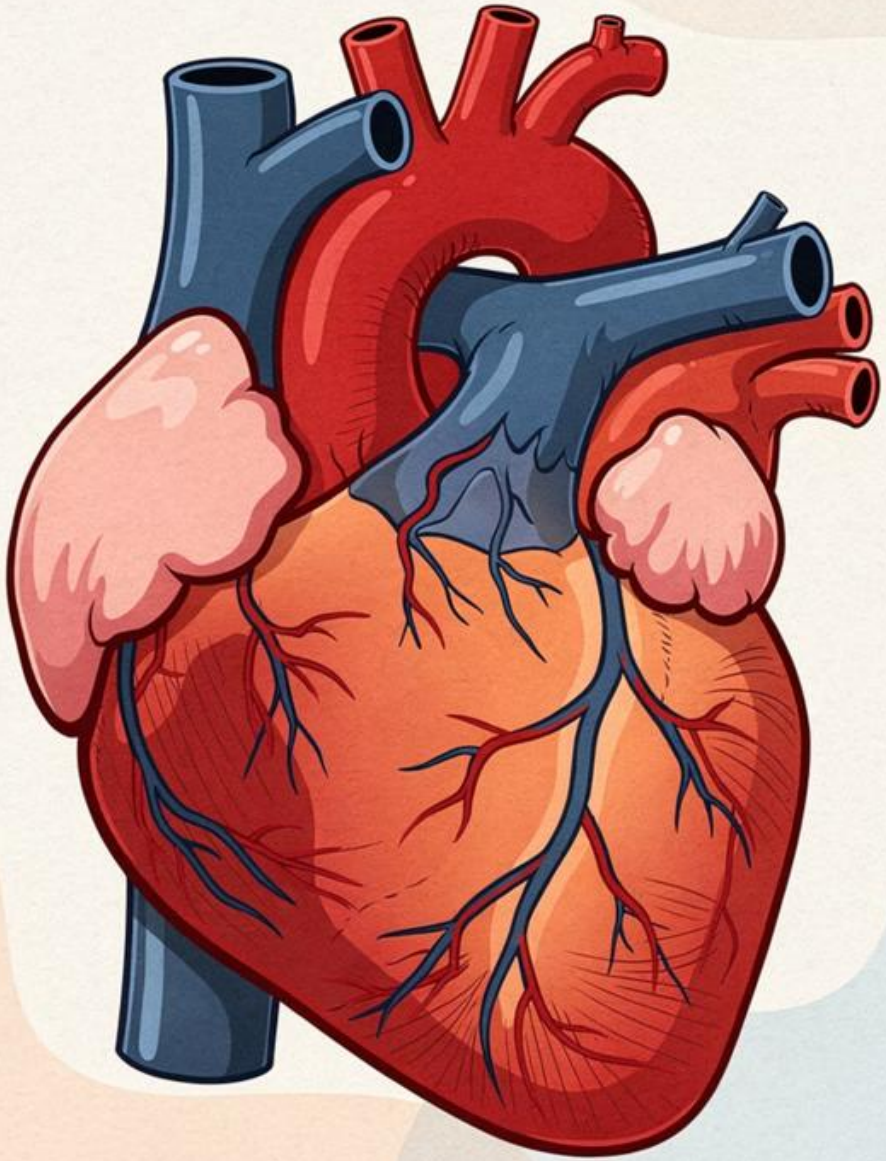

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Management of the Cardiometabolic Patient

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**No Conflict of Interest Disclosures*

Sentara®

April 2026

AGENDA

Objectives

1

Prevalence & Definition

Review the scope and definition of cardiometabolic disease and CKM syndrome, syndrome, including global and U.S.-specific specific burden data.

2

Effective Pharmacotherapy

Identify evidence-based pharmacologic strategies targeting the upstream risk factors of factors of cardiometabolic disease.

3

Multidisciplinary Approach

Reinforce the necessity of a coordinated, team-team-based approach to preventative cardiometabolic care.

Cardiometabolic Disease / Syndrome Prevalence

- It is estimated that **more than half** of the **world population** over the age of 5 is projected to be **overweight or obese by the year 2035**

- In the **US alone, it is projected that 58% of adults will be classified as obese with a BMI > or equal to 30 as of 2035**

- Per the CDC, **Heart disease remains the leading cause of death in the United States**
- About **1 in 20 adults** age 20 and older have CAD (about 5%).

Cardiometabolic Disease / Cardiovascular-Kidney- Metabolic syndrome (CKM)

Not a single condition – CKM syndrome is a group of interrelated risk factors that together dramatically amplify the likelihood of serious cardiovascular and metabolic events.

