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# UPDATES ON KIDNEY DISEASE

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**University of Alabama Chronic Kidney Disease Clinic**



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# FACULTY DISCLOSURE/CONFLICT OF INTEREST

**I, Rebecca Maxson, have  
no actual or potential  
conflict of interest in relation  
to this program.**



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# OBJECTIVES

- ▶ Recognize patients with chronic kidney disease (CKD) and their severity of disease.
- ▶ Describe current issues with access to care and inequities in CKD.
- ▶ Identify new medications for treating albuminuria and anemia of CKD.
- ▶ Describe the new kidney payment models and how pharmacists can participate.



# PATIENT STORY, MRS. SMITH

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Middle aged black female, has a university degree and previously worked in the hospital lab. Married with two children.

First CKD Clinic visit: Oct 2019

- ▶ Recently hospitalized with progressive SOB and BLE edema. Diagnosed with HFpEF
  - ▶ BL SCr 1.3-1.6, peak SCr 3.7, discharge 3.6
- ▶ PMH: T2DM (gastroparesis, retinopathy), HTN, IBS, CKD
- ▶ SCr 2.6 mg/dL (eGFR 19 mL/min/1.73m<sup>2</sup>), UACR 11,008 mg/g, BP 180/80 mmHg
- ▶ A1c 5.5 (Sept 2019)....14.5 (Sept 2013)
- ▶ Multiple AKI episodes while hospitalized

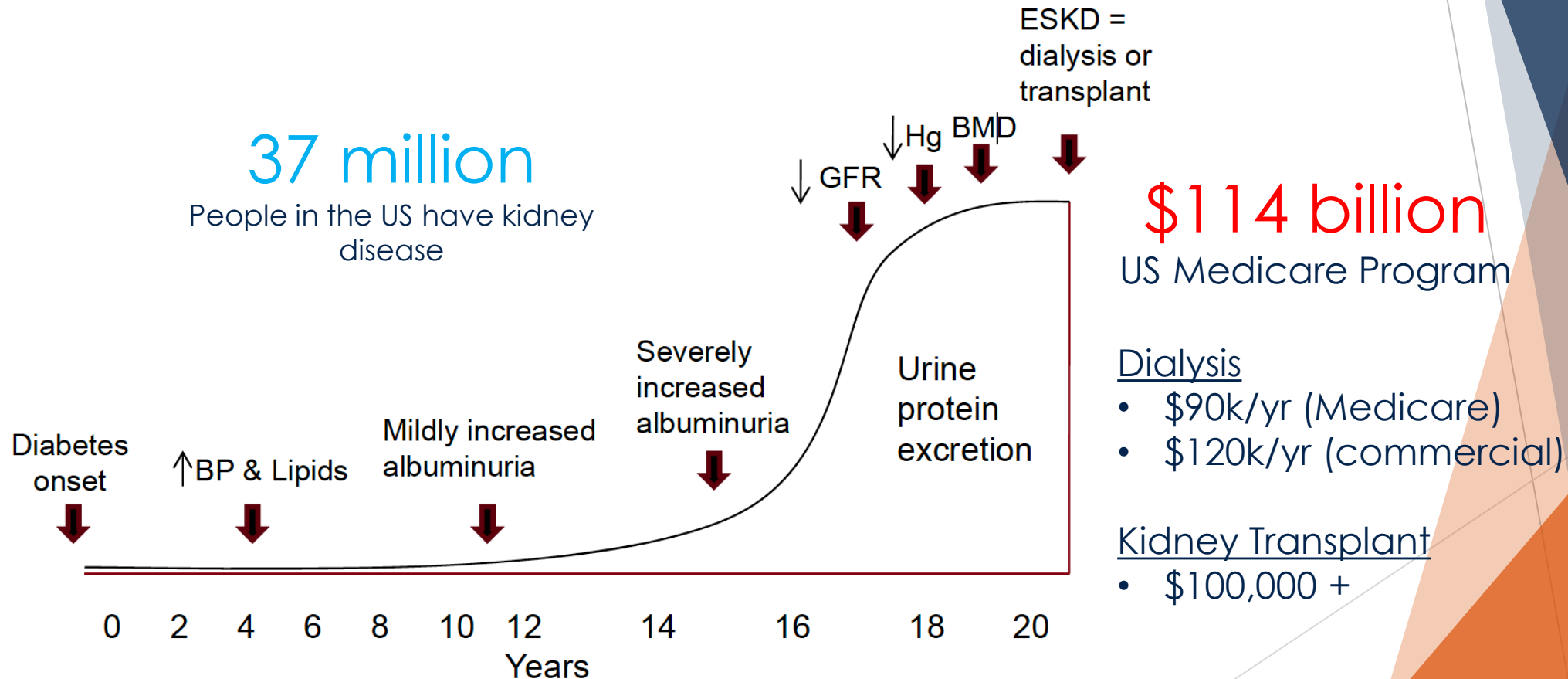
Started in-center hemodialysis April 2021



