



CKD for the PCP

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MedNet21
Center for Continuing Medical Education

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Disclosures

- None

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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

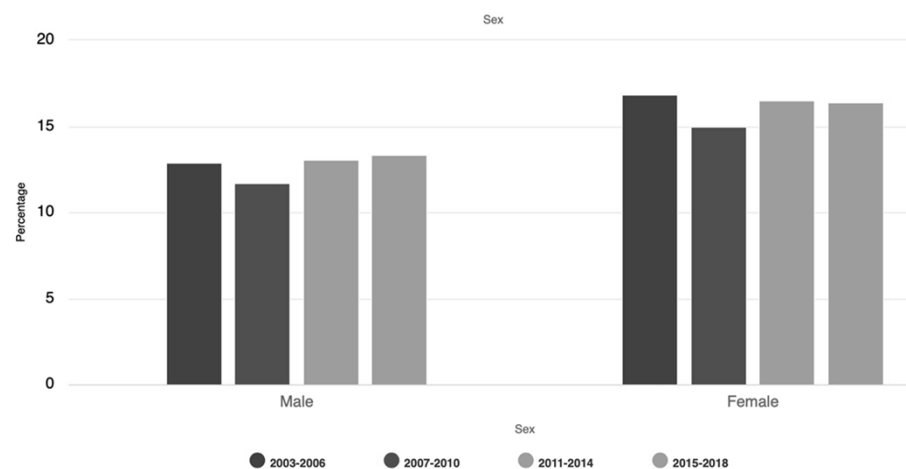
USRDS

(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



Prevalence of CKD in adults within sex, 2003-2018

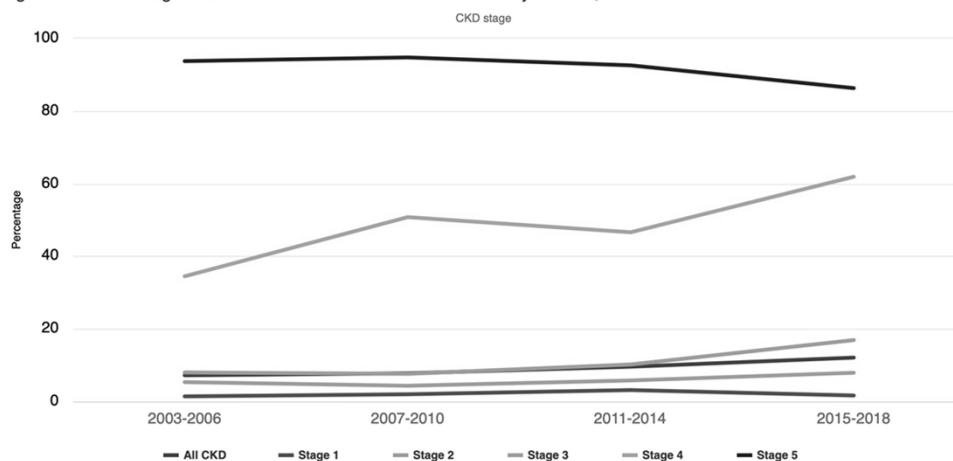


Data Source: 2020 United States Renal Data System Annual Data Report

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



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

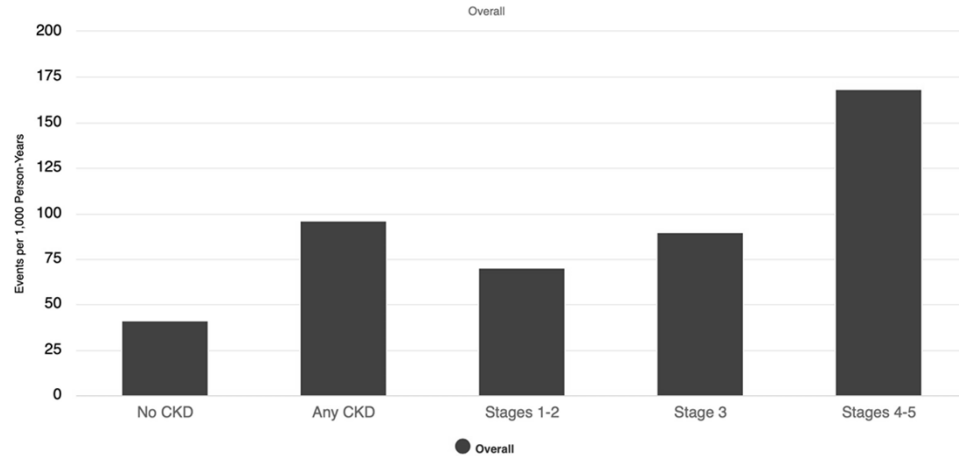


Data Source: 2020 United States Renal Data System Annual Data Report

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



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

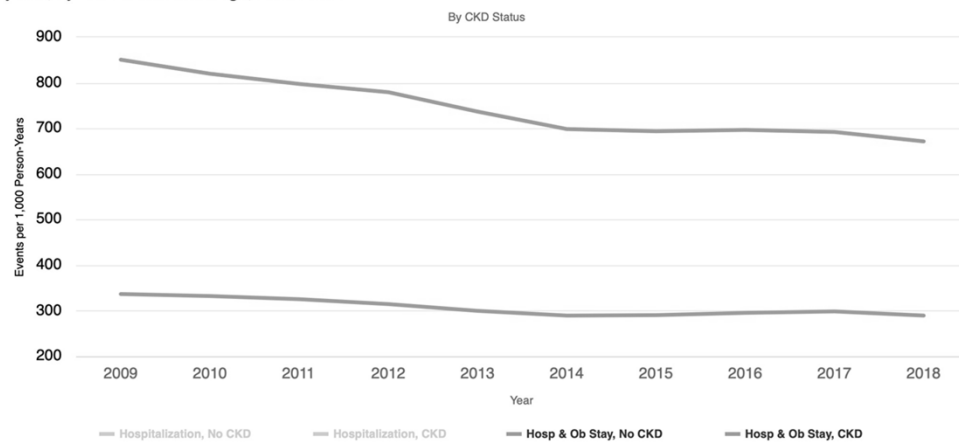


Data Source: 2020 United States Renal Data System Annual Data Report

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

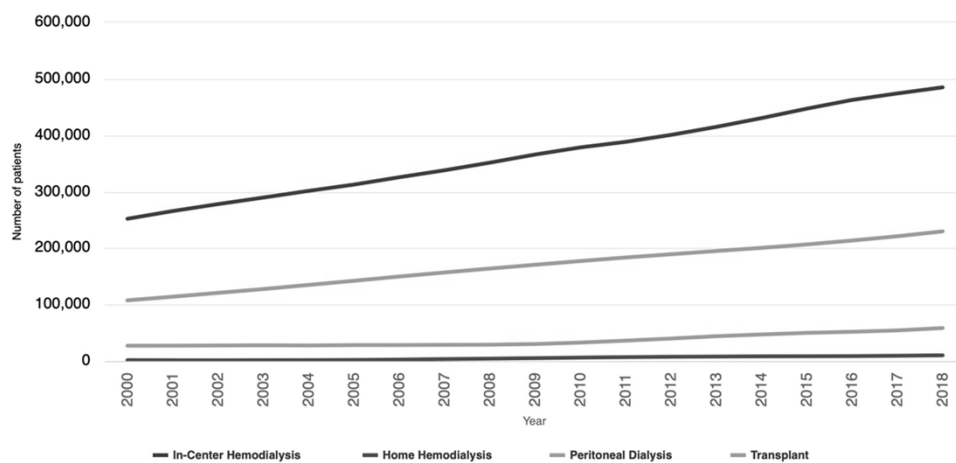


Figure 3.5 Adjusted rates of all-cause hospitalization and observation stays for Medicare beneficiaries aged ≥ 66 years, by CKD status and stage, 2009-2018.



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

USRDS

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

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CKD Basics

CKD Heat-map				Prognosis of CKD by GFR and albuminuria category		
Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012				Persistent albuminuria categories		
				Description and range		
				A ₁	A ₂	A ₃
				Normal to mildly increased <30 mg/g <3 mg/mmol	Moderately increased 30-300 mg/g 3-30 mg/mmol	Severely increased >300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m ²) Description and range	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 Suppl. 2013;3:1-150.						

CKD Heat-map

Table 1.1 Percentage of adults in the U.S. in KDIGO 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 ≥90 ml/min/1.73 m ²)	53.5	4.1	0.58	58.3
G2: Mildly decreased (eGFR 60-89 ml/min/1.73 m ²)	31.5	2.9	0.43	34.8
G3a: Mildly to moderately decreased (eGFR 45-59 ml/min/1.73 m ²)	3.9	0.84	0.27	5.0
G3b: Moderately to severely decreased (eGFR 30-44 ml/min/1.73 m ²)	0.88	0.40	0.17	1.5
G4: Severely decreased (eGFR 15-29 ml/min/1.73 m ²)	0.11	0.09	0.17	0.37
G5: Kidney failure (eGFR <15 ml/min/1.73 m ²)	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?!

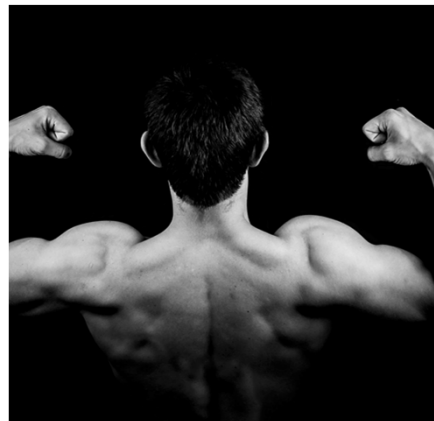


Metabolic by-product mainly produced by muscles

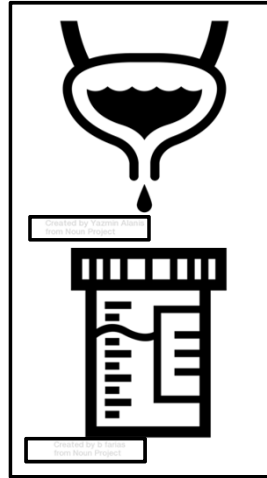


In steady-state; production = excretion

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

Persistent albuminuria categories Description and range

A₁
A₂
A₃

 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

GFR categories (ml/min/ 1.73 m ²)Description and range	G1	Normal or high	≥90			
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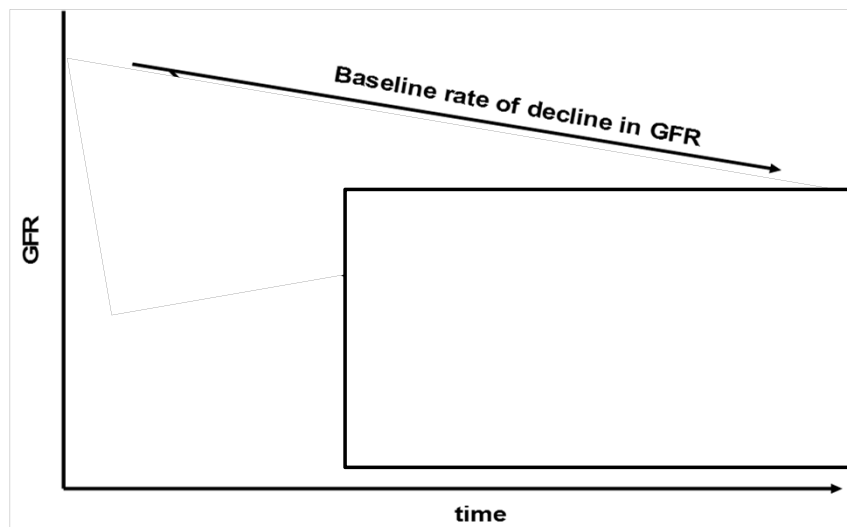
Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk;
Orange: high risk; Red, very high risk.

