

*Mount Sinai Health Partners:*  
**Excellence in Polychronic  
Disease Management**

Tuesday, May 17, 2022

*Course Director*

**Arshad K. Rahim, MD, MBA, FACP**

*Provided by*

Mount Sinai Health Partners (MSHP) and the  
Icahn School of Medicine at Mount Sinai

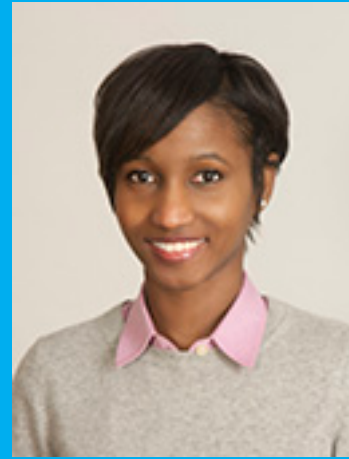


**Mount  
Sinai  
Health  
Partners**

# Welcome and Introduction



Shirley Chen,  
MD



Khadeen  
Cheesman,  
MD



Noah Moss,  
MD



Joji Tokita,  
MD

# Case Presentation



**Dr. Shirley Chen**  
Mount Sinai Doctors

## Patient Information: *First 2 PCP Visits*

### Demographic Information and Background

CC: Establishing Care with a New PCP

- 62 year old African American female
- Established care with PCP in January 2021 and completed follow up visit in February 2021
- Previously had an outside PCP near her house in Far Rockaway, Queens
- Established care with cardiologist at Mount Sinai Queens in June 2019 following multiple CHF-related admissions in 2019
- Commercial insurance

### Medical History

- CHF
- Atrial fibrillation
- Type II Diabetes (>10 years, many complications: retinopathy, neuropathy, microalbuminuria, CAD)
- Hypertension
- GERD
- Hyperlipidemia
- Multiple CHF-related admissions in 2019; ICD/CRT place in 2019 which found her Afib in 2020

### Social History

- Lives alone
- From the Caribbean
- Works night shifts as a home aide so often difficult to make appointments and coordinate transportation
- Cost is a concern for her medications

## Patient Information: *First 2 PCP Visits*

### Current Medications

- Amlodipine (CCB)
- Carvedilol (Beta-Blocker)
- Novolog 70/30 (insulin)
- Sitagliptan-metformin (DPP4 inhibitor, biguanides)
- Losartan (ARB)
- Simvastatin (statin)
- Warfarin (blood thinner)
- Omeprazole (GERD)

Patient reports she is not taking carvedilol due to difficulty obtaining it at her pharmacy.

She is only taking sitagliptan-metformin once daily instead of twice daily as prescribed because she feels it causes dizziness.

Patient has had insulin cost issues in the past, so she was switched to Novolog 70/30 insulin. She had inconsistent use of medication for the supply she had.

## Patient Physical Examination

BMI normal at 20.55 and stable weight over the past few months

Vitals	1/8/2020	12/30/2020	1/6/2021	2/10/2021
Systolic	125	128	122	124
Diastolic	80	83	60	70

General: No distress, pleasant elderly female

HEENT: NCAT, PERRLA

CV: RRR with no murmur

Pulm: Crackles at the Left Base, otherwise CTA

Abd: soft/nt/nd/nabs

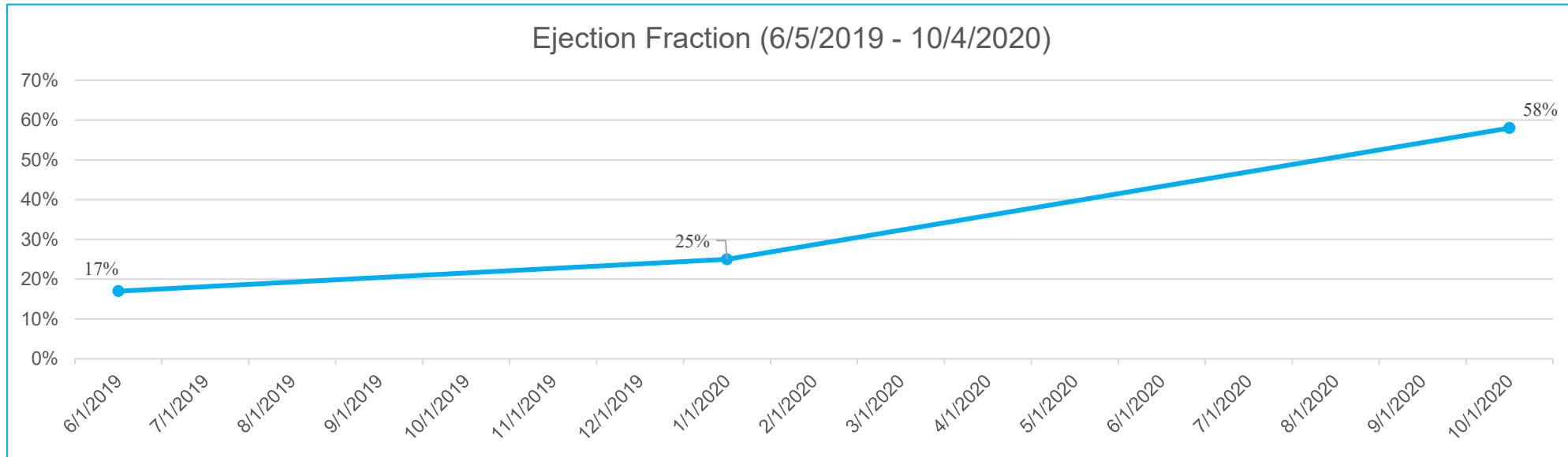
Ext: No edema, 2+ distal pulses

Psych: Normal mood and affect

## Relevant Lab Results

- ▶ A1c: 13.1% and the last one before that was a 14.5% in 2019
- ▶ Glucose: 328 mg/dL (fasting = 80-130 / after food <180)
- ▶ Blood urea nitrogen: 19 mg/dL (normal = 8-27)
- ▶ Creatinine: 1.22 mg/dL (normal = 0.57 – 1.00)
- ▶ Potassium: 4.2 mmol/L (normal = 3.5-5.2)
- ▶ Estimated glomerular filtration rate: 55 mL/min/1.73
- ▶ BNP: 150 (normal = 0-100 pg/mL)

# Procedural Results Include





# Audience Polling and Expert-Facilitated Group Discussion

## Poll Question #1

- ▶ What are the appropriate next steps to improve glycemic control in this case?
  - a) Increase Novolin (insulin)
  - b) Stop sitagliptin and prescribe metformin only
  - c) Education on glucose monitoring, diet, and lifestyle management
  - d) Refer to endocrinology
  - e) Refer to medication cost assistance programs
  - f) C and D
  - g) B, C, D, and E

## Poll Question #2

- ▶ What are some red flags that should prompt a referral to endocrinology?
  - a) For A1c > 9, despite 6 months of therapy
  - b) Recurrent hypoglycemia
  - c) Continuous subcutaneous insulin infusion (insulin pump) therapy
  - d) Multiple hospital admissions related to CHF
  - e) Behavioral health barriers
  - f) A and D
  - g) A, B, and C
  - h) All of the above

## Poll Question #3

- ▶ Are there additional medications we can add to provide renal protection and/or manage heart failure?
  - a) SGLT2i
  - b) Diuretics
  - c) ACE inhibitor
  - d) Increase dose of ARB
  - e) None
  - f) All of the above

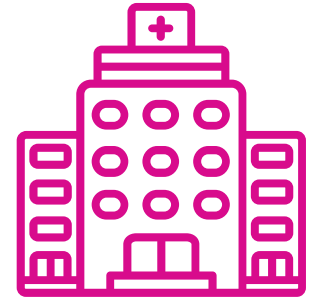
## Poll Question #4

- ▶ What are some next steps to improve diabetes medication adherence?
  - a) Medication reconciliation at every visit
  - b) Written patient instructions/list/schedule
  - c) 90-day fills
  - d) Home delivery
  - e) Blister packaging
  - f) Phone alerts
  - g) A, B, and C
  - h) All of the above

**One Year Later**

## Patient Hospitalized

- ▶ 1 hospitalization in 12/2021 for low blood sugar and kept having low BP in the hospital. At the discharge, they changed her to Xarelto not realizing the patient cannot afford this. Insurance does not cover other blood thinners outside of Coumadin.
- ▶ A few blood pressure readings chosen throughout the patient's hospitalization:



Vitals	12/11/2022	12/12/2022	12/12/2022	12/12/2022	12/13/2022	12/13/2022
Systolic	148	142	91	81	132	134
Diastolic	80	80	61	49	81	85

