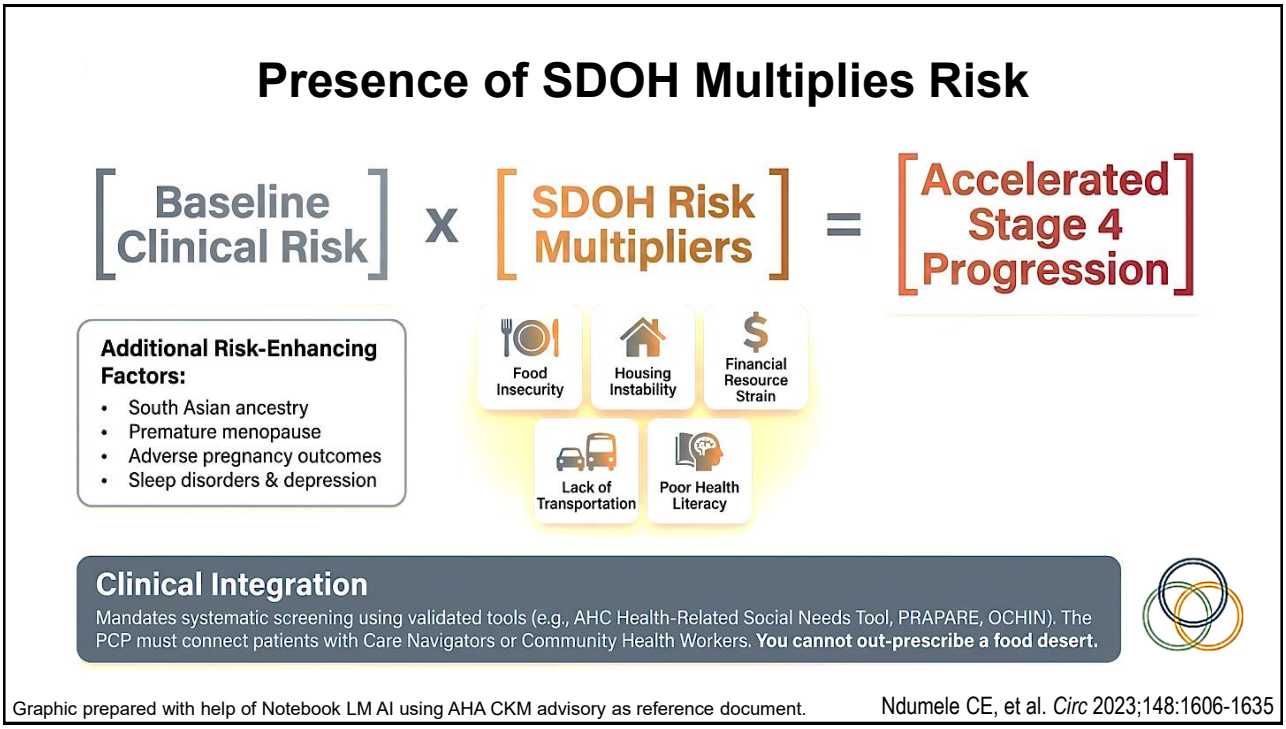

Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

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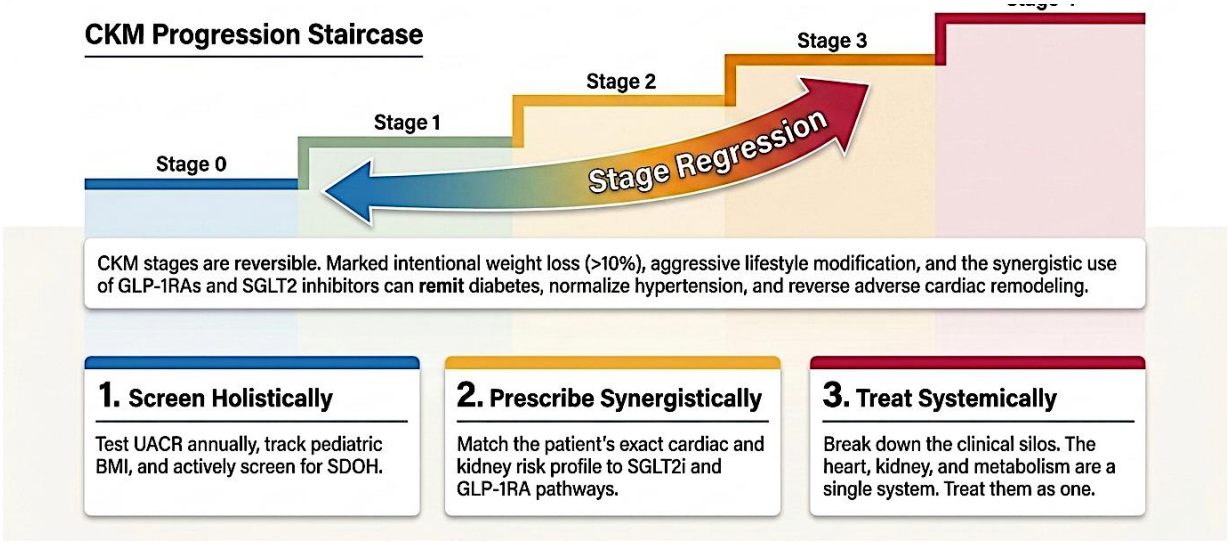
CKM Stages 3, 2 and 1 Can Be Reversed

