Refining Strategies for Enhancing Cardiorenal Outcomes With SGLT2 Inhibitors:

Optimizing the Cardiometabolic Care Mode

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Question & Answer Session

Be sure to submit your questions on the right-hand side of the screen

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Learning Objectives

- Examine the clinical traits of chronic kidney disease (CKD) for prompt diagnosis and treatment initiation
- Assess the real-world implications of recent clinical trial findings on SGLT2 inhibitors for disease progression in a diverse patient population with CKD and/or heart failure (HF)
- Incorporate the ADA-KDIGO consensus recommendations along with other guidelines, such as ESC-HF, ADA, and AHA, in designing treatment protocols for patients suffering from CKD and/or HF, irrespective of their diabetes status
- Develop strategies for using SGLT2 inhibitors in patients with and without diabetes to improve cardiorenal outcomes
- Apply approaches to coordinated interdisciplinary care for patients with cardiorenal metabolic disease

Cardiologist Best Practices in the Management of Cardiometabolic Renal Outcomes

Keith Miller, MD

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Cardiologist Best Practices in the Management of Cardiometabolic Renal Outcomes

- Comprehensive cardiac assessment
- HFrEF evaluation, assessment of risk
- Importance of GDMT (highlighting importance of findings associated with EMPEROR-Reduced
- CV impact of diabetes and CKD (considerations associated with cardioprotective effects of SGLT2)
- Patient education and counseling

PATIENT CASE

68-YEAR-OLD MAN WITH HX OF T2D, HTN, CKD (STAGE 3B), AND HFREF (LVEF: 38%)

Reports with worsening HF and high HbA1c, with SCr 1.8 mg/dL

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Case Description:

- Etiology of HFrEF
  - Valvular heart disease – fix if appropriate
  - Atrial fibrillation – manage
  - CAD – revascularize
  - Other contributors…alcohol, illicit drugs
- GDMT for HFrEF
  - 4 pillars of therapy for HFrEF (all class IA recommended)
- Consider other comorbidities when customizing HF therapy

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Case Description:

- Consider other comorbidities when customizing HF therapy
  - T2D: with or at high risk (>55 y.o. with 2+ RFs) of ASCVD
    - Class Ia indicated for GLP-1 RA, SGLT2i, in addition to ACEI and statin (ADA, AACE, ACC/AHA)
  - HTN: Treat to goal, <130/80 mmHg, regimen including RAS inhibitor
  - CKD 3b: Indicated for RAS inhibitor and SGLT2 inhibitor
    - Further risk stratify CKD with UACR (higher risk of CKD progression with decr eGFR and incr albuminuria)
  - CHF risk: NYHA functional class, recent hospitalization, bedside volume assessment, NT-proBNP
- Indications for SGLT2 inhibitor (he has ALL 4 OF THEM)
  - T2DM
  - Reduction of MACE in T2DM at high risk of ASCVD
  - CKD
  - CHF

SGLT2 Inhibitors:
Not Just Diabetes Drugs Anymore!

		Cardiac/Renal Indication			
Drug	Brand Name	CV risk reduction	Heart Failure		Kidney dz progression
			Reduced EF	Any EF	
Dapagliflozin	Farxiga®	√	√	√	√
Empagliflozin	Jardiance®	√	√	√	√
Canagliflozin	Invokana®	√			√

