CKD for the PCP

Khaled Boubes, MD, FASN, FASDIN
Assistant Professor of Medicine & Biomedical Engineering
Director of Interventional Nephrology
Division of Nephrology, Department of Internal Medicine
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University Wexner Medical Center

Disclosures

- None

The Ohio State University Wexner Medical Center

Outline

- CKD prevalence
- Is CKD a risk factor?
- CKD basics
- Decided to refer? What to do next?
  - CKD work-up
  - Things to AVOID
  - Things that we follow
  - Treatments
- New Treatments

The Ohio State University Wexner Medical Center

USRDS

(b) Trends in percentage in KDIGO CKD risk categories, 2003-2018

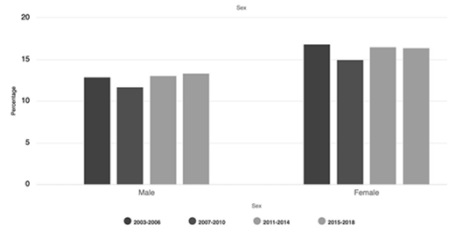
	2003-2006	2007-2010	2011-2014	2015-2018
Low risk	85.1	86.6	85.2	85.1
Moderately high risk	10.9	9.5	10.8	10.9
High risk	2.7	2.5	2.6	2.7
Very high risk	1.3	1.4	1.5	1.3
Total	100	100	100	100

2020 USRDS Annual Data Report: Epidemiology of kidney disease in the US. NIH, NIDDK

The Ohio State University Wexner Medical Center

USRDS

Prevalence of CKD in adults within sex, 2003-2018

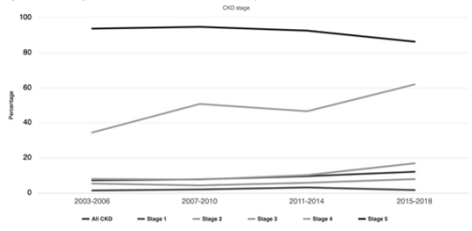


Data Source: 2020 United States Renal Data System Annual Data Report

2020 USRDS Annual Data Report: Epidemiology of kidney disease in the US. NIH, NIDDK

USRDS

Figure 1.11 Percentage of U.S. adults with CKD aware of their kidney disease, 2003-2018

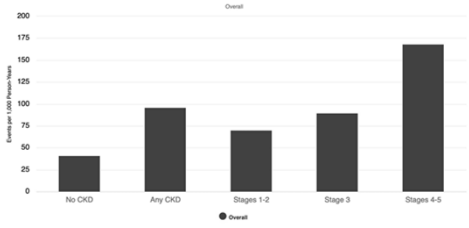


Data Source: 2020 United States Renal Data System Annual Data Report

2020 USRDS Annual Data Report: Epidemiology of kidney disease in the US. NIH, NIDDK

USRDS

Figure 3.1 Adjusted all-cause mortality in Medicare beneficiaries aged ≥66 years, by CKD status and stage, 2018

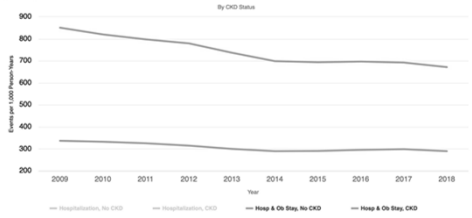


Data Source: 2020 United States Renal Data System Annual Data Report

2020 USRDS Annual Data Report: Epidemiology of kidney disease in the US. NIH, NIDDK

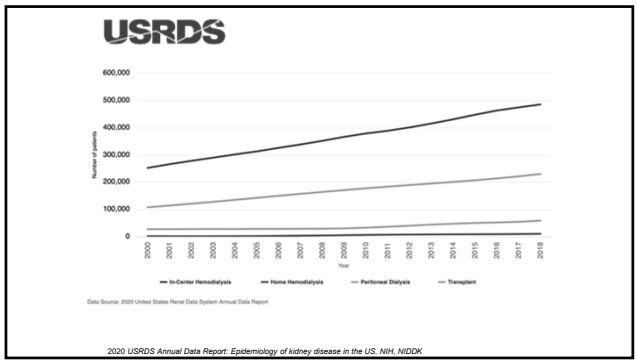
USRDS

Figure 3.5 Adjusted rates of all-cause hospitalization and observation stays for Medicare beneficiaries aged ≥66 years, by CKD status and stage, 2009-2018.



