Cardiovascular-Kidney-Metabolic (CKM) Syndrome: Addressing Complex Interrelationships Among Obesity, Diabetes, CKD and Heart Disease

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1

Disclosures

- No relevant financial disclosures
- I will not reference unlabeled/unapproved uses of drugs or products in this presentation

2

Objectives

By the end of this talk, the attendees will be able to:

- Describe the definition and rationale for the construct of Cardiovascular-Kidney-Metabolic (CKM) Health
- Describe qualitative and quantitative approaches to assessing risk in CKM Syndrome
- Understand approaches to enhance holistic care for patients across the CKM syndrome spectrum

3

Case: A Confluence of Risk

- **History:** 54-year-old woman with a history of obesity, hypertension and diabetes, coming to clinic to establish care after death of family member. Self-care and healthy lifestyle challenging as a single mother working both full and part time jobs. Smokes cigarettes to alleviate stress.
- **Meds:** Amlodipine, HCTZ, Metformin
- **Exam:** BP 144/92, BMI 38 kg/m^2, waist circumference 106 cm, JVP wnl, clear lungs, CV RRR s1s2 +s4, abdomen protuberant, extremities warm with trace edema
- **Labs:** A1c 9.2%, eGFR 55 nl/min/1.73 m^2, UACR 93 mg/g, Total chol 225 mg/dl, LDL 163 mg/dl, triglycerides 180 mg/dl, HDL-C 36 mg/dl

- ***What is contributing to her CVD risk?***
- ***How do we best classify and quantify her CVD risk?***
- ***What are the best strategies for optimizing her CKM health?***

4

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- *Multiple interconnected comorbidities*
- *High burden of adverse SDOH*
- *Uncontrolled risk factors*
- *Unrecognized "High Risk CKD"*
- *Opportunities to optimize CKM health with social support, lifestyle change and pharmacotherapy*

5

Circulation

AHA PRESIDENTIAL ADVISORY

Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association

Circulation

AHA SCIENTIFIC STATEMENT

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

6

Why Focus on Cardiovascular-Kidney-Metabolic Health?

7

Rationale for Emphasis on Cardiovascular-Kidney Metabolic Health:

- Close interplay among metabolic risk factors (obesity, diabetes, metabolic syndrome), CKD and the cardiovascular system
- Shifting causes of heart disease risk in the population, with increasing burden of obesity, diabetes and CKD, and earlier presentations with CVD
- CKM syndrome associated with premature mortality, primarily of cardiovascular etiology
- Major driver of disparities in CVD rates and outcomes
- **Key opportunities:** better scientific understanding, and multiple new therapies impacting metabolic, kidney and CVD outcomes

8

Changing Phenotype of Cardiovascular Risk

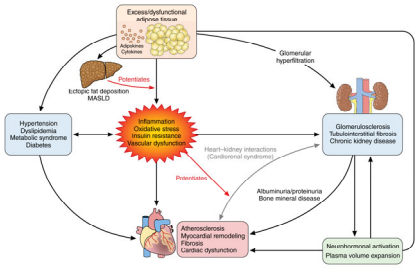
Over last 25 years:

- Less **hypertension/ hypercholesterolemia**
- More **obesity**, **CKD** + **severe hyperglycemia**

Lhoste et al. Nature Cardiovascular Research. **3**: 46–59 (2024)

9

Conceptual Diagram of CKM Syndrome



Ndumele, C.E. et al., A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic Syndrome: A Scientific Statement From the American Heart Association. 2023. Circulation.

10

CKM Syndrome and Premature Mortality

CKM Risk Factor	Survival Reduction
Severe Obesity (BMI 40-45)	8-10 years
Diabetes	13-14 years
CKD (stage 4 vs eGFR >60)	>20 years

- Confluence of CKM syndrome components is common and associated with synergistic increases in mortality risk. In nationwide sample, 10-year mortality rates for:
  - Diabetes: 7.7%
  - CKD: 11.5%
  - **Diabetes and CKD: 31.1%**

Afkarian et al. J Am Soc Nephrol. 2013;24:302–308

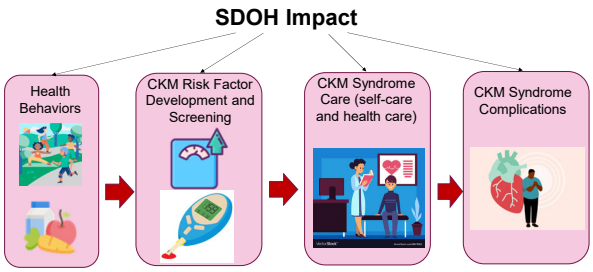
11

Importance of Social Determinants (or Drivers) of Health for CKM Health

- More adverse SDOH, at multiple levels, impact health behaviors and drive the development of CKM factors
- Adverse SDOH decrease the likelihood of early detection of CKM factors, and increase risk of disease complications, CVD events and mortality in those with existing CKM factors
- While there are a growing array of therapeutic options to support CKMH, access is limited and particularly restricted among populations that are marginalized with high social needs
- Navigating health systems with multiple providers/therapeutic plans particularly challenging with more adverse SDOH

12

SDOH Impact the Development and Clinical Consequences of CKM Syndrome



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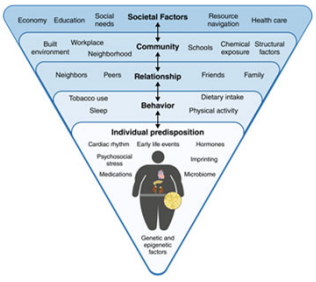
A Socio-ecological Framework for CKMH



For optimal CKM care, need to consider SDOH in:

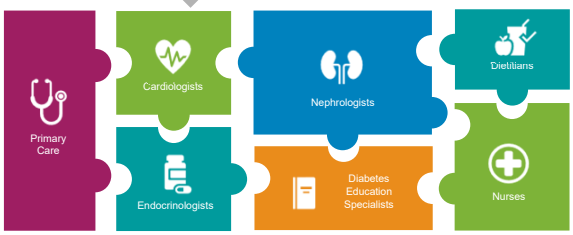
- Screening
- Risk prediction
- Clinical algorithms
- Composition of the clinical care team
- Real world Implementation

Ndumele, C.E. et al., A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic Syndrome: A Scientific Statement From the American Heart Association. 2023. Circulation.

