

# The Creatinine is Elevated: Who Needs to See a Nephrologist

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# Learning Objectives



Understand kidney disease burden, gaps in care and challenges for improving outcomes

Diagnosing, staging and risk profiling of chronic kidney disease

When to refer to a Nephrologist

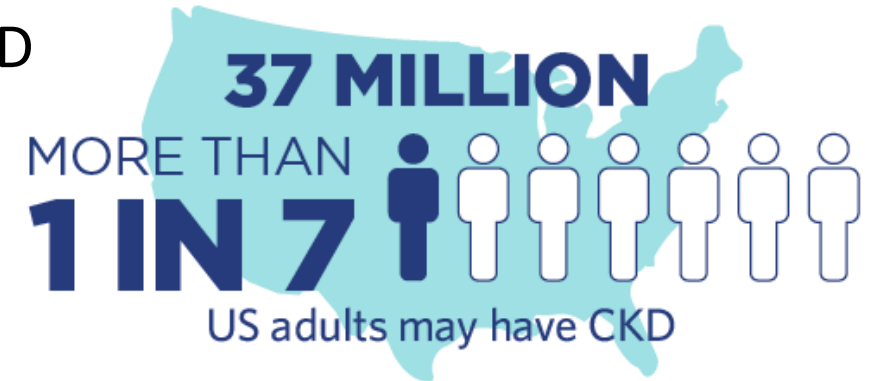
To understand the newer therapeutics and guidelines for management of CKD

# Crash Start Dialysis

- 72 year old male with history of long standing uncontrolled DM and HTN presents to ER with 1 week of lethargy and “just not feeling well”
- Labs show BUN 72
- Cr = Hb = K = 7.2
- Has never seen a nephrologist, is not aware that he has advanced CKD
  - Tunneled dialysis catheter placed
  - Starts urgent HD in hospital

# Chronic Kidney Disease: Prevalent, Deadly and Costly

- Diabetes and HTN are most common risk factors for CKD
- By 2030, 1 in 6 adults will have CKD
- Disease of aging
  - Age  $\geq 65$ , 40% have CKD
- Higher prevalence in African American and Hispanics
- Medicare spending for CKD and ESKD = \$124 B/year
  - CKD: \$87 B, ESKD: \$37 B
  - In-center dialysis costs: \$90,000/patient/year



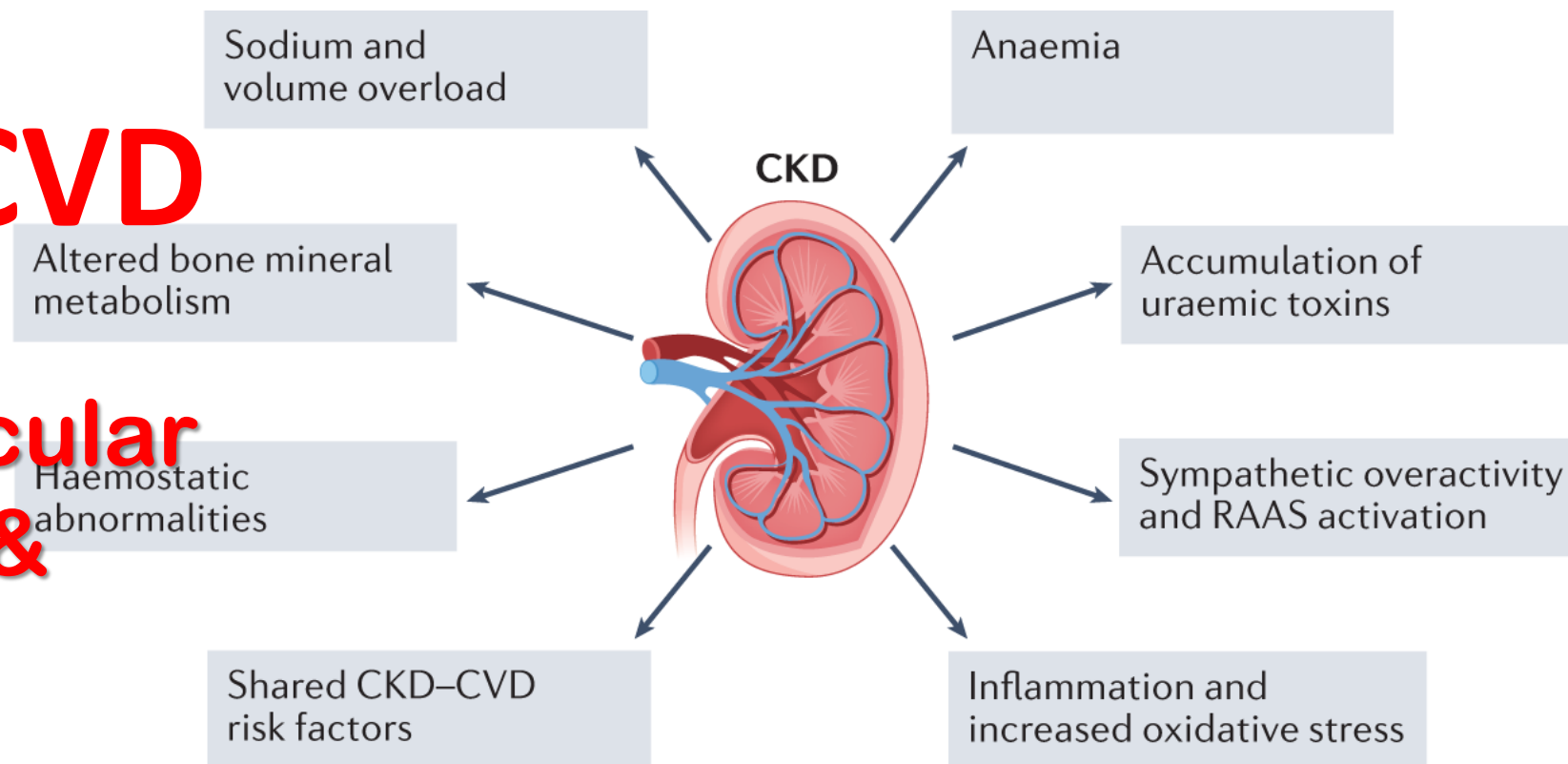
**Kidney failure kills more people than breast or prostate cancer**