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

CKD work-up - Management

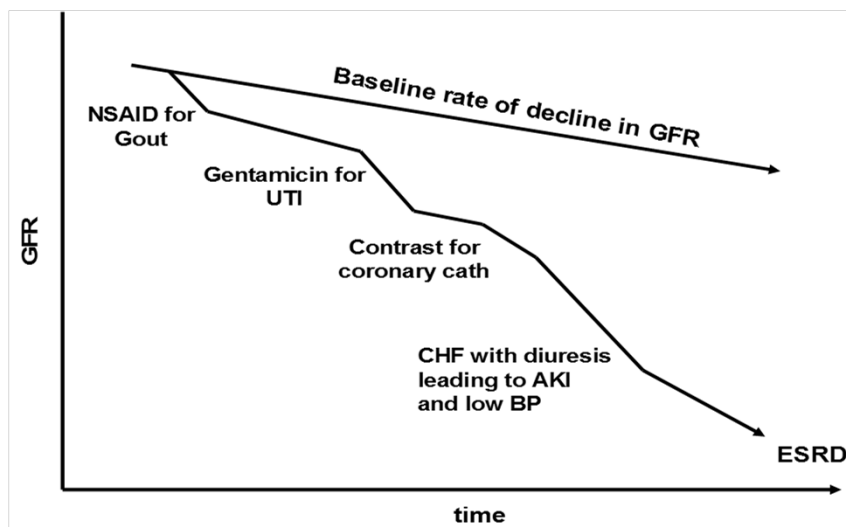
- Review medications: “*We are Medicine!*”
 - NSAID’s, NSAID’s, and *NSAID*’s!
 - Avoid dual RAAS blockade
 - Preferably avoid PPI’s
- Maximize DM control
- Maximize BP control
- Appropriate dosing of medications

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

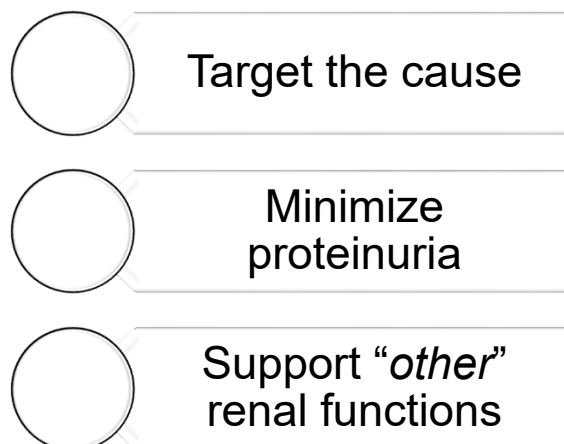
▪ Endocrine functions:

- Erythropoietin
- Active Vitamin D
 - Bone metabolism
- Renin
 - BP control

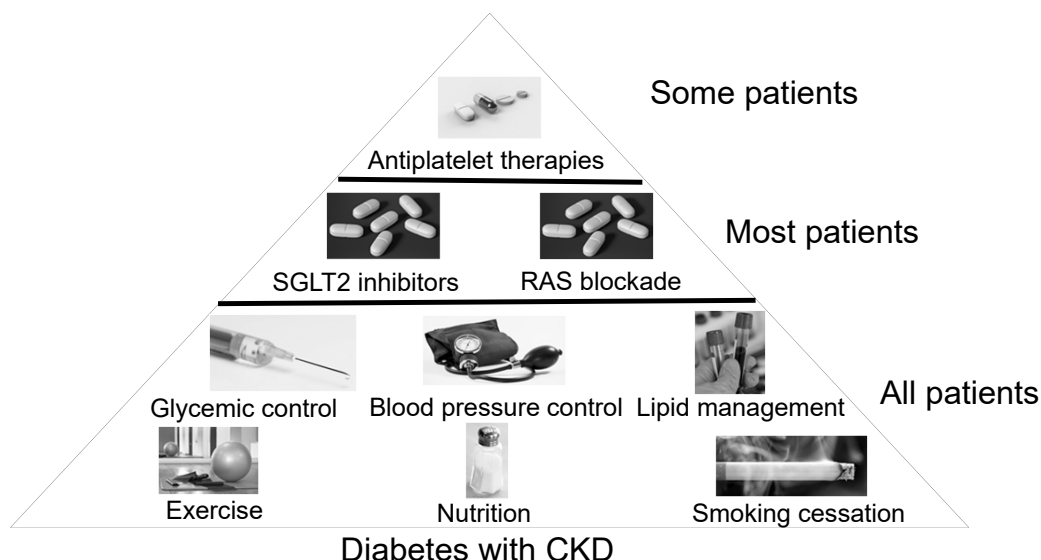
Things that *Nephrologists* will follow

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

Treatments



Executive summary of 2020 KDIGO DM Management in CKD Guideline

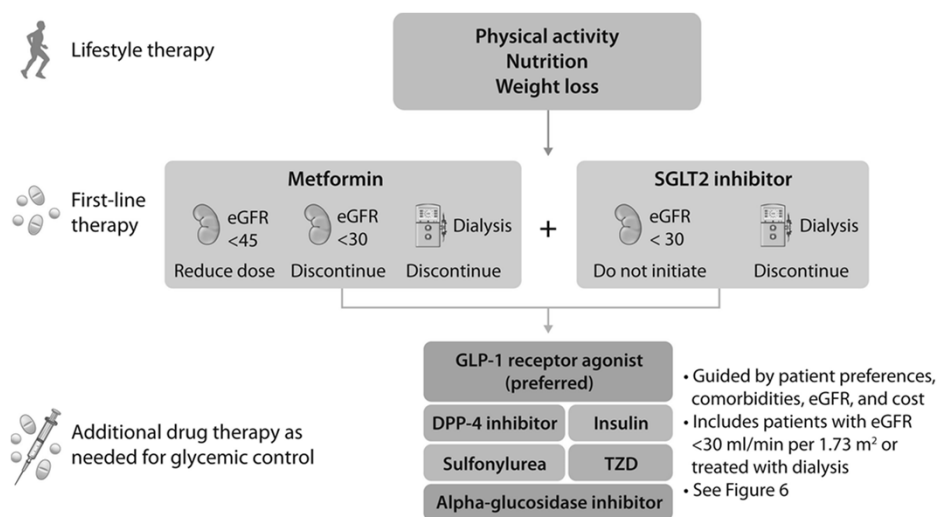


Kidney International 2020 98839-848DOI: (10.1016/j.kint.2020.06.024)