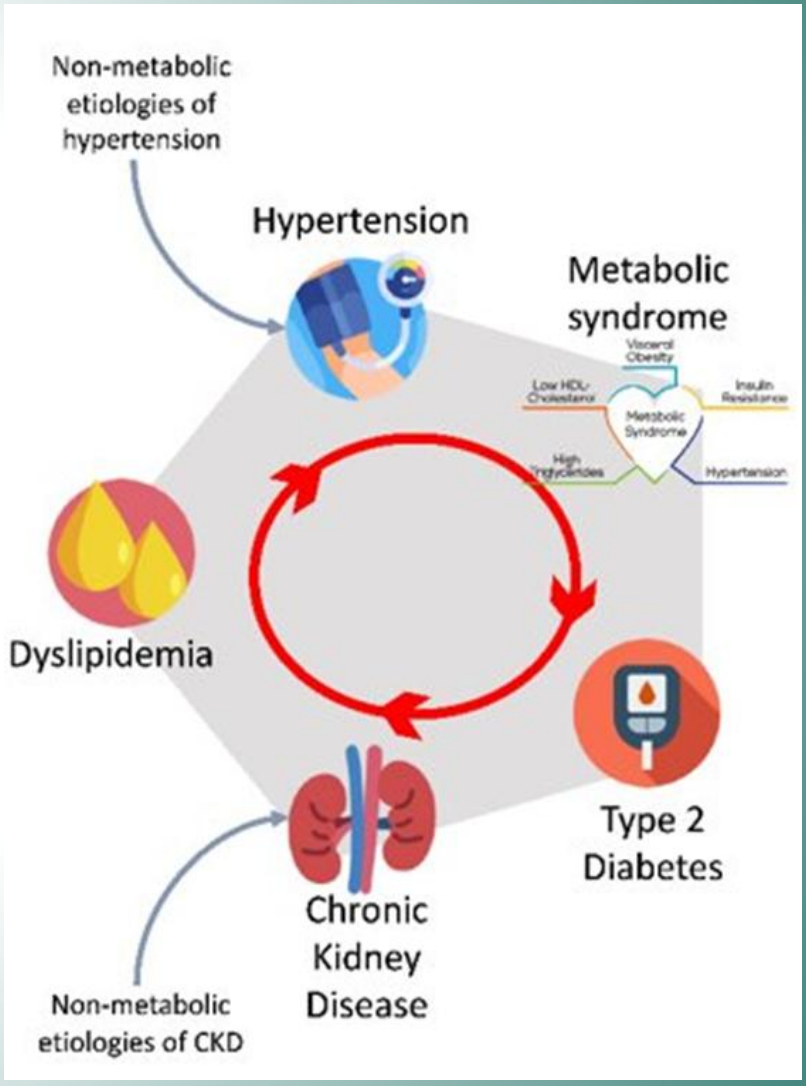
Risk Factors Include:

HTN	*Dyslipidemia*
Insulin Resistance / DM	*Obesity*
CKD	

When these risk factors cluster in one individual, the combined risk for cardiovascular events and metabolic disease is **substantially greater** than the sum of each factor in isolation.

Associated Outcomes:

- Heart attack & stroke
- Type 2 diabetes mellitus
- Chronic kidney disease progression
- Heart failure



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Cardiometabolic Disease/ CKM Prevalence

Cardiovascular-Kidney-Metabolic (CKM) syndrome is a health disorder arising from the connections among heart disease, kidney disease, diabetes, and obesity — leading to poor health outcomes.