14

Fragmented Patient Care

Multiple providers + lack of comprehensive/cohesive treatment plans



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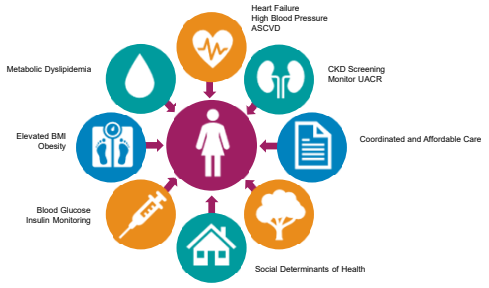
Patient-Centered

Harmonized Approach



16

Science Advisory Group

To address challenges related to CKM health, AHA convened a multi-disciplinary Science Advisory Group (SAG) on CKMH. SAG Co-Chairs:

Sheryl L. Chow, PharmD, FCCP, FAHA, FHFSA

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17

CKM Science Advisory Group


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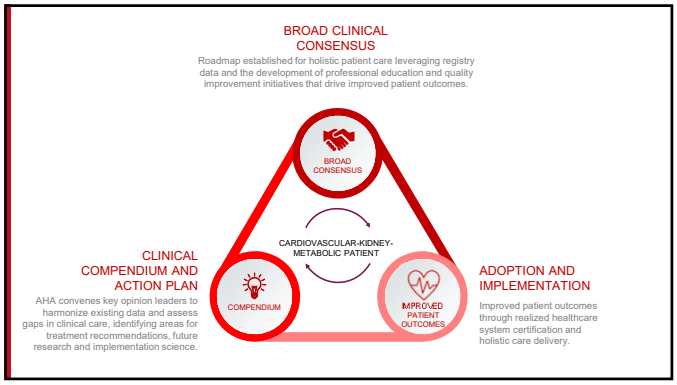
Jackson Wright, MD, PhD

18



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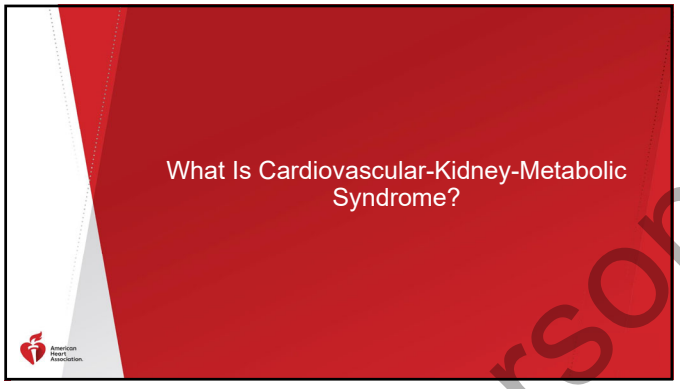

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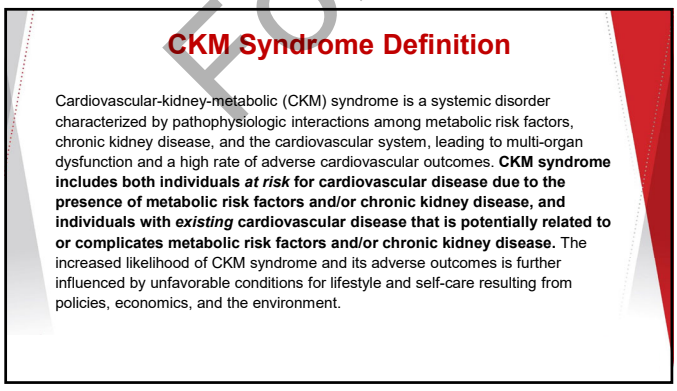


21

Abbreviated CKM Syndrome Definition
(for Health Care Professionals and Laypersons)

Cardiovascular-kidney-metabolic (CKM) syndrome is a health disorder due to connections among heart disease, kidney disease, diabetes, and obesity leading to poor health outcomes.

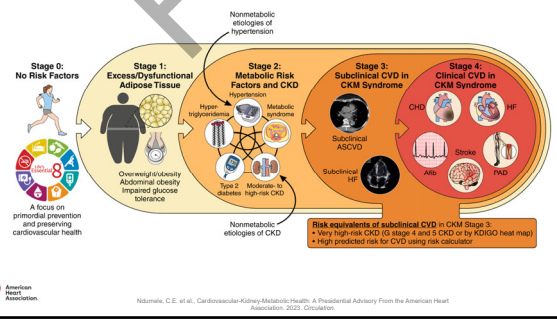
22

Rationale for CKMH Staging

- Reflects the progressive pathophysiology of CKM syndrome
- Improves identification of under-recognized clinical conditions, which are often initially asymptomatic but confer increased clinical risk
  - More than 90% of persons with CKD are unaware of the condition
- Each stage to represent a higher level of absolute risk → intensified therapies
  - Principal focus on cardiovascular disease to define the "at-risk" population and to identify those with end-organ injury. This is because the primary cause of premature mortality in relation to poor CKMH is CVD.
  - Additional focus on kidney failure, but CVD also primary cause of mortality in CKD
- Each stage represents window for preventive intervention, with goal of preventing progression to later CKMH stages
- Also supports the concept of CKM Stage regression with marked lifestyle change and/or weight loss