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# CLINICAL COURSE OF UNTREATED DIABETES LEADING TO ESKD



**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
<b>GFR categories (ml/min/ 1.73 m<sup>2</sup>) Description and range</b>	G1	Normal or high	≥90		<b>X</b>	
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			<b>X</b>
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			<b>X</b>
	G5	Kidney failure	<15			

- |                                                                                                                         |
|-------------------------------------------------------------------------------------------------------------------------|
| <p>2013</p> <ul style="list-style-type: none"> <li>• GFR &gt;60</li> <li>• UACR 150</li> <li>• A1c 14.5</li> </ul>      |
| <p>2018</p> <ul style="list-style-type: none"> <li>• GFR 56</li> <li>• UACR 4,725</li> <li>• A1c 6.6</li> </ul>         |
| <p>1<sup>st</sup> CKD visit, 2019</p> <ul style="list-style-type: none"> <li>• GFR 19</li> <li>• UACR 11,000</li> </ul> |

# INEQUITIES – MINORITY? POVERTY? BOTH?

- ▶ 13% of US population BUT 32% of CKD population
- ▶ Higher rates of HTN and DM than non-Hispanic whites
- ▶ Compared with non-Hispanic Whites
  - ▶ Higher rates of HTN and DM
  - ▶ Develop CKD a younger age
  - ▶ Progress faster, 3x number of new ESKD cases
- ▶ Community level poverty associated with higher ESKD cases
  - ▶ Stronger for AA than White patients

<https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>

Fryar CD, Ostchega Y, Hales CM, Zhang G, Kruszon-Moran D: Hypertension prevalence and control among adults: United States, 2015–2016. NCHS Data Brief (289): 1–8, 2017.

United States Renal Data System 2017 Annual Data Report Volume 2 Chapter 1,

[https://usrds.org/media/1688/v2\\_c01\\_incprev\\_17.pdf](https://usrds.org/media/1688/v2_c01_incprev_17.pdf), accessed 4.28.2021

Am J Kidney Dis. 2013; 62: 261–266. <https://doi.org/10.1053/j.ajkd.2013.01.012>

J Am Soc of Nephrol. 2008 doi: 10.1681/ASN.2008030276.



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# Assessing Race in eGFR equations



# RACE IN eGFR EQUATIONS

- ▶ MDRD equation
  - ▶ Invalid for GFR > 60
  - ▶ Most used in lab reporting

$$eGFR = 175 \times (SCr)^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if AA})$$

- ▶ CKD-EPI equation
  - ▶ Validated for all ranges of GFR
  - ▶ Preferred by KDIGO guidelines, available in < 20% of labs

$$eGFR = 141 \times \min(SCr/kappa, 1)^{\alpha} \times \max(Scr/kappa, 1)^{-1.209} \times 0.993^{age} \times 1.018 \text{ (if female)} \times 1.159 \text{ (if black)}$$

Kappa is 0.7 for females, 0.9 for males

Alpha is -0.329 for females, -0.411 for males

# ASN-NKF TASK FORCE ON RACE IN KIDNEY ESTIMATING EQUATIONS

## Statement 6

“Differences in health exist across racial and ethnic groups in the United States, and not all of these differences are accounted for by socioeconomic status, geographic regions (including urban versus rural setting), insurance, lifestyle and clinical factors. Disparities in healthcare exist across racial and ethnic groups and geographic regions (including urban versus rural setting) in the United States, even after accounting for insurance status, income, age, and disease severity.”

# ASN-NKF TASK FORCE ON RACE IN KIDNEY ESTIMATING EQUATIONS

## Statement 5

“A variety of factors influence kidney health across racial and ethnic groups, including delivery of healthcare, clinical/health policies, environment, genetics and health behaviors. These factors act with a different degree of influence along the life span of individuals and along the continuum from health to kidney disease. There are gaps in our understanding of these influences and how to interrupt their effect on creating health disparities. To eliminate disparities, multifaceted initiatives beyond an examination of estimating equations must be developed.”