There are ~30 million adults in the US with CKD 3 or greater, but only ~600,000 patients with ESRD or a kidney transplant.

Why the disparity?????

# Risk Factors for CVD in CKD

**CKD = CVD**  
**High cardiovascular morbidity & mortality**



## Representative CVD outcomes

- Coronary artery disease
- Stroke
- Heart failure
- Venous thromboembolism
- Sudden cardiac death
- Atrial fibrillation
- Abdominal aortic aneurysm
- Peripheral artery disease

# Provider Challenges to CKD care are two-fold

**Problem #1:  
Identifying those at high  
risk for progression**



- **<1% of CKD progress to dialysis**

**Problem # 2:  
Closing gaps in CKD care  
Newer guidelines for CKD  
Therapeutic Inertia & Disparities**

# Patient Challenges to Improving CKD care

## SILENT DISEASE

Even among those with stage 4 disease, less than 50% are aware

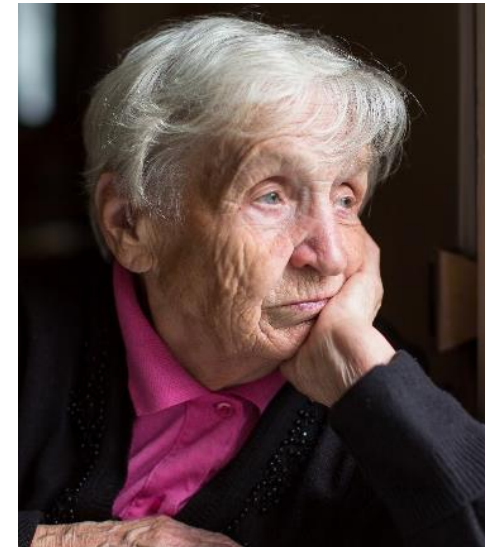
Stage 3 – only ~ 20% are aware

Most patients never see a nephrologist

Not prepared for dialysis, kidney transplant or conservative management

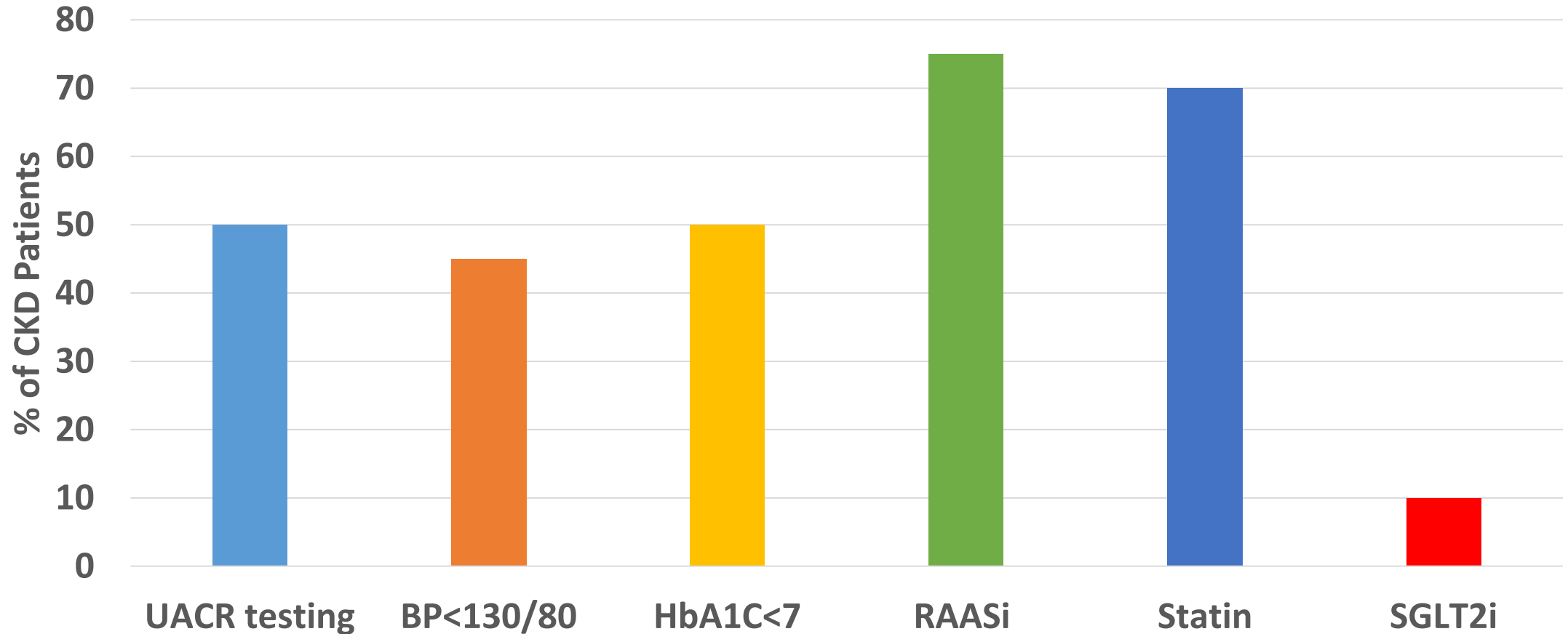
Many patients have a “crash start” dialysis in the hospital with a catheter