Figure 2

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

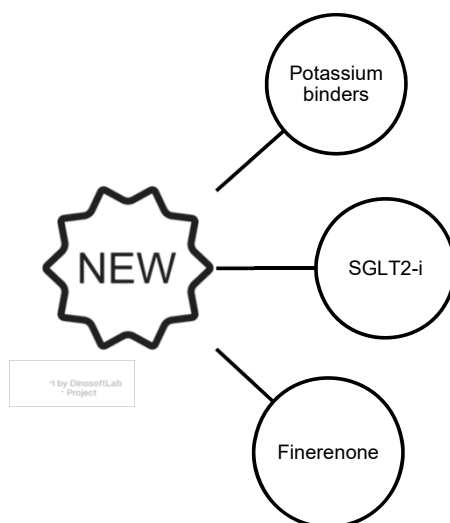
Executive summary of 2020 KDIGO DM Management in CKD Guideline



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

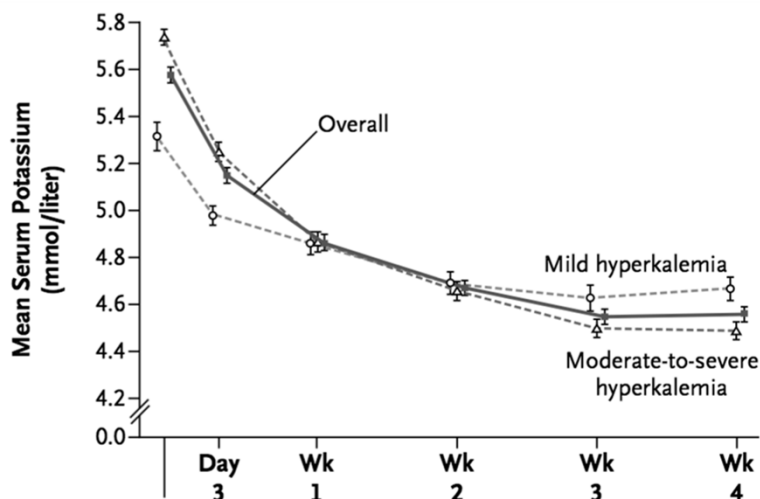
ESTABLISHED IN 1812

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*

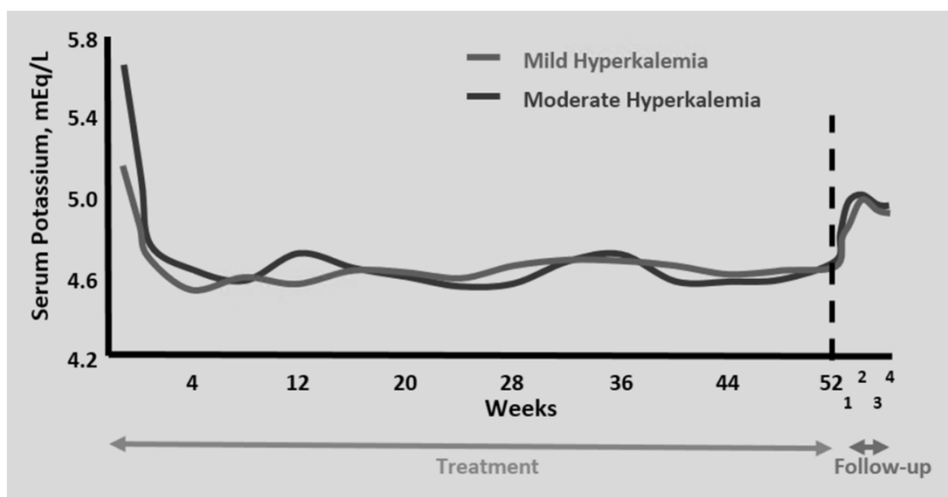


- The effect was sustained over 4 weeks
- Well tolerated

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.



JAMA. 2015;314(2):151-161. doi:10.1001/jama.2015.7446

The NEW ENGLAND JOURNAL of MEDICINE

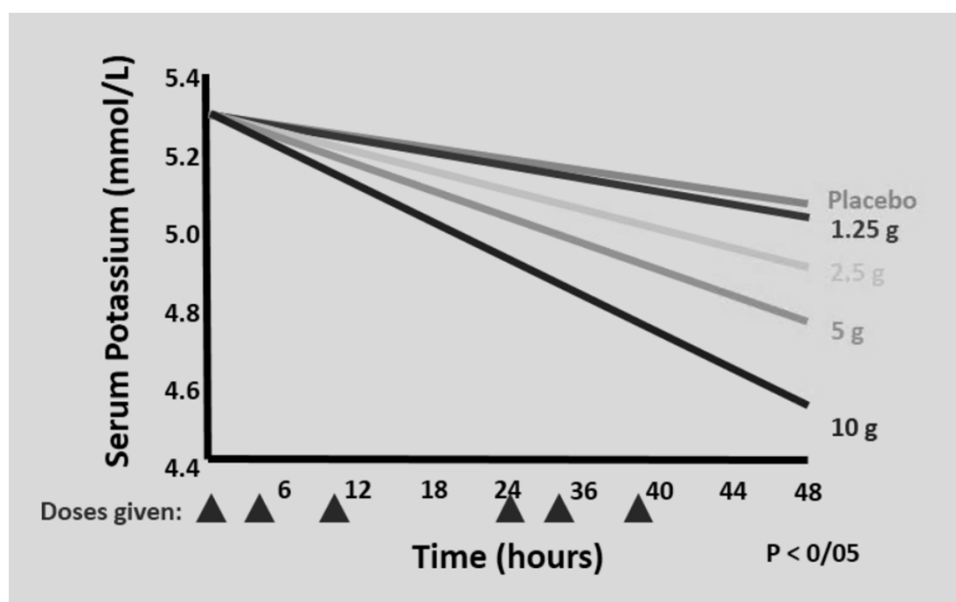
ORIGINAL ARTICLE

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 Cor

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

Division of Nephrology & Hypertension, Northwestern University, Feinberg School of Medicine, Chicago, IL 60611, United States