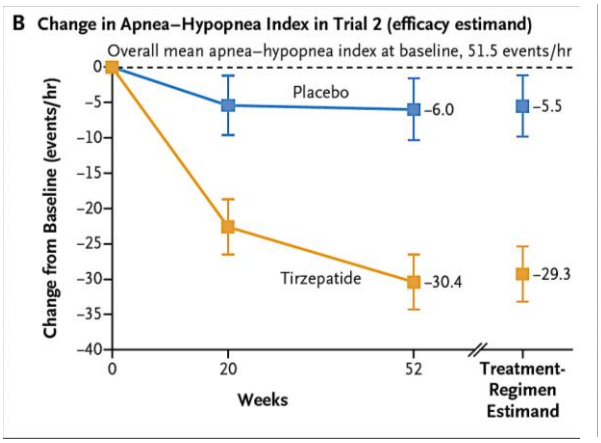


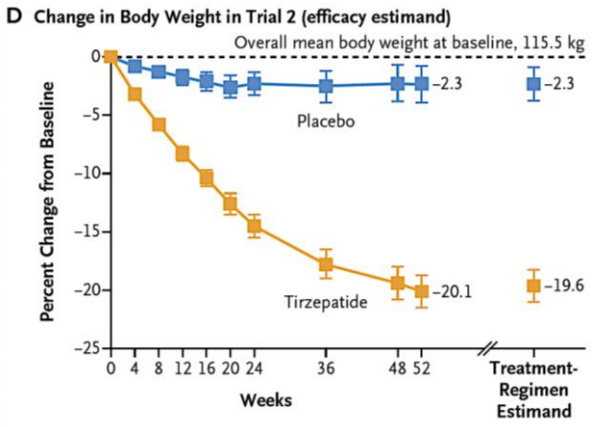
Graphic prepared with help of Notebook LM AI using AHA CKM advisory as reference document.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

47

Tirzepatide Treatment Resulted in Significant Reduction in AHI (25.6%) and Weight (-17.3%) in Persons With OSA and Obesity and Without Diabetes



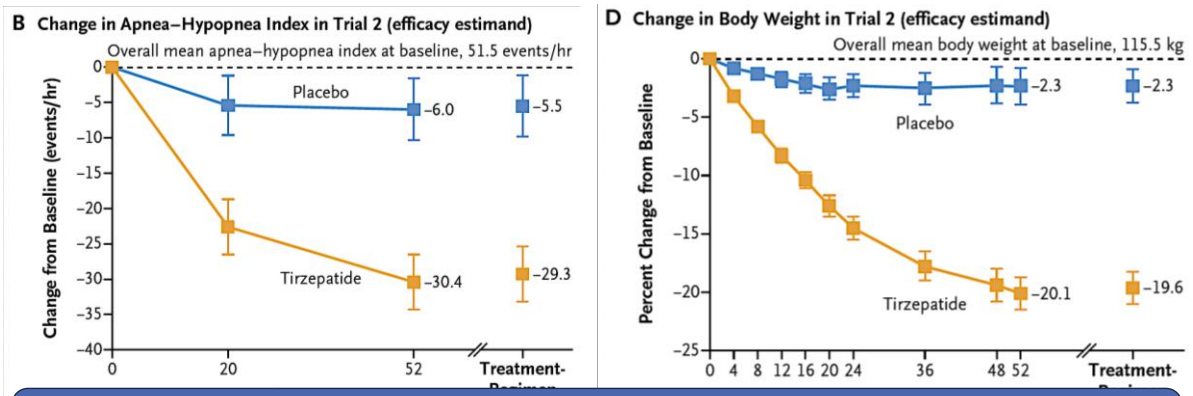


Low Wang

Malhotra A, et al. *N Engl J Med* 2024;141:107516

48

Tirzepatide Treatment Resulted in Significant Reduction in AHI (25.6%) and Weight (-17.3%) in Persons With OSA and Obesity and Without Diabetes



