CKD TREATMENT UPDATE

NDAFP BIG SKY MEETING

JANUARY 2026

CLARE HAWKINS MD FAAFP

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OBJECTIVES

- Family Physicians will categorize patients according to risk for dialysis using several measures of eGFR as well as proteinuria with uACR.
- Family Physicians will have stage-specific interventions with pharmacotherapy including ACE/ARB and newer SGLT2-I and NS-MRA medications.
- Family Physicians will know when to refer to nephrology appropriate workup and how to assist patients in choices for advanced Kidney Disease

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What is the best way to estimate CKD risk?

Question 1

A. Creatinine clearance eGFR
B. Urine albumin creatinine ratio uACR
C. Cystatin C based estimate of eGFR in patients with low muscle mass
D. All of the above

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MAIN CAUSES OF CKD

- **Elevated Blood Pressure Control**
- **Poor Glycemic Control in Patients with Diabetes**
- Obstructive Uropathy
- Infectious
- Autoimmune

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Albuminuria

- GFR groups
- Albinuria groups
- Albuminuria even with normal GFR is dangerous
- Suggestions about when to refer

CKD is classified based on:
Cause (C)*
GFR (G)†
Albuminuria (A)†

GFR categories (mL/min per 1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
G1	Normal or high	≥90		Screen 1	Treat 1	Treat and refer 3
G2	Mildly decreased	60–89		Screen 1	Treat 1	Treat and refer 3
G3a	Mildly to moderately decreased	45–59		Treat 1	Treat 2	Treat and refer 3
G3b	Moderately to severely decreased	30–44		Treat 2	Treat and refer 3	Treat and refer 3
G4	Severely decreased	15–29		Treat and refer‡ 3	Treat and refer‡ 3	Treat and refer 4+
G5	Kidney failure	<15		Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk

Kidney Disease Improving Global Outcomes KDIGO

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Screen for Early Kidney Damage

- For patients with Diabetes
  - eGFR and **uACR** one to 4 x per year (ADA 2025)
  - (Current uptake only 43% of Family Physicians are ordering)
- For patients with CKM
  - **uACR** and creatinine or cystatin C for KDIGO staging
  - Annually stage 2 CKM
  - More frequently with higher KDIGO risk
- For patients with CKD
  - KDIGO risk stratification

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UACR

- "**Microalbumin**" is the earliest amount of protein released from the glomerulus
- In 2012 KDIGO standardized this measurement to be a quantifiable ratio of albumin to creatinine in urine.
- "**Urine Albumin Creatinine Ratio**"
- Measure of early kidney damage in up to 30% of patients with diabetes and a normal eGFR
- In 2023 only 40% of Primary Care practices were ordering this as a test for patients with Diabetes

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THE DEVIL IS IN THE DETAILS "MICROALBUMIN"?

- CPT Codes 82043 urine creatinine, 82570 urine albumin
- Lab Specific Test Codes
  - What is on your Diabetes order-set?
  - What is on your "wellness lab" protocol?
  - What test does your E.H.R. button point to
  - What about point-of-care testing (dip-stick)?

Lab	Test Name	Lab Code
QUEST	Kidney Profile	39165
CPL	Kidney Profile Serum and Urine Test	9332
Lab Corp	Kidney Profile	140301

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WHAT ABOUT ESTIMATED GLOMERULAR FILTRATION RATE E-GFR

- It is great that every Comprehensive Metabolic Panel (CMP) gives us an automatic eGFR calculation
- 2021 NKFASN (National Kidney Foundation and American Society of Nephrology) recommended CKDEPI Refit calculation which does not separate by race
- Is Creatinine Clearance the best measure?
  - Not if there is low muscle-mass
  - Consider eGFR based on a measurement of Cystatin C

https://www.kidney.org/sites/default/files/02-10-8361_icb_egfr_summary_flyer.pdf

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OTHER WAYS TO ADDRESS HIGH UACR OR REDUCED EGFR

- Control BP
- Stop smoking
- Reduce weight
- Avoid NSAID
- Reconsider vitamins, minerals, herbs, weight loss or body building supplements
- Adjust other medication doses as appropriate