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

Pranav S. Garimella, MD, MPH
Tufts Medical Center, Boston, Massachusetts

Bertrand L. Jaber, MD, MS 
St Elizabeth's Medical Center, Boston, Massachusetts

"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

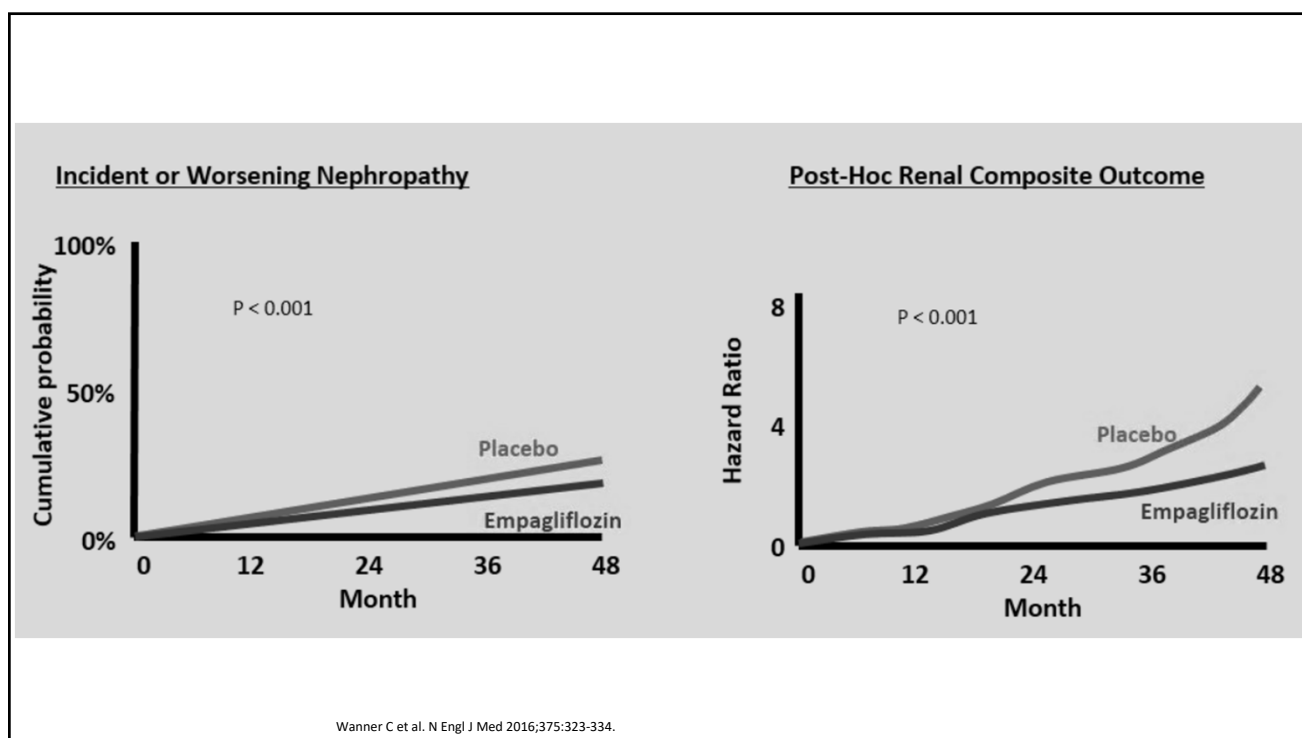
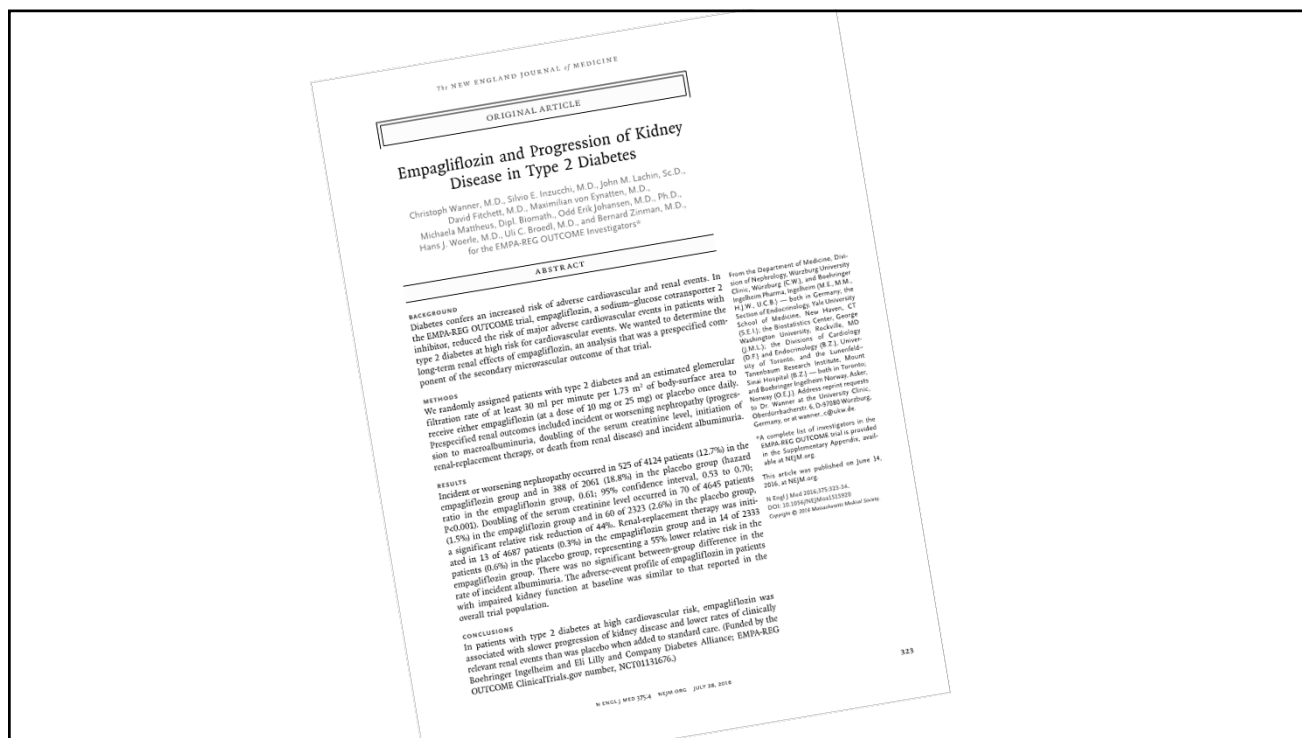
▪ Patiromer