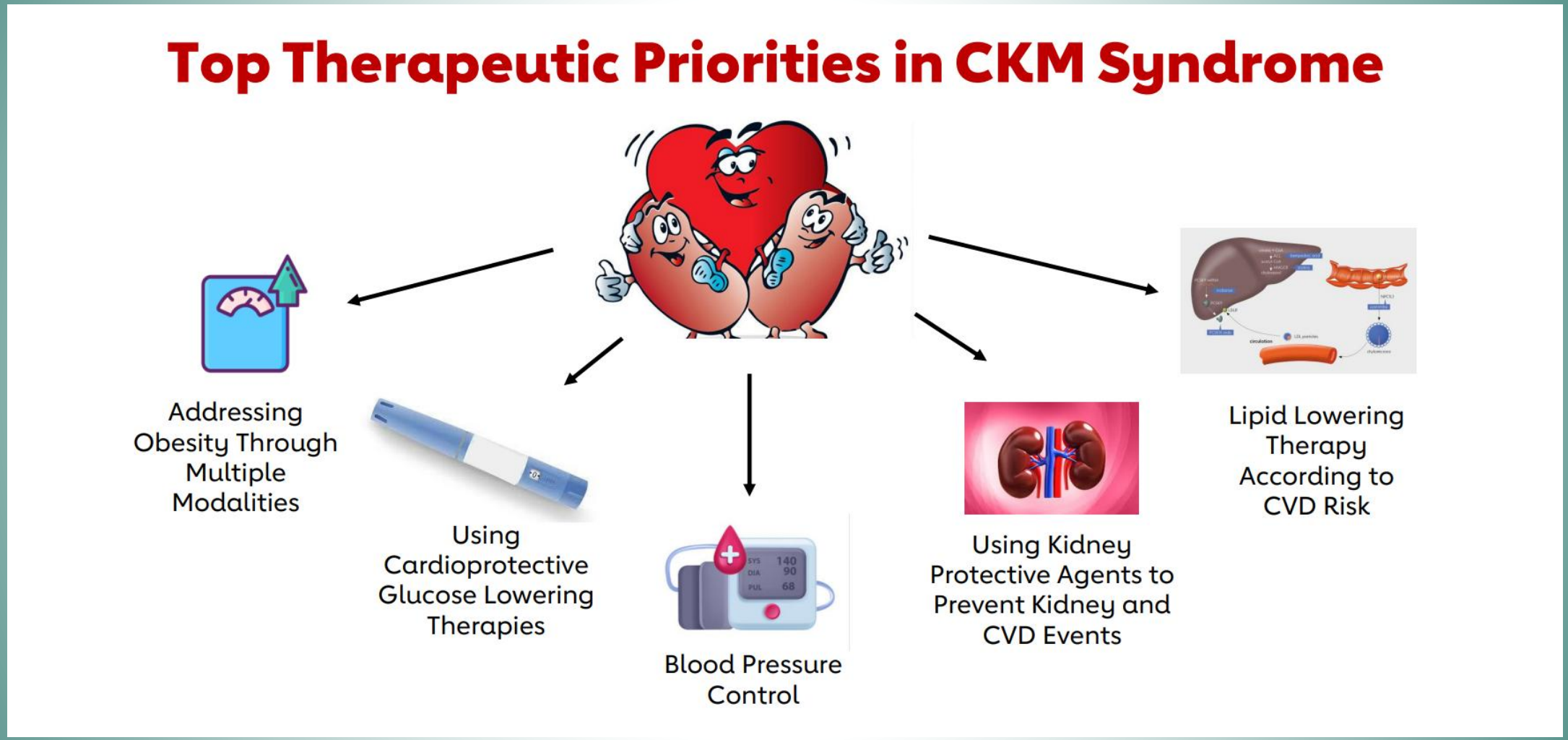
Despite the deeply interconnected pathophysiology of these conditions, current clinical practice often addresses each disease state **in isolation** — treating the downstream consequence rather than the root causes driving the syndrome.

Cardiometabolic Disease Prevalence

Current treatment tends to be focused towards treating the final disease process.

What if we be *stream*

Cardiometabolic Disease / CKM Prevalence



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Ndumele CE, Neeland IJ, Tuttle KR, et al. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association. Circulation

Lipid and HTN management

Risk factor modification-

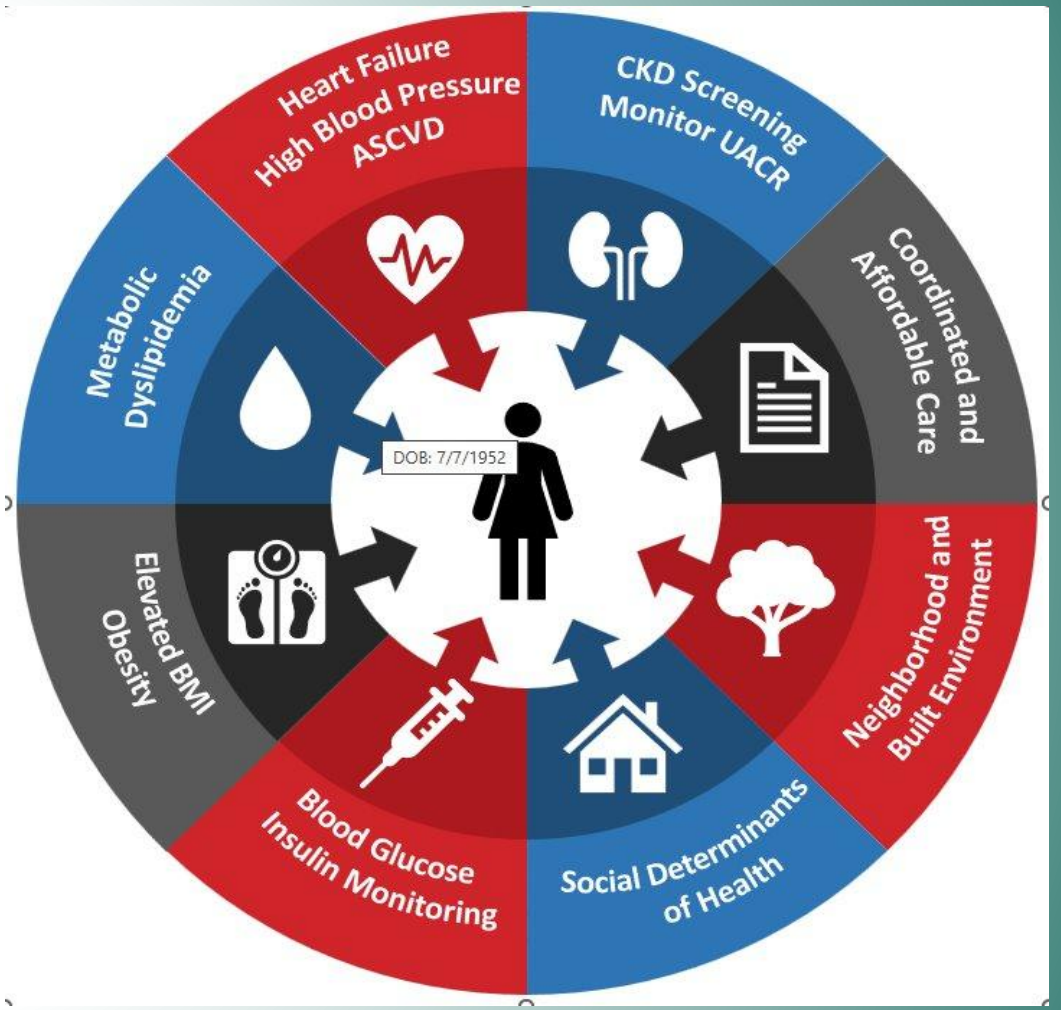
Goals will vary based on concomitant risk factors