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"NEPHRO**TOXINS**……..**"?**: ACE & ARB? …

- May decrease eGFR up to 30% but still valuable
- May be d/c in the hospital during a dehydration or ATN episode
- Don't forget at post-hospital follow-up to restart ACE/ARB!
- Caution with NSAID! Consider d/c for any stage of CKD

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RISK ASSESSMENT

- ASCVD risk estimator
- Estimating impact of treatment
- Adding other variables
- Refining for

CKD KDIGO risk

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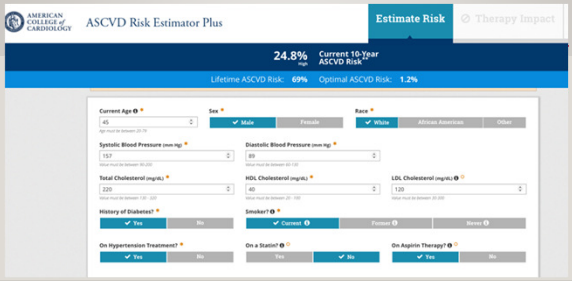
ASCVD RISK ESTIMATOR PLUS



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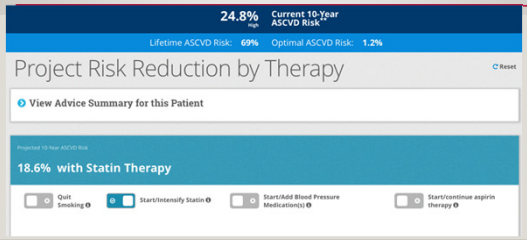
RISK REDUCTION FROM 24.8 TO 18.6 WITH STATIN!



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PREVENT SCORE

The American Heart Association PREVENT™ Online Calculator

Welcome to the American Heart Association **Predicting Risk of cardiovascular disease EVENTs** (PREVENT™). This app should be used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

- Update to the AHA/ACC Pooled Cohort Equations previously published in 2013. It now includes BMI, has expanded the age for which scores can be calculated
- Includes optional variables that better define the effect of cardiovascular-kidney-metabolic (CKM) condition
- uACR, Social Deprivation Index, or A1c
- Diabetes, **smoking**, using statins, BP, Total Cholesterol HDL

Khan SS, Coresh J, Pencina MJ, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. Circulation 2023; 148: 1982-2004

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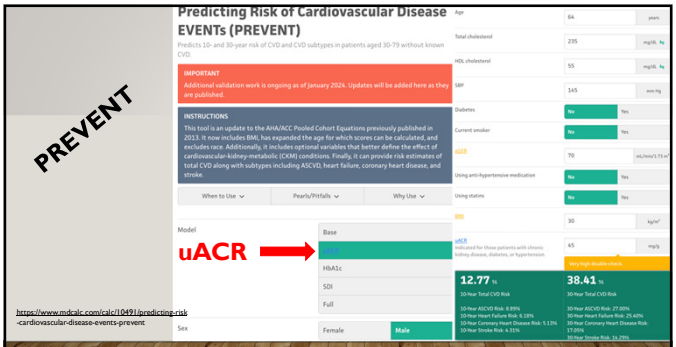
PREVENT



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CKD SCREENING FOR PEOPLE WITH DIABETES: **ADA** STANDARDS OF CARE 2025

- At least **annual urinary albumin**
  - (spot urinary **albumin-to-creatinine ratio**) and **EGFR**
- All patients with DMII **uACR 1-4 x per year** depending on CKD stage
- Optimize glucose control to prevent or slow CKD progression
- For DMII with CKD consider **SGLT-2** if GFR >20 and urinary albumin >300 and for CVD risk reduction
- **ACE/ARB, MRA, GLP-1**

https://care.diabetesjournals.org/content/44/Supplement_1

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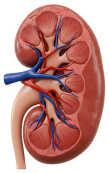
"**FAKE**" HYPOVOLEMIA: EVOLUTIONARY ADAPTATION

Activation of the Renin Angiotensin Aldosterone System

- Compensation for a perceived intravascular deficit
  - Fluid retention
  - Vasoconstriction
  - Elevated Blood Pressure