Data Source: 2020 United States Renal Data System Annual Data Report

2020 USRDS Annual Data Report: Epidemiology of kidney disease in the US. NIH, NIDDK



2020 USRDS Annual Data Report: Epidemiology of kidney disease in the US. NIH, NIDDK

CKD Basics

CKD Heat-map **Prognosis of CKD by GFR and albuminuria category**

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/1.73 m2)Description and range				Persistent albuminuria categories Description and range		
				A_1	A_2	A_3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Source: Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. Kidney Int Suppls. 2013;3:1-150.

CKD Heat-map

Table 1.1 Percentage of adults in the U.S. in KDGIO CKD risk categories, 2003-2018

	(a) Percentage by eGFR and ACR, 2015-2018			
eGFR Categories	A1: Normal to mildly increased (ACR <30 mg/g)	A2: Moderately increased (ACR 30-299 mg/g)	A3: Severely increased (ACR ≥300 mg/g)	Total
G1: Normal or high (eGFR ≥90ml/min/1.73m²)	53.5	4.1	0.58	58.3
G2: Mildly decreased (eGFR 60-89 ml/min/1.73m²)	31.5	2.9	0.43	34.8
G3a: Mildly to moderately decreased (eGFR 45-59 ml/min/1.73m²)	3.9	0.84	0.27	5.0
G3b: Moderately to severely decreased (eGFR 30-44 ml/min/1.73m²)	0.88	0.40	0.17	1.5
G4: Severely decreased (eGFR 15-29 ml/min/1.73m²)	0.11	0.09	0.17	0.37
G5: Kidney failure (eGFR <15 ml/min/1.73m²)	0.01	0.01	0.09	0.11
Total	90.0	8.3	1.7	100

2020 USRDS Annual Data Report: Epidemiology of kidney disease in the US. NIH, NIDDK

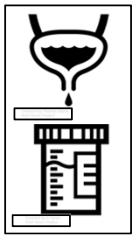
What is Creatinine?!

Metabolic by-product mainly produced by muscles

In steady-state; production = excretion

Is a serum Cr of 1.5mg/dL normal?

What should I order?



CKD work-up

- Chemistry
  - Rule out DM-2
- Urine analysis with microscopic evaluation
  - Blood is a red flag
- Protein: Urine albumin to creatinine
- Renal US
  - Look for structural abnormalities, bladder obstruction, etc…

CKD work-up

- Chemistry
- Urine
- Protein
- Ultrasound

CKD Heat-map — **Prognosis of CKD by GFR and albuminuria category**

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/1.73 m2) Description and range				Persistent albuminuria categories Description and range		
				A_1	A_2	A_3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

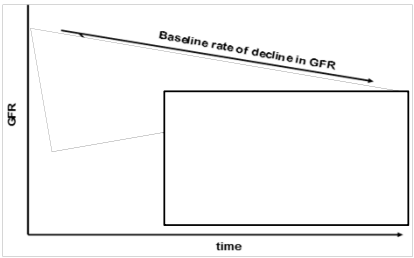
Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Source: Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. Kidney Int Suppls. 2013;3:1-150.

CKD work-up - Management

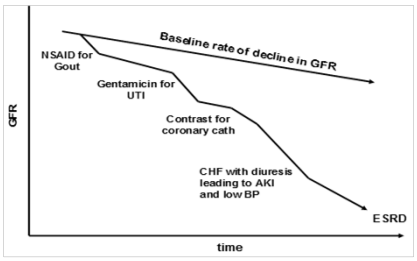
- Review medications: "*We are Medicine!*"
  - NSAID's, NSAID's, and *NSAID's*!
  - Avoid dual RAAS blockade
  - Preferably avoid PPI's
- Maximize DM control
- Maximize BP control
- Appropriate dosing of medications

CKD progression: biology vs "us"?



Fink, et al, AJKD, 2009

CKD progression: biology vs "us"?



Fink, et al, AJKD, 2009

Things that *Nephrologists* will follow

- **Excretory functions:**
  - Remove from the body
    - Toxic and waste products
    - Excess water
  - Maintain the balance of
    - Various electrolytes
- **Endocrine functions**:
  - Erythropoietin
  - Active Vitamin D
    - Bone metabolism
  - Renin
    - BP control

Things that *Nephrologists* will follow

- CKD Etiology–
- HTN– rule out secondary causes
- Anemia–
- Bone mineral disease– Ca, PO4, PTH and Vit D
- Acidosis–