Vitals	12/13/2022	12/13/2022	12/13/2022	12/13/2022	12/14/2022	12/14/2022
Systolic	124	110	76	132	124	146
Diastolic	79	61	55	73	81	94

## Care Team Engagement

- ▶ Very engaged with PCP and cardiologist, seeing them every 2-3 months
- ▶ Patient started seeing an endocrinologist in December 2021 after referral from PCP 7/21
- ▶ Enrolled in Medication Assistance Program (MAP) and received cost assistance with SGLT2i and insulin co-pays
- ▶ Recently enrolled in Care Management Program on 2/9/22



## Current Medications

- ▶ Aspirin
- ▶ Losartan
- ▶ Carvedilol
- ▶ Coumadin
- ▶ Omeprazole
- ▶ Rosuvastatin
- ▶ Sitagliptin
- ▶ Insulin glargine 100 unit/mL (3mL) pen
- ▶ Dapagliflozin
- ▶ Gabapentin

- ▶ **Stopped:** Novolog 70/30 insulin, simvastatin, sitagliptin-metformin, amlodipine
- ▶ Sitagliptin-metformin was stopped because the patient reported dizziness. She reported not tolerating metformin alone in the past, so her endocrinologist prescribed sitagliptin phosphate (JANUVIA).
- ▶ Patient continues to have cost and coverage challenges with medications and other resources are being scoped to support patient

## Physical Examination

► BMI most recent visit: 21

Vitals	1/6/ 2021	2/10/ 2021	4/7/ 2021	7/7/ 2021	9/7/ 2021	11/2/ 2021	12/20/ 2021	2/8/ 2022	2/25/ 2022	3/11/ 2022
Systolic	122	124	140	133	144	142	160	130	155	148
Diastolic	60	70	90	81	90	76	94	80	79	80
Pulse										
Temp	98.6	98.6	98.7	98.6	98.5	98.6	98.6	98.6	98.6	98.6

General: No distress, pleasant elderly female

HEENT: NCAT, PERRLA

CV: RRR with no murmur

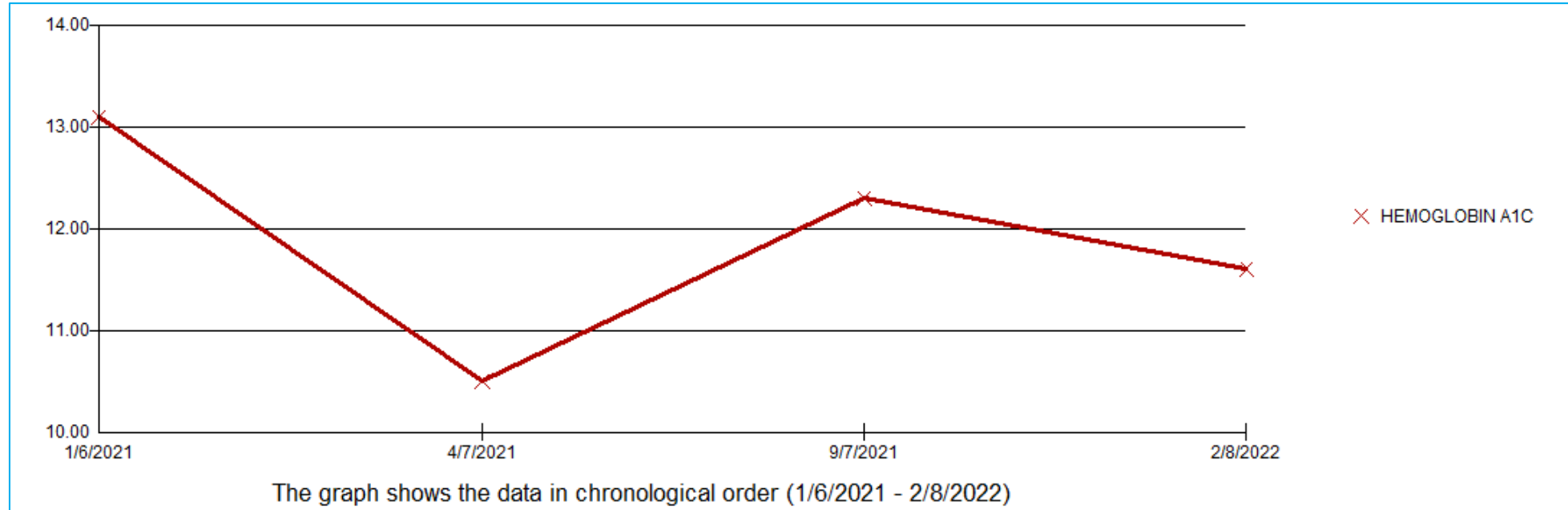
Pulm: Crackles at the Left Base, otherwise CTA