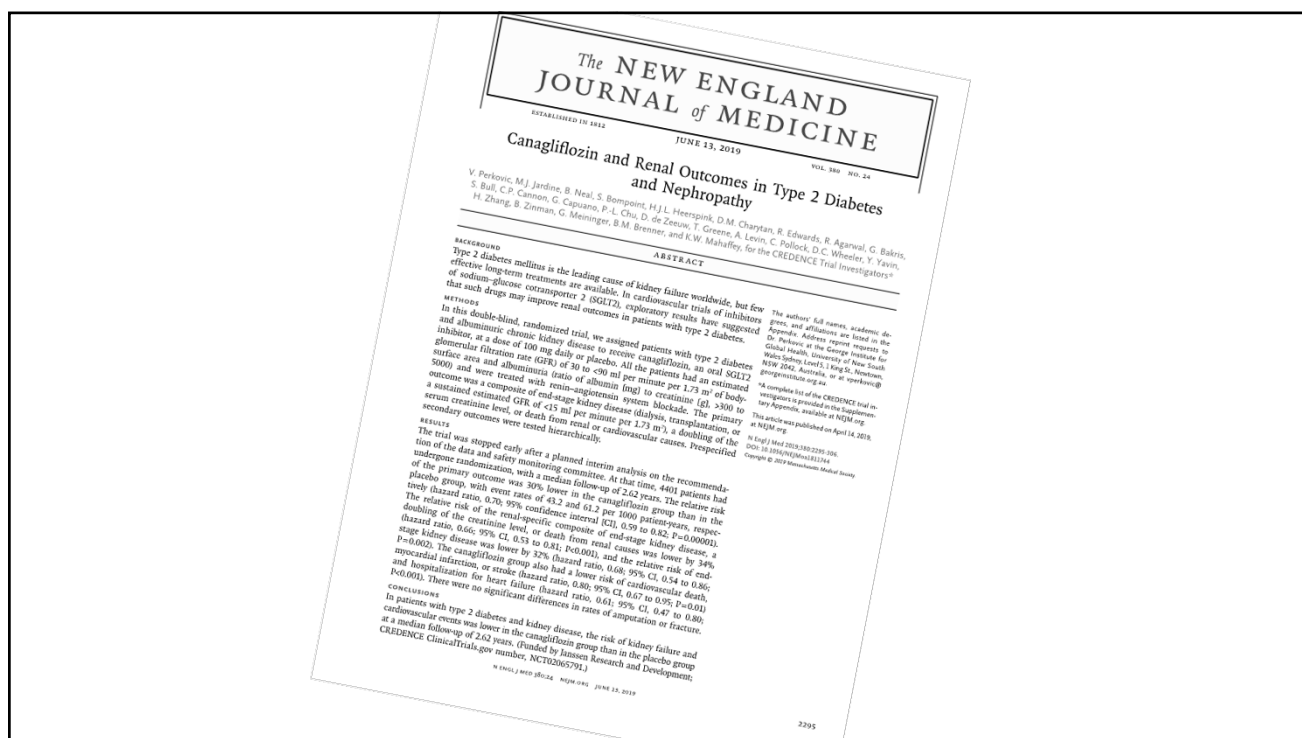
- Exchanges Ca for K
- Can cause low Mg
- On market since 2015
- Binds K in the colon
- Can be used in ESRD
- Cost: \$700-800/month

▪ ZS-9

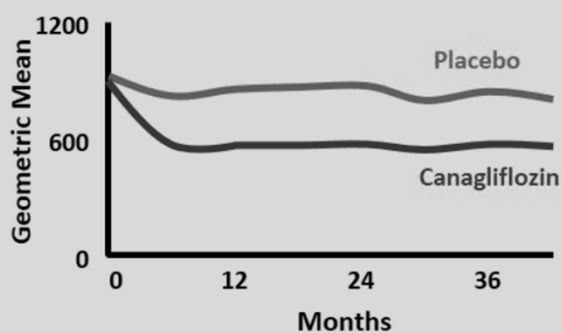
- Exchanges Na for K
- Can cause edema
- On market since 2019
- Binds K throughout the GI tract
- Can be used in ESRD
- Cost: \$600-700/month