Treatments

- Target the cause
- Minimize proteinuria
- Support "*other*" renal functions

Executive summary of 2020 KDIGO DM Management in CKD Guideline

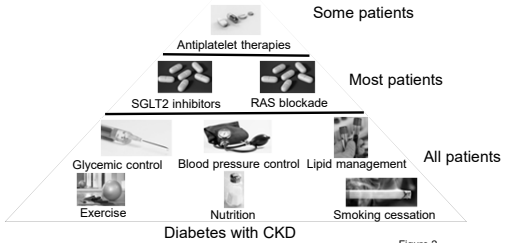
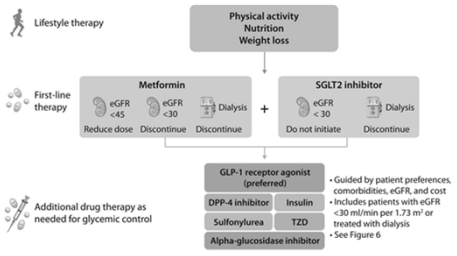


Figure 2

Kidney International 2020 98839-848DOI: (10.1016/j.kint.2020.06.024)

Executive summary of 2020 KDIGO DM Management in CKD Guideline			Primary outcome		Kidney outcomes		
Drug	**Trial**	**Kidney-related eligibility criteria**	**Primary outcome**	**Effect on primary outcome**	**Effect on albuminuria or albuminuria-containing composite outcome**	**Effect on GFR loss**	**Adverse effects**
SGLT2 inhibitors							
Empagliflozin	EMPA-REG OUTCOME	eGFR ≥30 ml/min per 1.73 m^2	MACE	⇩	⇩⇩	⇩⇩	Genital mycotic infections, DKA
Canagliflozin	CANVAS trials CREDENCE	eGFR ≥30 ml/min per 1.73 m^2 ACR >300 mg/g [30 mg/mmol] and eGFR 30–90 ml/min per 1.73 m^2	MACE Progression of CKD[b]	⇩ ⇩⇩	⇩⇩ ⇩⇩	⇩⇩ ⇩⇩	Genital mycotic infections, DKA, amputation Genital mycotic infections, DKA
Dapagliflozin	DECLARE-TIMI 58	CrCl ≥60 ml/min	Dual primary outcomes: MACE and the composite of hospitalization for heart failure or CV death[c]	⇔/⇩	⇩	⇩⇩	Genital mycotic infections, DKA

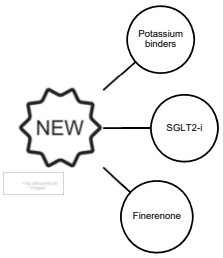
Executive summary of 2020 KDIGO DM Management in CKD Guideline



Kidney International 2020 98839-848DOI: (10.1016/j.kint.2020.06.024)

New kids on the block!

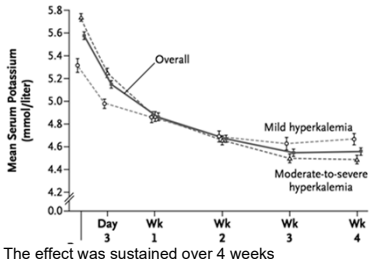
New Therapies



The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 15, 2015 VOL. 372 NO. 3

Patiromer in Patients with Kidney Disease and Hyperkalemia Receiving RAAS Inhibitors

Matthew R. Weir, M.D., George L. Bakris, M.D., David A. Bushinsky, M.D., Martha R. Mayo, Pharm.D., Dahlia Garza, M.D., Yuri Stasiv, Ph.D., Janet Wittes, Ph.D., Heidi Christ-Schmidt, M.S.E., Lance Berman, M.D., and Bertram Pitt, M.D., for the OPAL-HK Investigators*

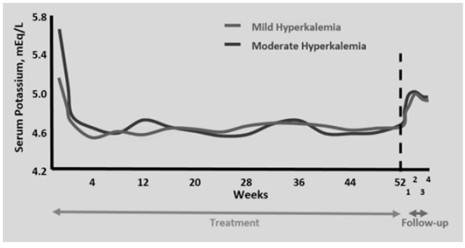


- The effect was sustained over 4 weeks
- Well tolerated

Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease

The AMETHYST-DN Randomized Clinical Trial

Bakris GL, et. al.



The NEW ENGLAND JOURNAL of MEDICINE

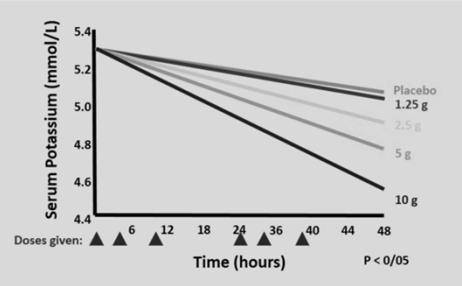
ORIGINAL ARTICLE

Sodium Zirconium Cyclosilicate in Hyperkalemia

David K. Packham, M.B., B.S., M.D., Henrik S. Rasmussen, M.D., Ph.D., Philip T. Lavin, Ph.D., Mohamed A. El-Shahawy, M.D., M.P.H., Simon D. Roger, M.D., Geoffrey Block, M.D., Wajeh Qunibi, M.D., Pablo Pergola, M.D., Ph.D., and Bhupinder Singh, M.D.