# Health Equity: Where should we set our sights and efforts? Look around!

**Drivers of Disparities**

eGFR Equations





# MRS. SMITH

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## October 2019 CKD visit

- ▶ Not taking most of her medications, education provided

## January 2020 CKD visit

BP 204/100 mm Hg, SCr 2.7 mg/dL, GFR 18 mL/min/1.73m<sup>2</sup>, UACR 8,616 mg/g

- ▶ Only taking the 2 free at Publix medications
- ▶ Should have Medicare. NP and I spent 10 + minutes talking to Medicare – they thought she had BCBS. Per patient and husband, they canceled this policy in November.



# MRS. SMITH

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## February 2020 CKD visit

BP 177/90 mmHg, SCr 2.7, eGFR 18 mL/min/1.73m<sup>2</sup>, UACR 10,293 mg/g

- ▶ No insulin in “a while”
- ▶ Taking lower doses of BP medications than prescribed

## March 2020 CKD visit – telemedicine

- ▶ Mrs. Smith can't read medication bottle labels

## April 2020 CKD visit - telemedicine

SCr 4.1 mg/dL, eGFR 11 mL/min/1.73m<sup>2</sup>, UACR 7,941 mg/g

- ▶ Medicare issues worked out
- ▶ Taking more medications



# MRS. SMITH

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## March 2021

- ▶ Dialysis access placed

## April 2021

- ▶ Starts in-center hemodialysis



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# Therapeutic Updates





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# REDUCING KIDNEY FUNCTION DECLINE

- ▶ Control HTN
- ▶ Control hyperglycemia
- ▶ Correct metabolic acidosis
- ▶ Lifestyle modifications
  - ▶ Stop smoking
  - ▶ Healthy diet
  - ▶ Reduce sodium consumption
- ▶ RAAS inhibition
  - ▶ New player: finerenone
- ▶ SGLT2 inhibitors



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# KDIGO 2021 Management of BP in CKD Guidelines

# KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease

VOLUME 99 | ISSUE 3S | MARCH 2021

[www.kidney-international.org](http://www.kidney-international.org)

- ▶ **Recommendation 1.1.** We recommend standardized office BP measurement in preference to routine office BP measurement for the management of high BP in adults (1B).
- ▶ **Recommendation 3.1.1.** We suggest that adults with high BP and CKD be treated with a **target systolic blood pressure (SBP) of < 120 mm Hg**, when tolerated, using standardized office BP measurement (2B).
- ▶ **Recommendation 3.2.1, 3.2.2, 3.2.3.** RASi recommendations
  - ▶ Recommend RASi for high BP, CKD and severely increased albuminuria without diabetes (1B)
  - ▶ Suggest RASi for high BP, CKD and moderately increased albuminuria without diabetes (2C)
  - ▶ Recommend RASi for high BP, CKD and moderately to severely increased albuminuria with diabetes (1B)
- ▶ **Recommendation 3.3.1.** We recommend avoiding any combination of ACEi, ARB, and direct renin inhibitor (DRI) therapy in patients with CKD, with or without diabetes (1B)

## FIGURE 2: CHECKLIST FOR STANDARDIZED OFFICE BLOOD PRESSURE MEASUREMENT

### 1 Properly prepare the patient

- 1 Have the patient relax, sitting in a chair (feet on floor, back supported) for > 5 min
- 2 The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement
- 3 Ensure patient has emptied his/her bladder
- 4 Neither the patient nor the observer should talk during the rest period or during the measurement
- 5 Remove all clothing covering the location of cuff placement
- 6 Measurements made while the patient is sitting or lying on an examining table do not fulfill these criteria

### 2 Use proper technique for BP measurements

- 1 Use a BP measurement device that has been validated, and ensure that the device is calibrated periodically
- 2 Support the patient's arm (e.g., resting on a desk)
- 3 Position the middle of the cuff on the patient's upper arm at the level of the right atrium (the midpoint of the sternum)
- 4 Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used
- 5 Either the stethoscope diaphragm or bell may be used for auscultatory readings