23

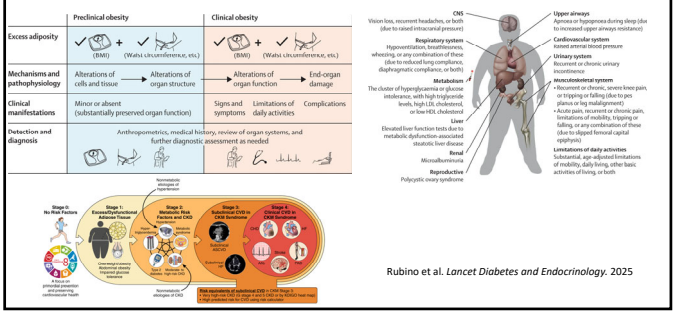
Stages of Cardiovascular-Kidney-Metabolic Syndrome



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

24

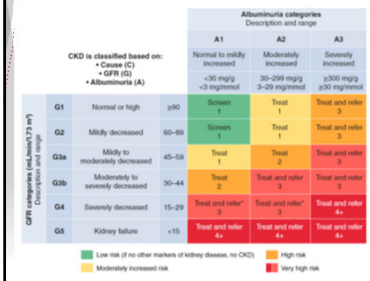
Lancet Obesity Commission:
Obesity as a Driver of Multi-System Compromise



Rubino et al. *Lancet Diabetes and Endocrinology*. 2025

25

KDIGO Heat Map

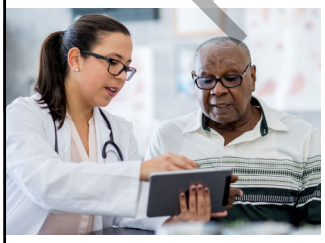


KDIGO risk categories based on eGFR and UACR linked to absolute risk for kidney failure, cardiovascular events, all-cause mortality and other adverse outcomes

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

26

Risk Enhancing Factors in CKM Syndrome



- Chronic inflammatory conditions
- High burden of adverse SDOH
- High risk demographic (South Asian ancestry)
- Mental health disorders
- Sleep disorders
- Sex-specific risk enhancing factors
  - *History of premature menopause*
  - *History of adverse pregnancy outcomes*
  - *Polycystic ovarian syndrome*
  - *Erectile dysfunction*
- Elevated high-sensitivity C-reactive protein
- Family history of kidney failure, diabetes

American Heart Association.

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

27

An Updated Approach to CVD Risk Prediction

The recognition of CKM syndrome required an updated prediction approach, which led to the development of PREVENT™. Key updates include:

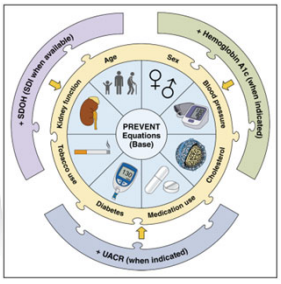
- Expanded outcome focus to ASCVD, heart failure and total CVD
- Expanded age range to 30-79 years
- Assessments of 10 and 30 year risk
- Added CKM syndrome components to prediction model
- Removed race and added SDI as measure of SDOH
- Improved calibration in all demographic groups

https://professional.heart.org/prevent

Khan et al. Circulation. 2024 Feb 6;149(6):430-449.

28

Role of Risk Prediction in CKM Syndrome



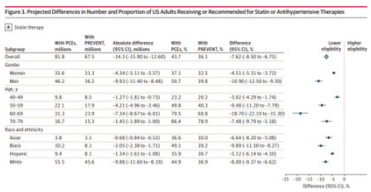
- Quantitative prediction is complementary to qualitative CKM staging approach
  - Stage 3 includes high CVD risk as a "risk equivalent"
  - In Stage 1 and 2, higher predicted CVD risk = greater net benefit from preventive therapies
- Helpful tool as we consider the use of non-statin pharmacotherapies in populations at-risk for CVD and kidney failure

Khan et al. Circulation. 2023 Dec 12;148(24):1982-2004.

29

A Need for New Risk Thresholds?

With PREVENT, correction of prior ~2-fold overprediction by PCEs = shift to lower predicted CVD risk estimates



Diao et al. JAMA. 2024; 332(12):989-1000

30

How Do We Address Cardiovascular-Kidney Metabolic Syndrome?

31

Overarching Therapeutic Consideration:
Addressing SDOH in Care Model

- **Systematic screening** for SDOH using validated tools
- **Integration of SDOH assessments** into clinical care workflow and EHR
- **Incorporation of community health workers (CHWs) and care navigators** into integrated care team, to help patients with access, self-management, health system navigation and connection to available social needs resources
- **Leveraging existing community resources and community programs** for those identified to have adverse SDOH limiting care

32

Overarching Therapeutic Consideration:
Interdisciplinary Care Models

Value-based care

- Support of remote interdisciplinary care team when any two of the following are present: CKD, diabetes, and subclinical/clinical CVD
- Interdisciplinary team
  - Primary care
  - Subspecialists
  - Pharmacy
  - Nursing
  - CKM coordinator
- CKM coordinators partner with PCPs and support patients in journey to optimizing CKM care and health

Volume-based care

- Targeted referrals to specialists
  - Nephrology
  - Endocrinology
  - Cardiology
- CKM coordinator assists with patient navigation across multiple subspecialists
- Use of telemedicine as needed
- Flexibility to rely more on value- or volume-based care