January 15, 2015 N Engl J Med 2015; 372:222-231

Sodium Zirconium Cyclosilicate in Hyperkalemia



January 15, 2015 N Engl J Med 2015; 372:222-231

Lokelma approved in the US for the treatment of adults with hyperkalaemia

PUBLISHED
18 May 2018

Lokelma provides rapid and sustained potassium control for patients in a condition with high unmet need

The US Food and Drug Administration (FDA) has approved Lokelma (sodium zirconium cyclosilicate), formerly ZS-9, for the treatment of adults with hyperkalaemia,[1] a serious condition characterised by elevated potassium levels in the blood associated with cardiovascular, renal and metabolic diseases.[2]

The risk of hyperkalaemia increases significantly for patients with chronic kidney disease (CKD) and for those who take common medications for heart failure (HF), such as renin-angiotensin-aldosterone system (RAAS) inhibitors, which can increase potassium in the blood.[2,3] To help prevent the recurrence of hyperkalaemia, RAAS-inhibitor therapy is often modified or discontinued, which can compromise cardio-renal outcomes and increase the risk of death.[3,4]

Editorial commentary

EDITORIAL

A Cov

A New Era for the Treatment of Hyperkalemia?

Julie R. Ingelfinger, M.D.
N Engl J Med 2015; 372:275-277 | January 15, 2015 | DOI: 10.1056/NEJMe1414112

In Focus

The Colon as the Potassium Target: Entering the Colonic Age of Hyperkalemia Treatment?

Daniel Batlle *, Khaled Boobés, Kiran G. Manjee

Patiromer for Hyperkalemia in Diabetic CKD: A New Kid on the Block

Pranav S. Garimella, MD, MPH
Bertrand L. Jaber, MD, MPH

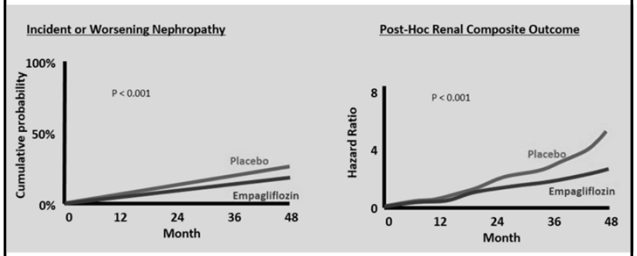
*"Given the gastro- intestinal side effects, unpleasant taste, and risk for colonic necrosis with sodium polystyrene sulfonate, its days as the primary treatment option for hyperkalemia are likely **numbered**."*

Comparison

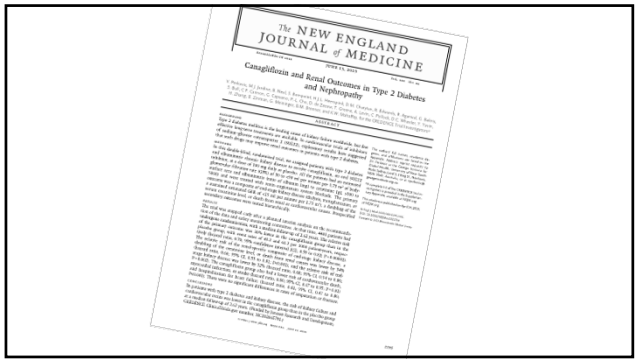
- Patiromer
  - Exchanges Ca for K
  - Can cause low Mg
  - On market since 2015
  - Binds K in the colon
  - Can be used in ESRD
  - Cost: $700-800/month
- ZS-9
  - Exchanges Na for K
  - Can cause edema
  - On market since 2019
  - Binds K throughout the GI tract
  - Can be used in ESRD
  - Cost: $600-700/month

SGLT2- inhibitors

Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes

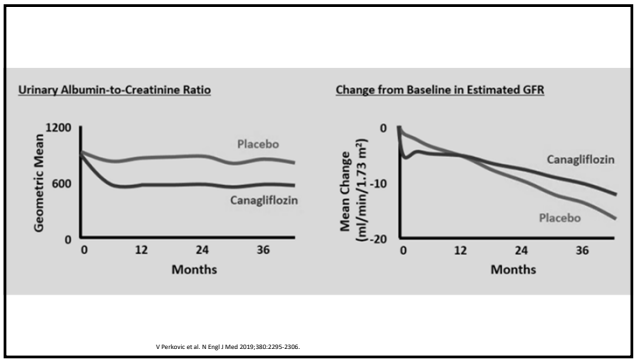


Wanner C et al. N Engl J Med 2016;375:323-334.