## FIGURE 2: CHECKLIST FOR STANDARDIZED OFFICE BLOOD PRESSURE MEASUREMENT

<b>3 Take the proper measurements needed for diagnosis and treatment of elevated BP</b>	<ol style="list-style-type: none"><li>1 At the first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings</li><li>2 Separate repeated measurements by 1–2 min</li><li>3 For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20–30 mm Hg above this level for an auscultatory determination of the BP level</li><li>4 For auscultatory readings, deflate the cuff pressure 2 mm Hg per second, and listen for Korotkoff sounds</li></ol>
<b>4 Properly document accurate BP readings</b>	<ol style="list-style-type: none"><li>1 Record SBP and DBP. If using the auscultatory technique, record SBP and DBP as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number</li><li>2 Note the time of most recent BP medication taken before measurements</li></ol>
<b>5 Average the readings</b>	Use an average of $\geq 2$ readings obtained on $\geq 2$ occasions to estimate the individual's level of BP
<b>6 Provide BP readings to patient</b>	Provide patients with the SBP/DBP readings verbally and in writing

# SBP GOAL < 120 MM HG

- ▶ SPRINT trial
- ▶ ACC/AHA BP Guidelines < 130/80
- ▶ Why the difference?
  - ▶ RCT specific inclusion and exclusion criteria limits generalizability to all HTN patients
  - ▶ BP measurements in RCT more consistent with guideline recommendations than is common in clinical practice → lower absolute values for SBP



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# KDIGO 2020 Diabetes Management in CKD Guidelines

# KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

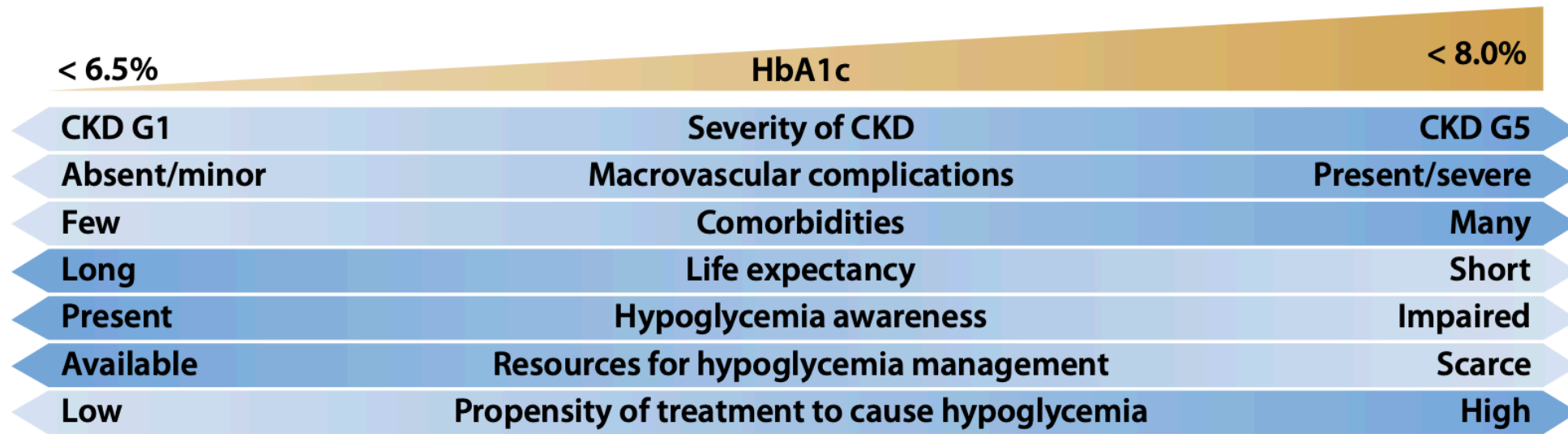
VOLUME 98 | ISSUE 45 | OCTOBER 2020

[www.kidney-international.org](http://www.kidney-international.org)

- ▶ **Recommendation 1.2.1.** Recommend RASi for patients with CKD, diabetes and albuminuria, titrated to maximum tolerated dose (1B).
- ▶ **Lifestyle recommendations**
  - ▶ Stop smoking
  - ▶ Limit sodium - < 2g per day
  - ▶ Limit protein – 0.8 g protein/kg/day
  - ▶ Moderate physical activity – 150 min/week



# GLYCEMIC TARGETS



**Figure 9 | Factors guiding decisions on individual HbA1c targets.** CKD, chronic kidney disease; G1, estimated glomerular filtration rate (eGFR)  $\geq 90$  ml/min per 1.73 m<sup>2</sup>; G5, eGFR  $< 15$  ml/min per 1.73 m<sup>2</sup>; HbA1c, glycated hemoglobin.