→ In 12/2024, the wt loss form was FDA-approved for moderate to severe obstructive sleep apnea (OSA) in adults with obesity

Low Wang

Malhotra A, et al. *N Engl J Med* 2024;141:107516

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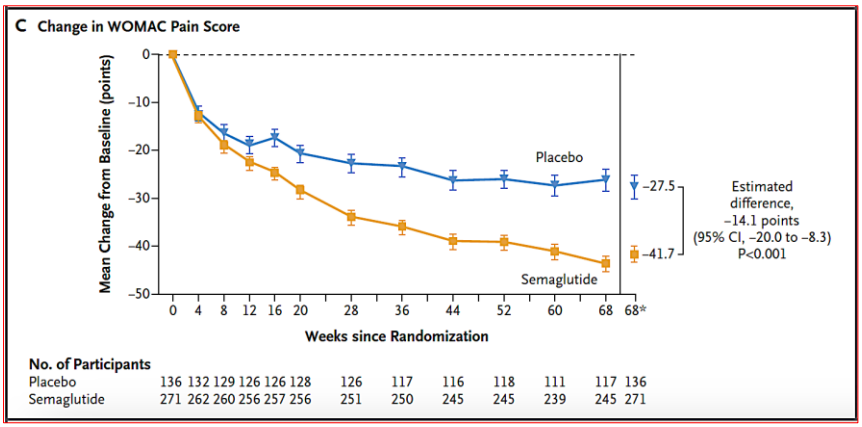
Semaglutide Treatment Reduced Pain in Persons with Obesity and Knee Osteoarthritis



Low Wang

Bliddal H, et al. *N Engl J Med* 2024;391(17):1573-1583

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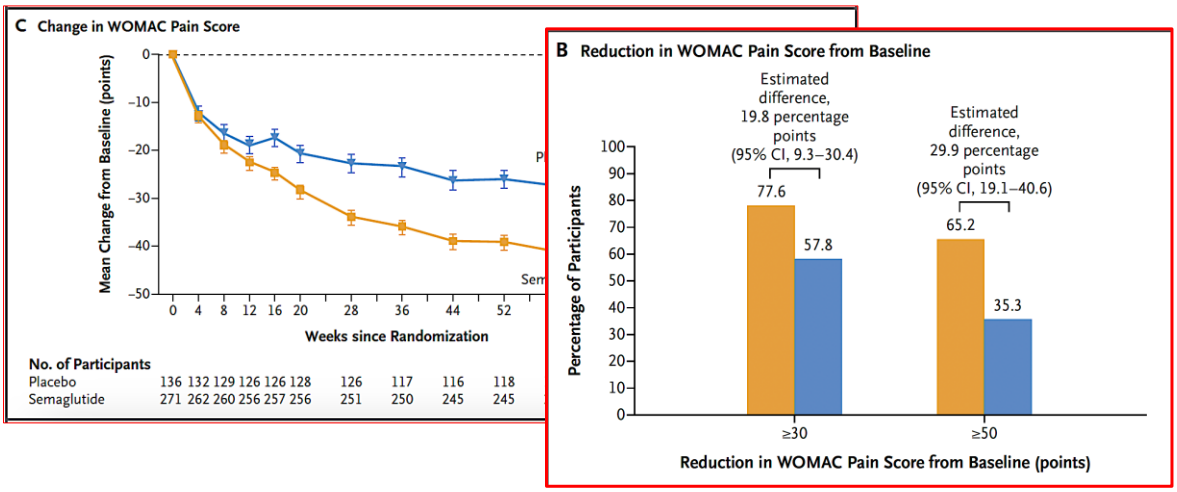
Semaglutide Treatment Reduced Pain in Persons with Obesity and Knee Osteoarthritis



Low Wang

Bliddal H, et al. *N Engl J Med* 2024;391(17):1573-1583

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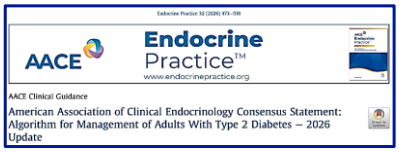
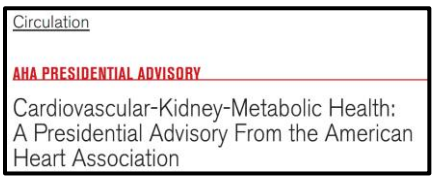
Outline

