

State-of-the-Art
Treatment of
DKD

Stephen A. Brunton, MD,
FAAFP, CDCEs
Executive Director
Primary Care Metabolic Group

Please take a moment to answer a
very brief pre-survey using the QR
Code or URL below.
URL: <https://www.pcmg-us.org/survey/pre/2024DKD2>



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Disclosures

• **Stephen Brunton, MD, FAAFP, CDCES**, has disclosed that he is on the advisory board and/or speakers bureau for Abbott Diabetes, AstraZeneca, Bayer, Biolinq, Boehringer Ingelheim, Lifescan, Lilly, Novo Nordisk, Sanofi, and holds stock options for Paracrine.

• All relevant financial relationships have been mitigated.

Learning Objectives

Participants in this presentation should be able to...

Identify patients at risk for CKD who should be screened for albuminuria, using UACR, and reduced eGFR to lessen diagnostic delays.

Incorporate newer agents such as SGLT-2 inhibitors and MRAs into treatment plans for eligible patients with CKD and T2D.

Review new and emerging data regarding the use of MRAs in patients with CKD and DKD.

Definitions: CKD and DKD

- KDIGO 2024 CKD definition:¹
 - “CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health”
- Broad definition of DKD²
 - The presence of CKD in patients with T1D or T2D, regardless of background

Criteria for CKD (KDIGO 2024)	
Markers of kidney damage (1 or more)	<ul style="list-style-type: none"> • Albuminuria • Urine sediment abnormalities • Persistent hematuria • Electrolyte and other abnormalities due to tubular disorders • Abnormalities detected by histology • Structural abnormalities detected by imaging • History of kidney transplantation
Decreased GFR	GFR <60 mL/min/1.73 m ²

1. KDIGO CKD Work Group. *Kidney Int.* 2024;105(4, Suppl):S117-S114.
 2. Pearson F, Rossing P. *Kidney Int Suppl.* 2018;8(1):2-7.

CKD, chronic kidney disease; DKD, diabetic kidney disease; KDIGO, Kidney Disease: Improving Global Outcomes; GFR, glomerular filtration rate; T1D, type 1 diabetes; T2D, type 2 diabetes

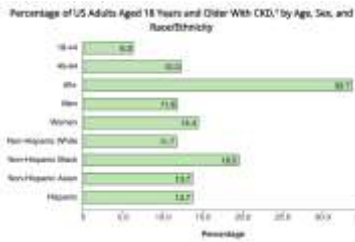
Chronic Kidney Disease (CKD) and Diabetes in the United States

- More than 1 in 7 adults in the United States (U.S.) are estimated to have CKD, equating to ~35.5 million people¹
 - Approximately 1 in 3 adults with diabetes have CKD
- CKD is commonly encountered in primary care, yet it remains underdiagnosed²
 - Early stages of CKD are often characterized by asymptomatic presentation
 - Diagnosis may be overlooked if appropriate screening is not performed



1. Centers for Disease Control and Prevention. Chronic kidney disease initiative. Reviewed February 27, 2023. Accessed April 4, 2024. <https://www.cdc.gov/kidneydisease/index.html>. 2. Chan TY, et al. JAMA. 2019;321(15):1294-1304.

CKD by Age, Sex, and Race/Ethnicity



Centers for Disease Control and Prevention. Chronic kidney disease initiative. Reviewed February 27, 2023. Accessed April 4, 2024. <https://www.cdc.gov/kidneydisease/index.html>.

10-Year Mortality in T2D by CKD Manifestation

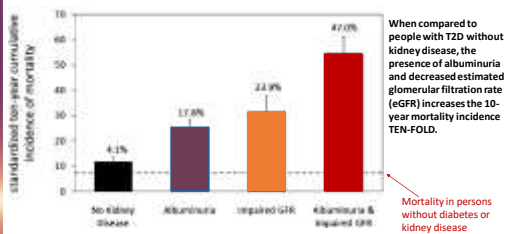


Image used with permission from Afarián M, et al. Kidney disease and increased mortality risk in type 2 diabetes. J Am Soc Nephrol. 2013;24:302-308.