# FIGURE 18: TREATMENT ALGORITHM



Lifestyle therapy

Physical activity  
Nutrition  
Weight loss



First-line therapy

**Metformin**

eGFR < 45	eGFR < 30	Dialysis
Reduce dose	Discontinue	Discontinue

+

**SGLT2 inhibitor**

eGFR < 30	Dialysis
Do not initiate	Discontinue



Additional drug therapy as needed for glycemic control

GLP-1 receptor agonist (preferred)

DPP-4 inhibitor

Insulin

Sulfonylurea

TZD

Alpha-glucosidase inhibitor

- Guided by patient preferences, comorbidities, eGFR, and cost
- Includes patients with eGFR < 30 ml/min per 1.73 m<sup>2</sup> or treated with dialysis
- See Figure 20



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# Mineralocorticoid Receptor Antagonists (MRA)



# MR IN CKD

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- ▶ Overactivation of the MR → inflammation and fibrosis → CKD progression
- ▶ Spironolactone adjunctive to ACEi/ARB to reduce proteinuria in patients with CKD
- ▶ Less evidence with eplerenone



# FINERENONE

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- ▶ Nonsteroidal selective mineralocorticoid receptor antagonist
  - ▶ Stronger MR binding potential than steroidal MRAs
  - ▶ No active metabolite
  - ▶ Shorter half-life
- ▶ Phase III trials in diabetic nephropathy and albuminuria
  - ▶ FIDELIO-DKD
  - ▶ FIGARO-DKD
- ▶ Anticipate approval in July 2021



# FIDELIO-DKD

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- ▶ 2,833 finerenone vs 2,841 placebo in diabetic CKD patients
  - ▶ ~ 65 yoa, 70% male, 63% white, 4.8% black, 25% Asian
  - ▶ 99% on ACEI/ARB
- ▶ Dosing
  - ▶ 10 mg eGFR 25 to < 60 or 20 mg eGFR 60 or more
  - ▶ Titrated to 20 mg if K < 4.8 mEq/L and eGFR stable
- ▶ Primary Composite Outcome
  - ▶ Kidney failure or sustained decrease of at least 40% in eGFR over 4 weeks or death from renal causes
- ▶ Key Secondary Composite Outcome
  - ▶ CV death or nonfatal MI or nonfatal stroke or HF hospitalization

# FIDELIO-DKD

Outcome	Finerenone	Placebo	Hazard Ratio	NNT
Primary Composite	504 (17.8%)	600 (21.1%)	0.82 (0.73-0.93), p=0.001	30
Key Secondary Composite	367 (13%)	420 (14.8%)	0.86 (0.75-0.99), p=0.03	56

## Other key outcomes:

- 3 year follow up
- UACR less in finerenone group
- Mean serum K remained similar to baseline in both groups
- Similar rates of ADRs between groups



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# Emerging treatment for anemia of CKD