33

Evidence for Benefit of Coordinated Care Models

CKM Care Coordination has been effective in enhancing coordinated and holistic care in CKM syndrome when provided:

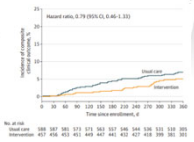
- Virtually or in person
- Using nurses or pharmacists

In a recent cluster randomized trial, engagement of a multidisciplinary team and "implementation specialist" for patients with type 2 diabetes resulted in:

- >4 fold increase in use of multiple classes of preventive therapies

	No. (%)		Adjusted	
	Intervention (n = 457)	Usual care (n = 588)	OR (95% CI)[a]	P value
Primary outcome				
Prescribed all 3 groups of recommended, evidence-based therapies[b]	173 (37.9)	85 (14.5)	4.38 (2.49-7.71)	<.001
Secondary outcomes				
Prescribed individual groups of recommended therapies				
High-intensity statins	323 (70.7)	334 (56.8)	1.73 (1.06-2.83)	.03
ACEIs or ARBs[c]	372 (81.4)	402 (68.4)	1.82 (1.14-2.91)	.01
SGLT2 inhibitors and/or GLP-1RAs	276 (60.4)	209 (35.5)	3.11 (2.08-4.64)	<.001
Prescribed ≥2 groups of recommended therapies	361 (79.0)	326 (55.4)	4.68 (2.58-8.51)	<.001
Prescribed all 3 groups of recommended therapies without metformin monotherapy with hemoglobin A_{1c} <7% option	142 (31.1)	50 (8.5)	6.90 (3.55-13.40)	<.001

Secondary clinical outcome: all-cause mortality, hospitalization for CVD event or urgent revascularization



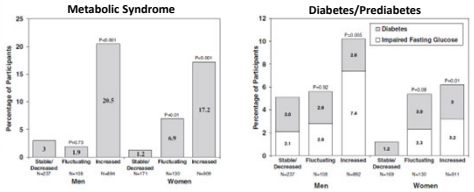
Pagidipati N et al. *JAMA*. 2023;329(15):1261-1270

34

Stage 0: Preserving Ideal Cardiovascular Health

Stage 0

STAGE 0
- Attaining and maintaining ideal CVH linked to decreased CVD and mortality
- Multilevel school-based and family-based interventions increase likelihood of ideal CVH
- Avoiding weight gain with aging decreases likelihood of developing CKM risk factors



Avoiding weight gain with aging associated with lower risk of developing metabolic risk factors

Lloyd-Jones al. *Circulation*. 2007;115:1004-1011

35

Stage 1: Addressing Excess/Dysfunctional Adiposity

Stage 1

STAGE 1
- Nonjudgmental weight loss counseling increases the likelihood of weight loss attempts
- A comprehensive lifestyle intervention is most effective for sustained behavioral changes
- 5%–10% weight loss associated with improved BP, glycemia, and lipids
- ≥10% weight loss associated with lower CVD event rates
- Incretin analogues* induce >15% weight loss and improve metabolic risk factors
- Bariatric surgery associated with reductions in metabolic risk factors, CVD events, and mortality

Achieving clinically significant weight loss (≥ 10%)			
Not judged+not discussed	188	REF	–
Judged+not discussed	15	1.71	0.34–8.49
Judged+discussed	112	2.70	0.05–7.63
Not judged+discussed	284	4.36	1.99–9.56

PCP primary care provider.

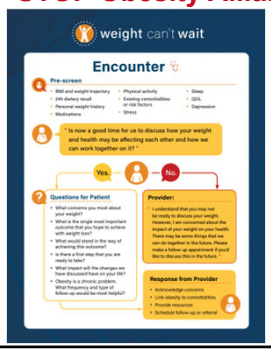
a Logistic regression model adjusted for patient age, patient sex, patient race, patient BMI, duration of PCP relationship, PCP race and perceived PCP BMI. Estimates generated using survey weights.

Nonjudgmental weight loss discussions associated with a greater likelihood of clinically significant weight loss

Gudzune KA et al. *Prev Med*. 2014;62:103-107

36

STOP Obesity Alliance Toolkit



Obesity presently addressed in a minority of eligible encounters

Effectively addressing obesity with the 6 As:

- Ask
- Assess
- Advise
- Agree
- Assist
- Arrange

37

Stage 2: Addressing Metabolic Risk Factors and Moderate to High-risk CKD

Stage 2

STAGE 2

Hypertension
- BP control reduces risk for multiple CVD outcomes; goal of <130/80 mmHg
- Pharmacotherapy for those with diabetes, CKD, age ≥65 y or ≥10% CVD risk; ACEi/ARB if CKD or diabetes with albuminuria

Hypertriglyceridemia
- Initial focus on lifestyle changes and addressing secondary causes; use statins if intermediate or higher ASCVD risk
- In those with diabetes + risk factors + triglycerides ≥135 mg/dL, icosapent ethyl lowers CVD risk

MetS
- Lifestyle changes/weight loss improve MetS components and other pathophysiologic features
- Lifestyle changes accompanied by targeted pharmacotherapy for risk factor control lowers CVD event rates

Diabetes
- Statins lower CVD event rates; ezetimibe helps achieve 50% LDL-C reduction and further lowers ASCVD risk
- SGLT2i decrease adverse kidney events, HF events, and MACE/CVD mortality
- GLP-1RA reduce weight, glycemia, MACE, and CVD mortality
- Metformin in concert with SGLT2i useful for achieving glycemic targets if HbA1c ≥7.5%