Abd: soft/nt/nd/nabs

Ext: No edema, 2+ distal pulses

Psych: Normal mood and affect

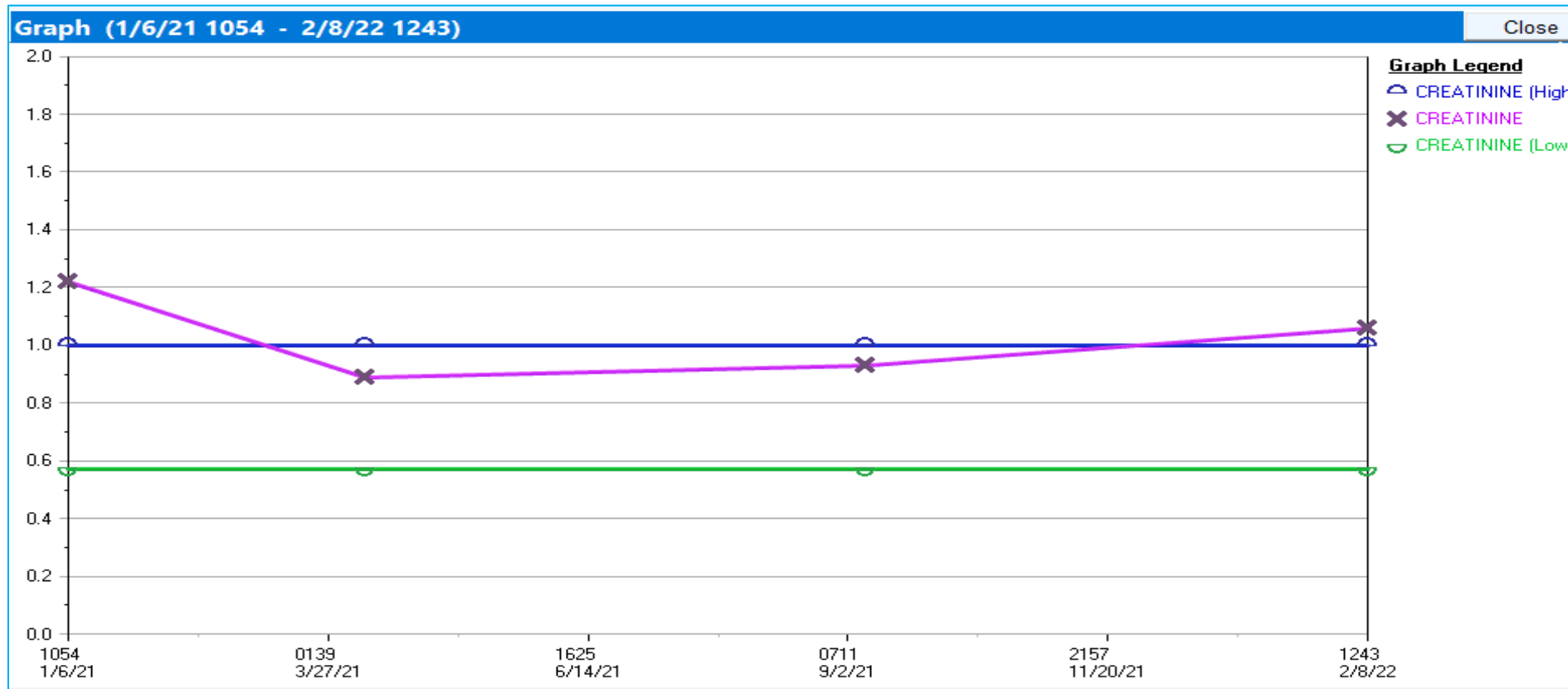
## Relevant Lab Result: Hgb A1c trend



## Relevant Lab Results from Endocrine Visit on 2/8/22

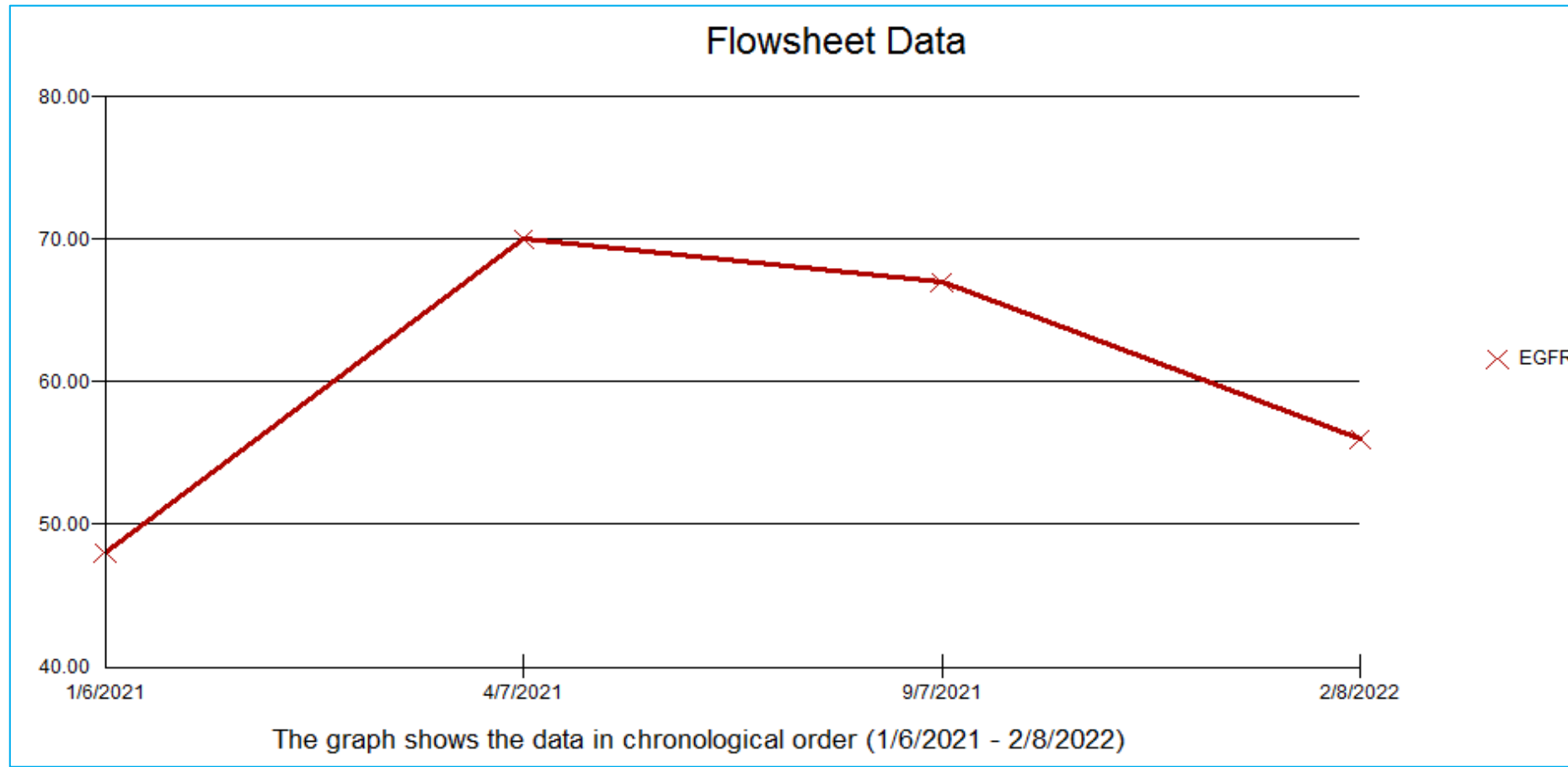
- ▶ Random blood glucose: 302 mg/dL
- ▶ Potassium: 4.1 (normal = 3.5-5.2 mmol/L)
- ▶ Blood urea nitrogen: 24 (normal = 8-27 mg/dL)
- ▶ Creatinine: 1.06 (normal = 0.57 -1.00 mg/dL)

- ▶ Microalb/Creat Ratio: 67 mg/g



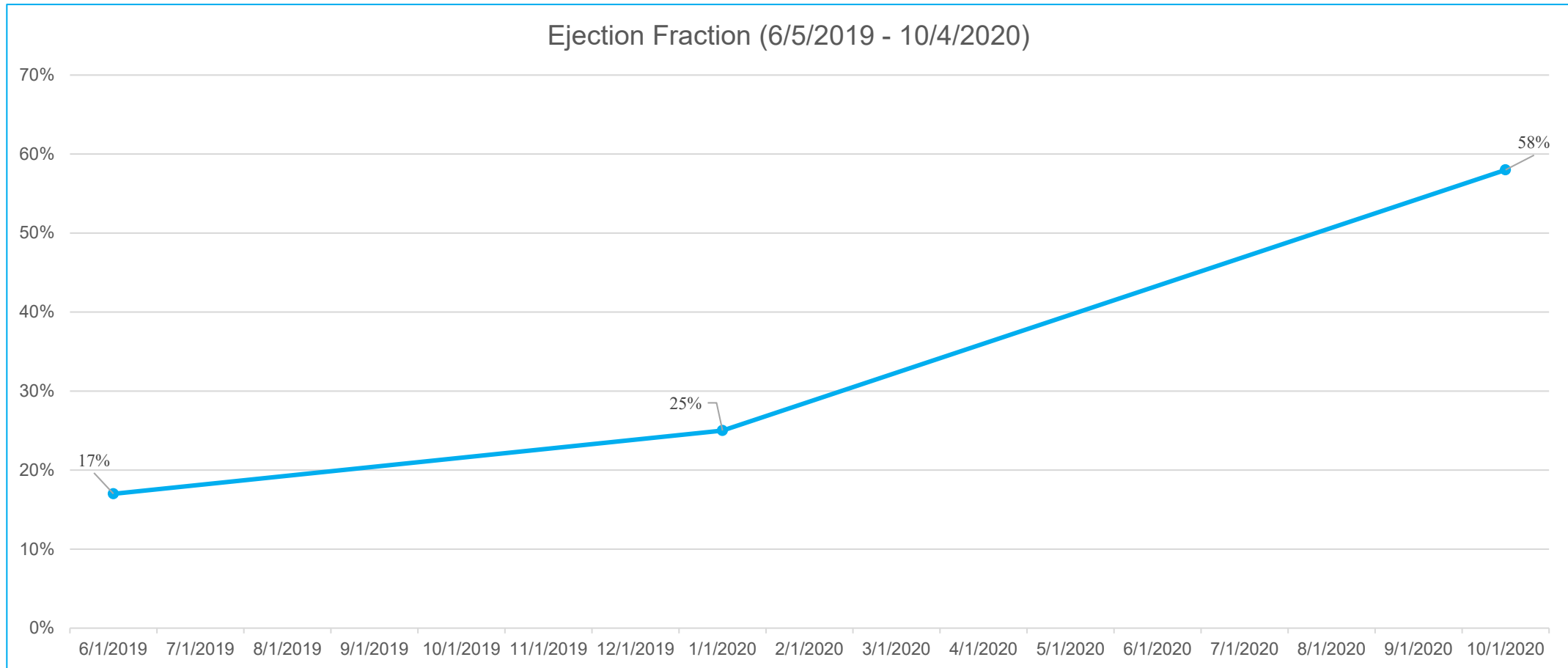
## Relevant Lab Results from Endocrine Visit on 2/8/22 *Continued ...*

- ▶ **Estimated glomerular filtration rate:** 55 mL/min/1.73 from 2/8/2022 and trending below



# Relevant Historical Results from Cardiology Visits on 3/17/2022 *Continued ...*

BNP: 110 (normal = 0-100 pg/mL)



## Current Medical Management

- Patient remains on guideline directed medical therapy for Heart Failure and has not had a CHF hospitalization since 2019.
- Beta-blocker has been adjusted due to fluctuating BP and dizziness. The patient cannot be maximized on GDMT due to symptomatic orthostatic hypotension.
- Patient is back on the Coumadin dose because Direct Acting Oral Anticoagulants are not covered. She has no bleeding issues but INRs not stable (often sub-therapeutic).
- Patient's blood pressure is suboptimal due to dizziness as noted above
- Patient's fear of needles has improved to start to check blood sugar about 1 time a day.
- Patient continues to have cost and coverage challenges with medications and other resources are being scoped to support patient.

