Management of CKM Syndrome: Integrated Multidisciplinary Approach

Amanda K. Kitten, PharmD, MSc, BCPS

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CKM: Cardiovascular-kidney-metabolic

Objectives

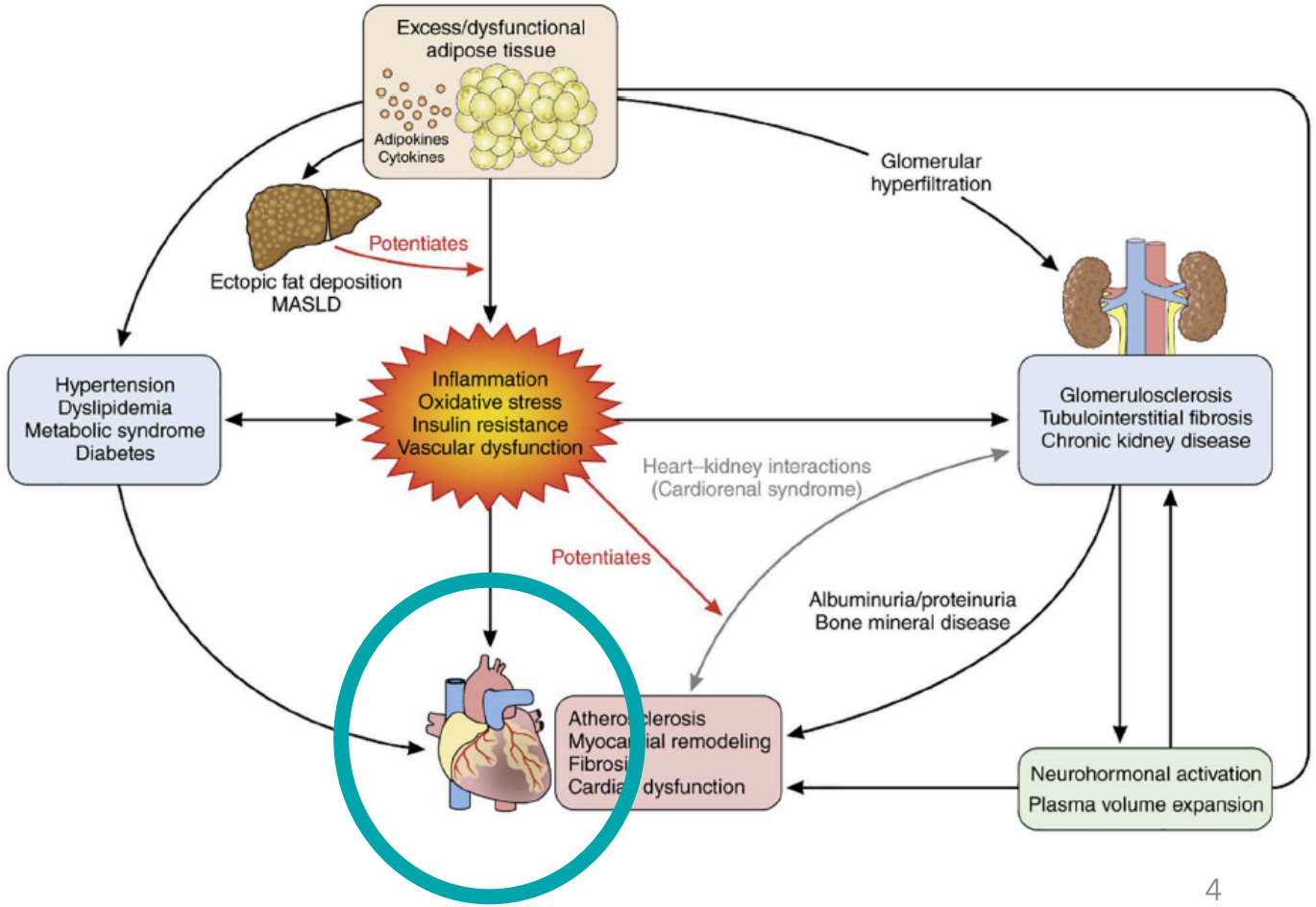
- Determine the role of pharmacists in the management of cardiovascular-kidney-metabolic syndrome
- Discuss strategies to incorporate pharmacists into the management of cardiovascular-kidney-metabolic syndrome