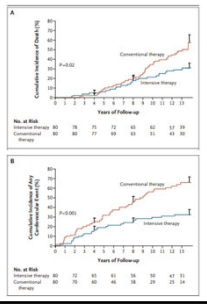
CKD
- ACEi/ARB in albuminuric CKD decrease adverse kidney and CVD events
- SGLT2i in CKD with eGFR >20 mL/min/1.73 m^2 decrease adverse kidney and CVD events
- Finerenone in CKD with diabetes with eGFR >25 mL/min/1.73 m^2 reduces adverse kidney and CVD events

Priorities:
- Risk factor control with lifestyle change + targeted pharmacotherapy
- Utilization of novel therapies targeting multiple axes of CKM health

38

Risk Reduction with Lifestyle Change Plus Pharmacotherapy

- STENO-2 trial: 160 patients with overweight/obesity, type 2 diabetes and albuminuria
- Usual care vs lifestyle change + pharmacologic therapy to reach glycemic, lipid and BP goals
  - HR for mortality 0.54 (95% CI: 0.32-0.89)
  - HR for CVD 0.41 (95% CI: 0.25-0.67)

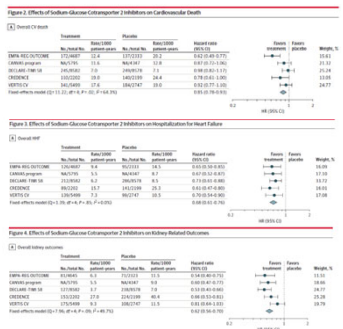


Gaede P et al. *N Engl J Med*. 2008; 358:580-591

39

CKM Therapies: SGLT2 Inhibitors

- Modest glycemic benefits
- Decreased MACE and CVD mortality
- Reduced HF hospitalizations
- Decreased kidney events

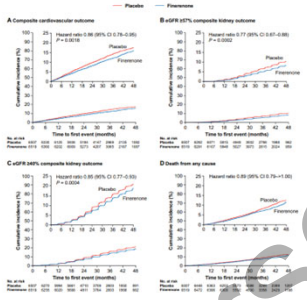


Mcguire DK et al. *JAMA Cardiol.* 2021;6(2):148-158.

40

CKM Therapies: Finerenone (Non-steroidal MRA)

- Reduced adverse kidney events in those with diabetes
- Reduced CVD event rate (heart failure) largely driven by protection against kidney function decline
- Finerenone reduces HF events in HFpEF/ HFmrEF

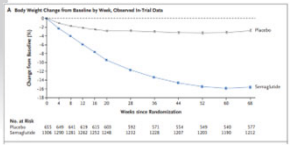


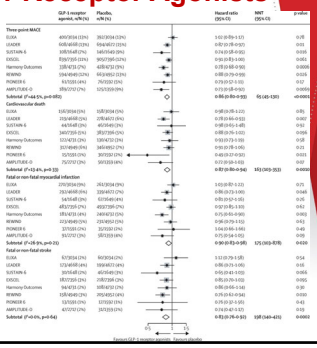
Agarwal R et al. *Eur Heart J.* 2022;43(6):474-484; Solomon SD et al. *N Engl J Med.* 2024;391:1475-1485

41

CKM Therapies: GLP-1 Receptor Agonists

- Marked weight loss (>15%)
- Improved glycemic control and metabolic risk factors
- Reduced MACE/CVD Mortality



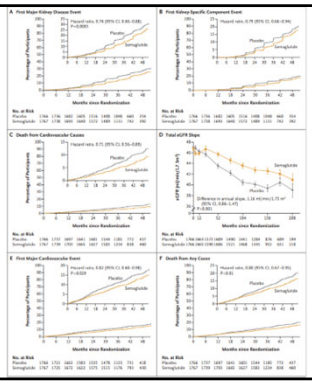


Wilding J et al. *N Engl J Med 2021.* 384:989-1002
Sattar N et al. *Lancet Diabetes Endocrinol.* 2021;9(10):653-662.

42

Kidney Benefits of GLP-1RA therapy
FLOW Trial

- In patients with diabetes and CKD, semaglutide 1.0 mg reduced
  - Adverse kidney events
  - MACE
  - CVD mortality
  - All-cause mortality

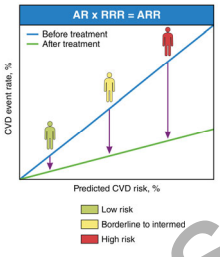


Perkovic et al. *NEJM*. 2024

43

Predicted Risk and CKM Therapies?
Considering Absolute Risk Reduction

- For a therapy with a given relative risk reduction, those with higher baseline risk will experience greater absolute risk reduction (ARR)
- Prioritizing therapy for those expected to have higher ARR associated with high clinical utility (lower number needed to treat) and greater cost effectiveness



AR = absolute risk
ARR = absolute risk reduction
RRR = relative risk reduction

Khan et al. Circulation. 2023 Dec 12;148(24):1982-2004.

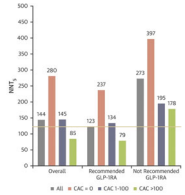
44

Stage 3: Addressing Subclinical CVD and Risk Equivalents

Stage 3

STAGE 3
Subclinical ASCVD
- Presence of CAC favors statin therapy in those with borderline-intermediate ASCVD risk
- CAC score ≥100 indicates greater net benefit from aspirin and other preventive therapies

Subclinical HF
- In asymptomatic LV systolic dysfunction, ACEi and β-blockers associated with less HF/CVD mortality
- In diabetes, SGLT2i decrease the risk for incident HF



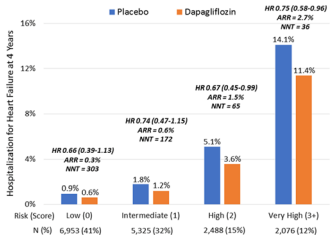
Greater absolute risk reduction for therapies:

Estimated number needed to treat with GLP-1 lower with higher CAC

Cainzos-Achirica M et al. *JACC Cardiovasc Imaging*. 2021;14(7):1470-1472.