HTN management

- Aim for established goal of SBP < 130 in most patients with some individualization based on comorbidities, frailty, and tolerability
- In patients with Diabetes Mellitus, prioritize AceI/Arb for additive renal and cardiovascular protection

Lipid management

- Consider lower goals for higher risk patients (ex LDL goal of < 55 rather than < 70 in established ASCVD)
- Maximize statin therapy and consider addition of supportive agents:
- Add Ezetimide or bempedoic acid + ezetimibe (combination)
- Consider PSK9 inhibitors or inclisiran for persistent elevation
- Icosapent ethyl or Fibrates for elevated triglycerides



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Organ protection- Kidney/Heart

Beyond traditional risk factor management, targeted pharmacotherapy for cardio-renal protection should be considered in patients with CKD or heart failure with or without diabetes.

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SGLT2 inhibitors

- Dapagliflozin (*Farxiga*)
- Empagliflozin (*Jardiance*)

MRAs

- Eplerenone *(Inspra)*

Emphasis HF trial ~ 37% reduction in cardiovascular death or HF hospitalization in HFrEF

EPHESUS trial - addition of eplerenone to optimal medical therapy reduces morbidity and mortality among patients with acute MI complicated by LV dysfunction and heart failure.

- Spironolactone *(Aldactone)*

TOPCAT trial – showed decreased readmission for HFpEF.

RALES trial - showed improved morbidity and mortality in HFrEF

- Finerenone *(Kerendia)*

nsMRA with proven renal and CV benefits in CKD with DM)

FINEARTS — reduced CV death (7%) and total HF events (18%)in patients with **HF with EF >/= 40%*** currently not FDA approved for HFrEF

FIGARO-DKD — reduced risk of CV events in pts with CKD associated with DM II

FIDELIO-DKD – reduced risk of renal progression in pts with CKD with DM II

GLP-1RAs

Obesity and Glycemic management- *The Historical Gap*

Obesity is not simply a comorbidity. It plays a central role in CKM syndrome often amplifying:

- HTN
- HLD (often increases TG and reduces HDL)
- Insulin resistance leading to DM
- Systemic Inflammation

•Lifestyle modifications alone have demonstrated limited long-term efficacy for sustained weight loss

•Historical lack of effective, tolerable pharmacotherapy

•Significant clinical and societal stigma surrounding obesity treatment

But that is rapidly changing with the emergence of GLP-1 receptor agonists...

Obesity and Glycemic management

GLP-1 receptor agonists (GLP-1 RAs) exert their therapeutic effects through multiple complementary mechanisms, producing meaningful improvements in both glycemic control and body weight.

- ***Appetite Suppression***

  GLP-1 acts centrally in the brain to suppress appetite and promote satiety, reducing caloric intake.

- ***Delayed Gastric Emptying***

  Slows gastric emptying, prolonging the sensation of fullness and blunting postprandial glucose absorption.

- ***Insulin Sensitization & Secretion***

  Improves insulin sensitivity and stimulates glucose-dependent pancreatic insulin release after meals.

- ***Glucagon Inhibition***

  Suppresses glucagon secretion, thereby reducing hepatic glucose output and fasting hyperglycemia.

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Obesity and Glycemic management

There are many GLP-1 medications with varying approvals or proven benefits.