Abbreviations

ACEi	Angiotensin-converting enzyme inhibitor
ARB	Angiotensin II receptor blocker
ARNI	Angiotensin II receptor blocker/neprilysin inhibitor
ASCVD	Atherosclerotic cardiovascular disease
CAC	Coronary artery calcium
CKM	Cardiovascular-kidney-metabolic
CVD	Cardiovascular disease
DM	Diabetes mellitus
GDMT	Guideline-directed medical treatment
GLP1RA	Glucagon-like peptide 1 receptor agonist
HF	Heart failure
HTG	Hypertriglyceridemia
HTN	Hypertension
LDL-C	Low-density lipoprotein cholesterol
MAP	Medication assistance program
MetS	Metabolic syndrome
MRA	Mineralocorticoid receptor agonist
SGLT2i	Sodium-glucose cotransporter 2 inhibitor

Introduction to CKM Syndrome

- **Definition**: a systemic disorder distinguished by dysregulation of three connected systems: metabolic, kidney, and cardiovascular



Circulation 2023.148:1636-1664.

Evidence-based Benefits of Multidisciplinary Approach

- Comprehensive Care
- Improved Patient Outcomes
- Cost-effectiveness

Kidney News Online. 15;12:1-6.

Importance of a Multidisciplinary Approach

- Prevention of gaps in care
- Value-based approach

Circulation. 2023;148:1606–1635

Healthcare Providers Involved in the Interdisciplinary Team

- Primary care providers
- Cardiologists
- Nephrologists
- Endocrinologists
- **Pharmacists**
- Nurses
- Care navigators
- Social Workers
- Community health workers

Review of Evidence for CKM Stages

CKM Stage	Evidence
0	• Maintain CVH • Avoid weight gain with aging
1	• 5-10% OR ≥10% weight loss • Incretin analogues for >15% weight loss, improvement in metabolic factors
2	• HTN: BP control (<130/80 mmHg), pharmacotherapy for those with diabetes, CKD, age ≥65 years or ≥10% CVD risk; ACEi/ARB if CKD or diabetes with albuminuria • HTG: lifestyle and secondary causes; icosapent ethyl • MetS: lifestyle changes/weight loss; targeted pharmacotherapy • DM: statins, ezetimibe for further LDL-C lowering; SGLT2i; GLP-1RA, metformin

3	• <u>Subclinical ASCVD</u>
	  • Presence of CAC → statin therapy if borderline intermediate ASCVD risk
	• <u>Subclinical HF</u>
	  • Asymptomatic LV systolic dysfunction → ACEi and beta-blocker
	  • Diabetes → SGLT2i

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	  • Diabetes → **SGLT2i**

Review of Evidence for CKM Stages

CKM Stage	Evidence
4	• All ASCVD: aspirin or P2Y12i + high-intensity statin • All HF: 4 pillars of GDMT (beta-blocker, ARNI, MRA, SGLT2i) • Obesity: Weight loss, exercise, weight-management teams, incretin analogues for >15% weight loss, bariatric surgery • HTG and CVD: statin therapy, icosapent ethyl • HTN and CVD: goal BP <130/80, ACEi/ARB in CVD with CKD or diabetes; in African American patients with HFrEF, hydralazine/isosorbide dinitrate after 4 pillars of GDMT • DM and CVD: lifestyle modification, SGLT2i in HF and ASCVD, GLP-1RA in ASCVD • CKD and CVD: statin continuation, ACEi/ARB, SGLT2i in eGFR >20mL/min/1.73m^2, finerenone in CKD with DM and eGFR>25mL/min/1.73m^2, ARNI in HF