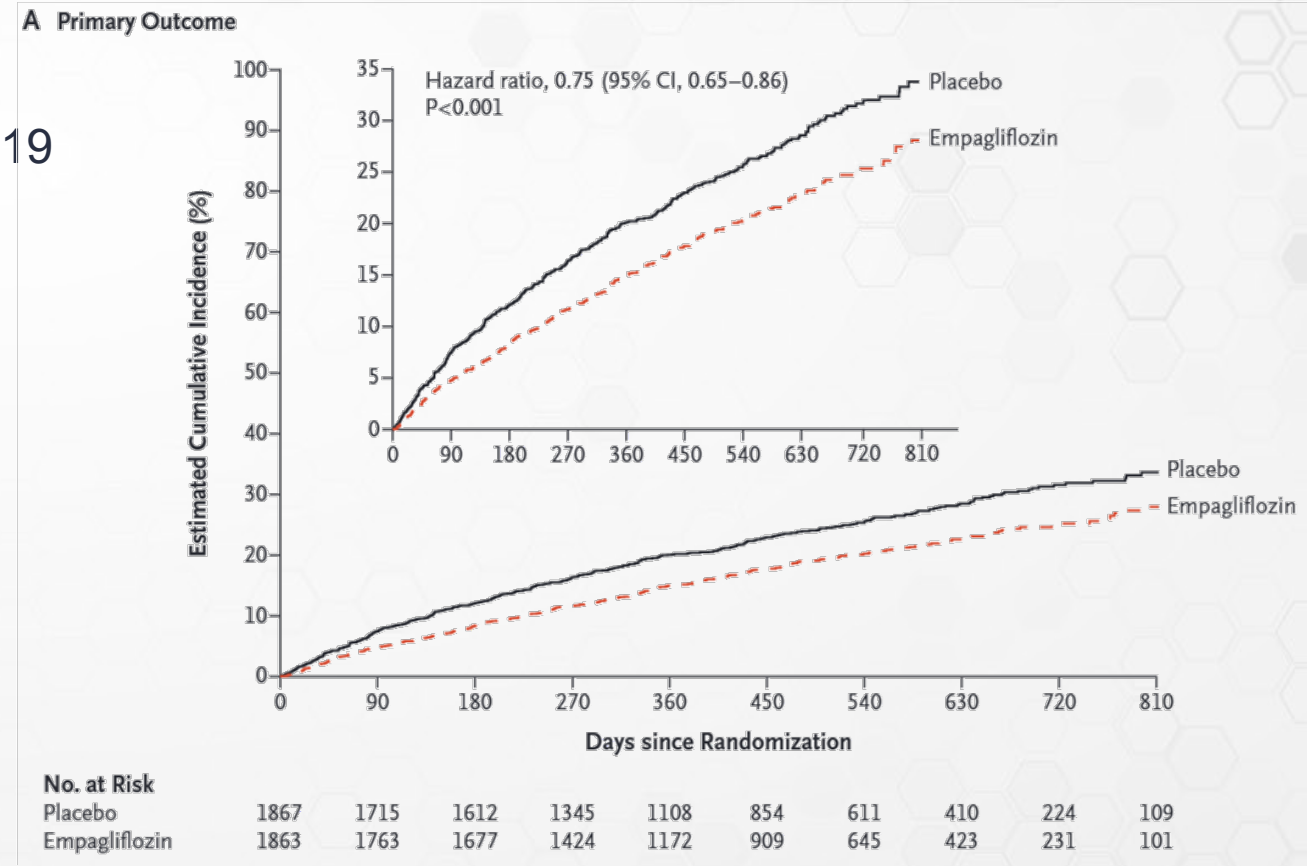
EMPEROR-REDUCED Clinical Trial

- HF with EF ≤ 40% (HFrEF)
- N = 3,730 1:1 empagliflozin vs placebo
- Enrollment: April 2017 through November 2019
- Mean follow-up: 16 months
- **<u>Primary outcome</u>: composite outcome of death from cardiovascular causes or hospitalization for heart failure**
- **Significant reduction in worsening HF events withing 12 days of initation**

25% RRR

5.3% ARR

NNT 19
Median of 16 months



Packer M, et al. *N Engl J Med.* 2020;383(15):1413-1424.