- Obesity tracks with Type 2 Diabetes (T2D)
- Pathophysiology of T2D: insulin resistance, beta-cell deficiency, and blunted incretin response
- Obesity drives metabolic risk
- CKM Syndrome – what is it? Why is it important?
- How to choose between SGLT2i and GLP1RA in T2D
- Adjunctive use of GLP1RA in T1D





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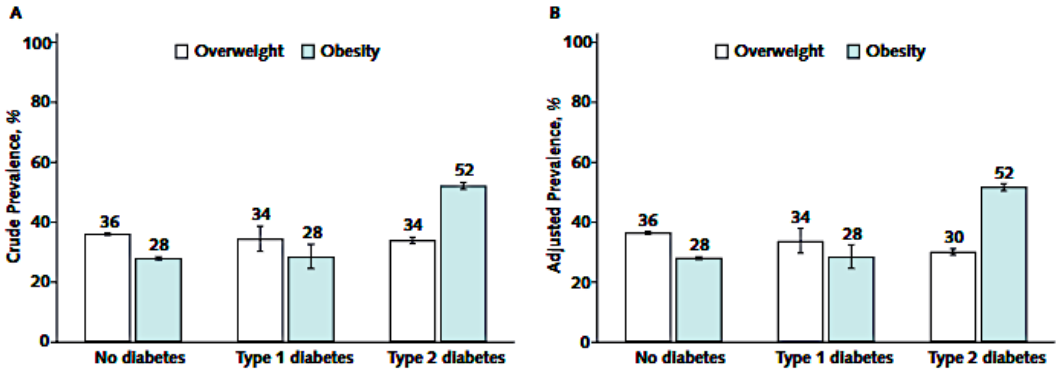
The Prevalence of Overweight and Obesity in Type 1 Diabetes Continues to Increase



Fang M, et al. Prevalence and management of obesity in US adults with type 1 diabetes. *Ann Intern Med* 2023;176(3):427-429.

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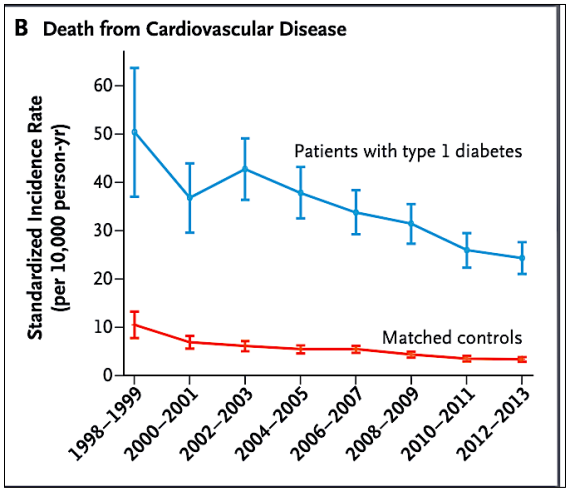
Individuals with Type 1 Diabetes Have a Higher Incidence of CV Death, Not Just from Hyperglycemia



	HR: CV death
Time-updated mean A1c - # events/total #	2326/200,539
Reference (controls)	1.00
≤ 6.9%	2.92 (2.07-4.13)
7-7.8%	3.39 (2.49-4.61)
7.9-8.7%	4.44 (3.32-5.96)
8.8-9.6%	5.35 (3.94-7.26)
≥ 9.7%	10.46 (7.62-14.37)

Lind M, et al. Glycemic control and excess mortality in type 1 diabetes. *N Engl J Med* 2014;371:1972-1982.
Rawshani A, et al. Mortality and cardiovascular disease in type 1 and type 2 diabetes. *N Engl J Med* 2017;376(15):1407-1418.