Brand Name (generic name)	Route	Frequency	Type 2 Diabetes Indication	Obesity Indication†	Cardiovascular Benefit Data
Dual glucagon-like peptide (GLP-1) receptor agonist / glucose-dependent insulinotropic polypeptide (GIP)					
Zepbound (tirzepatide)	SC	Weekly		✓	Trial in progress
Mounjaro (tirzepatide)	SC	Weekly	✓		Trial in progress
Glucagon-like peptide (GLP-1) receptor agonists					
Wegovy (semaglutide)	SC	Weekly		✓	✓
Ozempic (semaglutide)	SC	Weekly	✓		✓
TBD (semaglutide)* *FDA approval pending for obesity in 2024*	Oral	Daily		✓	
Rybelsus (semaglutide)	Oral	Daily	✓		
Saxenda (liraglutide)	SC	Daily		✓	
Victoza (liraglutide)	SC	Daily	✓		✓
Trulicity (dulaglutide)	SC	Weekly	✓		✓

*Zepbound -also approved for management of mod-severe OSA

- **Victoza, Ozempic, Trulicity**- have shown a reduction in MACE in patients with DM II

Wegovy - reduce the risk of major CV events in overweight/obese individuals with preexisting CVD- regardless of diabetes status (SELECT trial).

MACE Definition: Major Adverse Cardiac Events: CV death, Nonfatal MI, non-fatal stroke

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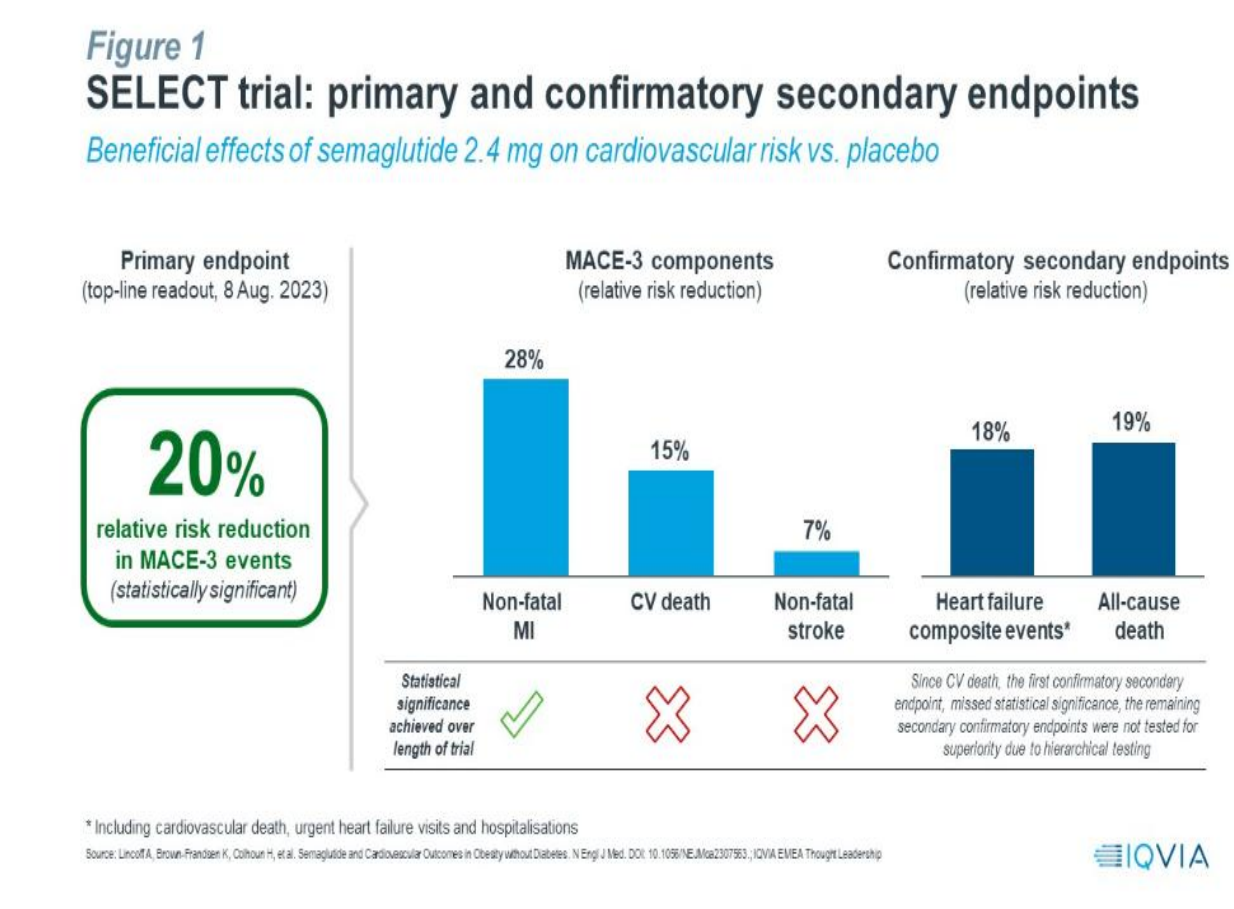
Preparing Your Plan for the GLP-1 Era | Optum Rx

Select Trial- Semaglutide vs. Placebo in Overweight or Obese Patients With Pre-Existing CVD, But Without Diabetes



- The SELECT trial showed that in patients with overweight or obesity and established CVD but without diabetes, once-weekly subcutaneous **semaglutide was associated with a 20% decreased risk of MACE (CV death, nonfatal MI, and stroke)** compared with placebo.