Potential Consequences of CKD/DKD

- Kidney diseases are a leading cause of mortality in the United States
- CKD can progress to kidney failure, likely requiring dialysis or kidney transplantation
- CKD markedly increases CV risk
- CKD is associated with multiple additional complications:
 - Hypertension
 - Volume overload
 - Electrolyte abnormalities
 - Metabolic acidosis
 - Anemia
 - Metabolic bone disease

Centers for Disease Control and Prevention. Chronic kidney disease initiative. Reviewed February 27, 2023. Accessed April 4, 2024.
<https://www.cdc.gov/kidneydisease/index.html>; American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(suppl_1):S219-S230.

Role of the Primary Care Clinician (PCC) in CKD and DKD

- Facilitate early screening and diagnosis
- Implement interventions early when indicated to prevent cardiovascular morbidity/mortality and slow CKD progression
 - Lifestyle interventions
 - Optimized risk factor management
- Initiation of agents with evidence of CV and kidney benefit
 - SGLT-2 inhibitors
 - Nonsteroidal mineralocorticoid receptor antagonists (ns-MRAs)
 - GLP-1 RAs
- Refer to nephrology when appropriate

CV, cardiovascular; SGLT-2, sodium-glucose cotransporter-2; GLP-1 RA, glucagon-like peptide-1 receptor agonists

Shubrook JH, et al. PostgradMed. 2022;13(4):376-387.

Underuse of Newer Therapies in T2D and CKD

- Cross-sectional analysis of ~1.2 million patients from the Veterans Health Administration Database
- Of patients with T2D and CKD:
 - Only **12%** were prescribed an SGLT-2 inhibitor
 - Only **10%** were prescribed a GLP-1 RA

Those with more severe kidney disease and higher cardiovascular and kidney risk were less likely to be prescribed a SGLT-2 inhibitor or a GLP-1 RA

Langriss-Montallegre JA, et al. Diabetes Care. 2022;29(9):2006.

Remember the question from your pre-survey?

Which of the following is true about implementing newer agents for treating T2D and CKD based on a real-world study of ~1.2 million patients in the Veterans Health Administration Database?

- Only **12%** were prescribed an SGLT-2 inhibitor

Lamprea-Montallegre JA, et al. Diabetes Care. 2022;2900-2906.

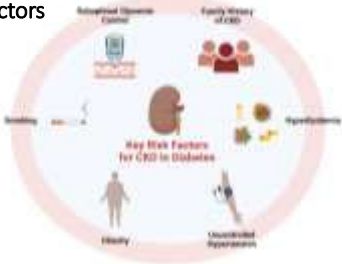
Identification, Screening, and Diagnosis of Patients with CKD

Importance of Early Diagnosis and Intervention

- Early detection and treatment is critical for patients with CKD because progressive disease is associated with adverse outcomes, including ESKD, CV disease, and death¹
- Since CKD is often asymptomatic, especially in early stages, laboratory detection is critical for early-stage diagnosis²
- Treatment of early stages of CKD can often be successfully implemented in primary care¹

1. Chen TK, et al. JAMA. 2019;322(13):1294-1304. 2. de Boer H, et al. Diabetes Care. 2022;45:3075-3080.

Key Risk Factors for CKD in Diabetes



Centers for Disease Control and Prevention. Chronic kidney disease initiative. Reviewed February 27, 2023. Accessed April 4, 2024. <https://www.cdc.gov/kidneydisease/index.html>

Classification and Staging of CKD

- Risk of CKD progression, frequency of visits, and referral to nephrologist according to GFR and albuminuria shown.
- Risk of progression indicated by color grading.
- Numbers in boxes are a guide to how many times per year the patient should be seen.
- "Refer" suggests that nephrology services are recommended.

GFR category (mL/min/1.73 m ²)	Albuminuria (mg/24 hr)	CKD is classified based on: • GFR (G1-G5) • Albuminuria (A1-A3)	Albuminuria ranges by GFR category and range		
			G1-G3 Normal to mildly increased	G4-G5 Moderately increased	G4-G5 Severely increased
G1	Normal or high	A1	Green	Yellow	Red
G2	Mildly decreased	A1-A2	Green	Yellow	Red
G3a	Mild to moderately decreased	A1-A2	Yellow	Orange	Red
G3b	Moderately to severely decreased	A1-A2	Yellow	Orange	Red
G4	Severely decreased	A1-A2	Red	Red	Red
G5	Kidney failure	A1-A3	Red	Red	Red

de Boer IH, et al. Diabetes Care. 2022;45:3075-3090. Reprinted with permission of the American Diabetes Association, copyright 2022.