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Role of the Pharmacist in CKM Management

MEDICATION MANAGEMENT

PATIENT EDUCATION/ COUNSELING

PROTOCOL DEVELOPMENT

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Medication Management

1. Medication initiation
   - Based on CKM stage
2. Dose titration
   - Medication effect
   - Goal dose for HF GDMT
3. Medication access
   - SDOH

Medication Access

Medication class	Generic availability	Cost
ACEi/ARB	Multiple	$
Statins	Multiple	$
Metformin	Yes	$
Beta-blockers	Multiple	$
Ezetimibe	Yes	$$
P2Y12i	Clopidogrel, prasugrel	$-$$$
Icosapent ethyl	Yes	$$$
GLP1RA	Liraglutide	$$$$
GLP1/GIP-RA	None	$$$$
SGLT2i	Dapagliflozin	$$$$
Finerenone	None	$$$$

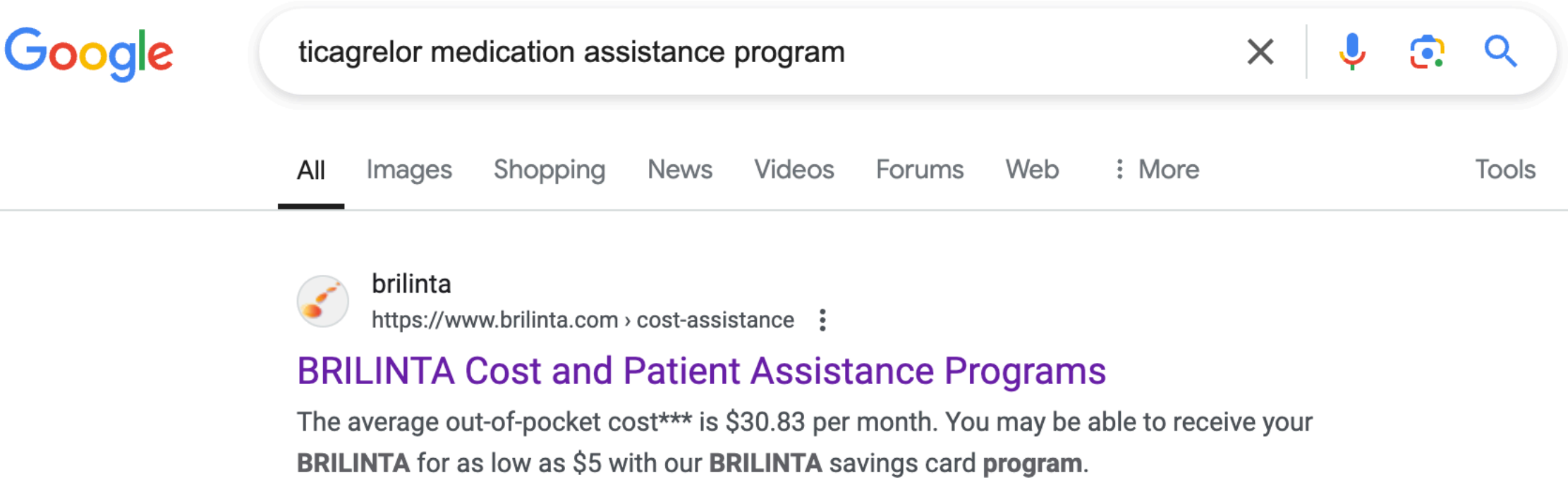
Monthly cost in dollars: $ <10, $$ 10-50, $$$ 50-300, $$$$ >300