- **28% reduction in heart attacks and 19% reduction in all- cause mortality** among patients who received semaglutide

Patients DID NOT have to lose weight or have altered glucose control to get this benefit!

Beyond obesity: Novo's SELECT re-defines cardiovascular risk management | IQVIA

Daniel J. Drucker; Efficacy and Safety of GLP-1 Medicines for Type 2 Diabetes and Obesity. *Diabetes Care* 21 October 2024; 47 (11): 1873–1888. https://doi.org/10.2337/dci24-0003

Types of GLP1 medications

Ozempic (Semaglutide)

Indicated for type II DM

Formulations:

SQ Pen injector (weekly):

0.25 --> 0.5 --> 1 --> 2 mg

Oral tablet (daily) *previously rybelsus*: 1.5 --> 4 --> 9 mg

Take with sip of water 30 min prior to any food/drink or other meds

Wegovy (Semaglutide)

Indicated for chronic weight management *and* reducing major cardiovascular risk in pts with established CV *disease* and obesity

Formulations:

SQ pen injector (weekly):

0.25--> 0.5 --> 1 --> 1.7 --> 2.4 mg

-->and ***now NEW HD 7.2 mg dose***

New Oral tablet (daily):

1.5--> 4 --> 9 --> 25 mg daily

Take with sip of water 30 min prior to any food/drink or other meds

Types of GLP1 medications

Mounjaro (Tirzepatide)

Indicated for type II DM

Preparations:

SQ Pen injector (weekly):

2.5 --> 5 --> 7.5 --> 10 --> 12.5 -->15 mg

Zepbound (Tirzepatide)

Indicated for chronic weight management* *and* for patients with moderate to severe OSA

Preparations:

SQ Pen injector (weekly):

2.5 --> 5 --> 7.5 --> 10 --> 12.5 -->15 mg

New oral tablet Foundayo (orforglipron) (daily)

0.8 mg --> 2.5 mg --> 5.5 mg -->9 mg --> 14.5 mg -->17.2

Take with or without food

**obesity OR overweight with at least one comorbid weight related condition*

Beyond Glycemic control and Weight: Other GLP1 Benefits

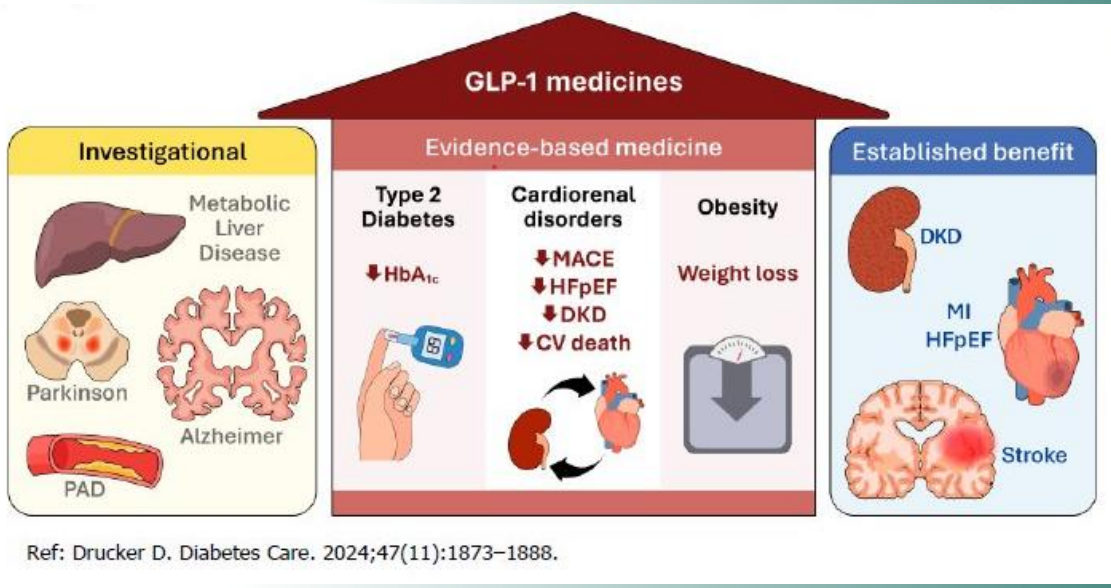
Additional Benefits:

CV Event Reduction
Significant MACE reduction in patients with and without T2DM

Kidney + Heart Failure
Reduces HFpEF, CKD progression, and CV death by >10% in diabetic patients