Older patients experience more morbidity and mortality





# Gaps in CKD Care Lead to Rapid progression to ESKD



In the US, patients with CKD receiving goal-concordant care has NOT increased over time

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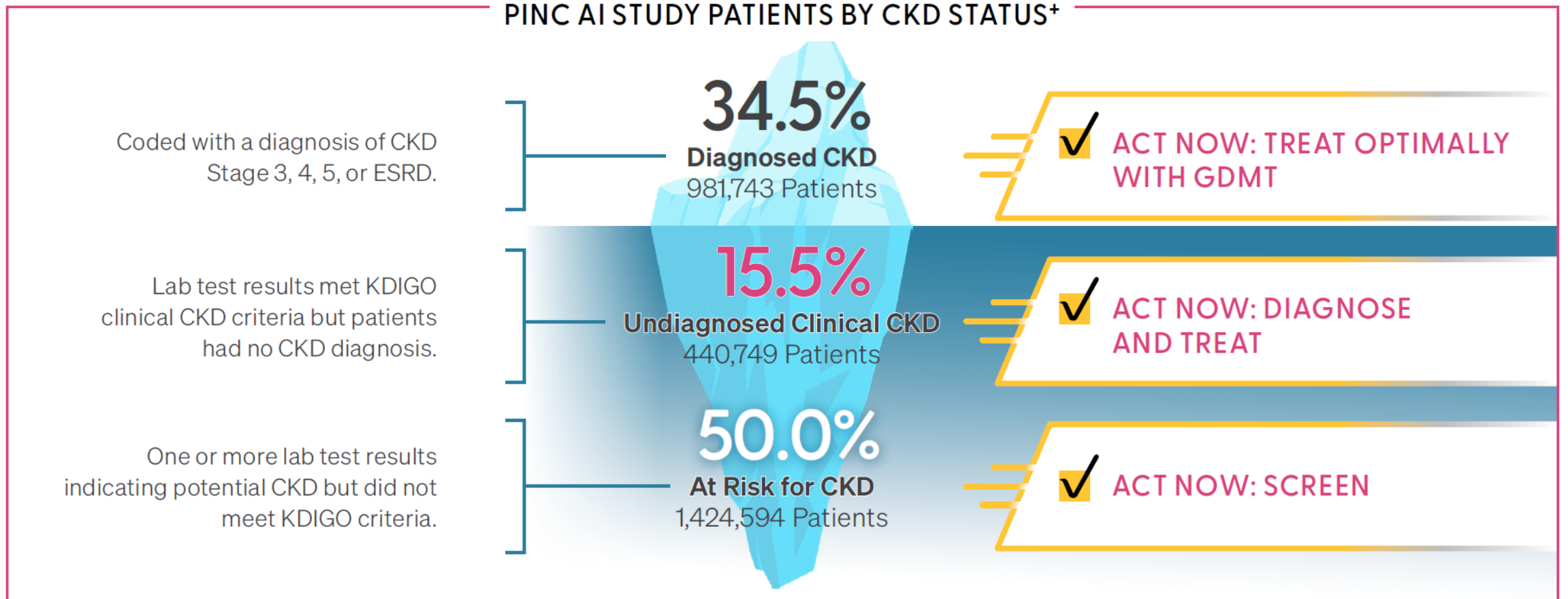
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# CKD is Under-diagnosed

## HOW MANY PATIENTS HAVE UNDIAGNOSED CLINICAL CKD OR ARE AT RISK BASED ON LABORATORY TEST RESULTS?



# Stages of CKD (KDOQI 2002)

Stage	Description	GFR (ml/min/1.73m <sup>2</sup> )
1	Kidney damage (structural or functional) with normal or ↑ GFR	≥90
2	Kidney damage (structural or functional) with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	<15 or dialysis