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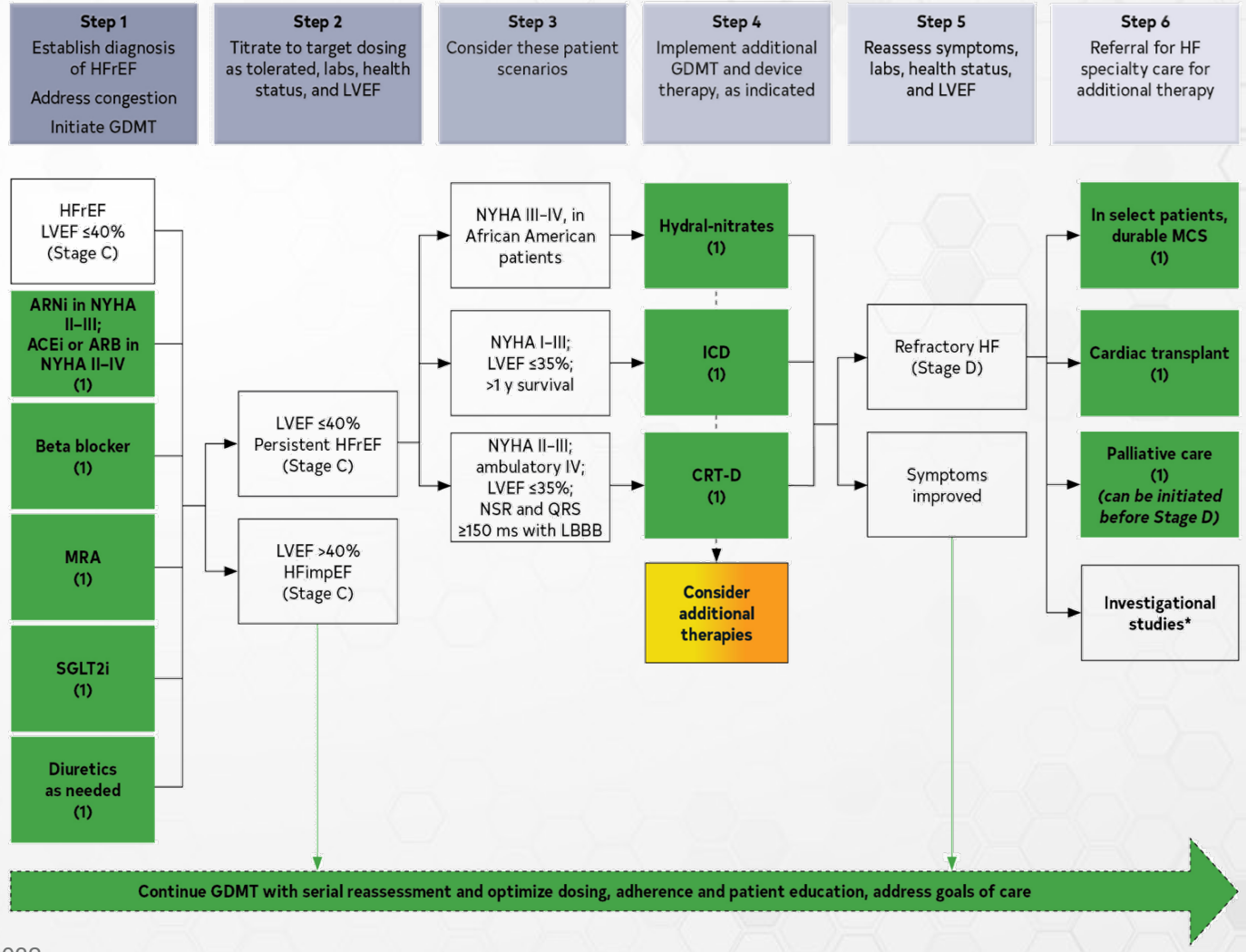
Treatment of HFrEF Stages C and D

Treatment recommendations for patients with HFrEF are displayed. Step 1 medications may be started simultaneously at initial (low) doses recommended for HFrEF. Alternatively, these medications may be started sequentially, with sequence guided by clinical or other factors, without need to achieve target dosing before initiating next medication. Medication doses should be increased to target as tolerated.



Heidenreich PA, et al. *Circulation*. 2022;145(18):e895-e1032.

PATIENT CASE

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Case Description:

- **Individualized** treatment of CHF in setting of multiple comorbidities
  - Beta-blocker
  - If already on RAS inhibitor (ACE or ARB), no immediate change
  - Prioritize **early initiation** of SGLT2 inhibitor:
    - Needs improved A1c (caution if A1c very high because of excess glucosuria)
    - Rapid benefit in HFrEF worsening HF events
    - Additional indications of CKD, ASCVD risk reduction in T2DM
    - Assess volume status, NT-proBNP before initiating and adjust diuretic accordingly
- Close follow-up, monitoring of BG, kidney function, electrolytes
- Attention to BG, adjustment of other T2DM medications
- Consideration of continuous glucose monitor, especially if taking insulin
- Lifestyle counseling
- Titrate GDMT for HFrEF to achieve target doses, switch to sacubitril/valsartan if appropriate