Emerging/Investigational Areas

- *Peripheral Vascular Disease*
- *Neurodegenerative Disorders*
- *Addiction-Related Behaviors*
- *Metabolic Liver Disease*
- *Type 1 Diabetes*



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Beyond MACE- Other GLP1 Benefits-

Supportive Endpoints of the Select Trial

Supportive endpoint data from SELECT trial suggests that semaglutide contributes to clinically meaningful reductions in blood pressure, cholesterol, and A1c likely mediated by weight loss and offering additional cardiometabolic benefit beyond MACE reduction alone

Confirmatory secondary end points:
Change from baseline to week 104 in[3]:

Waist circumference:
5.7-inch reduction
2-inch reduction with placebo

Systolic blood pressure:
5.7 mm Hg reduction
1.6 mm Hg reduction with placebo

Supportive secondary end points: Change from baseline to week 104 in[3]:

Lipid profile:

Total cholesterol	LDL	HDL	Triglycerides
3.3% reduction 1.4% increase with placebo	**6.1% reduction** 2.7% reduction with placebo	**9.6% increase** 8.1% increase with placebo	**19% reduction** 3.7% increase with placebo

Diastolic blood pressure:
4.4 mm Hg reduction
0.8 mm Hg reduction with placebo

A1c:
0.4% reduction
0.1% reduction with placebo

[Chronic Weight Management Trial Results | Wegovy® (semaglutide)]

Sentara Cardiometabolic Clinic- *What are we doing?*

- An APP run specialty clinic dedicated to seeing established Sentara Cardiology patients with known CAD (ideally hx MI- STEMI, NSTEMI type I or II) and BMI> 27, start them on an appropriate GLP-1 agonist, arrange initial follow up for titration (via nurse phone calls monthly and in person for 3 mo appt and further as needed).
- Focusing on appropriate GLP-1 initiation and addressing other risk factors as needed in follow up
- Started October 2025 staffed by general cardiology APPs at the Princess Anne Office.

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Eligible Patients - How to Refer

To refer a patient to the Sentara Cardiology Cardiometabolic Clinic, the referring provider must be a **Sentara Cardiology provider (NP, PA, MD, or DO)** referring an **established Sentara Cardiology patient**. The referring team agrees to manage weight loss medications long-term after the patient reaches a maintenance dose.

The provider will be prompted to answer questions to ensure your patient is a candidate to be seen in this clinic

Not a Sentara Cardiology Provider?

Contact the patient's Cardiologist at Sentara Cardiology

The Cardiologist or Cardiology APP will place the internal Epic referral if appropriate:

"Referral to Cardiometabolic clinic"

Qualifiers:

- **Does patient have a history of CAD?**
- **Does Patient have a BMI ≥ 27?**
  (If BMI > 40, consider also referring to the Sentara Weight Loss Clinic for additional support.)
- **Are you a Sentara Cardiology Provider (NP, PA, MD, or DO) AND is this an established Sentara Cardiology patient?**
- *(Important: The Referring provider/care team agrees to manage potential weight loss medications long-term after the patient reaches a maintenance dose.)*
- **Is this patient on insulin?**
- *(If on insulin, endocrine specialists would be best suited to manage these medications.)*
- **Is this patient on Dialysis?**
- *Patient cannot be on dialysis (PD or HD)*

If you have answered "No" to any of these questions, your patient may be a candidate for GLP-1 medications; however, they are not a candidate for referral to the Sentara Cardiology Metabolic Clinic at this time. Consider referral to the Sentara Weight Loss Clinic, Endocrinology, or Primary Care for management if felt appropriate.

Cardiology Cardiometabolic Team

Kristen McElhaney, PA

General Cardiology APP Team Coordinator

Sydney Alexander, PA

Cardiometabolic Clinic and General Cardiology APP

Jacqueline Knox, PA

Cardiometabolic Clinic and General Cardiology APP

The First Visit- What to expect

Comprehensive History
Weight history, exercise habits, diet, possible contraindications to use of GLP-1 medications *(ex prior pancreatitis or GI blockage, pregnancy intentions)* will be reviewed

Baseline Measurements
Weight, BMI, lipids, A1c, waist circumference (to estimate visceral fat loss)

Education and Initiation
Nutrition counseling, pen injector demonstration, and referrals as needed (weight loss clinic, sleep study, surgical subspecialties, nutritionists)

Follow up Plan
Monthly nurse phone calls for titration support, In person or telehealth 3 mo visit and additional follow up as clinically indicated to address multiple risk factors

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GLP-1 Intiation support

An Epic smartphrase has been created to support GLP-1 initiation across providers and specialties – even outside the Cardiometabolic clinic.