Glomerulus

- Reduced afferent arterial flow (vasoconstriction?)
- But …. Increased intraglomerular pressure
- Leaky Filter: proteinuria



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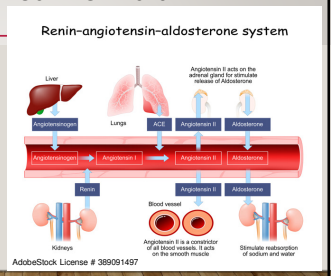
RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM

- Vasoconstriction
- Sodium Retention
- All systems are integrated
- Kidney, Blood Pressure, Vascular System related



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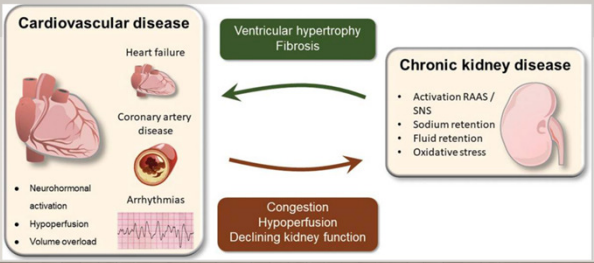
NEUROHORMONAL ACTIVATION: HYPERTROPHY & FIBROSIS



Circ Res. 2023 Apr 14; 132(8): 902–914.

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SGLT2 INHIBITION

- Evidence accumulating on this category of medications
- For Type II Diabetes
- For Kidney Disease intervention
- For Heart Failure Treatment
- ADA 2025 Standards of Care
  - *"type 2 diabetes and CKD, use of a sodium–glucose cotransporter 2 (SGLT2) inhibitor with demonstrated benefit is recommended o reduce CKD progression and cardiovascularevents in individuals with eGFR >20 mL/min/1.73 m²"*

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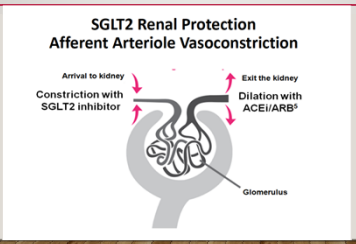
SGLT-2 AT THE GLOMERULUS TRANSIENT CREATININE RISE THEN IMPROVEMENT



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SGLT-2 EXAMPLES, COST AND COPAY

Chemical Name	Trade Name	Good RX/with coupon
Canagliflozin	Invokana	$730/600
Canagliflozin/metformin	Invokamet	$730/600
Dapagliflozin	Farxiga	$700/288
Dapagliflozin/metformin extended release	Xigduo SR	$700/580
Dapagliflozin/saxagliptin	Qtern	$135/120
Empagliflozin	Jardiance	$750/620
Empagliflozin/linagliptin	Glyxambi	$750/620

Good RX average estimates June 2025

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Empagliflozin		Dapagliflozin		Canagliflozin	
FDA indications	HFrEF HFpEF	FDA	HFrEF	FDA	CKD HFrEF HFpEF
Trials	EMPA-REG Emperor-Reduced Emperor – Preserved	Trials	DAPA-HF PRESERVED – HF DELIVER - HF	Trials	CREDENCE CHIEF-HF

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SGLT2I IF CKD, **GFR >20**, (OR BELOW?) & DMII

1. Even if on other glucose-lowering agents, add SGLT2i for CVS protection
2. Choose SGLT2i with proven CVS benefits and monitor GFR
3. Withhold SGLT2i during fasting, surgery or critical illness to reduce ketosis risk
4. If risk for hypovolemia, decrease diuretic and worn patients about dehydration and hypotension
5. A small reversible GFR drop is expected when starting SGLT2i
6. **Tolerate up to a 20 ml/min GFR drop**
7. Insufficient evidence for SGLT2i in transplant recipients

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PERIPROCEDURAL / PERIOPERATIVE SGLT2I

1. Inform patients about risk of ketoacidosis
2. Withhold SGLT2i the day of day-stay procedures
3. Limit fasting to minimum required
4. Withhold SGLT2i at least 2 days in advance and the day of procedures/surgery requiring 1 or more days in hospital and/or bowel preparation
5. Measure both blood glucose and blood ketone levels on hospital admission (proceed with procedure/surgery if the patient is clinically well and ketones are <1.0 mmol/l)
6. Restart SGLT2i after procedure/surgery only when eating and drinking normally