Comprehensive Management of the Patient With Chronic Cardiovascular Disease

Then

- ASCVD?
- CHF (β-blocker, ACE/ARB/ARNI, MRA)
- Lipid management
- Hypertension

Now

- ASCVD?
- CHF (β-blocker, ACE/ARB/ARNI, MRA, **SGLT2i**)
- Lipid management
- Hypertension
- **Type 2 diabetes?**
- **Chronic kidney disease**
  - **eGFR**
  - **UACR**

Nursing Best Practices in the Management of Cardiometabolic Renal Outcomes

Melissa Magwire, RN, MSN, CDE

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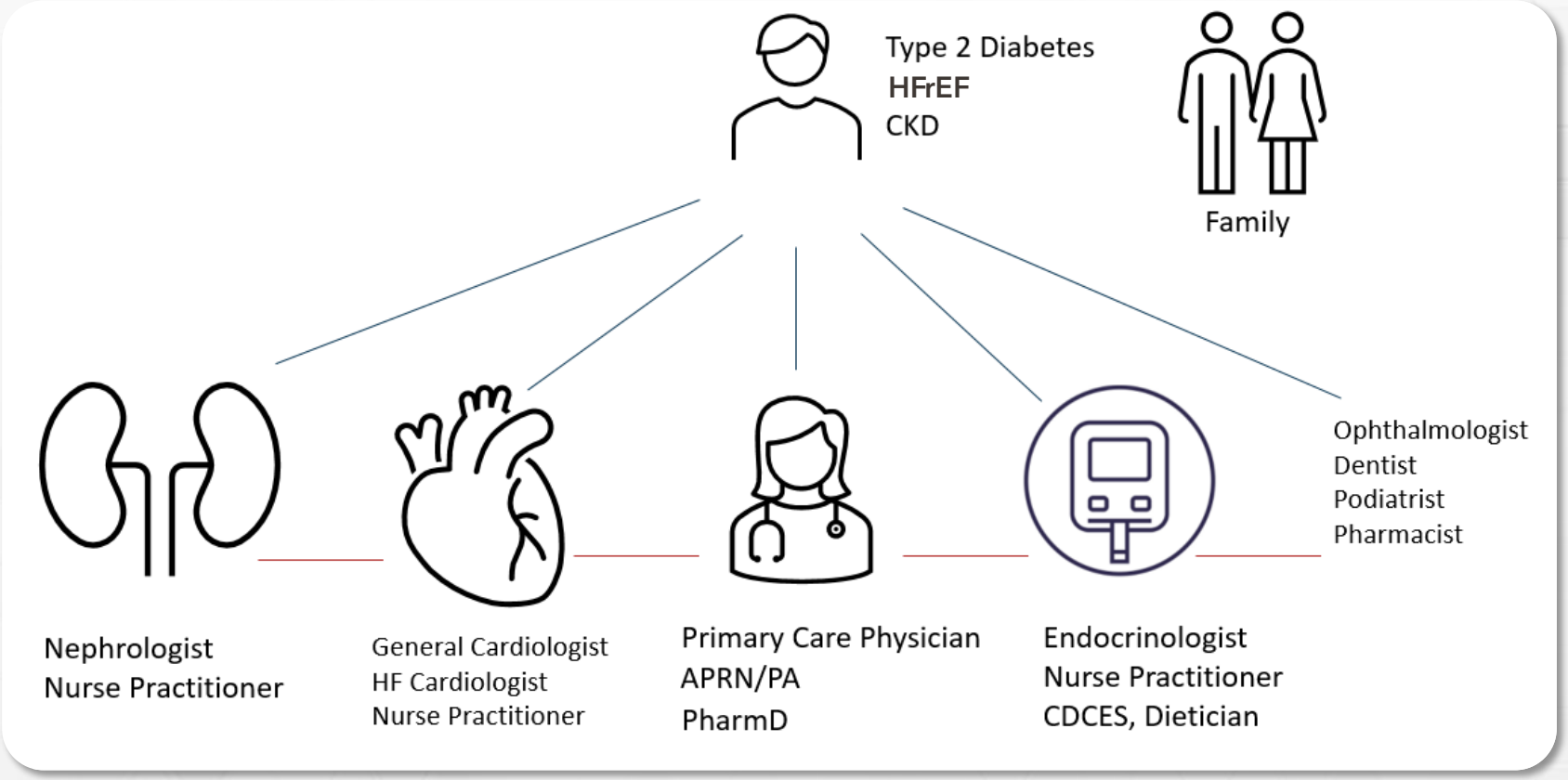
Comorbid Conditions Require a Coordinated Approach