# Q&A Polling and Expert-Facilitated Group Discussion



## Poll Question #5

- ▶ Does the patient currently have CKD? If so, what stage is this patient for CKD?
  - a) No
  - b) Yes, stage 1
  - c) Yes, stage 2
  - d) Yes, stage 3a
  - e) Yes, stage 3b
  - f) Yes, stage 4

## Poll Question #6

- ▶ What are some of the heart failure medical interventions that improved the patient's EF?
  - a) Cardiac resynchronization therapy
  - b) SGLT2i
  - c) Beta Blockers
  - d) Diuretics
  - e) A, B, and C
  - f) All of the above

# Group Discussion

# Update on CKD with a Focus on Management of DM, HF, and BP

## Joji Tokita, MD

Clinical Director, Division of Nephrology  
Associate Professor of Medicine  
Icahn School of Medicine at Mount Sinai



**Mount  
Sinai  
Health  
Partners**

## Example Clinical Case

Chief Complaint: Routine follow up

58 year old man with HTN, **T2DM**, asthma, elevated BMI, dyslipidemia, and **CKD Stage G2A2** seen for routine follow up in clinic. HTN has been reasonably well controlled. He has been compliant with medications but difficulty with dietary restriction and does not exercise regularly. Non-smoker.

- ▶ Type 2 Diabetes since 2015
  - Hemoglobin A1c in 7s, most recently **7.5%**
  - Microalbuminuria: **UACR 121mg/g**
  - Managed with **metformin 1000mg BID**
  - Does not have documented retinopathy
  - Diet and lifestyle changes have been difficult for him
- ▶ HTN with ambulatory blood pressure 124/84
  - On **Losartan 100mg daily** and Nifedipine ER 30mg daily

## Additional Information

### ► Past Medical History

- HTN
- DM2
- CKD G2A2
- Asthma
- BMI 29
- Dyslipidemia

### ► Medications

- Losartan 100mg daily
- Nifedipine ER 30mg daily
- Metformin 100mg BID
- Atorvastatin 40mg daily
- Albuterol MDI PRN

### ► Examination

- VS: 128/86 75 19
- Gen: well appearing in NAD
- Neck: No JVD
- Pulm: Chest clear
- CV: regular, no MRG
- Abd: soft/NT
- Ext: no peripheral edema

140	108	23	8.6	eGFR 66ml/min
4.2	22	1.2	121	HbA1c 7.1-7.5%
			3.6	

UA: no glucose, LE/nitrite, protein 100, no RBC/WBC  
UACR: 121mg/g

**KidneyIntelX Score: 88**

# Outline

- ❑ CKD Burden in the general population is underappreciated
- ❑ Correct Classification Using Urine Albumin to Creatinine Ratio (UACR)
- ❑ Risk stratify early in course of CKD (beyond GFR) and take action to prevent progression
- ❑ Options include Blood Pressure Management (<120/80), use ACE/ARB to max dose if possible, use SGLT2i
  - ❑ This will also save the heart
- ❑ Use the Mount Sinai CKD Ambulatory Care Pathway and/or consider Nephrology referral

# CKD is a Worldwide Public Health Problem

## Affects 850 Million Individuals Globally

### Chronic Kidney Disease

**37M**

Americans currently estimated with CKD

**20%**

Of the CMS budget is related to CKD or ESRD

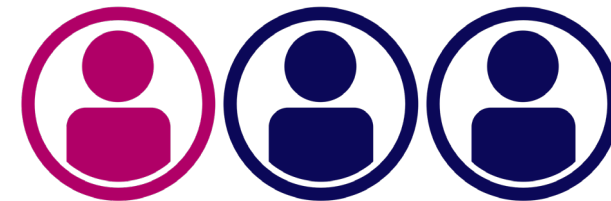
**90%**

9 out of 10 adults with CKD don't know they have it

### Diabetic Kidney Disease

**~60M**

Adults in the U.S. expected to be diagnosed with diabetes by 2060



**1 in 3**

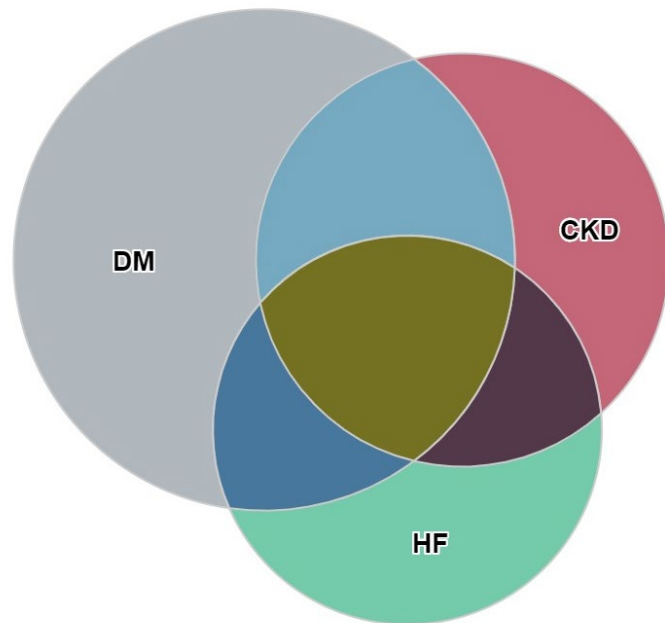
Adults with diabetes develop CKD



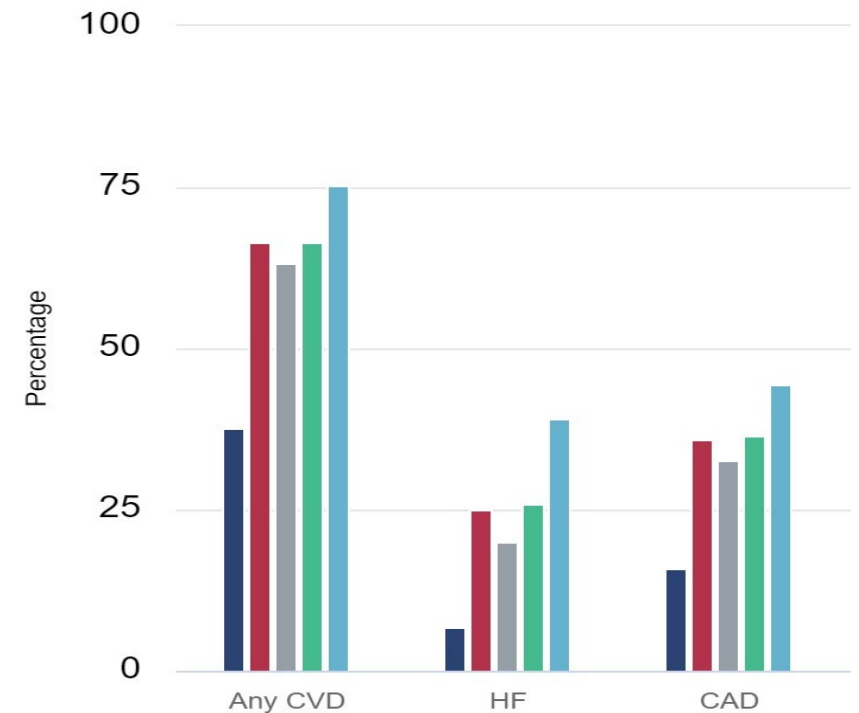
# Major Overlap Between Kidney Disease, Type 2 DM, and CVD

## Management of CKD Vital for Improving Outcomes

Annual Medicare Spending on CKD, DM2, Heart Failure  
**\$295 Billion**



### Increase in Risk for Cardiovascular Disease by CKD



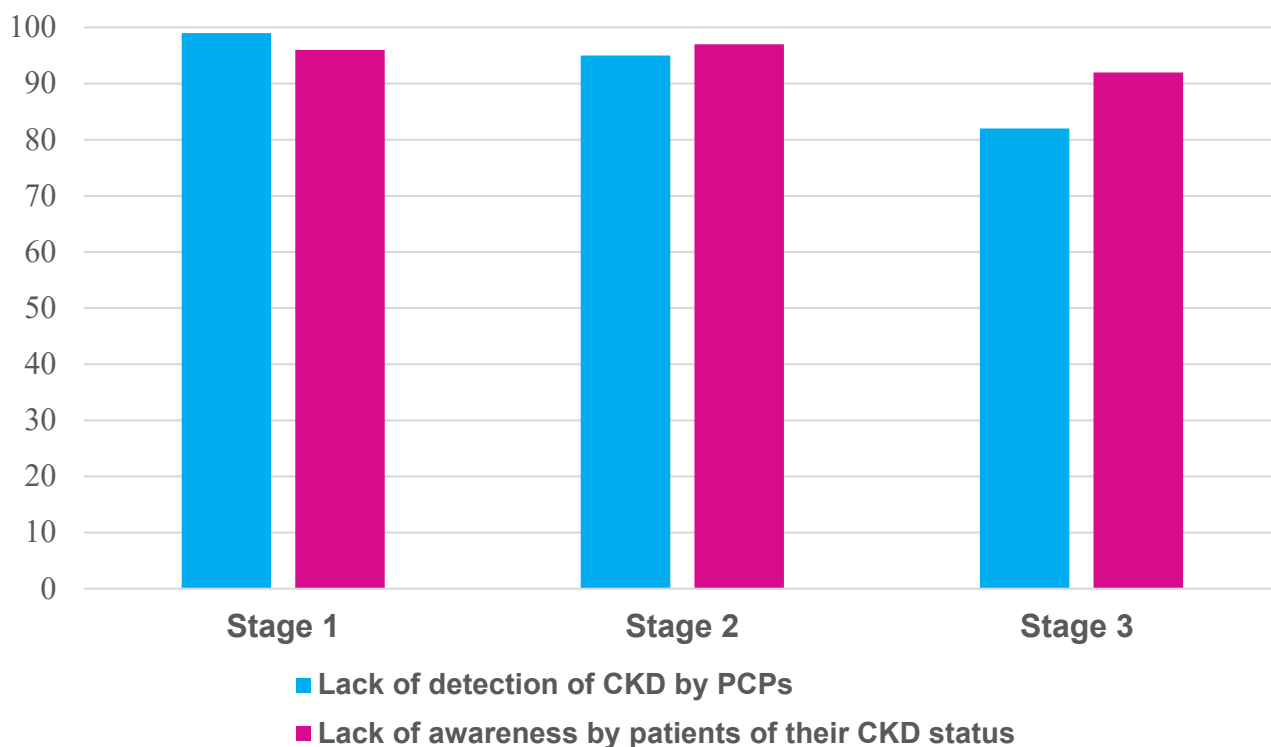
● No CKD ● Any CKD ● Stages 1-2 ● Stage 3 ● Stages 4-5