**Proteinuria is a very significant independent risk factor for morbidity and mortality**

**Important to quantify proteinuria**

For CKD diagnosis and staging:  
eGFR

Urine albumin-creatinine ratio

CKD diagnosis = 2 abnormal tests in either at least 3 months apart

“Normal” serum Creatinine may not be normal

Some medications may spuriously elevate Creatinine - Bactrim

# CKD Staging (KDIGO 2012)

## HEAT MAP

				Albuminuria stages, description and range (mg/g)				
				A1		A2	A3	
				Optimal and high-normal		High	Very high and nephrotic	
				<10	10-29	30-299	300-1999	≥2000
GFR stages, description and range (mL/min per 1.73 m <sup>2</sup> )	G1	High and optimal	>105					
			90-104					
	G2	Mild	75-89					
			60-74					
	G3a	Mild-moderate	45-59					
	G3b	Moderate-severe	30-44					
	G4	Severe	15-29					
G5	Kidney failure	<15						

# THE KIDNEY FAILURE RISK EQUATION

Find out your real risk of kidney failure



KIDNEY FAILURE  
RISK CALCULATOR

LEARN MORE ABOUT  
YOUR KIDNEYS

## KIDNEY FAILURE RISK CALCULATION

If you don't have the information required below talk to your doctor.

Age (Yrs)

Sex

Select ▾

Region

Select ▾

GFR (ml/min/1.73m<sup>2</sup>)

 ?

Urine Albumin: Creatinine Ratio

 ?

Units

Select ▾



# YOUR RESULTS

500 mg/g  
URINE ALBUMIN

M  
SEX

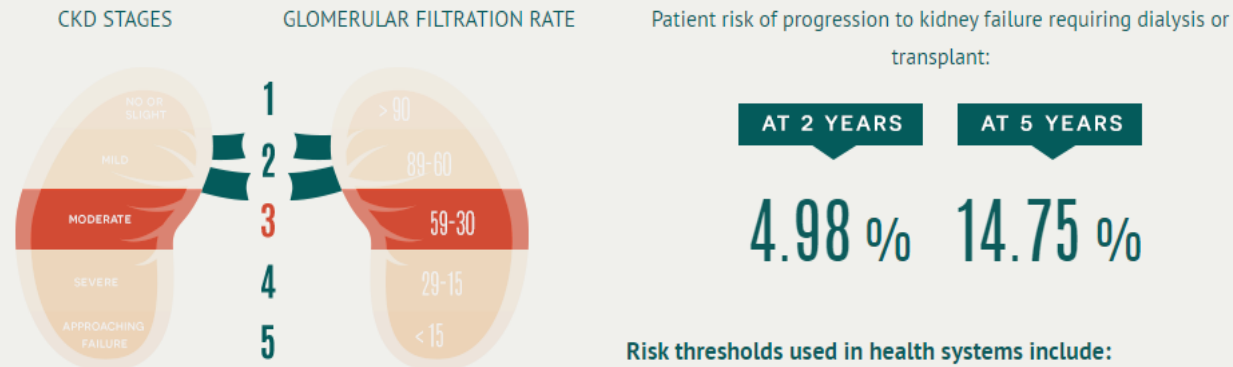
71  
AGE

35 mL/min/1.73 m<sup>2</sup>  
GFR

## ASSESSMENT

### STAGE 3

MODERATE DECREASE IN FUNCTION



**5-year KFRE  
>5% - Refer  
to a  
Nephrologist**

#### Risk thresholds used in health systems include:

- 3-5 % over 5 years for referral to a kidney doctor
- 10 % over 2 years for team based care (Kidney Doctor, Nurse, Dietician, Pharmacist)
- 20-40 % over 2 years for planning a transplant or fistula

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# Appropriate Nephrology Referral is Key

AJKD

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**Too Many for Too Few: Finding Appropriate Nephrology Referrals for Patients With CKD That Optimize Outcomes**

*Chi D. Chu, Julio A. Lamprea-Montealegre, and Michelle M. Estrella*

1 Nephrologist



3000 CKD Patients



**Primary  
Care  
Provider**

# Nephrology Referral

- CKD stage 4
  - Volume overload
  - Complications – electrolyte disorders, anemia, bone mineral disease
- 5-year KFRE > 5%
- Rapidly declining eGFR ( $\geq 5$  ml/min/yr)
- Hematuria
- Heavy proteinuria
- Suspected genetic disease (eg. polycystic kidney disease)

# Late Nephrology referral

- Poor preparation for starting dialysis
  - 50% of patients in US crash into hemodialysis
- Poor education and uptake of home dialysis
  - Home dialysis rate is ~10% in the US
- Low access to transplantation
- Untreated CKD complications – anemia, secondary hyperparathyroidism
- More hospitalizations
- Higher mortality

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# Guidelines for CKD management

- Optimize treatment with **ACEi or ARB** in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the **highest approved dose that is tolerated**
- Upto 30% drop in eGFR is acceptable after starting or dose adjusting