CKD Screening and Diagnosis in Diabetes

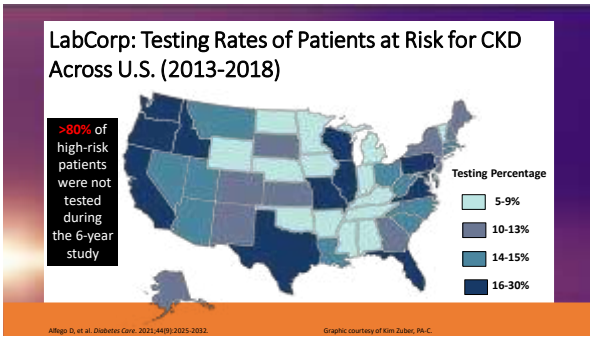
Who and when to screen?

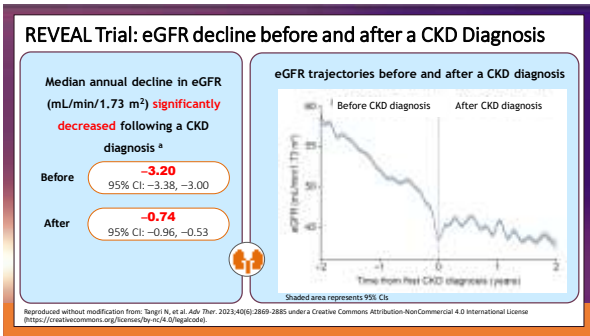
- T1D** Yearly starting 5 years after diagnosis
- T2D** Yearly starting at diagnosis

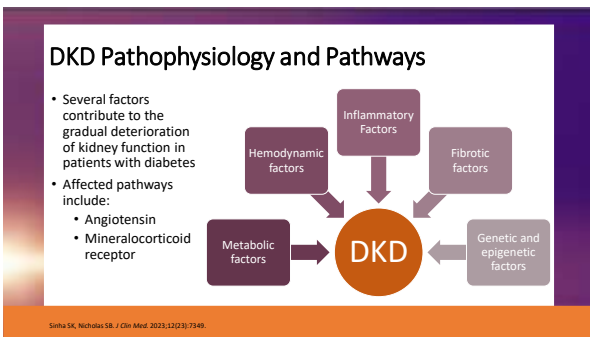
How to screen?

- Spot urine ACR
- and
- eGFR

de Boer IH, et al. Diabetes Care. 2022;45:3075-3090. Reprinted with permission of the American Diabetes Association, copyright 2022.







CKD Screening and Diagnosis

What defines CKD diagnosis?

- Persistent urine ACR ≥ 30 mg/g and/or
- Persistent eGFR < 60 mL/min/1.73 m² and/or
- Other evidence of kidney damage

What to do with a positive result?

Repeat and monitor:

- Evaluate possible triggers or adjust doses
- Consider using nephrotic C and creatinine to track proteinuria and/or
- Only patients diagnosed with CKD

Initiate evidence-based treatments

de Boer M, et al. Diabetes Care 2022;45:3075-3090. Reprinted with permission of the American Diabetes Association, copyright 2022.

Considerations for Nephrology Referral: ADA*

Uncertain etiology of kidney disease	Difficult management issues [†]
eGFR < 30 mL/min/1.73 m ²	Rapidly progressing kidney disease

*Referral threshold may vary.
[†]Anemia, secondary hyperparathyroidism, significant increase in albuminuria despite good BP management, metabolic bone disease, resistant hypertension, electrolyte disturbances.

American Diabetes Association Professional Practice Committee. Diabetes Care 2024;47(Suppl. 1):S219-S230.

Evidence-Based Management of CKD and DKD in Primary Care

Overall Management Goals for Patients with T2D and CKD

• ADA/KDIGO Consensus Statement:

- All patients with T1D or T2D and CKD should be treated with a comprehensive plan, outlined and agreed upon by healthcare professionals and the patient together, to optimize nutrition, exercise, smoking cessation, and weight, upon which are layered evidence-based pharmacologic therapies aimed at preserving organ function and other therapies selected to attain intermediate targets for glycemia, blood pressure, and lipids.