United States Renal Data System (USRDS). USRDS Annual Report, 2020

## CKD is Missed in Early Stages

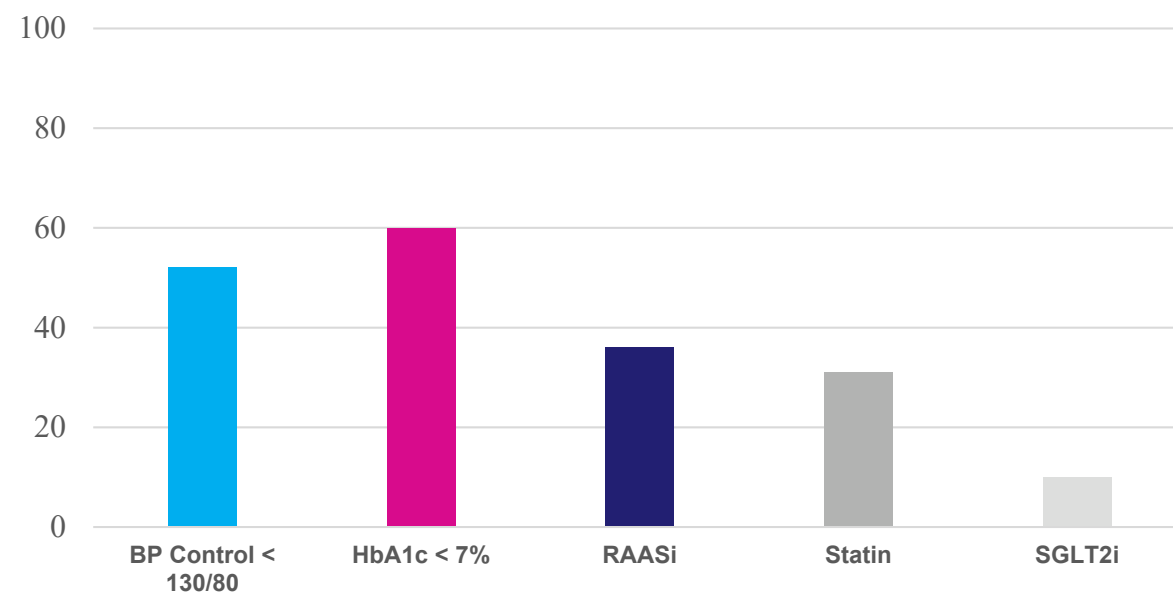
There is an Opportunity to Improve the Quality of CKD Care to Prevent Progression to ESKD

Inadequate Detection of CKD by Physicians  
Lack of Awareness of CKD by Patients



Source: PCP Data: Szczech LA, et al. Plos One 2014  
Patient Awareness Data: NHANES 2018 Data

Inadequate Treatment of CKD by Physicians

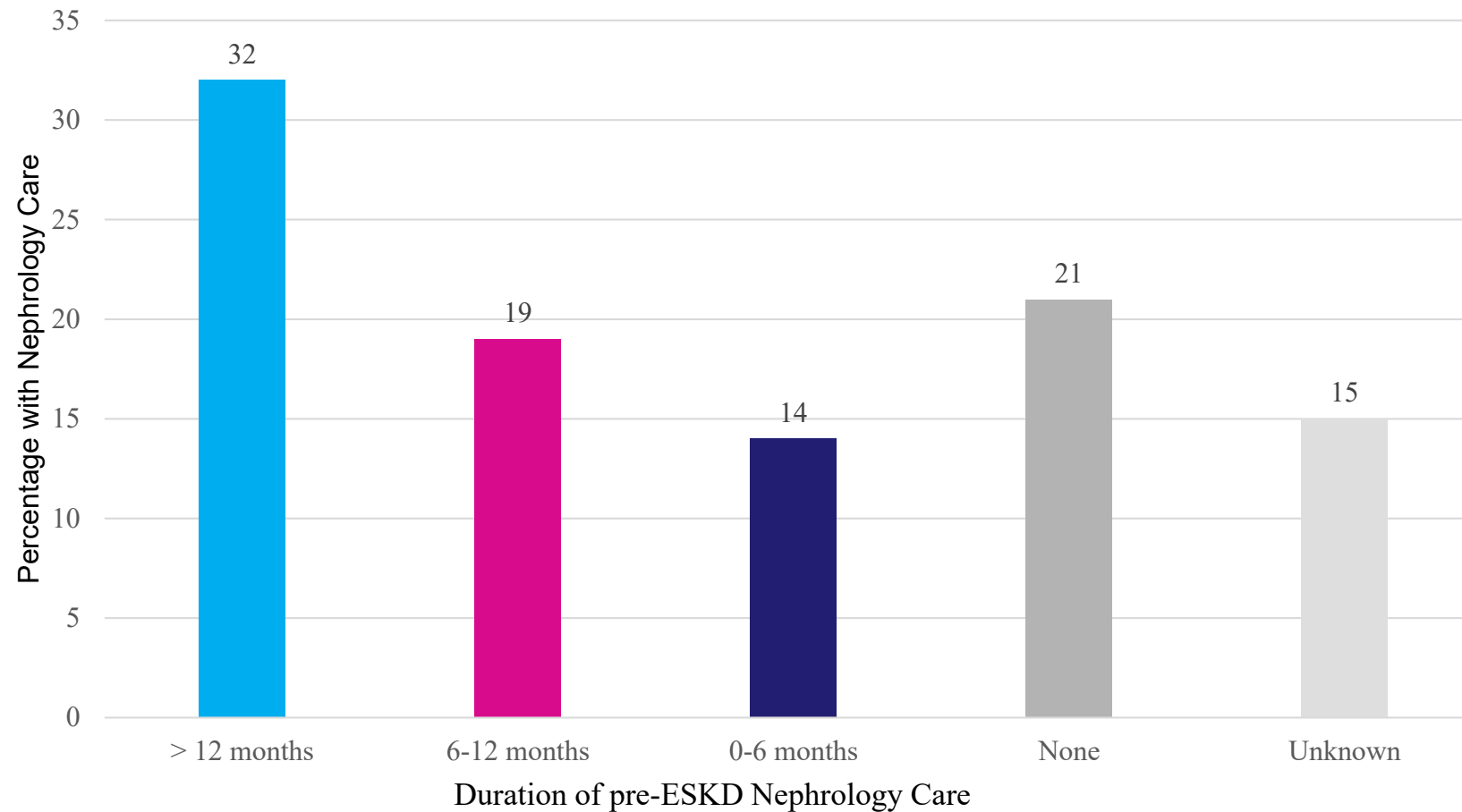


Sri Lekha Tummalapalli, Neil R. Powe and Salomeh Keyhani  
CJASN August 2019, 14 (8) 1142-1150

# An Assessment of Early-Stage CKD Care in the US

## Late and Inadequate Referrals in US

Only 32% of Patients Starting Long-term Dialysis Were Under the Care of Nephrologist for > 1 Year