Medication Access: MAP

Medication class	Generic availability	Cost	MAP
P2Y12i	Clopidogrel, prasugrel	$-$$$	Ticagrelor
Icosapent ethyl	Yes	$$$	Yes
GLP1RA	Liraglutide	$$$$	Exenatide, liraglutide, lixisenatide, semaglutide, dulaglutide
GLP1/GIP-RA	None	$$$$	Tirzepatide
SGLT2i	Dapagliflozin	$$$$	Dapagliflozin, empagliflozin, canagliflozin
Finerenone	None	$$$$	Yes

Monthly cost in dollars: $ <10, $$ 10-50, $$$ 50-300, $$$$ >300. MAP: medication assistance program

Medication Access: MAP



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PROTOCOL DEVELOPMENT

Patient Education & Counseling

- Medication rationale
- CKM syndrome
- Lifestyle modifications

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Protocol Development

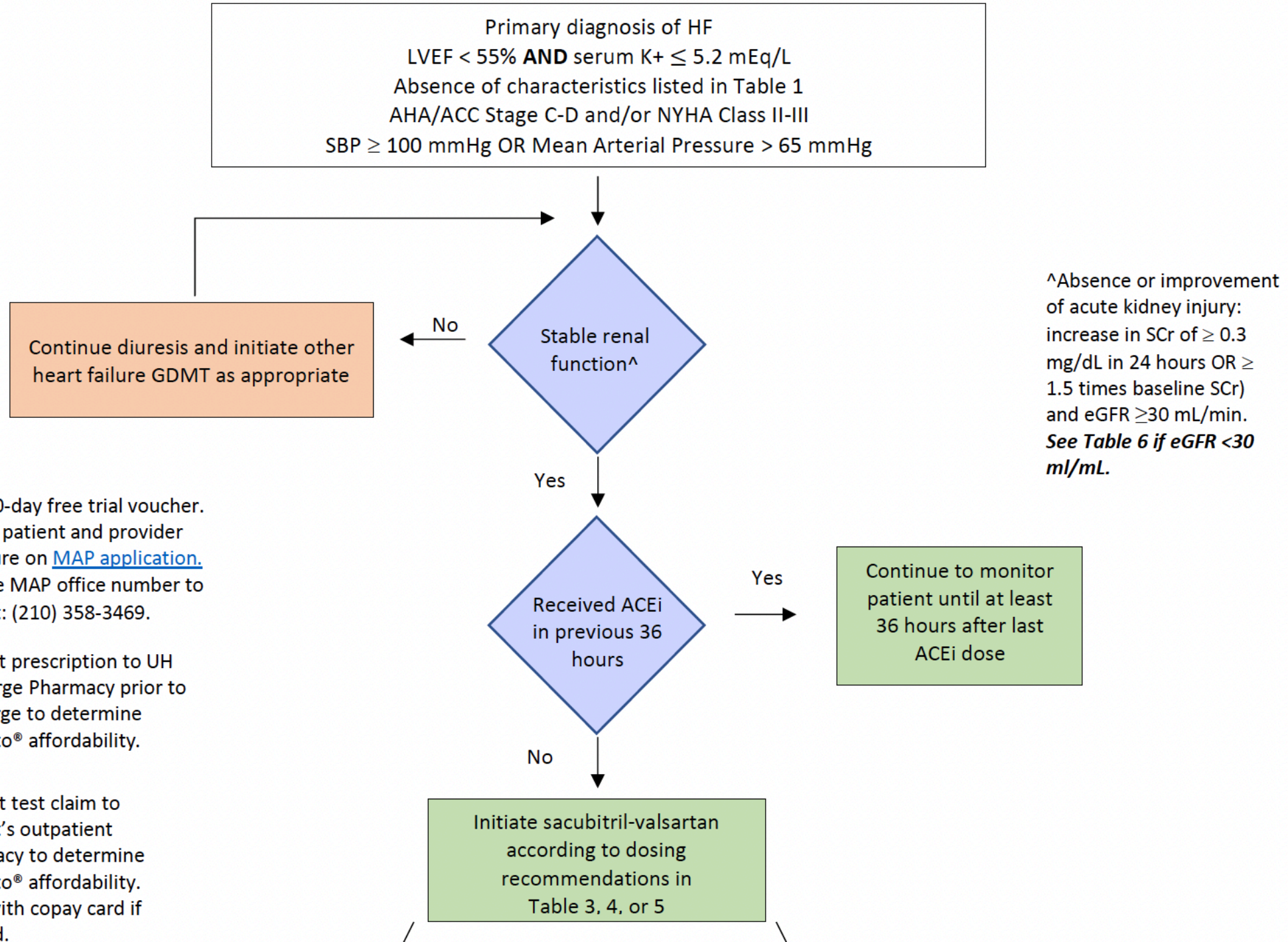
- Algorithms to aid in identifying which patients will benefit most from specific GDMT
- May include dosing
- May include steps to improve medication access