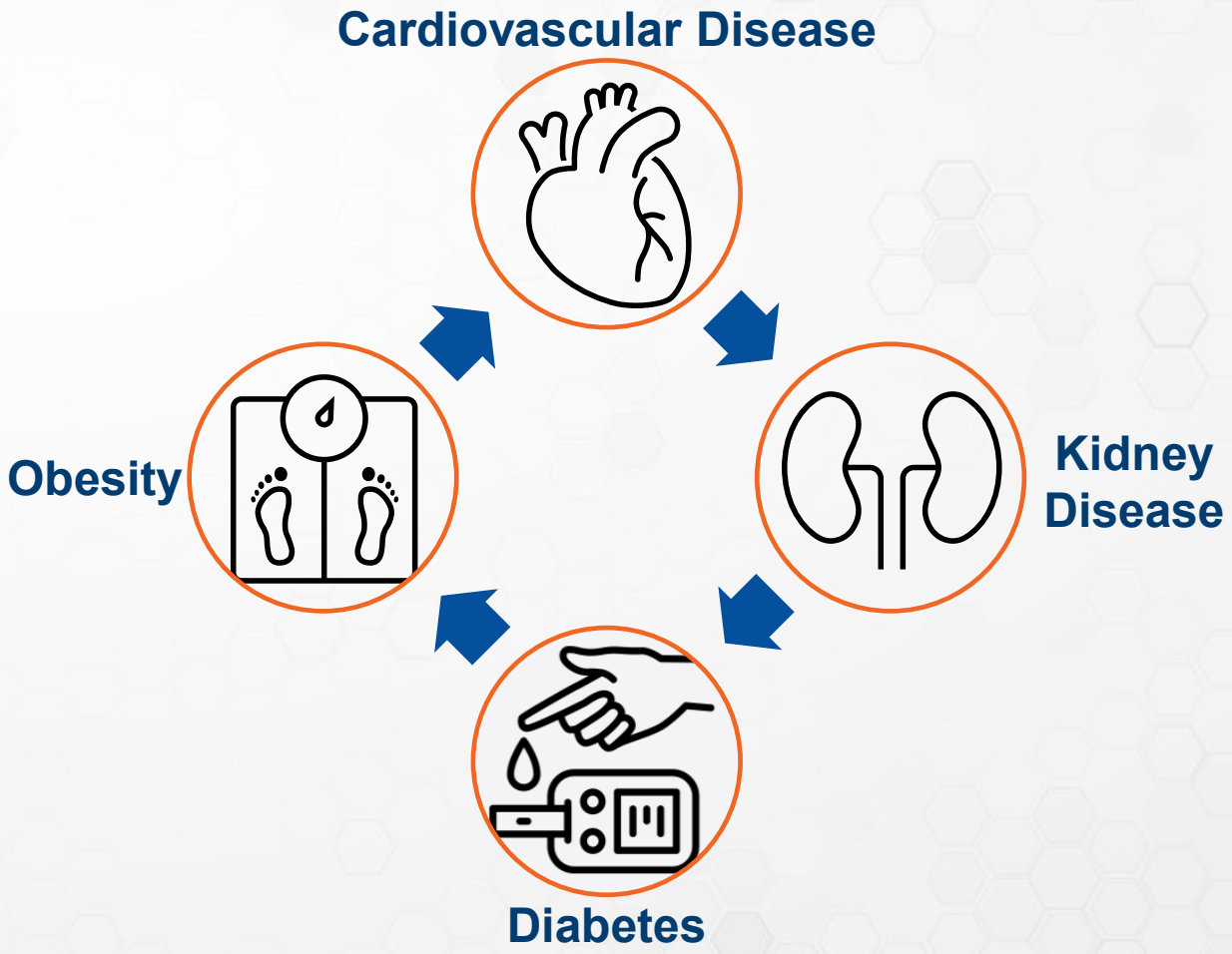


Coordination of care and patient education are key elements needed for successful patient participation in their care plan

Karam M, et al. *Int J Integr Care.* 2021;21(1):16.