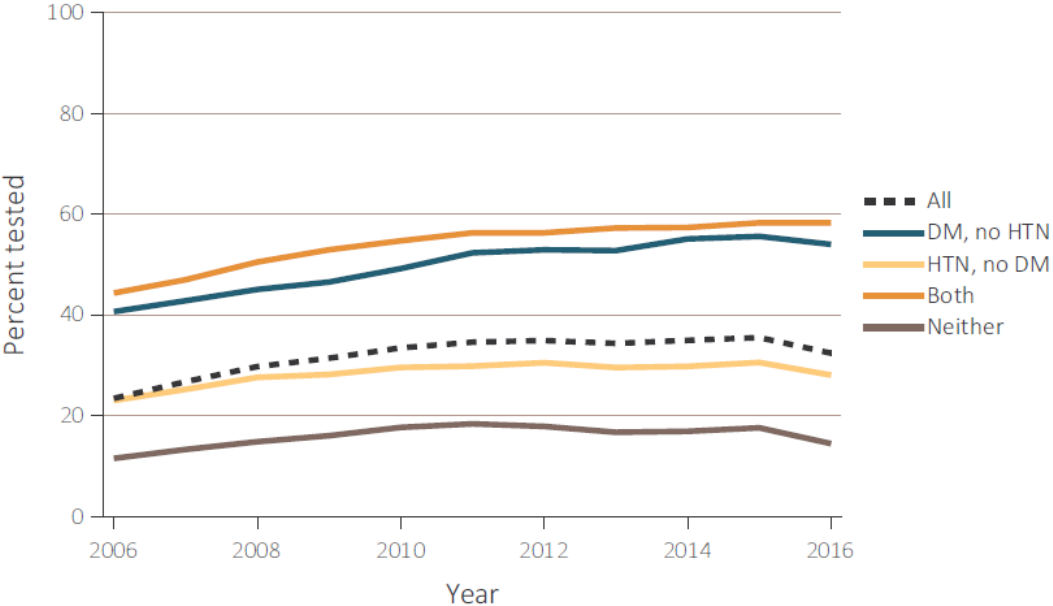


# Outline

- ❑ CKD Burden in the general population is underappreciated
- ❑ **Correct Classification Using Urine Albumin to Creatinine Ratio (UACR)**
- ❑ Risk stratify early in course of CKD (beyond GFR) and take action to prevent progression
- ❑ Options include Blood Pressure Management (<120/80), use ACE/ARB to max dose if possible, use SGLT2i
  - ❑ This will also save the heart
- ❑ Use the Mount Sinai CKD Ambulatory Care Pathway and/or consider Nephrology referral

# Use of UACR: Underutilized, but Necessary for Classification of CKD, and part of Guidelines and HEDIS Measures

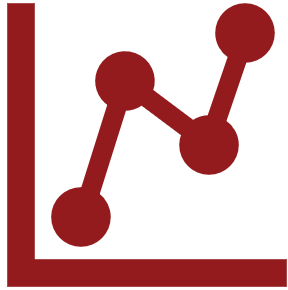
Nearly 50% of patients with CKD Do NOT Get Urine Albumin Testing



				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 per 1.73 m <sup>2</sup> ) 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			

# Even with eGFR and UACR Testing, There are Still Nuances to Consider

## High biological variability of UACR and eGFR



Intra-individual variability:  
UACR 55-125%  
eGFR 16-20%

## Lack of precision in eGFR by race



NKF/ASN have dropped race from eGFR calculation

## Hyperfiltration precedes DKD progression



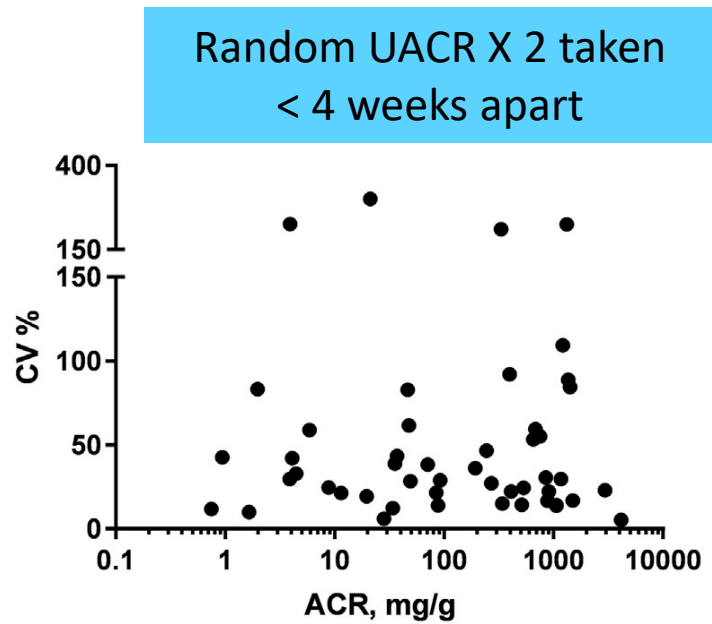
Hyperfiltration masks early DKD while kidney injury continues

## Most kidney protective drugs decrease kidney function over first 1-2 years of Rx

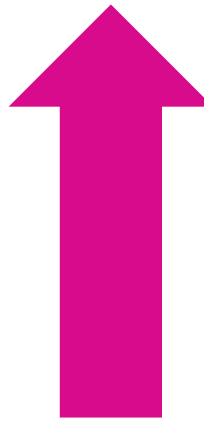


RAAS inhibitors and SGLT2i both result in drops in eGFR

# Significant Intra-Individual Variability in UACR Within Short-time Period



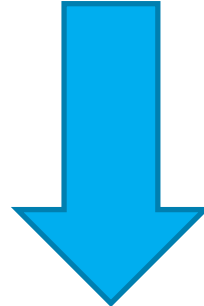
CV<sub>w</sub> = 30%



124% increase



Given a median CV<sub>w</sub> = 30%, an increase from baseline of 124% or a decrease of 55% can be expected by chance



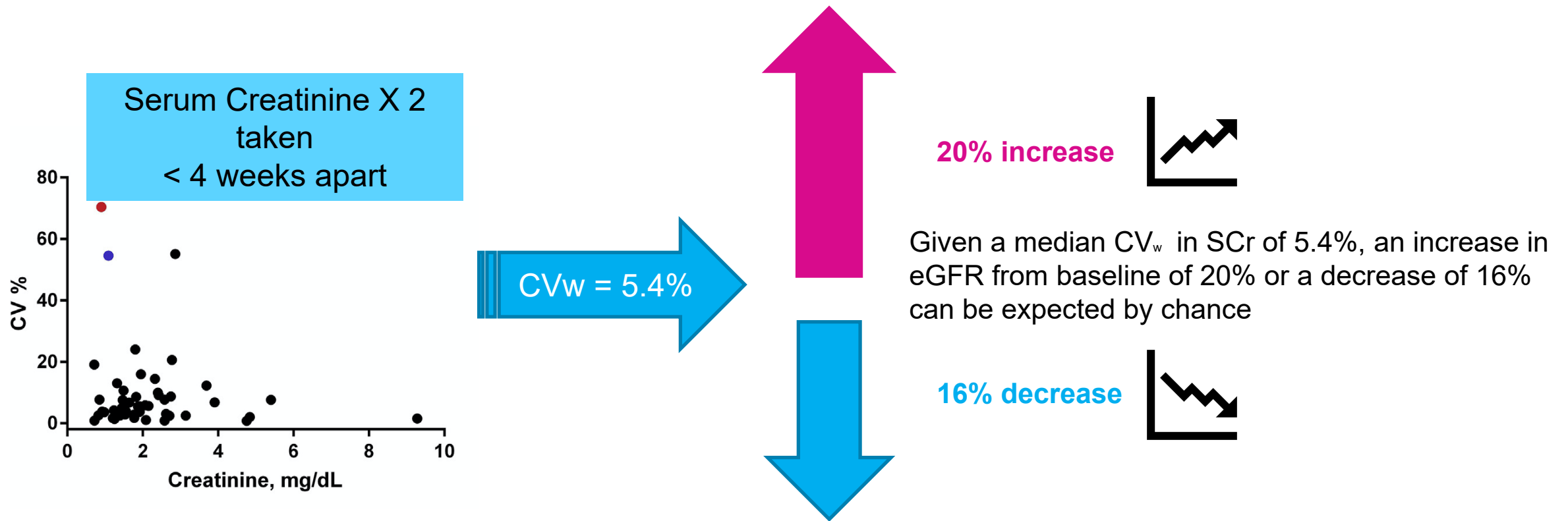
55% decrease



Abbreviations: CV<sub>w</sub>= Within person coefficient of variation



# Significant Intra-Individual Variability in eGFR Within Short Time Period (Continued)

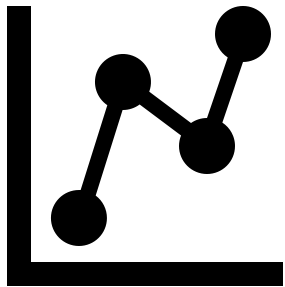


Abbreviations: CV<sub>w</sub>= Within person coefficient of variation

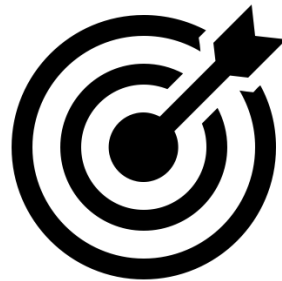
# Issues with Current Standard of Care

## Measures of Kidney Function

High Biological  
Variability



Lack of precision  
by race



Hyperfiltration precedes  
DKD progression

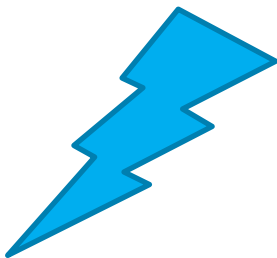


Most kidney protective drugs  
decrease kidney function  
over first 1-2 years of Rx