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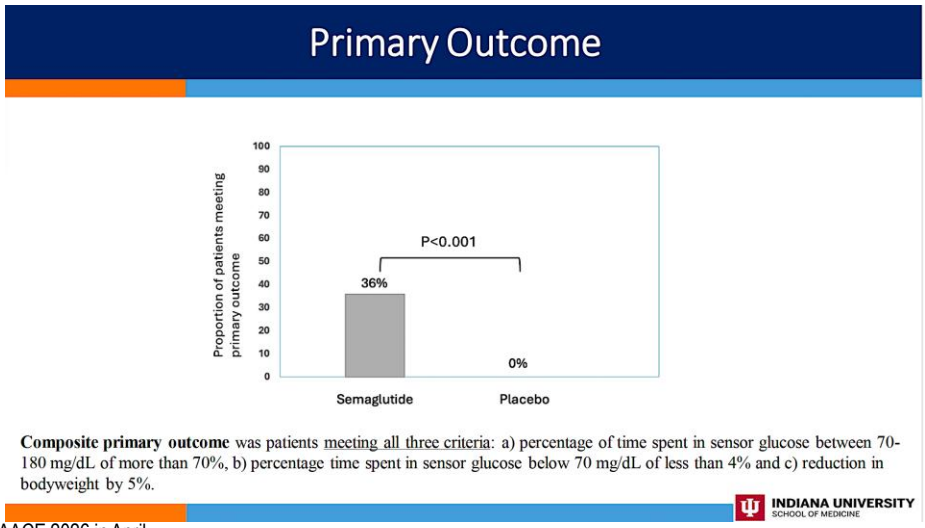
Semaglutide 1 mg SQ Qwk x 6 Months Allowed Patients to Achieve ≥70% TIR and Lose ≥5% Weight Without Unsafe Level of Time Below Range (TBR)



V Shah, presented at AACE 2026 in April

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The ADA Recommends Approaching Obesity Management in Type 1 Diabetes as with the General Adult Population

- **8.29** Apply obesity management strategies used in the general adult population, including GLP-1 RA–based therapy **B** and metabolic surgery **C** to adults with type 1 diabetes who have obesity (BMI ≥30.0 kg/m2, or ≥27.5 kg/m2 in Asian American individuals). Shared decision-making should inform individualized care.

ADA PPC. 8. Obesity and Weight Management for the Prevention and Treatment of Diabetes - Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S166-S182.

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Step-by-Step Approach to Navigating GL1RA and SGLT2i Selection in Your Patients with Diabetes and Obesity:

1. **Does your patient have vascular or renal comorbidities?**
2. **If so, which one(s)?** (HF-CKD-ASCVD/TIA/CVA-MASLD)
3. **Is weight management a primary focus?**

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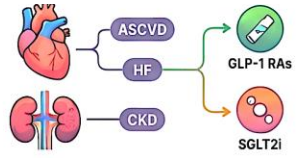
Type 2 Diabetes: Comorbidity- and Weight-Centric Management



Comorbidity-Independent Therapy
Prioritize GLP-1 RAs or SGLT2i for those with ASCVD, HF, or CKD, regardless of A1C.

Weight Management as a Primary Goal
Use high-potency GLP-1 RAs or Tirzepatide when weight loss is a key treatment objective.

GLP-1 Based Therapy vs. Insulin
For those requiring injectable therapy, GLP-1 based options are preferred over starting insulin.

T2D Glucose-Lowering Drug Class Efficacy & Benefits

	Glucose Lowering Efficacy	Weight Effect	Primary Benefit
Tirzepatide / Semaglutide	Very High	Very High Loss	Glycemic & Weight
SGLT2 Inhibitors	Intermediate/High	Intermediate Loss	HF & CKD Protection
Metformin	High	Neutral	Cost & Safety

Graphic prepared with help of Notebook LM AI using ADA & AACE guidelines, AHA CKM advisory as reference documents.

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Obesity Pharmacotherapy Is Advancing Rapidly

- Orforglipron (Foundayo) – small molecule GLP1RA pill approved April 1, 2026, for QD dosing
- High-dose semaglutide SQ (Wegovy) 7.2 mg approved March 19, 2026 (dose increase Q4 wk: 0.25 mg → 0.5 mg → 1 mg → 1.7 mg → 2.4 mg → 7.2 mg Qwk)
- Semaglutide PO (Wegovy) approved in December 2025 (dose increase Q30 days: 1.5 mg → 4 mg → 9 mg → 25 mg QD)

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Nutrient-Stimulated Hormone (NUSH) Mimetics in Development

GLP-1 Agonists
Beinaglutide
Utreglutide (GL0034)
MET-097i
Orforglipron
Aleniglipron (GSBR-1290)
CT-996
ECC5004
TERN-601
HRS-7535
Semaglutide 50 mg