64. Rhee PL, et al. Diabetes Care. 2022;45:3075-3090.

Overall Management Goals for Patients with T2D and CKD

• ADA Standards of Care:

- Optimize glucose control to reduce the risk or slow the progression of CKD.
- Optimize blood pressure control and reduce blood pressure variability to reduce the risk or slow the progression of CKD.

American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(Suppl. 1):S219-S230.

Glycemic Targets in T2D and CKD

KDIGO

- Individualized A1c target ranging from 6.5% to 8.0% for patients with CKD and diabetes not on dialysis
- More stringent goal if mild CKD (G1)
- Less stringent goal (e.g., <8.0%) if:
 - Severe CKD (G5)
 - Macrovascular complications
 - Many comorbidities
 - Short life expectancy
 - Impaired hypoglycemia awareness
 - Lack of resources for hypoglycemia management
 - High risk of hypoglycemia

KDIGO. *kidney int.* 2022;102(Suppl 5):S1-S127.

A1c, glycated hemoglobin; KDIGO, Kidney Disease: Improving Global Outcomes

Glycemic Targets in T2D and CKD

American Diabetes Association (ADA):

- A1c <7.0% for most
- Less stringent A1c goal (e.g., <8.0%) if:
 - History of severe hypoglycemia
 - Limited life expectancy
 - **Advanced microvascular or macrovascular complications**
 - Extensive comorbidities
 - Long-standing diabetes in which the A1c goal is difficult to achieve despite self-management education, appropriate glucose monitoring, effective doses of multiple glucose-lowering agents including insulin

American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(Suppl. 1):S111-S125.

Other Management Goals for Patients with CKD

- **KDIGO¹**
 - KDIGO recommends a systolic blood pressure of < 120 mm Hg to slow progression in CKD.
 - First line medication is an ACE inhibitor (ACEi) or angiotensin II receptor blocker (ARB) titrated to the maximum highest tolerated dose.
- **DKD: ADA Standards of Care²**
 - Optimize glucose control to reduce the risk or slow the progression of CKD.
 - Optimize blood pressure control and reduce blood pressure variability to reduce the risk or slow the progression of CKD.

1. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. Kidney Int. 2021;99(3):S1-S67.
2. American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(Suppl. 1):S213-S228.

Other Management Goals for Patients with CKD

Lipid Management in T2D (consensus statement):

- High-intensity statin for patients with clinical ASCVD for secondary prevention
- High-intensity statin for patients at high risk of ASCVD aged 40-75 years for primary prevention
- Moderate-intensity statin for patients aged 40-75 years without high CV risk for primary prevention

64 Boer JH, et al. Diabetes Care. 2022;45:3075-3090.





ADA/KDIGO Consensus Statement: First Line Glucose-Lowering Therapies

- An SGLT-2 inhibitor with proven kidney or CV benefit is recommended for patients with T2D, CKD, and eGFR ≥ 20 mL/min/1.73m². Once initiated, the SGLT-2 inhibitor can be continued at lower levels of eGFR.
 - SGLT-2 inhibitor therapy recommended to be continued until initiation of dialysis or transplant
- Metformin is recommended for patients with T2D, CKD, and eGFR ≥ 30 mL/min/1.73m²; the dose should be reduced to 1,000 mg daily in patients with eGFR 30-44 mL/min/1.73m² and in some patients with eGFR 45-59 mL/min/1.73m² who are at high risk of lactic acidosis.

de Boer IH, et al. Diabetes Care. 2022;45:3075-3090.

SGLT-2 Inhibitors: Recommended Dosing by eGFR†

	Stage 3b (eGFR 30-44)	Stage 4 (eGFR 15-29)	Stage 5 (eGFR <15)
Bexagliflozin	20 mg daily	Use not recommended	
Canagliflozin	Maximum 100 mg daily	<ul style="list-style-type: none"> Initiation not recommended May continue 100 mg daily if tolerated for kidney and cardiovascular benefit until dialysis* 	
Dapagliflozin	10 mg daily	<ul style="list-style-type: none"> Initiation not recommended with eGFR <25 mL/min/1.73 m² May continue if tolerated for kidney and cardiovascular benefit until dialysis* 	
Empagliflozin	No dose adjustment required	<ul style="list-style-type: none"> Initiation not recommended with eGFR <20 mL/min/1.73 m² May continue if tolerated for kidney and cardiovascular benefit until dialysis* 	
Ertugliflozin	Not recommended if eGFR <45		Use not recommended
Sotagliflozin	200 to 400 mg daily	<ul style="list-style-type: none"> Initiation not recommended with eGFR <25 mL/min/1.73 m² May continue if tolerated for kidney and cardiovascular benefit until dialysis* 	