## HYPERKALEMIA

- Mild hyperK – 5.0-5.4 meq/L – Do not discontinue ACEi/ARB – manage with diet and diuretics
- Moderate-severe hyperK  $\geq 5.5$  meq/L
  - Do NOT use kayexalate – intestinal necrosis
  - New binders
    - Patiromer (Veltassa) – 8.4g once daily to max 25.2 g/d
    - Sodium Zirconium cyclosilicate (Lokelma) – 5- 10 gm once daily, max maintenance dose 15 g/d

# Newer guidelines for CKD management

**SGLT2i predicted to delay ESKD by 15 years**

## **American Diabetes Association Guidelines 2020**

“Among patients with type 2 diabetes who have established atherosclerotic CVD or indicators of high risk, or heart failure, or CKD, **an SGLT2 inhibitor or GLP-1 Ra is recommended independent of baseline A1C**”

Additionally, in non-diabetic patients:

- SGLT2i approved for heart failure (May 2020)
- SGLT2i approved for non-diabetic CKD with proteinuria (May 2021)



# SGLT2i guidelines for CKD and CVD in **Diabetes type 2**

American Diabetes Association (2020)

Kidney Disease Improving Global Outcomes (2020)

American Heart Association (2020)

European Society for Cardiology (2019)

SGLT2i Recommended in  
CKD  
ASCVD (established or high risk)  
Heart Failure

# Sodium Glucose co-Transporter 2 Inhibitors (SGLT2i)

## Farxiga, Jardiance, -flozins

- Very compelling data for effectiveness in improving renal and CV outcomes and safety in diabetic (Type 2 DM only) and non-diabetic CKD
- Decrease risk of ESKD, cardiovascular death, MI, stroke and heart failure hospitalizations
- Reduce HbA1C (by about 0.5-1%)
  - Their glucose-lowering effects are modest, especially in people with  $eGFR < 45 \text{ mL/min/1.73 m}^2$
- Reduce BP (~ 2-5 mmHg decrease in SBP/1-2 mmHg decrease in DBP)
- Weight loss 1-2kg

# Sodium Glucose co-Transporter 2 Inhibitors (SGLT2i)

## Farxiga, Jardiance, -flozins

- Do not cause hypoglycemia in non diabetic CKD
- Only approved for eGFR>20 ml/min [ADA recommendation May 2022 ]
- Can cause upto 30% drop in eGFR acutely – no need to stop
- Once an SGLT2i is initiated, it is reasonable to continue it even if eGFR falls <20 ml/min, unless it is not tolerated or kidney replacement therapy is initiated
- Side effects - genital mycotic skin infections/UTIs, volume depletion, rarely euglycemic DKA

# Glucagon-like Peptide-1 Receptor agonists

## **GLP-1Ra**

### **Trulicity, Ozempic, Victoza, -glutide**

- Slow CKD progression, CV benefits, and decrease mortality
- Reduce HbA1C (by about 0.5-1.5%)
- Weight loss ~ 2-3 kg
- No eGFR cutoff
- Side effect – GI intolerance - Start at low dose and uptitrate slowly

# Non-steroidal Mineralocorticoid Receptor Antagonist

## Finerenone (Kerendia)

- Mineralocorticoid receptor antagonist (similar to spironolactone)
- Slow CKD progression, CV benefits
- Less hyperK than spironolactone
- ADA May 2022
- In patients with CKD who are at **increased risk for cardiovascular events or chronic kidney disease progression or are unable to use a SGLT2i, a nonsteroidal mineralocorticoid receptor antagonist (finerenone) is recommended** to reduce chronic kidney disease progression and cardiovascular events. [A level evidence]

Indicated in:

eGFR  $\geq 25$  ml/min per 1.73 m<sup>2</sup>

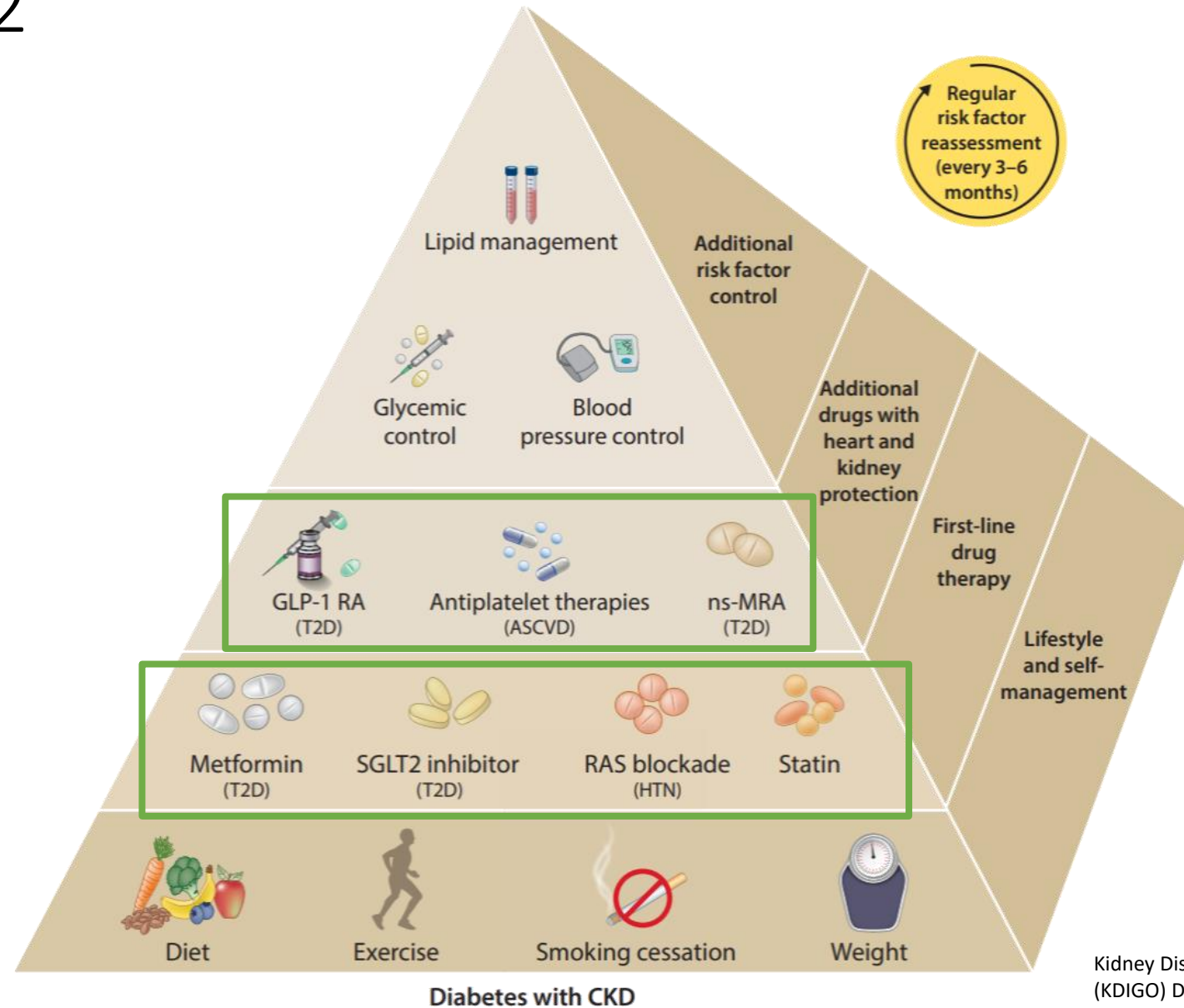
normal serum potassium (  $K \leq 5$  meq/L)

albuminuria ( $\geq 30$  mg/gram Cr) despite maximally tolerated RAS inhibitor dose

# KDIGO 2022 Guidelines Summary

# Guideline Based Management of Diabetic CKD

## KDIGO 2022



# KDIGO CKD in Type 2 DM guidelines 2022

- Recommend that treatment with **ACEi or ARB** be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the **highest approved dose that is tolerated** (1B).
- Recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR >20 ml/ min per 1.73 m<sup>2</sup> with an **SGLT2i** (1A).
- In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i treatment, or who are unable to use those medications, we recommend a long-acting **GLP-1 RA** (1B).
- Suggest a **nsMRA** for patients with T2D, an eGFR >25 ml/min per 1.73 m<sup>2</sup> , normal serum potassium concentration, and albuminuria (>30 mg/g) despite maximum tolerated dose of RASi (2A)