45

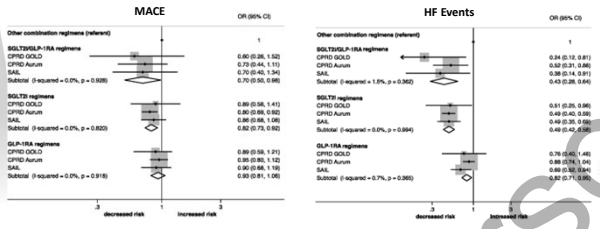
Predicted Absolute Risk May Help to Optimize Targeting of Cardioprotective Therapy in Diabetes



Berg et al. Circulation. 2019;140(19):1569-1577

46

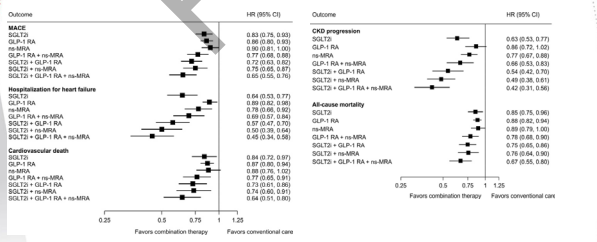
Observational Data: Combination SGLT2i + GLP-1RA Potentially Linked to Lower Risk



Wright AK et al. *Diabetes Care*. 2022;45(4):909-918.

47

Estimated Long-term Risk Reduction with SGLT2i + GLP-1RA + Finerenone



Clinical benefits of combination therapy must be balanced against costs and challenges related to polypharmacy; likely prioritized for those who are at higher absolute risk (e.g. stage 3)

Neuen BL et al. *Circulation*. 2024;149(6):450-462.

48

Stage 4: Address CKM Risk in Patients with CVD

Stage 4

STAGE 4
- All ASCVD: Aspirin or P2Y12S + high-intensity statin indicated to reduce ASCVD events; use of additional LDL-C-lowering agents based on the presence of high risk ASCVD and LDL-C thresholds.
- All HF: 4 pillars of GDMT (β-blockers, ARNi, MRAs, SGLT2i) to improve HF outcomes/mortality, particularly for HFrEF

Obesity and CVD
- Nonjudgmental approach to weight loss discussion improves effectiveness
- Exercise training in obesity and HFpEF improves functional status
- Integrated weight management teams facilitate patient-centered approach
- Incretin analogues induce >15% weight loss, improve QOL, and reduce recurrent CVD events
- Bariatric surgery reduces recurrent CVD events and mortality

Hypertriglyceridemia and CVD
- Statin therapy modestly reduces triglycerides (10%–30%) and lowers ASCVD risk
- Icosapent ethyl reduces CVD events and mortality

Hypertension and CVD
- BP control reduces recurrent CVD events and mortality; goal <130/80 mmHg
- ACEi/ARB in CVD with CKD or diabetes; in African American patients with HFrEF, hydralazine/isosorbide after 4 pillars of GDMT

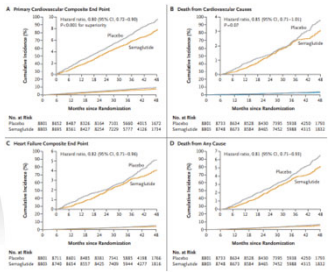
Diabetes and CVD
- Lifestyle modification improves control of glycemia/risk factors and QOL
- In HF, SGLT2i improve QOL, reduce HF hospitalizations, and reduce mortality risk
- In ASCVD, SGLT2i reduce MACE and HF hospitalizations
- In ASCVD, GLP-1RA reduce weight, glycemia, and MACE

CKD and CVD
- Statin continuation recommended for reducing recurrent ASCVD events
- ACEi/ARB reduce adverse kidney events and reduce morbidity and mortality rates in CVD
- SGLT2i in CKD with eGFR >20 mL/min/1.73 m^2 reduce adverse kidney events, HF hospitalizations, MACE, and CVD mortality
- Finerenone in CKD with diabetes with eGFR >25 mL/min/1.73 m^2 reduces adverse kidney events and CVD events
- ARNi reduces adverse kidney events, HF hospitalizations, and CV death in HF

Priority:
- Addressing CKM Risk Factors (obesity, diabetes, CKD) in those with existing CVD

49

Stage 4: Addressing CKM Risk in Patients with CVD - SELECT Trial



In patients with overweight/obesity and ASCVD but no diabetes, semaglutide (vs placebo) resulted in:

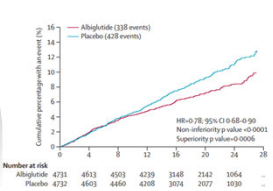
20% reduction in major adverse CV events

Lincoff AM et al. N Engl J Med 2023; 389:2221-2232

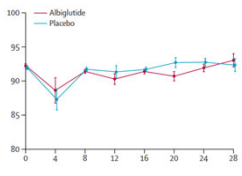
50

Weight Independent Effects of Incretin Analogues on CVD: Harmony Outcomes *(albiglutide)*