*Glucose-lowering efficacy is reduced with SGLT-2 inhibitors as eGFR declines, but kidney and CV benefits are preserved
†HF, heart failure
Bexagliflozin: Prescribing information, Takeda Pharmaceuticals, 2023. Accessed April 4, 2024. Invokana: Prescribing information, Janssen Pharmaceuticals, Inc., 2023. Accessed April 4, 2024. Farxiga: Prescribing information, AstraZeneca, 2024. Accessed April 4, 2024. Jardiance: Prescribing information, Boehringer Ingelheim Pharmaceuticals, Inc., 2023. Accessed April 4, 2024. Stegatin: Prescribing information, Merck Sharp & Dohme LLC, 2023. Accessed April 4, 2024. Iqalio: Prescribing information, Lexicon, 2024. Accessed April 4, 2024.

ADA/KDIGO Consensus Statements: Additional First Line Therapies

- An ACE inhibitor (ACEi) or angiotensin II receptor blocker (ARB) is recommended for patients with T1D or T2D who have hypertension and albuminuria, titrated to the maximum antihypertensive or highest tolerated dose.
- A statin is recommended for all patients with T1D or T2D and CKD, moderate intensity for primary prevention of atherosclerotic cardiovascular disease (ASCVD) or high intensity for patients with known ASCVD and some patients with multiple ASCVD risk factors.

de Boer IH, et al. Diabetes Care. 2022;45:3075-3090.

Approach for Improving Outcomes in Diabetes and CKD: Intensification of Glucose-Lowering Therapies



de Boer IH, et al. Diabetes Care. 2022;45:3075-3090. Reprinted with permission of the American Diabetes Association. copyright 2022.

ADA/KDIGO Consensus Statements: Additional Glucose-Lowering Therapies

- A GLP-1 RA with proven CV benefit is recommended for patients with T2D and CKD who do not meet their individualized glycemic target with metformin and/or an SGLT-2 inhibitor or who are unable to use these drugs.

de Boer IH, et al. Diabetes Care. 2022;45:3075-3090.

GLP-1 Receptor Agonists: Dosing in CKD

	Stage 3b (eGFR 30-44)	Stage 4 (eGFR 15-29)	Stage 5 (eGFR <15)
Exenatide	Caution initiating or increasing dose; avoid once-weekly formulation	Use not recommended	
Dulaglutide*	No dose adjustment required		
Liraglutide*	No dose adjustment required		
Lixisenatide	No dose adjustment required		Use not recommended
Semaglutide**	No dose adjustment required		
Tirzepatide**	No dose adjustment required		

de Boer IH, et al. Diabetes Care. 2022;45:3075-3090.
 Moumjid A. Prescribing Information. Eli Lilly and Company; 2023. Accessed April 4, 2024.
<https://pi.lilly.com/us/mounjaro-uspi.pdf>
 *GLP-1 RA with expanded indications for CVD
 **Injectable semaglutide carries a CVD indication
 **GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) dual agonist

Approach for Improving Outcomes in Diabetes and CKD



de Boer IH, et al. Diabetes Care. 2022;45:3075-3090.
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ADA/KDIGO Consensus Statements: Nonsteroidal Mineralocorticoid Receptor Antagonist

- An ns-MRA with proven kidney and CV benefit is recommended for patients with T2D, eGFR ≥ 25 mL/min/1.73m², normal serum potassium concentration, and albuminuria (ACR ≥ 30 mg/g) despite maximum tolerated dose of renin-angiotensin system (RAS) inhibitor.

de Boer IH, et al. Diabetes Care. 2022;45:3075-3090.

Pillars of DKD Management

Foundation	Lifestyle intervention (diet/exercise)
1st Pillar	ACE inhibitor/ARB at maximum tolerated dose
2nd Pillar	SGLT-2 inhibitor with primary evidence of reducing CKD progression
3rd Pillar	ns-MRA (finerenone)
4th Pillar	GLP-1 RAs*

*GLP-1 RAs are an "emerging pillar," with the recent FLOW trial demonstrating kidney and CV benefits with semaglutide in patients with T2D and CKD

Agarwal A, Fouga D. Nephrol Dial Transplant. 2023;38(2):253-257.