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MINERALOCORTICOID RECEPTORS

- Subfamily of nuclear hormone receptors and is expressed in several tissues/cell types
  - Kidney & Heart
  - Vasculature
  - Immune cells & Fibroblasts
- Regulating fluid, electrolytes, and blood pressure
- Overactivated in CKD and heart failure
- May abrogate the progression of CKD and reduce cardiovascular morbidity and mortality.

Agarwal R. et al. Investigating new treatment opportunities for patients with chronic kidney disease in type 2 diabetes: the role of Finerenone. Nephrol Dial Transplant. 2022 May 25;37(6):1014-1023.

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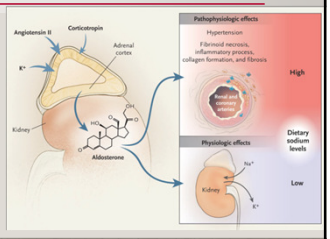
MINERALOCORTICOID EFFECTS

- Sodium retention
- Potassium loss in the kidneys
- Aldosterone induced myocardial fibrosis
- Cardiac remodeling with **collagen formation** and **vascular fibrosis** and dysfunction
- Baroreceptor dysfunction
- Reduced myocardial uptake of norepinephrine



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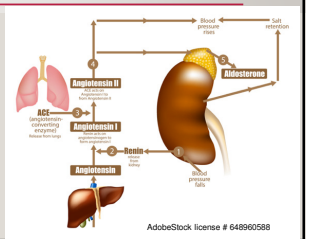
MINERALOCORTICOID METABOLISM IN HOMEOSTASIS

- ACE or ARB to prevent conversion of Angiotensin I to Angiotensin II
  - Initial mechanism to support perceived low blood pressure
- Aldosterone promoting salt retention to compensate for perceived low-blood pressure
- MRA to block aldosterone



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FINERENONE STUDIES

- FIDELIO-DKD
- FIGARO-DKD
- Significantly reduced the combined primary endpoint (chronic kidney disease progression, kidney failure, or kidney death) vs. placebo
- Recommended in ADA 2025 standards of care, in KDIGO guideline and 2023 CKM guideline from ACC

Pitt B Figaro DKD N Engl J Med 2021
Bacris GL Fidelio DKD N Engl J Med 2020

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FINERENONE

- High selectivity toward the mineralocorticoid receptor along with a low affinity for androgen, glucocorticoid, progesterone, and estrogen receptors
- In high-risk patients, such as those with CKD and diabetes mellitus (DM).
- ARTS-HF: 5-10 mg significantly reduced CV hospitalizations, or emergency presentation for worsening HF

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HYPERKALEMIA WITH FINERENONE

Below 4.8

- **Initiate Finerenone**
- **10mg daily if eGFR 25-59**
- **20 mg daily if egfr?60**
- **Monitor K at 1 m after initiation and q4m**
- **Increase dose to 20 mg daily if on 10**
- **Restart 10mg/d if previously held for high K and now less than 5**

Up to 5.5

- **Continue Finerenone 10 or 20 mg**
- **Monitor every 4 m**

Above 5.5

- **Hold Finerenone**
- **Consider adjustments to diet or concomitant medications to mitigate hyperkalemia**
- **Recheck K**
- **Consider reinitiation if/when K < 5**

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GLP-1/ GIP

- For weight loss
- For metabolic impact in Diabetes
- For Kidney protection
  - "*Among people with type 2 diabetes who have established **ASCVD** or established **kidney disease**, a sodium–glucose cotransporter 2 (SGLT2) inhibitor **or glucagon-like peptide 1 receptor agonist** (GLP-1 RA) is recommended as part of the comprehensive **cardiovascular risk reduction** and/or glucose-lowering treatment plans*"

ADA standards of care 2025

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November 2023

Circulation
Volume 148, Issue 20, 14 November 2023; Pages 1606-1635
https://doi.org/10.1161/CIR.0000000000001184