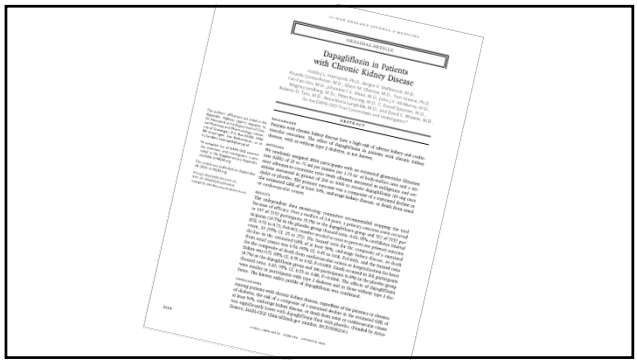


The NEW ENGLAND JOURNAL of MEDICINE

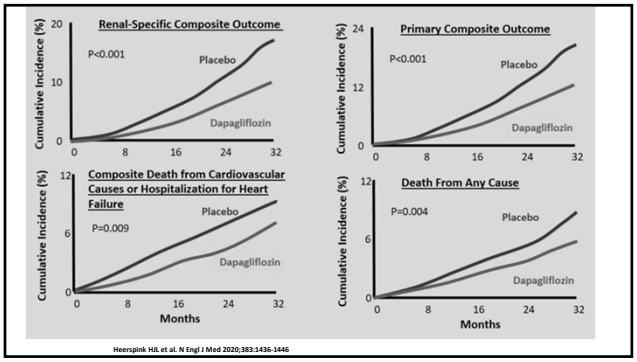
Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy



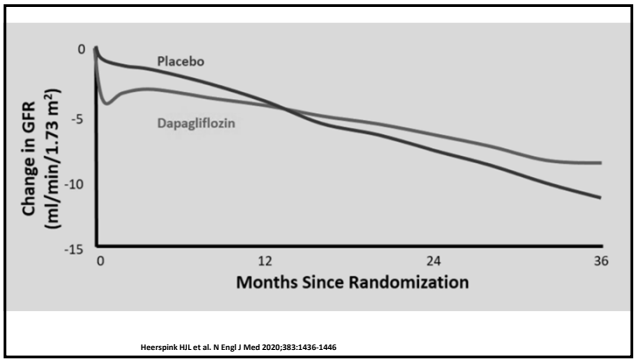
V Perkovic et al. N Engl J Med 2019;380:2295-2306.



Dapagliflozin in Patients with Chronic Kidney Disease

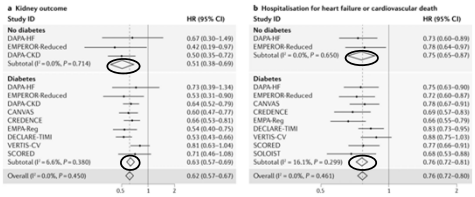


Heerspink HJL et al. N Engl J Med 2020;383:1436-1446



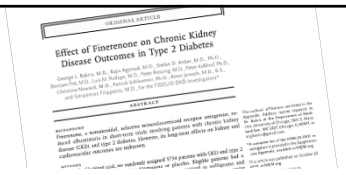
Heerspink HJL et al. N Engl J Med 2020;383:1436-1446

SGLT2-Inhibitors



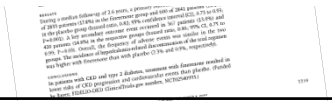
Kang, A., Jardine, M.J. SGLT2 inhibitors may offer benefit beyond diabetes. Nat Rev Nephrol 17, 83–84 (2021).

Finerenone


ORIGINAL ARTICLE

Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

ABSTRACT


CONCLUSIONS

In patients with CKD and type 2 diabetes, treatment with finerenone resulted in lower risks of CKD progression and cardiovascular events than placebo. (Funded by Bayer; FIDELIO-DKD ClinicalTrials.gov number, NCT02540993.)

In Summary…

- CKD is *common*
- CKD = ***higher*** risk

- CKD basics.
  - Heat map
  - Decided to refer?
    - CKD work-up- Chemistry, UA with micro, UPC, renal US
    - *Avoid* **NSAIDs**

- New Treatments are available:
  - K binders
  - ***SGLT2-I***
  - ***Finerenone***