SGLT2- inhibitors

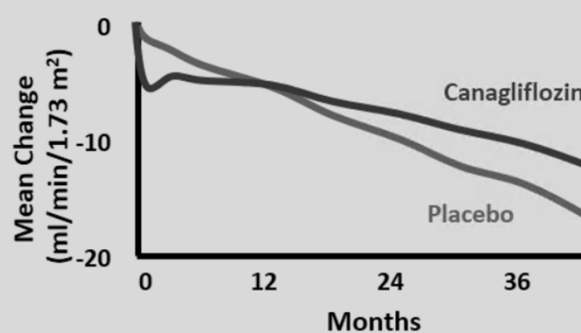


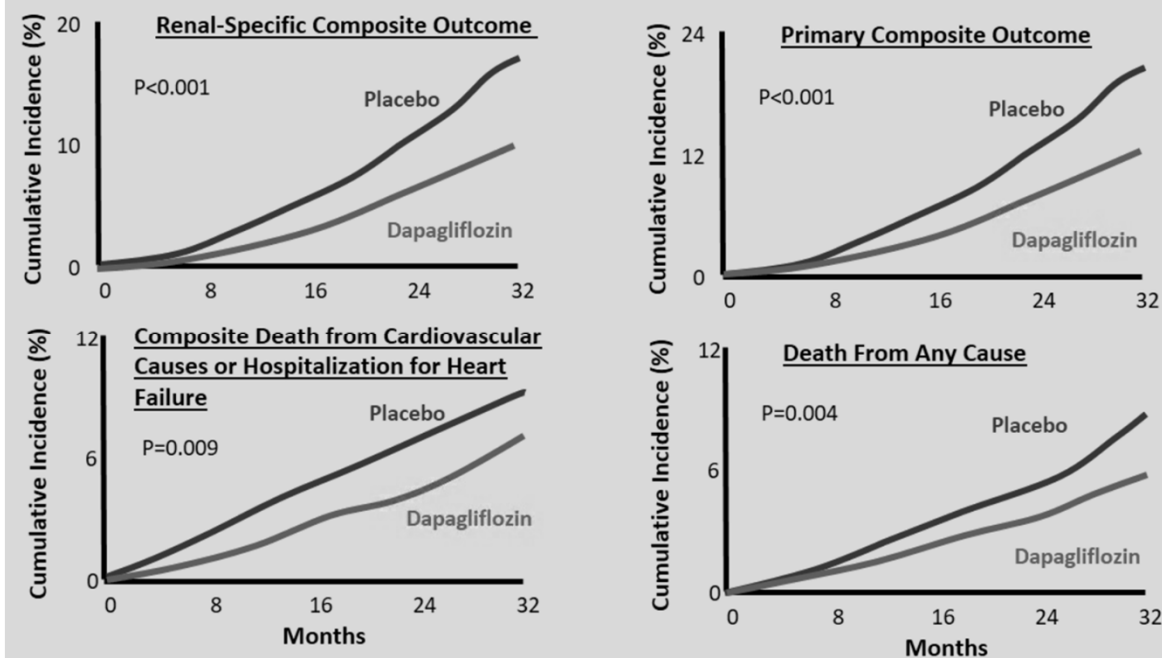
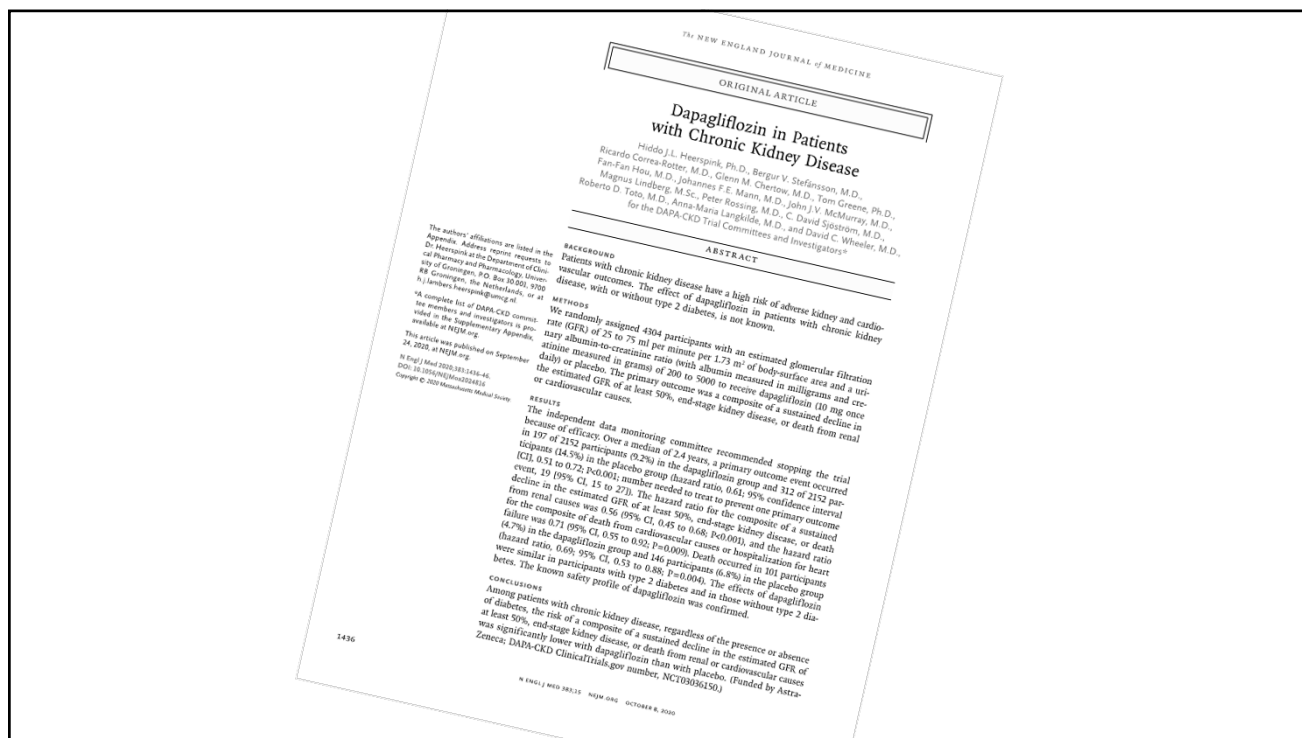