FLOW Trial: DKD Outcomes with Semaglutide

- Patients: 3533 adults with T2D and CKD randomized 1:1 to semaglutide 1.0 mg once weekly or placebo
- Trial stopped early at median follow-up of 3.4 years
- Results (all statistically significant in favor of semaglutide):

Outcome	Semaglutide vs Placebo
Primary outcome: major kidney disease events, a composite of the onset of kidney failure, at least a 50% reduction in the eGFR from baseline, or death from kidney or cardiovascular causes	HR 0.76; 95% CI, 0.66 to 0.88; <i>P</i> = .0003
Kidney-specific components of the primary outcome	HR 0.79; 95% CI, 0.66 to 0.94
Death from cardiovascular causes	HR 0.71; 95% CI, 0.56 to 0.89
Risk of major adverse cardiovascular events	HR 0.82; 95% CI, 0.68 to 0.98; <i>P</i> = .029
Risk of death from any cause	HR 0.80; 95% CI, 0.67 to 0.95; <i>P</i> = 0.01

Conclusion: semaglutide reduced the risk of clinically important kidney outcomes and death from CV causes in patients with T2D and CKD

Perovic V, et al. N Engl J Med. 2024. May 24 online ahead of print. doi:10.1056/NEJMoa2403347

Remember the question from your pre-survey?

Foundation	Lifestyle intervention (diet/exercise)
1st Pillar	ACE inhibitor/ARB at maximum tolerated dose
2nd Pillar	SGLT-2 inhibitor with evidence in kidney disease
3rd Pillar	ns-MRA (finerenone)
4th Pillar	GLP-1 RAs*

Diuretics are NOT one of the 4 Pillars!

Agarwal A, Fouca D. *Nephrol Dial Transplant.* 2023;38(2):253-257.

What is a mineralocorticoid receptor antagonist (MRA)?

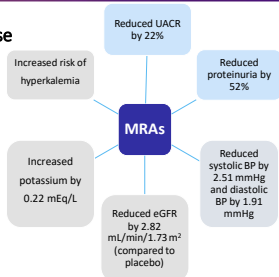
- MRAs have been around for decades.
- “MRAs are well known for their utility in treating heart failure, refractory hypertension, and diverse nephropathies, namely, diabetic nephropathy. As their name denotes, MRAs inhibit the action of aldosterone at the mineralocorticoid receptor, preventing receptor activation. This prevents remodeling, decreases inflammation, and improves proteinuria.”¹

Rico-Mesa JS, et al. *Curr Cardiol Rep.* 2020;10:22(11):140.

Mineralocorticoid Receptor Antagonists in Kidney Disease

2019 Meta-analysis

- 35 randomized, controlled trials
- Intervention: MRA alone or added to ACE-I or ARB
- Comparator: placebo or active treatment



Maria Elise A et al. *J Hypertens.* 2019;37(12):2307-2324

Comparison of MRAs

	Potency	Selectivity	Metabolites	Tissue Distribution* (Kidney/Heart)	FDA-Approved Indications
Steroidal					
Spiroinolactone	High	Low	Multiple, active	Higher in kidney	<ul style="list-style-type: none"> Hypertension HF Edema Primary hyperaldosteronism
Eplerenone	Low	Medium	No active metabolites	Higher in kidney	<ul style="list-style-type: none"> Hypertension HF post-MI
Non-Steroidal					
Finerenone	High	High	No active metabolites	Balanced in heart and kidney	<ul style="list-style-type: none"> To improve kidney and CV outcomes in T2D and CKD

*Based on standard whole-body quantitative analysis in healthy rats.

Agarwal R, et al. *European Heart Journal*. 2023;42(2):157-163.
Clinical Pharmacology Online. Available at: <https://doi.org/10.1093/cpo/cbab007>

Finerenone

- **FDA approved in 2021**
- **Non-steroidal MRA**
 - Less steroidal side effects (e.g., gynecomastia) and hyperkalemia when compared to steroidal MRAs
- **Indication:**
 - To reduce the risk of sustained eGFR decline, ESKD, CV death, nonfatal MI, and hospitalization for HF in adult patients with CKD associated with T2D.