Making the CKM Connection for Patients

- Estimated that 1 in 3 US adults has at least 3 risk factors contributing to CMK:
  - Extra body fat, especially around the waist
  - Prediabetes or diabetes
  - High cholesterol
  - High triglycerides
  - High blood pressure
- Having more than one CKM condition puts you at risk for developing others



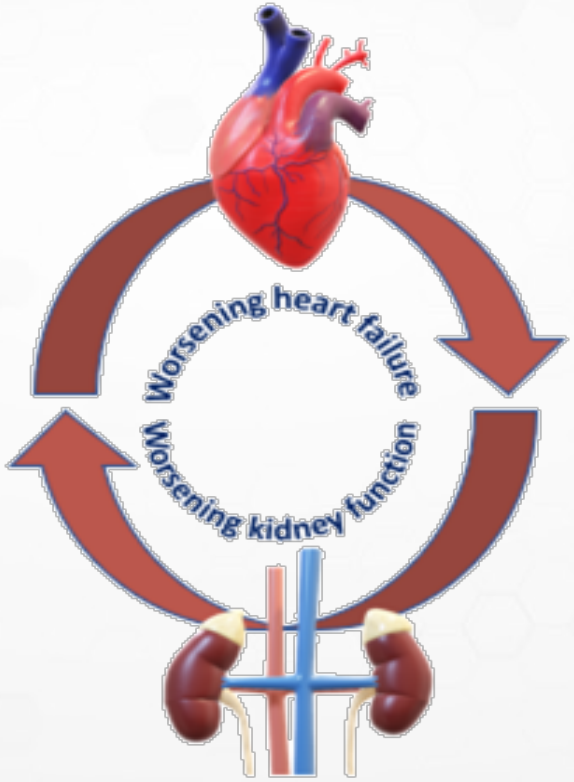
Ndumele CE, et al. *Circulation*. 2023;148(20):1636-1664.

The Heart Kidney Connection…

Heart Failure Education Points

Heart Failure is the term used to describe a heart that can't keep up with the body's needs for oxygen and blood

Ejection Fraction – compares the amount of blood in the heart to the amount of blood the heart pumps out



DKD/CKD Education Points

UACR and eGFR testing is essential
UACR measures kidney damage
eGFR measures kidney function

<u>Reducing Albuminuria Levels to Slow Progression</u>
In patients with CKD who have ≥30 mg/g urinary albumin, a reduction of **30% or greater** in urinary microalbumin is recommended to slow CKD progression (11.6- B)

More than 60% of patients with heart failure have some level of kidney disease

Papademetriou V, et al. *Am J Med*. 2017;130(12):1465.e27-1465.e39. Jankowski J, et al. *Circulation.* 2021;143(11):1157-1172.

Empower Patients to Take an Active Role in Their Health

Get Healthy Sleep: Adults should aim for 7-9 hours of sleep per night

QUIT Tobacco

Manage Blood Pressure: Keep your blood pressure in range – 120/80 is optimal (>130/80 is considered high blood pressure)

Control Cholesterol: Non-HDL and LDL levels are a target for decreasing heart disease risk

Eat Better: Whole foods, fruits and vegetables, lean protein, nuts and seeds

Be More Active: Aim for 150 minutes of moderate or 75 minutes of intense physical activity

Manage Blood Sugar: Monitor HbA1c levels to manage long-term control of glucose

Manage Weight: Achieve and maintain a healthy weight; optimal BMI is between 18.5 to less than 25

Breeman LD, et al. *Heart Lung.* 2024;69:31-39.

Explain the Who, Why, Where, and When of Medications to Ensure Successful Adherence

Who may benefit from taking an SGLT2i?

People with:

- ☐ Type 2 diabetes
- ☐ Heart failure
- ☐ Kidney disease
- ☐ Heart and blood vessel disease (ASCVD)
- ☐ High risk for heart failure or ASCVD

Why should I take my SGLT2i?

To lower risks of heart failure worsening, heart attack, stroke, and dying from heart disease

To reduce the risk of worsening kidney function

To decrease* blood sugar with minimal risk of low blood sugar

Additional benefits

To promote modest weight loss

To help decrease blood pressure

Where does my SGLT2i work?