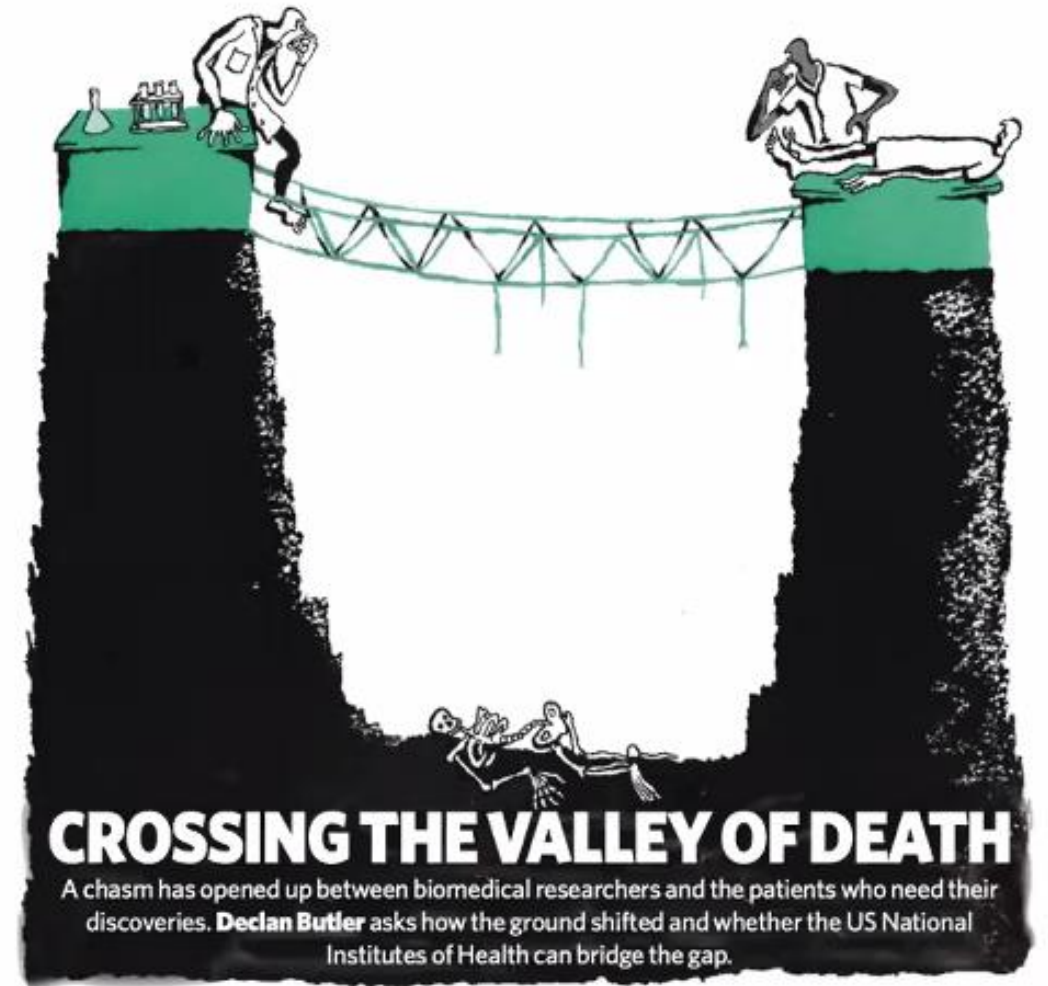
# Guidance for non diabetic CKD

- SGLT2i approved for non-diabetic CKD at risk of progression to reduce CKD progression, ESKD, CV death and hospitalization