Composite CVD Outcome



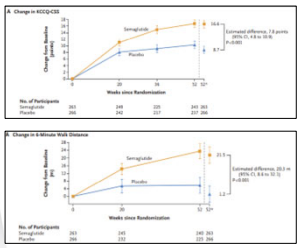
Weight



Hernandez et al. Lancet. 2018;392(10157):1519-1529

51

Obesity a Target in HFpEF: STEP-HFpEF



In 529 HFpEF patients with obesity, semaglutide (vs placebo) resulted in:

- Improved QOL (KCCQ-CSS) and functional capacity (6 minute walk distance)
- Reductions in hsCRP
- **Reductions in NT-proBNP and some echocardiographic improvements**

Exploratory end points assessed in the overall population			
Percentage reduction from baseline to week 52 in NT-proBNP level	−20.9	−5.3	0.84 (0.71 to 0.98)‡§

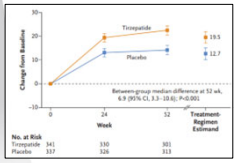
Kosiborod MN et al. N Engl J Med 2023;389:1069-84

52

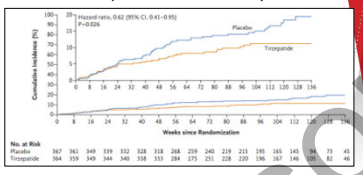
SUMMIT Trial (Tirzepatide)

In 731 patients with HFpEF and obesity, tirzepatide (vs placebo) resulted in:

Change in KCCQ Score (6.9 difference between groups)



Primary Endpoint: CVD Death or Worsening HF Event (38% Relative Risk Reduction)

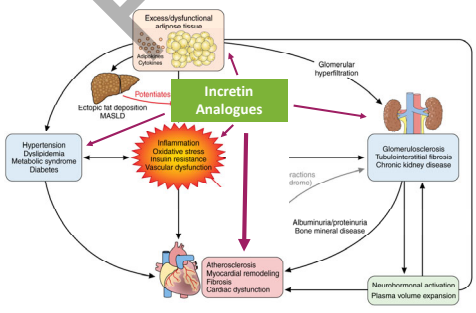


- Further demonstration of favorable cardiac remodeling by cardiac magnetic resonance imaging in patients with obesity and established HFpEF

Packer et al. N Engl J Med 2025;392:427-437

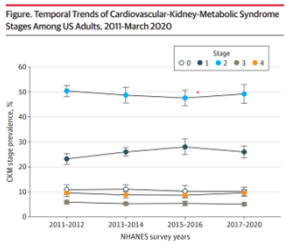
53

Impacting Multi-Morbidity in CKM Syndrome



54

The Epidemiology of CKM Syndrome

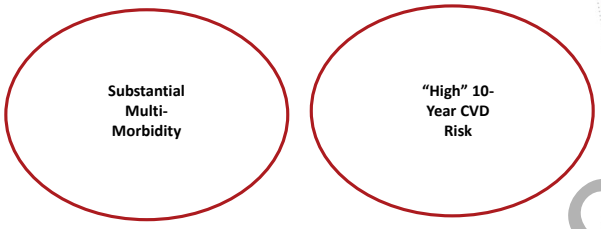


- Among US Adults, 90% in CKM Syndrome Stages 1 through 4
- Most have some indication for incretin therapy (excess weight, diabetes, +/- CKD, concomitant ASCVD or heart failure)
- **How to prioritize utilization?**

Aggarwal et al. JAMA. 2024;331(21):1858-1860.

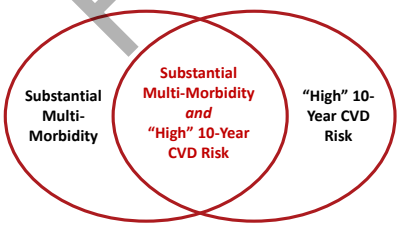
55

Potential Approaches for Prioritizing Incretin Pharmacotherapy



56

But What About Where They Don't Overlap?



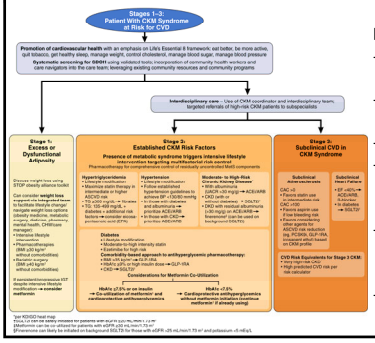
Younger adults with adverse CKM risk profile and high 30-year but low 10-year CVD risk

Older adults with isolated CKM risk factor or persons with mostly non-CKM risk factors (smoking, pure hypercholesterolemia)

Key questions to study and contend with moving forward

57

Algorithm for CKM Syndrome Management Stages 1-3

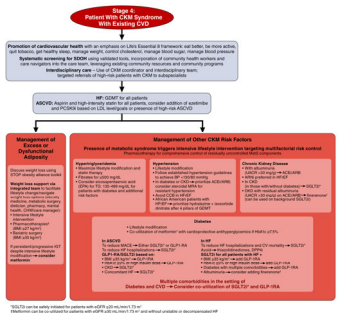


Key Highlights

- Interdisciplinary care for confluent risk; address SDOH
- Address obesity through multiple modalities
- Address/control CKM risk factors
- Comorbidity-based approach to selecting cardioprotective anti-hyperglycemic agents
- Prevent CKD progression with RAASi/SGLT2i and/or finerenone/GLP-1RA (in diabetes)
- More intensive and combination therapy in higher risk