Epic Smart phrase:
"RECSCARDIOMETCLINIC"

Can serve as a go-to Assessment and Plan when initiating GLP1s on your own

Assessment
Starting Weight: ***
Current Weight: @PTWT@
Starting BMI: ***
Current BMI: @BMI@
Starting Waist Circumference: ***
Current Waist Circumference: ***
Starting A1C: ***
Current A1C: @LABBRIEF(HBA1CAG)@
Starting LDL: ***
Current LDL: @@LABBRIEF(LDL)@
Sleep Evaluation: ***

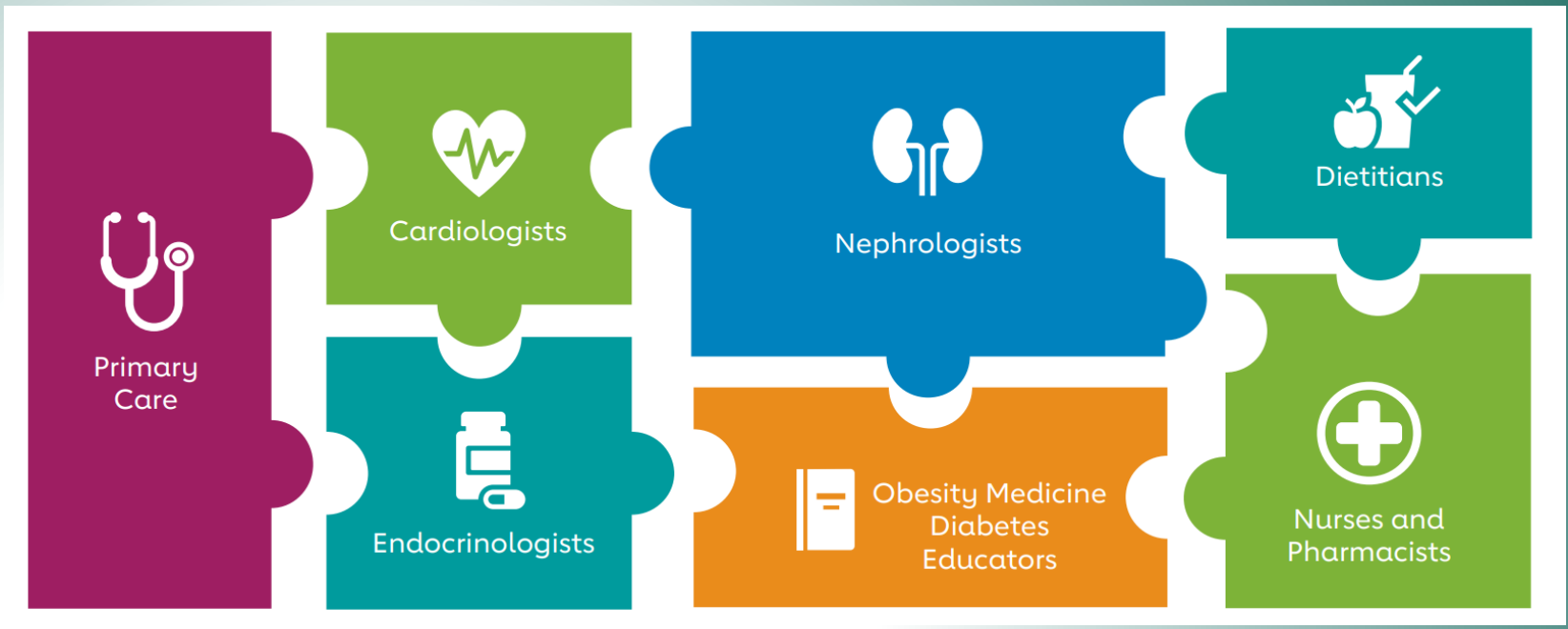
***Add full problem list

Plan:
Obesity / CAD / DM***

With hx of prior MI/CAD with concurrent obesity (and ***other risk factors) having already attempted traditional diet/exercise modifications for weight loss, pt would benefit from GLP-1 initiation for cardiovascular event risk reduction. Will prescribe *** and await prior auth approval. Should *** be denied, would next consider ***.

Discussed known contraindications/cautions for use of GLP-1 medications including: hx of pancreatitis, Type 1 DM, hx of thyroid cancer or genetic predisposition/family history of medullary thyroid cancer or MEN 2A or 2B and pt denies any history of such.
Caution in severe inflammatory bowel disease
IF applicable, we discussed pregnancy intentions and note increased fertility possible with weight reduction (Ozempic babies). Rec to D/c at least 2 months prior to planned pregnancy

In Summary



CKM is a syndrome – not a single disease

Treat the cluster of risk factors: HTN, HLD, insulin resistance, obesity, and CKD

Target Upstream Risk-

Early Aggressive intervention of metabolic risk factors prevents downstream CV events

GLP1- RAs can be cardioprotective

Evidence from the SELECT trial confirm meaningful MACE reduction- independent of weight loss or glucose lowering

Team Based Care Works

The Sentara Cardiometabolic Clinic demonstrates how a coordinated, multidisciplinary approach can close the treatment gap

Ndumele, C.E. et al., Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. 2023. Circulation

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