Kidneys: Works with my kidneys to flush sugar out of my urine* and may improve my heart's ability to pump blood to my body

When should I take my SGLT2i?

Take in the morning with or without food

Don't forget the How…..

Possible side effects and how to prevent them

Infection: Itching, irritation, or discharge in the genital area; may include genital yeast or urinary tract infections

- Usually mild and treatable
- Risk of infection decreases with improved blood glucose levels
- Keep genital area clean and dry

Dehydration: Dizziness, thirst, fast heart rate, lightheadedness (especially standing)

- Stay well hydrated, avoiding alcohol and caffeine
- Use caution when active or in hot weather
- Monitor blood pressure more often

Low blood sugar*: Shakiness, sweatiness, dizziness, fatigue, irritability

- Avoid skipping meals
- Time medications based on meals
- Monitor blood sugar more often
- If needed, discuss changes to other diabetes medication with my doctor

Less common side effects: Ketoacidosis (increased ketones in blood or urine—higher acid levels)

Pharmacy Best Practices in the Management of Cardiometabolic Renal Outcomes

Matt Bullington, PharmD

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SGLT2 Inhibitors

- Bexagliflozin (Brenzavvy)
- Canagliflozin (Invokana)
- Dapagliflozin (Farxiga)
- Empagliflozin (Jardiance)
- Ertugliflozin (Steglatro)

- Lower A1c by 0.4% - 1.16%
- Reduce systolic and diastolic blood pressure by 4 to 6 mmHg and 1 to 2 mmHg, respectively
- Low risk of hypoglycemia as monotherapy; the risk increases when utilized in addition to insulin and/or sulfonylureas
- Low risk for drug-to-drug interactions as a class
  - Potent UGT inducers (rifampin, phenytoin, phenobarbital, and ritonavir) interact with canagliflozin and significantly reduce area under the curve
  - Polypharmacy concerns are related to combined effects with other medications (eg, dehydration when used with diuretics)

SGLT2 Drug Class Overview. *Cardiometabolic Center Alliance.* https://www.cardiometabolicalliance.org/wp-content/uploads/SGLT2i-Drug-Class-Overview.pdf Accessed 19 November 2024.
Preda A, et al. *Cardiovasc Res.* 2024;120(5):443-460.

Renal / Cardiovascular Effects

- Natriuresis
- Glycosuria
- Ketogenesis
- Altered NHE activity
- Reduced plasma uric acid levels