58

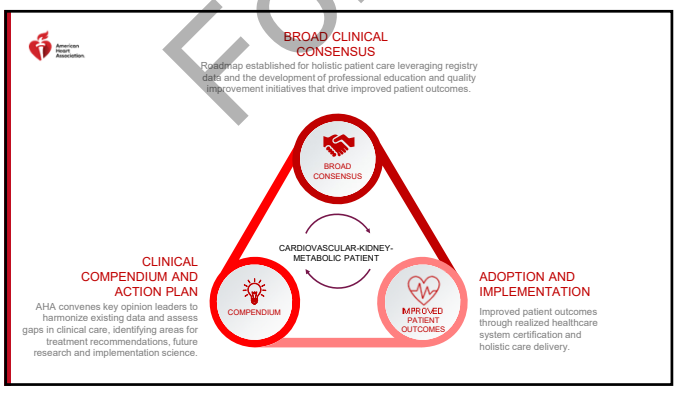
CKM Syndrome Management Stage 4



Key Highlights

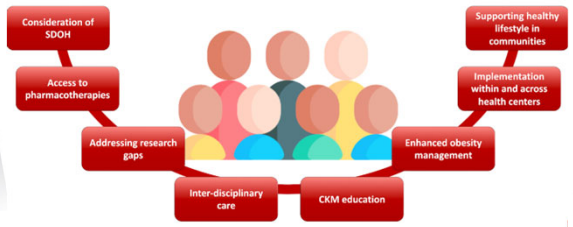
- Support interdisciplinary care and address SDOH
- Address obesity and CVD with integrated teams; consider obesity pharmacotherapy
- Address/control CKM risk factors
- Cardioprotective anti-hyperglycemic agent in all with CVD plus diabetes; combination therapy for very high risk/ multiple comorbidities
- Prevent CKD progression with RAASi/SGLT2i and/or finerenone/ GLP-1RA (in diabetes)

59



60

Patient-Centered Implementation Focus



61

Cardiovascular-Kidney-Metabolic Syndrome Call to Action

Access to Pharmacotherapies

- Utilization of pharmacists and social workers on the interdisciplinary CKM team to facilitate access
- Advocacy for policy level changes to ensure access
- Incorporate representation of health systems, payors, patients, and caregivers into policy change advocacy measures

Ndumele, C.E. et al., A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic Syndrome: A Scientific Statement From the American Heart Association. 2023. Circulation

62

Cardiovascular-Kidney-Metabolic Syndrome Call to Action

Implementation Within and Across Health Centers

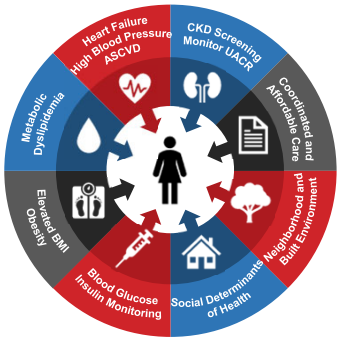
- CKM Implementation Project Across 150 Health Centers over 4 years
- Informed by the AHA's CKMH initiative, validated CKMH measures and center-specific performance across registry-based data
- AHA CKMH certification program, allowing for the designation of an AHA Center for CKMH Excellence for institutions that meet criteria for optimal implementation
- CKMH certification could activate implementation of key CKMH quality improvement metrics and hospital certification programs not only across GWTG hospitals in the US, but also in 13 other countries globally where the AHA is currently engaged

Ndumele, C.E. et al., A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic Syndrome: A Scientific Statement From the American Heart Association. 2023. Circulation

63

Cardiovascular-Kidney-Metabolic Syndrome

Patient-Centered Implementation Focus



Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; BMI, body mass index; CKD, chronic kidney disease; and UACR, urine albumin-creatinine ratio.

American Heart Association.

Ndumele, C.E. et al., A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic Syndrome: A Scientific Statement From the American Heart Association. 2023. Circulation

64

Case: A Confluence of Risk

- **History:** 54-year-old woman with a history of obesity, hypertension and diabetes, coming to clinic to establish care after death of family member. Self-care and healthy lifestyle challenging as a single mother working both full and part time jobs. Smokes cigarettes to alleviate stress.
- **Meds:** Amlodipine, HCTZ, Metformin
- **Exam:** BP 144/92, BMI 38 kg/m^2, waist circumference 106 cm, JVP wnl, clear lungs, CV RRR s1s2 +s4, abdomen protuberant, extremities warm with trace edema
- **Labs:** A1c 9.2%, eGFR 55 nl/min/1.73 m^2, UACR 93 mg/g, Total chol 225 mg/dl, LDL 163 mg/dl, triglycerides 180 mg/dl, HDL-C 36 mg/dl

- ***10y CVD risk 31% (CKM Stage 3)***
- ***SDOH screening and CHW/social work support***
- ***Interdisciplinary teams and help with navigation***
- ***RAASi for HTN with CKD/albuminuria***
- ***Cardioprotective anti-hyperglycemic (likely GLP-1RA 1st)***
- ***Statin for DM and high global risk***

65

Summary

- CKM health reflects interplay of metabolic risk factors, CKD and the cardiovascular system
- CKM syndrome is highly prevalent, with disproportionate burden in those with adverse SDOH, and a key predictor of premature mortality
- Fragmented care further impacts clinical outcomes in CKM syndrome
- Steps taken with CKMH initiative:
  - Definitions
  - Staging and screening to promote prevention across the life course
  - Updated AHA prediction model reflecting needs related to CKM syndrome
  - Overarching considerations of SDOH and interdisciplinary care
  - Strategies for CVD prevention and management, linked to CKM staging, reflecting harmonization across major guidelines and emerging scientific evidence
  - Framework for optimizing CKM health in the overall population

American Heart Association.

Ndumele, C.E. et al., A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic Syndrome: A Scientific Statement From the American Heart Association. 2023. Circulation

66

67