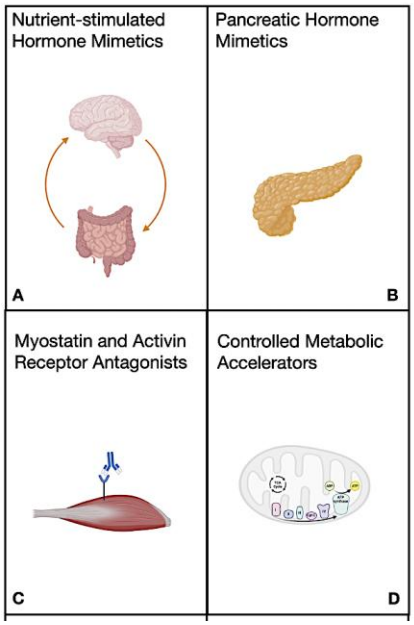
GLP-1/GIP Co-agonists
CT-868
CT-388
VK2735
HRS-9531

GLP-1 Agonist/GIP Antagonist
MariTide

GLP-1/GLP-2 Co-agonists
Dapiglutide

PYY
CIN-110

Bimagrumab
Garetosmab
Trevomugrab



Amylin Agonists
Petrilintide (ZP8396)
AZD6234
GUBamy

GLP-1/Amylin Co-agonists
CagriSema
Amycretin

GLP-1/Glucagon Co-agonists
Mazdutide
Pemvidutide
Survodutide
Cotadutide
Efinopegdutide

GLP-1/GIP/Glucagon Co-agonists
Retatrutide
UBT251

HU-6

Park C, et al. *Front Endocrinol* 2025; 10.3389/fendo.2025.1630199.

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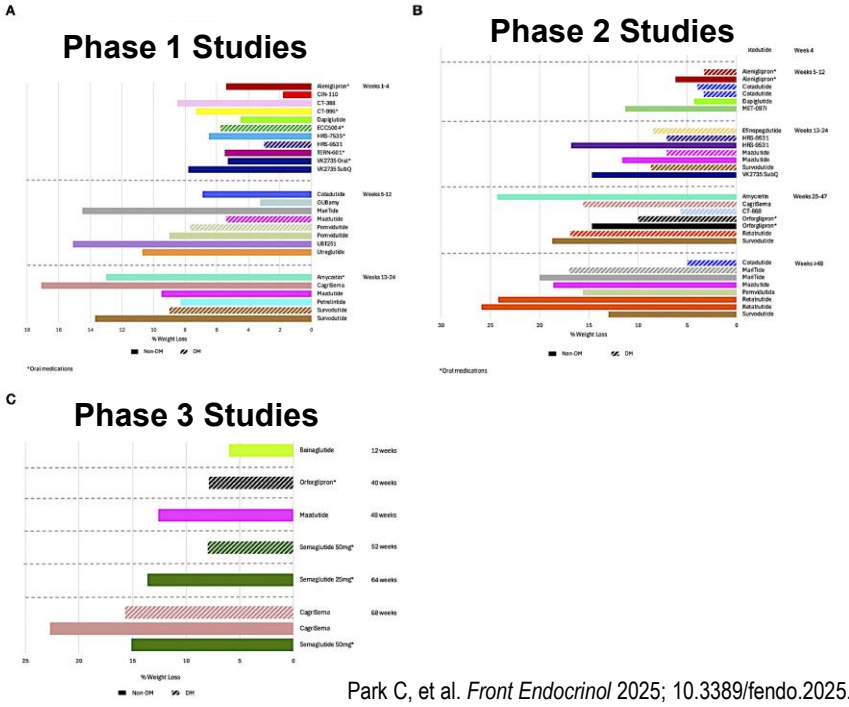
Therapies on the Horizon: NUSH Clinical Trials



Park C, et al. *Front Endocrinol* 2025; 10.3389/fendo.2025.1630199.

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ARS Question #1

In the AHA Cardio-Kidney-Metabolic Syndrome Paradigm, in Which Stage Are Individuals with Hypertension and/or Type 2 Diabetes?

A. Stage 0
B. Stage 1
C. Stage 2
D. Stage 3
E. Stage 4

CONTINUING EDUCATION COMPANY

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Take-Home Points for GLP1RA and SGLT2i

- The underlying pathophysiology of type 2 diabetes is related to insulin resistance (much of it related to **obesity**), beta-cell deficiency, and blunted incretin response.
- Obesity is the main driver of metabolic risk in most T2D.
- CKM syndrome provides a useful framework that integrates metabolic, kidney, and CV risk factors and care.
- PREVENT equations quantify risk for CVD, ASCVD, & HF.
- A step-by-step approach can guide decisions about GLP1RA vs SGLT2i (or both): HF? CKD? ASCVD? Stroke? MASLD? Weight?

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