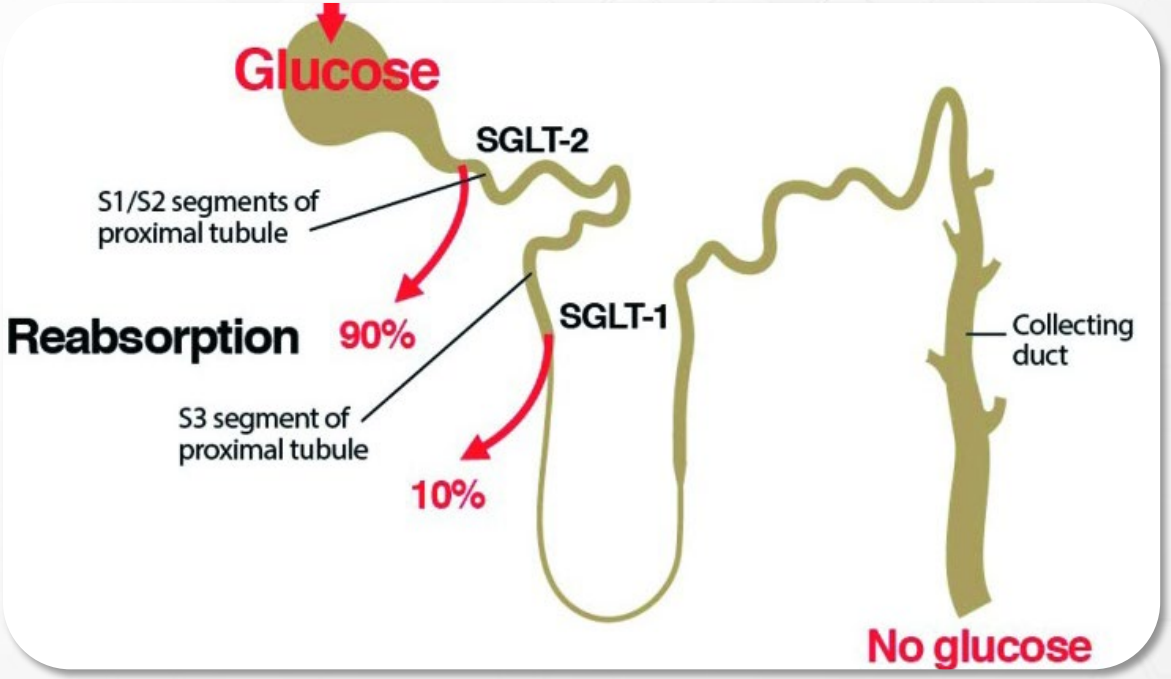

Figure Legend:
Renal glucose handling. In healthy individuals, the vast majority of the glucose filtered by the kidney is reabsorbed by SGLT-2 in the S1 and S2 segments of the proximal convoluted tubule, and the remaining glucose is reabsorbed by SGLT-1 in the S3 segment.[20]

Chao EC. *Clin Diabetes.* 2014;32(1):4-11.

GDMT Optimization

- Optimal guideline-directed medical therapy
  - Type 2 diabetes + CKD
    - SGLT2 inhibitor
    - RAS blockade
    - Nonsteroidal MRA
    - High-intensity statin
  - Heart failure (HFrEF)
  - SGLT2 inhibitor
  - ARNI
  - sMRA
  - Beta-blocker
  - Diuretic
- Clinical trial benefits of GDM
  - Meta-analysis of EMPA-REG OUTCOME, CANVAS Program, and DECLARE-TIMI (SGLT2i)
    - Overall reduction of composite endpoint of worsening renal function, ESRD, or renal death was 45%
  - DAPA-HF – RR reduction of 26% as regards to the primary outcome (composite of CV death, HF hospitalization, and urgent visit for worsening of HF)
  - EMPEROR-Reduced – primary outcome of CV death or HF hospitalization was reduced by 25%

Zinman B, et al. *N Engl J Med.* 2015;373(22):2117-2128. Neal B, et al. *N Engl J Med.* 2017;377(7):644-657. Wiviott SD, et al. *N Engl J Med.* 2019;380(4):347-357. McMurray JJV, et al. *N Engl J Med.* 2019;381(21):1995-2008. Packer M, et al. *N Engl J Med.* 2020;383(15):1413-1424.
Care Coordination. Agency for Healthcare Research and Quality. https://www.ahrq.gov/ncepcr/care/coordination.html

APP Best Practices in the Management of Cardiometabolic Renal Outcomes

Dawn Denicola, NP

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Review of History and Ongoing assessment

APP performs ongoing assessment, understanding level of patient insight into their illness

Complementing the cardiologist

- Review history (HF, DM, CKD)
- Most recent lab and testing
- Review SDOH

Care Coordination. Agency for Healthcare Research and Quality. https://www.ahrq.gov/ncepcr/care/coordination.html

Heart Failure Status

- Evaluate stage and assess class
- Worsening? Medications, treatments beyond GDMT?
- Advanced therapies (MCS, transplant), palliative cardiology vs hospice

Congestive Heart Failure Stages

Stage	Severity	Definition
Stage A	At Risk	At risk of heart failure but with no structural disease or symptoms of heart failure
Stage B	Pre-HF	Structural heart disease is present but without symptoms of heart failure
Stage C	HF	Structural heart disease and symptoms of heart failure present
Stage D	Advanced HF	Severe refractory heart failure

Congestive Heart Failure Symptoms

NYHA Class	Symptoms
Class I	No symptoms and can perform ordinary physical activity without limitations
Class II	Mild symptoms and slight limitation of physical activity; No symptoms at rest
Class III	Marked limitation of physical activity (even with less than ordinary activity) due to symptoms; Comfortable at rest
Class IV	Unable to carry out any physical activity; Severe limitations; Symptoms present even at rest

Education and Lifestyle

- SGLT2i education
- Lifestyle modification
- Plan for follow-up, management, and medication adjustment

Expert Panel Discussion: Pulling It All Together

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Live Q & A