Protocol Development Example

University Health System

Sacubitril-Valsartan (Entresto®) Algorithm for Inpatient and Outpatient Use in Adults

Purpose: To provide guidance for initiation and continuation of sacubitril-valsartan (Entresto®) in adults for the treatment of heart failure (HF). This includes criteria for use, insurance coverage, dosing and monitoring parameters.



^Absence or improvement of acute kidney injury: increase in SCr of ≥ 0.3 mg/dL in 24 hours OR ≥ 1.5 times baseline SCr) and eGFR ≥30 mL/min. ***See Table 6 if eGFR <30 ml/mL.***

[1]Use 30-day free trial voucher. Obtain patient and provider signature on MAP application. Provide MAP office number to patient: (210) 358-3469.

[2]Submit prescription to UH Discharge Pharmacy prior to discharge to determine Entresto® affordability.

[3]Submit test claim to patient's outpatient pharmacy to determine Entresto® affordability. Send with copay card if needed.

Cardiometabolic Center of Excellence:

A Novel Care Delivery Model for Secondary Prevention of CVD

- *Nurse navigators** cross-trained in management of DM and CVD
- Healthcare providers involved:
  - Certified diabetes educator, dietitian, pharmacist
- Providers utilized evidence- and guideline-based protocols and standardized processes of care

Circ Cardiovasc Qual Outcomes. 2021;14:e007682.

CMC Results

Participants	Intervention	Comparator	Outcomes
• Patients with CVD and type 2 DM	Patients followed at the CMC (n=129)	Comparator: matched cohort of patients with CVD and type 2 DM treated in other care settings* (n= 387) Matched using PSM	• GDMT 41.1% vs 2.3% [RR 17.75 (8.94-35.26); p<0.0001] • Weight loss -10.9 vs -1.5 lbs (p<0.001)

*primary care, general cardiology. PSM: propensity-score matching. GDMT: high-intensity statin, antiplatelet or anticoagulant, ACEi/ARB, and either SGLT2i or GLP1RA.

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Comparison of GDMT Therapies at Follow-up

	CMC (n= 129)	Control (n = 387)	RR (CI)	P-value
GDMT	53 (41.1%)	9 (2.3%)	17.75 (8.94–35.26)	<0.0001
SGLT2i/GLP1RA	124 (96.1%)	99 (25.7%)	3.61 (3.03–4.30)	<0.0001
ACEi	39 (30.2%)	35 (9.1%)	2.77 (1.78–4.31)	<0.0001
Statin	111 (86.0%)	299 (77.7%)	1.08 (0.99–1.19)	0.07
High-intensity statin	81 (62.8%)	190 (51.4%)	1.25 (1.07–1.46)	<0.01
ARB	39 (30.2%)	128 (33.2%)	0.95 (0.71–1.28)	0.76

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Strategies to Incorporate Pharmacists

- Collaborative Practice Agreements
- Interdisciplinary Team Meetings
- Pharmacist-Led Clinics
- Telehealth Service

Questions?