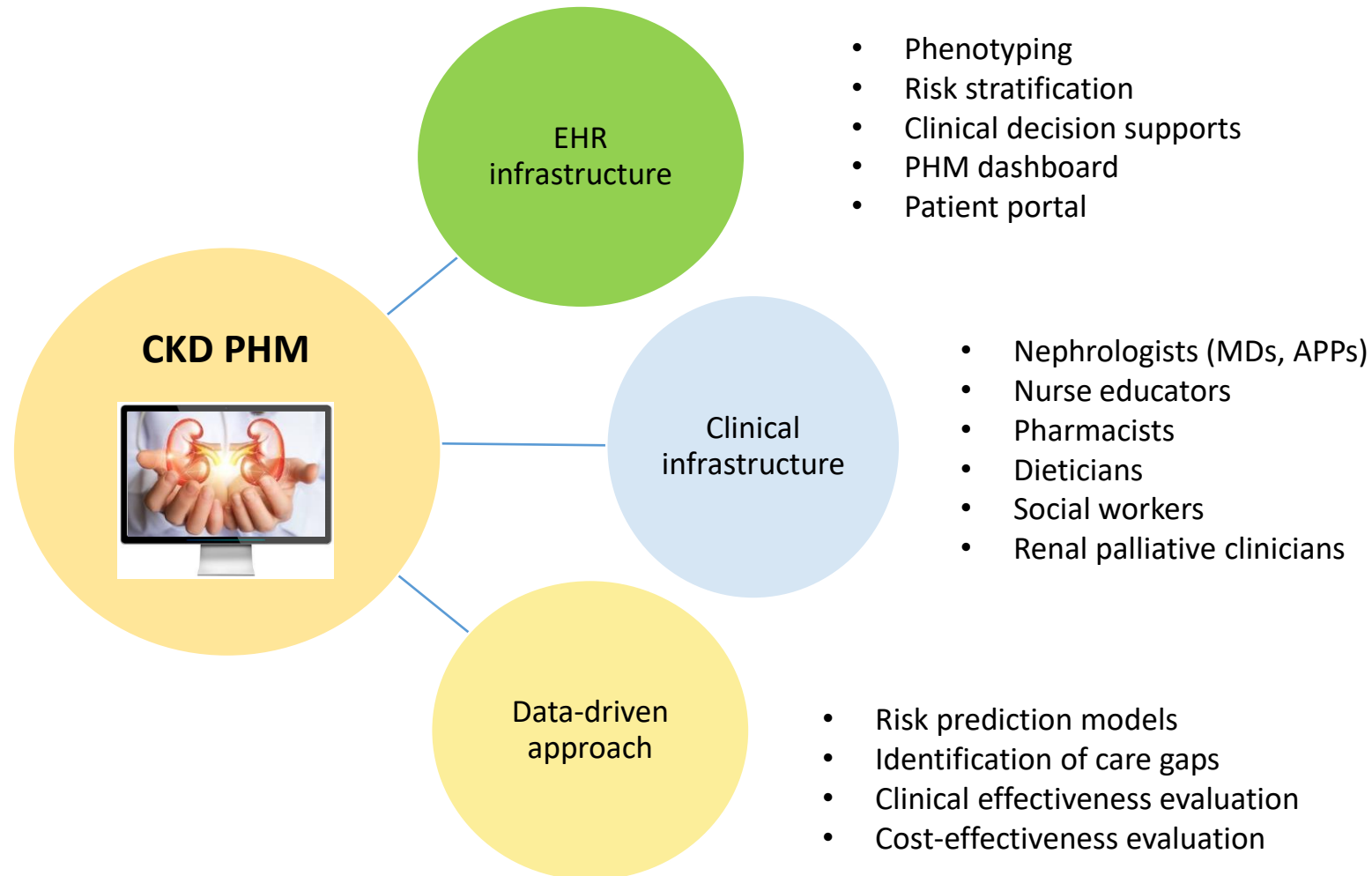
# Implementation gap

- Timeline for research to translate to practice – 17 years

**TIME to ACT**



# Value-Based Model of CKD Care

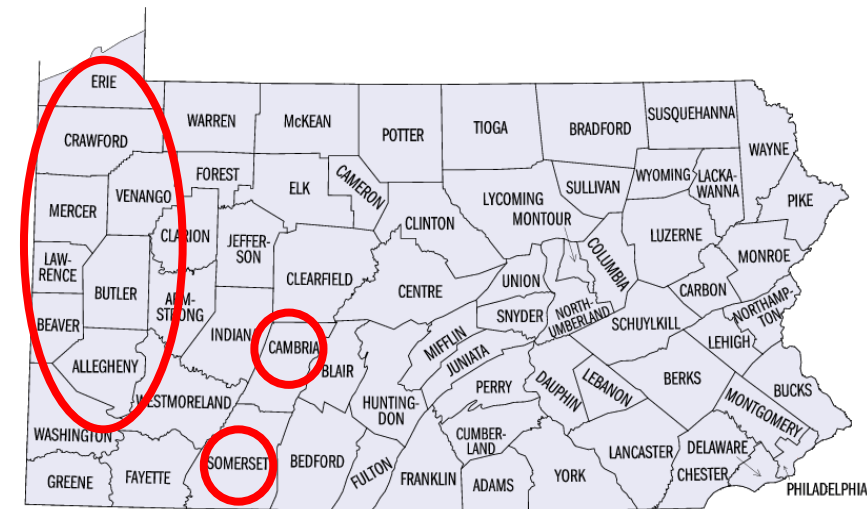
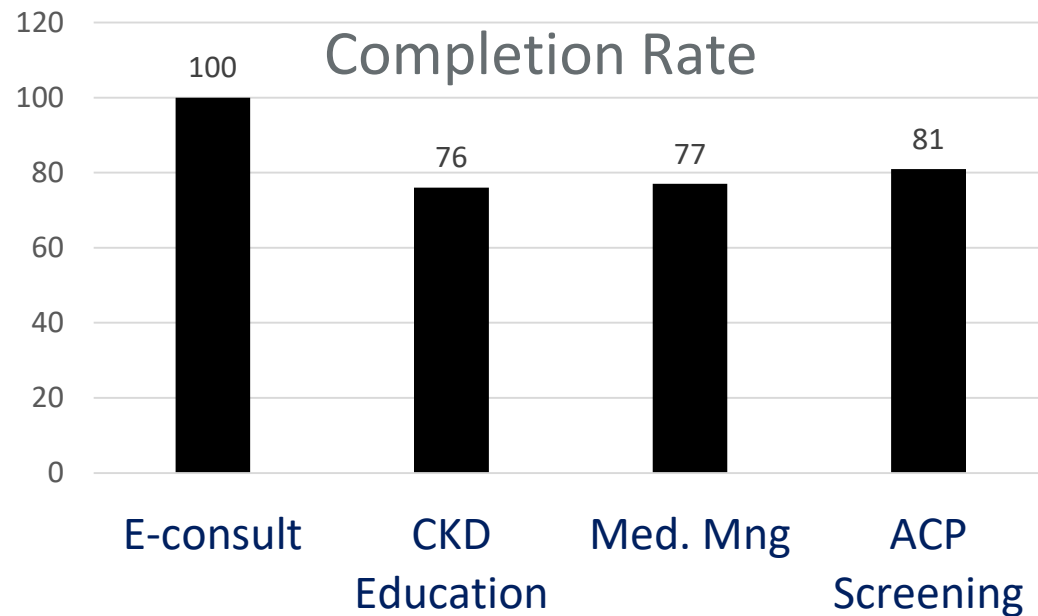


# Impact of CKD Program

Active in 102 UPMC PCP practices

Enrolled 2,251 patients (80-100 new patients per month)

Completed: 4,000 E-consults; 3,600 Medication Reviews; 2,700 Education sessions



# Take Home Points

- ❖ Patients with CKD have high cardiovascular morbidity and mortality
- ❖ CKD is under-diagnosed
- ❖ CKD diagnosis and staging – eGFR and Urine albumin-Creatinine ratio
- ❖ Three new drug classes for CKD management - SGLT2i, GLP-1Ra and nsMRA
- ❖ Decrease adverse cardiovascular and renal outcomes, and mortality in patients with type 2 DM with CKD
- ❖ SGLT2i also beneficial in Non diabetic CKD