# Implications for Black Adults in US due to Dropping AA from Calculation of eGFR

Instantaneous



## eGFR Calculation (CKD-EPI)

$GFR = 141 \times \min(Scr/\kappa, 1)^\alpha \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018[\text{if female}] \times 1.159[\text{if black}]$

$\kappa = 0.7$  if female  
 $\kappa = 0.9$  if male

$\alpha = -0.329$  if female  
 $\alpha = -0.411$  if male

min = The minimum of  $Scr/\kappa$  or 1  
max = The maximum of  $Scr/\kappa$  or 1

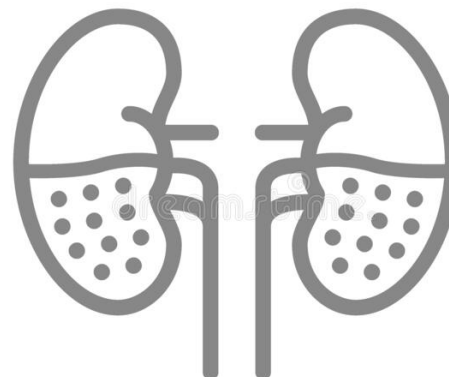
Scr = serum creatinine (mg/dL)



No change in true  
biology or disease



New CKD



20% Relative Increase  
1.2m new “cases” CKD

Progression of CKD



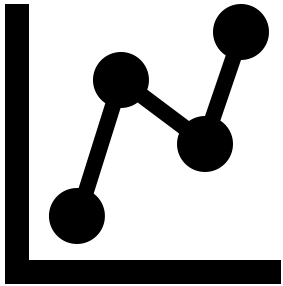
29% Relative Increase  
1.5m with worse stage of CKD

Diao JA, et al. Clinical implications of removing race from estimates of kidney function (Research Letter). *JAMA* [published online ahead of print]. doi: 10.1001/jama.2020.22124

# Issues with Current Standard of Care

## Measures of Kidney Function

High Biological  
Variability



Lack of precision  
by race



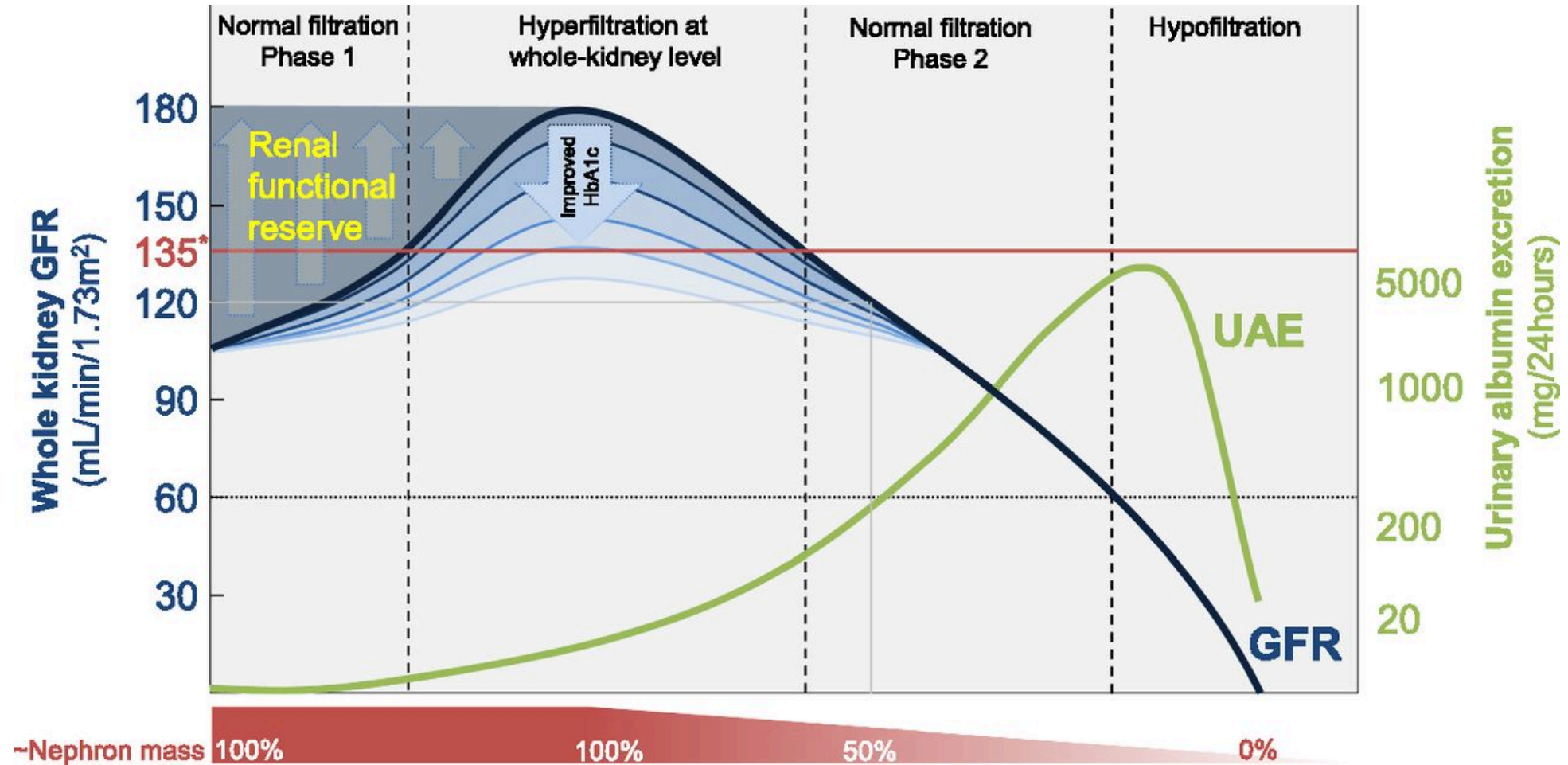
Hyperfiltration precedes  
DKD progression



Most kidney protective drugs  
decrease kidney function  
over first 1-2 years of Rx