AHA PRESIDENTIAL ADVISORIES

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

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CARDIOVASCULAR KIDNEY METABOLIC SYNDROME CKM (AHA ACC 2023)

- Treating Diabetes, Kidney Disease & CVD has converged
- Same pathophysiologic process underlying each
  - Obesity
  - Metabolic Dysfunction
  - Inflammation

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INTERVENTIONS FOR CKD AND CVD

Non-Pharmacologic
Exercise
Weight Loss
If Diabetes: CGM
Pharmacologic
ACE/ ARB
SGLT2-I
GLP-1
MRA (steroidal or non-steroidal)

Life's Essential 8

- Healthy diet
- Physical activity
- Avoidance of nicotine
- Healthy sleep
- Healthy weight
- Healthy lipids
- Healthy blood glucose
- Healthy blood pressure

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CHRONIC KIDNEY DISEASE (CKM GUIDELINE)

- With albuminuria (UACR > 30 mg/g) ->ACEi/ARB
- ARNi* preferred in HFrEF**
- In CKD (in those with/without diabetes) - SGLT2*
- DKD with residual albuminuria (UACR >30 mg/g) on ACE/ARB

Finerenone *** (can be used on background SGT2i)

*Angiotensin Receptor Blockade with Neprilysin Inhibitor
**Heart Failure with reduced Ejection Fraction
*** Finerenone is the only current Non Steroid Mineralocorticoid Receptor Antagonist (MRA)

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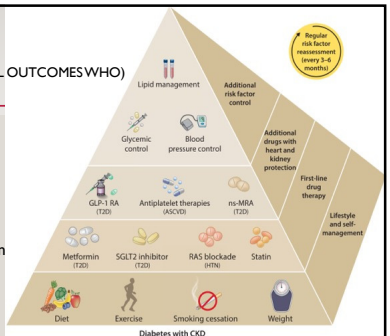
KDIGO 2023 DM & CKD
(KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES WHO)

Control Blood Sugar
Control BP
Control Lipids

GLP-1 RA, Antiplatelet, ns-MRA

Metformin, SGLT2i, RAS blockade, Statin

Diet, Exercise, Smoking Cessation
Weight Management



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HYPERTENSION DETECTION, TREATMENT AND MEDICATION ADHERENCE (KDIGO)

- Lifestyle modification
- Follow established hypertension guidelines to achieve BP <130/80 mmHg
- In diabetes or CKD, prioritize ACE/ARB; consider steroidal MRA for resistant hypertension
- Avoid CCB in HErEF
- African American patients with HFrEF -> prioritize hydralazine + isosorbide dinitrate after 4 pillars of GDMT

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PREVENTION

1. "Drink Plenty of Water" ?
2. Avoidance of NSAID where possible
3. Other "nephrotoxins" .....
4. Less common kidney injury from obstruction, infection or autoimmune

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MASH

Calculate Fib-4 Score

- Resmetirom (REZDIFFRA) has accelerated approval from the Food and Drug Administration (FDA) for the treatment of MASH with stage 2 or 3 liver fibrosis
- GLP-1 Semaglutide in Phase 3 trial for the treatment of type 2 diabetes and overweight or obesity. Essence Study (not yet approved for MASH)
  - Limit Statin Doses, GB and Liver and CYP2C8 metabolic interactions
- SGLT2i and Pioglitazone off-label

Sanyal AJ, et al. Phase 3 Trial of Semaglutide in Metabolic Dysfunction–Associated Steatohepatitis New Engl J Med April 2025
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Practice Recommendations

1. Screen patients with Diabetes using uACR and eGFR
2. Initiate RAAS blockade early (ACE/ARB, MRA) in CKD and in HF
3. Incorporate CKD measures into ASCVD calculation
4. Secondary RF modification with BP control, smoking cessation & statin +
5. Use of GDMT for HF will also address CKD and DM
6. SGLT2i and GLP-1 GLP1-GIP can help patients even without Diabetes to improve both cardiovascular and renal outcomes
7. Work with Specialists, APPs, PT, and others to help patients meet health goals

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Additional Questions? Contact Me.

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