Urinary Albumin-to-Creatinine Ratio

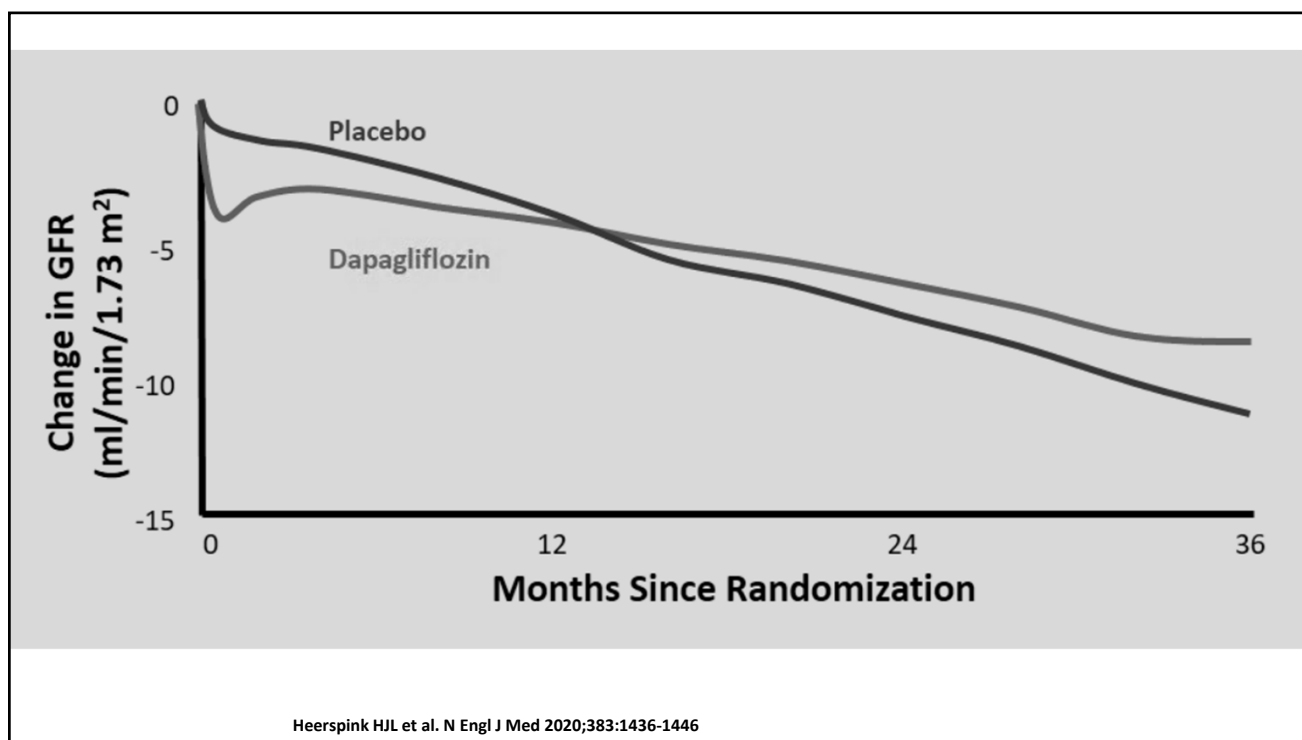


Change from Baseline in Estimated GFR

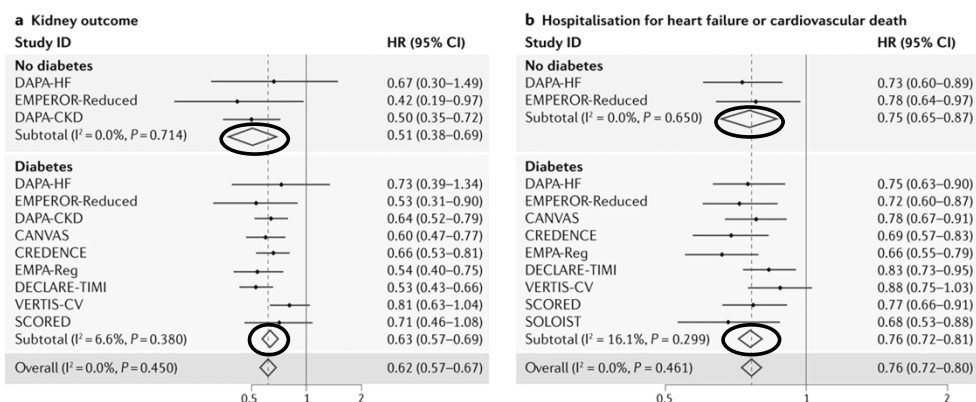




Heerspink HJL et al. N Engl J Med 2020;383:1436-1446

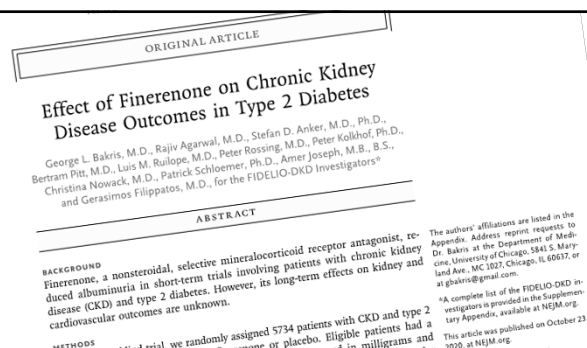


SGLT2-Inhibitors



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

Finerenone



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.)

RESULTS
During a median follow-up of 2.6 years, a primary outcome of 2841 patients (17.8%) in the finerenone group and 600 of 2841 patients (21.2%) in the placebo group (hazard ratio, 0.82; 95% confidence interval [CI], 0.73 to 0.93; $P=0.001$). A key secondary outcome event occurred in 367 patients (13.0%) and 420 patients (14.8%) in the respective groups (hazard ratio, 0.86; 95% CI, 0.75 to 0.99; $P=0.003$). Overall, the frequency of adverse events was similar in the two groups. The incidence of hyperkalemia-related discontinuation of the trial regimen was higher with finerenone than with placebo (2.3% and 0.9%, respectively).

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.)

2219

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**