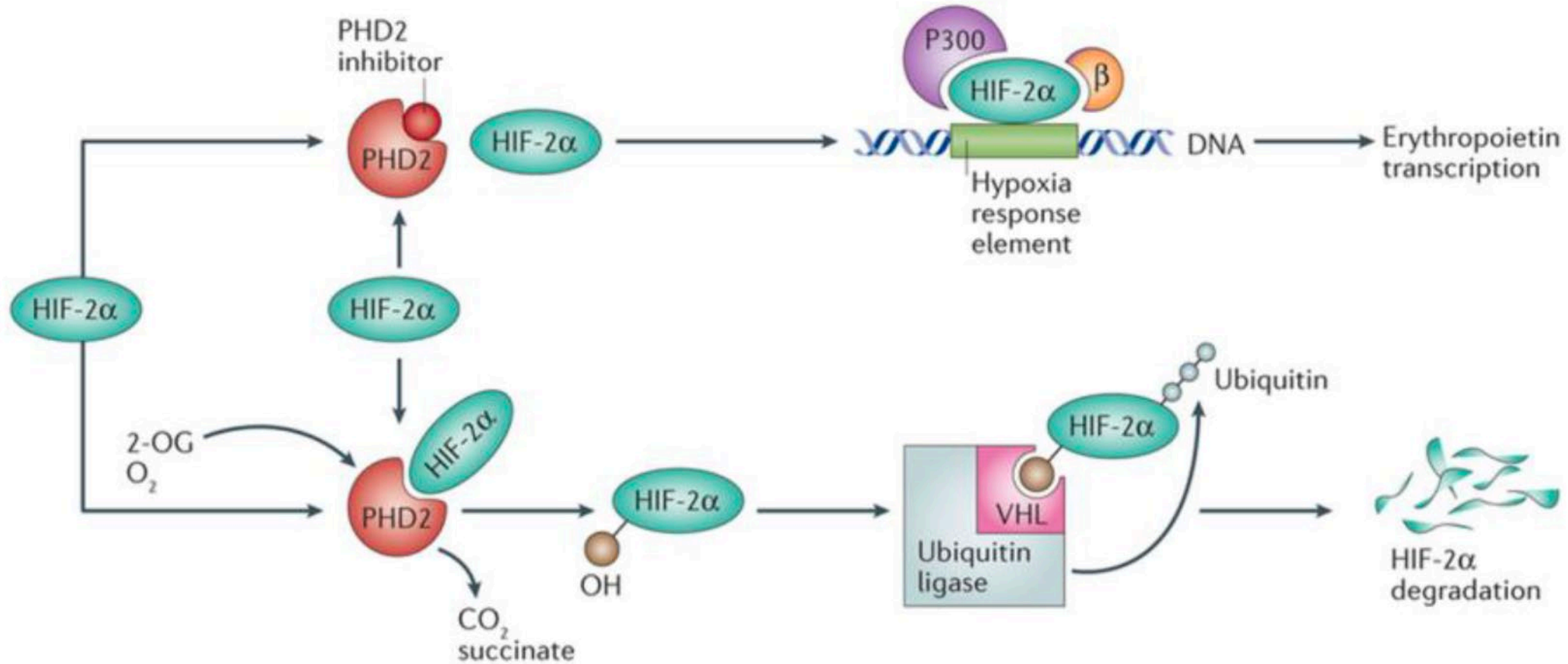


# ANEMIA OF CKD

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- ▶ With kidney function decline, decreased production of erythropoietin occurs
- ▶ Iron absorption and utilization are impaired
  - ▶ Gut edema
  - ▶ Inflammatory state increases hepcidin (responsible for iron sequestration)
- ▶ Current treatments
  - ▶ Oral iron
  - ▶ IV iron
  - ▶ Erythropoiesis Stimulating Agents

# HYPOXIA INDUCIBLE FACTORS



Nature Reviews | Nephrology



# HIF-PHI

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## Mechanism of Action

- ▶ Inhibits degradation of HIF → transcription for EPO → increase in EPO production
- ▶ Improves iron absorption
- ▶ Improves mobilization of storage iron
- ▶ Indirectly reduces hepcidin levels

## Key Characteristics

- ▶ Oral
- ▶ Daily or TIW

Blood. 2013 Aug 8; 122(6): 885–892.

Locatelli F, et al. Am J Nephrol. 2017;45(3):187-199.



# ROXADUSTAT

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- ▶ CKD-ND Trials
  - ▶ ALPS
  - ▶ ANDES
  - ▶ OLYMPUS
  - ▶ DOLOMITES, only with active ESA comparator arm
- ▶ CKD-D Trials, all compared with ESA therapy
  - ▶ PYRENES
  - ▶ ROCKIES
  - ▶ SIERRAS
  - ▶ HIMALAYAS
- ▶ NDA currently under consideration by FDA



# VADADUSTAT

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- ▶ CKD-NDD Trials
  - ▶ PRO<sub>2</sub>TECT – compared to darbepoetin
- ▶ CKD-D Trials
  - ▶ INNO<sub>2</sub>VATE – compared to darbepoetin



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# DAPRODUSTAT

- ▶ Completed trial in Japan only
- ▶ Global phase III trial ongoing

# LONG-TERM SAFETY CONCERNS, PHASE IV TRIALS

- ▶ Theoretical oncogenic risk
- ▶ Predisposition to pulmonary arterial hypertension and thromboembolic disease
- ▶ Increased angiogenesis → diabetic retinopathy
- ▶ Increased CKD progression
- ▶ Increased cyst size in polycystic kidney disease patients
- ▶ Metabolic effects: hyperglycemia, hyperuricemia, hyperkalemia