Agarwal R, et al. *Nephrol Dial Transplant*. 2022;37(9):1014-1023.
Kerenida. Prescribing information. Bayer Healthcare Pharmaceuticals Inc.; 2022. Accessed April 4, 2024. https://labeling.bayerhealthcare.com/html/products/pi/Kerenida_PI.pdf

Finerenone Phase 3 Trials in T2D and CKD

	FIDELIO-DKD ¹	FIGARO-DKD ²
Design	Randomized, double-blind, placebo-controlled, multicenter, phase 3, event-driven	
Subjects	Adults (N = 5734) with: <ul style="list-style-type: none"> • T2D • Treated with ACE-I or ARB • UACR 30-300 eGFR 25-60 and diabetic retinopathy or UACR \geq300 and eGFR 25-75 	Adults (N = 7437) with: <ul style="list-style-type: none"> • T2D • Treated with ACE-I or ARB • UACR 30-300 and eGFR 25-90 or UACR \geq300 and eGFR \geq60
Randomized treatment	Finerenone 10 or 20 mg/d or placebo Titration based on potassium level and change in eGFR	
Primary endpoint	Composite of time to first occurrence of kidney failure, sustained decrease of eGFR \geq 40% over \geq 4 wks, or kidney-related death	Composite of time to first occurrence of CV death, nonfatal myocardial infarction, nonfatal stroke, or HF hospitalization
Median follow up	2.6 years	3.4 years
Results published	October 2020	August 2021

UACR in mg/g and eGFR in mL/min/1.73 m²

1. Bakris GL, et al. *N Engl J Med*. 2020;383(23):2219-2229. 2. Pitt B, et al. *N Engl J Med*. 2021;385(24):2252-2263.

FIDELIO-DKD All Outcomes^{1,2}

Outcome	Hazard ratio (95% CI)	P value
Primary composite ¹	0.82 (0.73-0.93)	0.001
Sustained decrease \geq 40% in eGFR ¹	0.81 (0.72-0.92)	–
Secondary composite ¹	0.86 (0.75-0.99)	0.03
Secondary kidney composite ¹	0.76 (0.65-0.90)	–
Sustained doubling of SCr for \geq 4 wks ¹	0.68 (0.55-0.82)	–
New-onset atrial fibrillation/atrial flutter* ²	0.71 (0.53-0.94)	0.016

1. Bahris G, et al. *N Engl J Med*. 2020;383(23):2219-2229; 2. Filippatos G, et al. *J Am Coll Cardiol*. 2021;78(2):142-152.

FIGARO-DKD All Outcomes^{1,2}

Outcome	Hazard ratio (95% CI)	P value
Primary composite ¹	0.87 (0.76-0.98)	0.03
Hospitalization for HF ¹	0.71 (0.56-0.90)	–
Secondary composite ¹	0.87 (0.76-1.01)	–
Secondary kidney composite ¹	0.77 (0.60-0.99)	–
End-stage kidney disease ¹	0.64 (0.41-0.995)	–
New-onset HF ²	0.68 (0.50-0.93)	0.016

1. Pitt B, et al. *N Engl J Med*. 2021;385(24):2252-2263; 2. Filippatos G, et al. *Circulation*. 2022;145:437-447.

Key Finerenone Product Information

How supplied	10-mg and 20-mg tablets
Recommended dosing (eGFR expressed in mL/min/1.73m ² ; serum potassium expressed as mEq/L)	<p>Recommended starting dose (do not initiate if serum potassium >5.0 prior to initiation):</p> <ul style="list-style-type: none"> eGFR \geq60: 20 mg once daily eGFR \geq25 to <60: 10 mg once daily eGFR <25: initiation not recommended <p>Recommended dose adjustments:</p> <p>If current dose is 10 mg once daily:</p> <ul style="list-style-type: none"> Serum potassium \leq4.8: increase dose to 20 mg once daily Serum potassium >4.8 to 5.5: maintain 10 mg once daily Serum potassium >5.5: hold finerenone; consider restarting when serum potassium \leq5.0 <p>If current dose is 20 mg once daily:</p> <ul style="list-style-type: none"> Serum potassium \leq4.8: maintain 20 mg once-daily dose Serum potassium >4.8 to 5.5: maintain 20mg once-daily dose Serum potassium >5.5: hold finerenone; restart at 10 mg once daily when serum potassium \leq5.0