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# Advancing Kidney Health through Optimal Medication Management (AKHOMM)





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# ADVANCING AMERICAN KIDNEY HEALTH INITIATIVE

- ▶ Summer 2019, Executive Order
- ▶ Bold goals
  - ▶ Decrease number of Americans developing kidney failure by 25% by 2030
  - ▶ Aim for 80% of new kidney failure patients in 2025 receiving either home dialysis or a transplant
- ▶ Value-based payment models from CMS incentivize
  - ▶ Earlier intervention in CKD 4 and 5
  - ▶ Reward increased utilization of home dialysis modalities
  - ▶ Rewards and bonuses for kidney transplants



# AAKH PAYMENT MODELS

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- ▶ Kidney Care Choices Models (CKCC)
- ▶ Quality Measures
  - ▶ Patient Activation (PAM score, NQF-2483)
  - ▶ Depression Remission (NQF-1885)
  - ▶ Total cost of care reduction
- ▶ Benefit enhancements
  - ▶ Kidney Disease Education
  - ▶ Post Discharge Home Visits
- ▶ ESKD Treatment Choices (ETC)
  - ▶ Dialysis providers incentivized toward home modalities and transplant



# AKHOMM

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**Vision:** Every person with kidney disease receives optimal medication management through team-based care including a pharmacist to ensure their medications are safe, effective and convenient for them to use.

**Mission:** Engage pharmacists and key stakeholders to develop partnerships for optimal medication management in persons with kidney disease to improve health outcomes and reduce healthcare costs.



**Advancing Kidney Health**  
Through Optimal Medication Management



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# PHARMACISTS CAN ENHANCE NEPHROLOGY PRACTICES

- ▶ Models allow for other providers
- ▶ Allow nephrologists to see more patients
- ▶ Performance based components require optimal medication management
  - ▶ Patient activation: improve adherence
  - ▶ Depression remission
  - ▶ Reduced cost of care
    - ▶ Decrease CV and infectious hospitalizations
    - ▶ Optimize HTN, DM, HF, DLD, anemia and anti-infective regimens
  - ▶ Planned future metrics: CKD progression, optimal use of ACEI/ARB/SGLT2i
- ▶ Meet the quadruple aim



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# PHARMACISTS PROVIDING CMM

## Quadruple Aim

- ▶ Improve patient experience
  - ▶ Patient activation: improve adherence
  - ▶ Depression remission
- ▶ Improve population health
- ▶ Reduce costs
  - ▶ Decrease CV and infectious hospitalizations
  - ▶ Optimize HTN, DM, HF, DLD, anemia and anti-infective regimens
  - ▶ Planned future metrics: CKD progression, optimal use of ACEI/ARB/SGLT2i
- ▶ Improve care team well being
  - ▶ Reduce burden on nephrologists as practice can see more patients

# HOW WILL WE IMPLEMENT THIS

Develop a National Learning and Action Collaborative

Structure Built on Established  
Business Development, Quality Improvement &  
Implementation Science Methods

Monthly Coaching

+

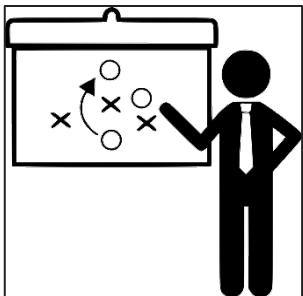
Virtual "All Team"  
Events

+

Face-to-Face  
Pacing Events

+

Tools and  
Resources





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# AKHOMM AND LAC RESOURCES

- ▶ Nephrology PRN Opinion Paper: Pharmacists' Perspectives on the Advancing American Kidney Health Initiative
  - ▶ J of the Am Coll of Clin Pharm. 2020;3(7);1355-1368
- ▶ University of Minnesota College of Pharmacy – Clinical Seminar Series
- ▶ “Policy Change for Pharmacy: Advancement Opportunity or Boondoggle?”
  - ▶ [https://mediaspace.umn.edu/media/t/1\\_jyb3a9eo](https://mediaspace.umn.edu/media/t/1_jyb3a9eo)
- ▶ Patients and Pharmacists: The New “Disrupters” in Healthcare
  - ▶ <https://www.youtube.com/watch?v=ajmT93H2RpA>



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