Kerenida. Prescribing information. Bayer HealthCare Pharmaceuticals Inc.; 2022. Accessed April 4, 2024. https://labeling.bayerhealthcare.com/html/products/pi/kerenida_pi.pdf

Key Finerenone Product Information

Recommended monitoring	Measure serum potassium 4 weeks after initiation, 4 weeks after a dose adjustment, and throughout treatment to guide dose adjustments
Common side effects (occurring in ≥1% of patients and more frequently than placebo)	<ul style="list-style-type: none"> Hyperkalemia Hypotension Hyponatremia
Select drug interactions	Finerenone is a CYP3A4 substrate: <ul style="list-style-type: none"> Concomitant use with strong CYP3A4 inhibitors is contraindicated Monitor serum potassium during drug initiation or dose adjustment of either finerenone or moderate/weak CYP3A4 inhibitors Avoid concomitant use with strong or moderate CYP3A4 inducers
Contraindications	<ul style="list-style-type: none"> Concomitant use with strong CYP3A4 inhibitors Patients with adrenal insufficiency

Karenida. Prescribing information. Bayer HealthCare Pharmaceuticals Inc.; 2022. Accessed April 4, 2024. https://labeling.bayerhealthcare.com/html/products/pi/karenida_pi.pdf

Combined SGLT-2 Inhibitor and MRA Benefit

Joint analysis of randomized trials (CREDESCENCE, FIDELIO-DKD, and DAPA-CKD)

Outcome	Combination Treatment Events/Patients	Conventional Treatment Events/Patients	Hazard Ratio (95% CI)
Doubling of SCr, ESKD, or death due to kidney failure	405/5035	550/5040	0.50 (0.44–0.57)
ESKD	324/5035	400/5040	0.59 (0.51–0.69)
All-cause mortality	387/5035	445/5040	0.75 (0.65–0.86)

- Patients had T2D and CKD
- Conventional Treatment: ACE inhibitor or ARB
- Combination treatment: SGLT-2 inhibitor and nonsteroidal MRA

Estimated event-free survival from composite kidney outcome incremental gain was 6.7 years with combination treatment

Herrington DM, et al. Diabetes Care. 2023; 46(10):1113-1123

Overcoming Barriers to Optimal DKD Treatment in Primary Care

- Barriers to successful DKD management
 - Clinical inertia
 - Low CKD awareness among patients
 - Primary care-specific barriers
- Overcoming barriers leads to more patients receiving the right therapies at the right time—early in the disease course to prevent adverse outcomes

Primary Care-Specific Barriers
Lack of clinician awareness and knowledge of CKD
Lower priority of CKD compared to other conditions
Complex patient characteristics
Lack of clinician time and resources
Inadequate collaboration with and access to specialists
Lack of clear parameters for specialist referral and difficult referral processes

Nee R, et al. Nephrol Dial Transplant. 2023;38(3):532-541; Shubrook R, et al. Postgrad Med. 2022;134(4):376-387.

Learning Objectives

In this presentation, you've learned to...

Identify patients at risk for CKD who should be screened for albuminuria, using UACR, and reduced eGFR to lessen diagnostic delays.

Incorporate newer agents such as SGLT-2 inhibitors and MRAs into treatment plans for eligible patients with CKD and T2D.

Review new and emerging data regarding the use of MRAs in patients with CKD and DKD.

State-of-the-Art Treatment of DKD

Resource Toolkit:

Additional resources and a video of this presentation are available using the URL or QR code below.



<https://www.pcmg-us.org/toolkit/dkd>

State-of-the-Art Treatment of DKD

Stephen A. Brunton, MD, FAAFP, CDCES

Executive Director
Primary Care Metabolic Group

Summary:

- CKD in T2D is associated with increased risk for CV events, kidney disease progression, and mortality.
- Annual CKD screening is recommended for patients with T2D, including albuminuria (UACR) and eGFR assessment.
- Risk factor management, including optimization of glycemia and blood pressure, are recommended to prevent and/or slow progression of DKD.
- Use of RAS inhibitors, SGLT-2 inhibitors, and/or finerenone are recommended for organ protection in patients with T2D and CKD.

State-of-the-Art
Treatment of
DKD

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Executive Director
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Please take the post-survey using
the QR Code or URL below.
URL: <https://www.pcmg-us.org/survey/post/2024DKD2>