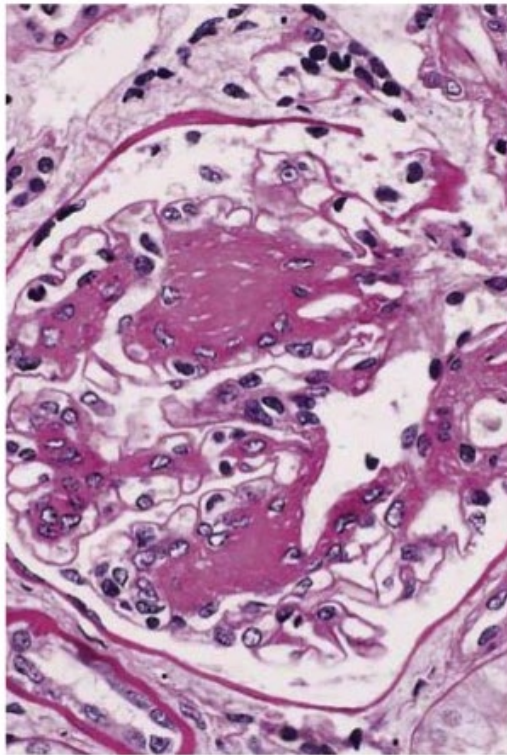


# Hyperfiltration in Early Stages of DKD Provides False Sense of Security

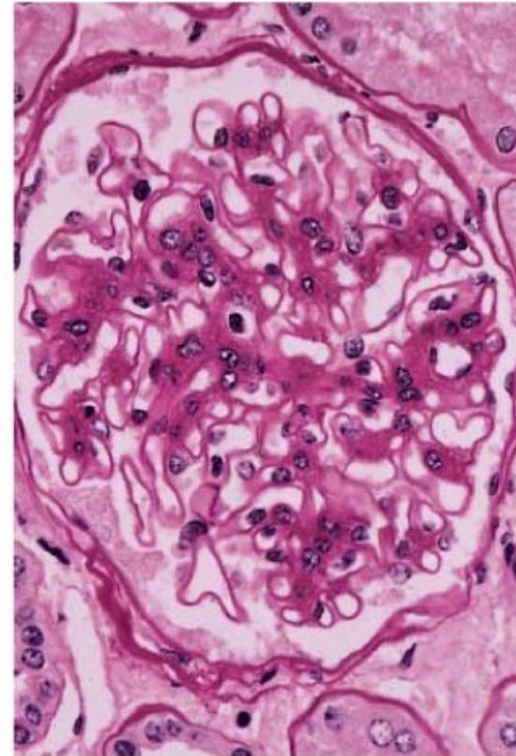


Can lose half of nephron mass with no decrement in GFR

# Marked Kidney Damage in Individuals with Diabetes and Normal Levels of Kidney Function



eGFR 84 ml/min/1.73 m<sup>2</sup>

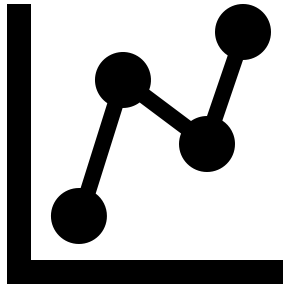


eGFR 110 ml/min/1.73 m<sup>2</sup>

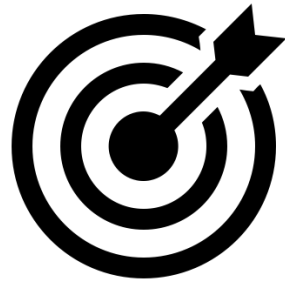
# Issues with Current Standard of Care

## Measures of Kidney Function

High Biological  
Variability



Lack of precision  
by race



Hyperfiltration precedes  
DKD progression

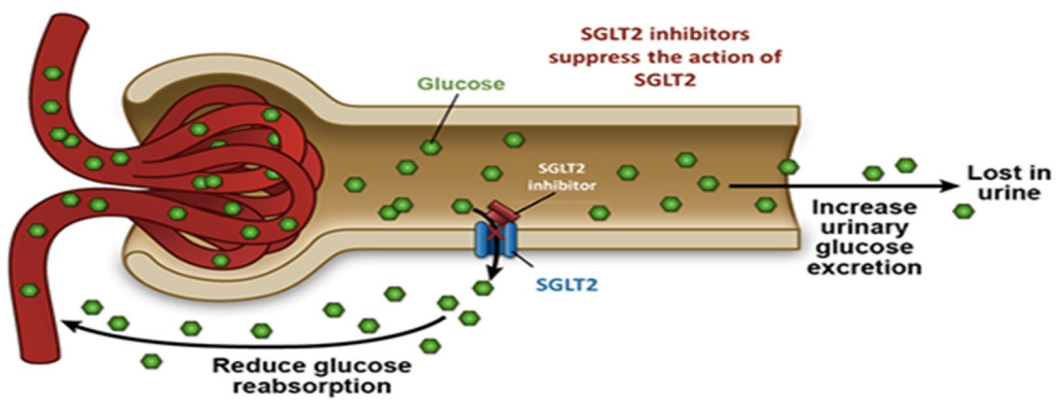
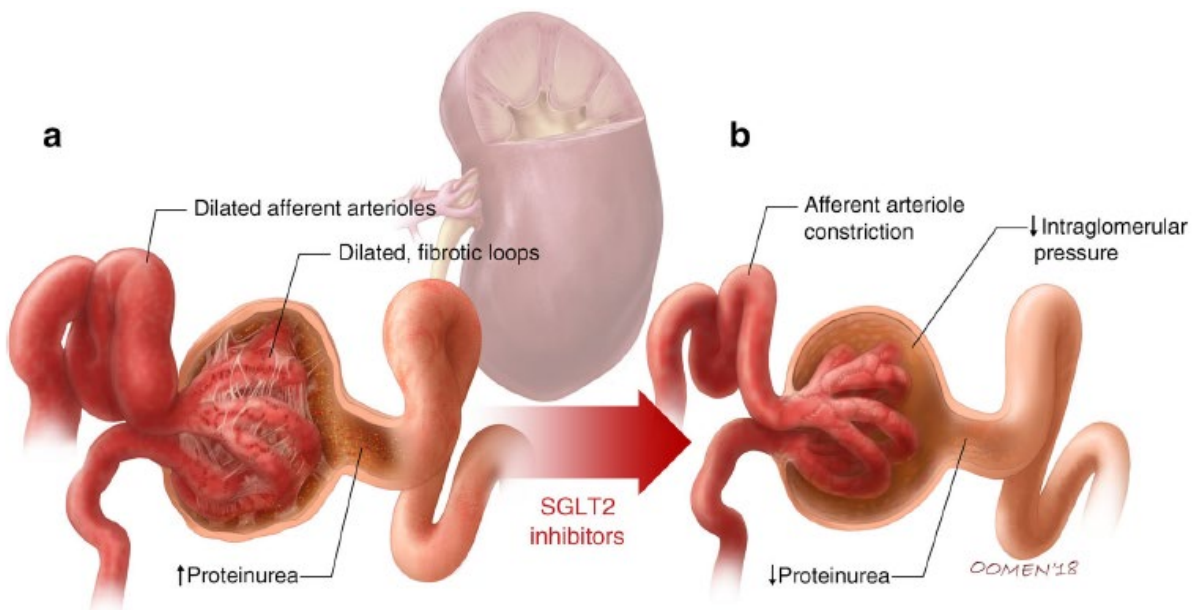


Most kidney protective drugs  
decrease kidney function  
over first 1-2 years of Rx



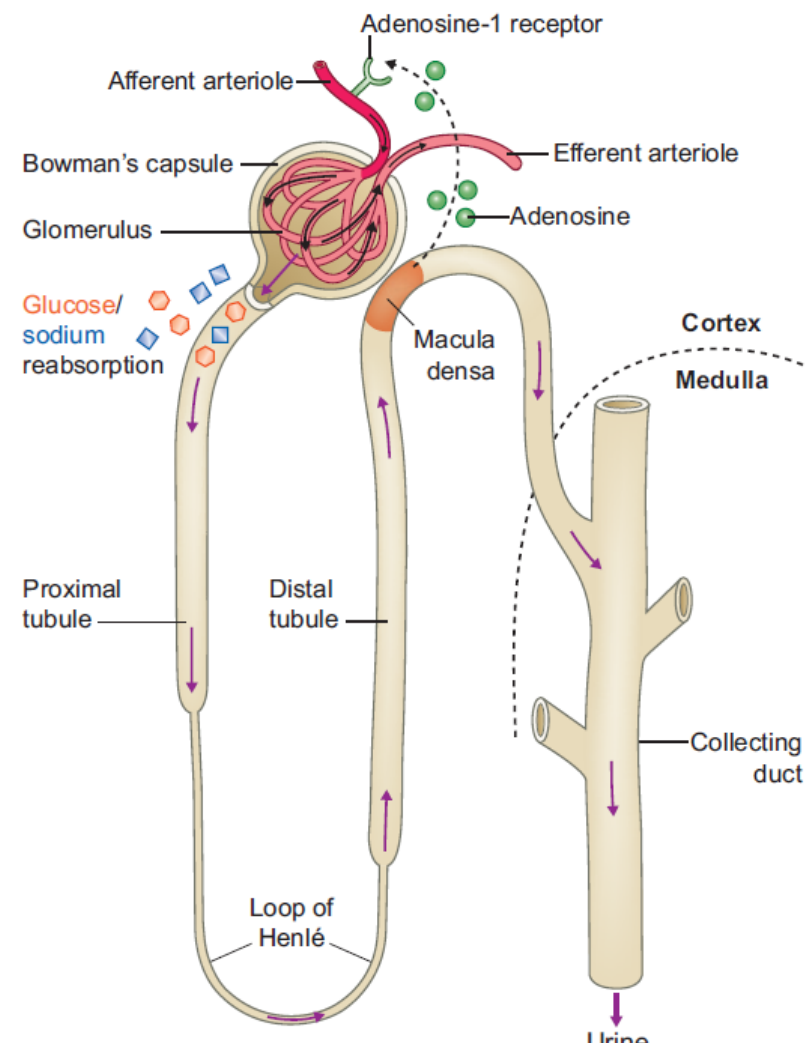


# The Goal for DKD is to Decrease Intraglomerular Pressure



Wright EM, et al. *Physiol Rev.* 2011;91:733-794.

Verma and McMurray *Diabetologia* 2018



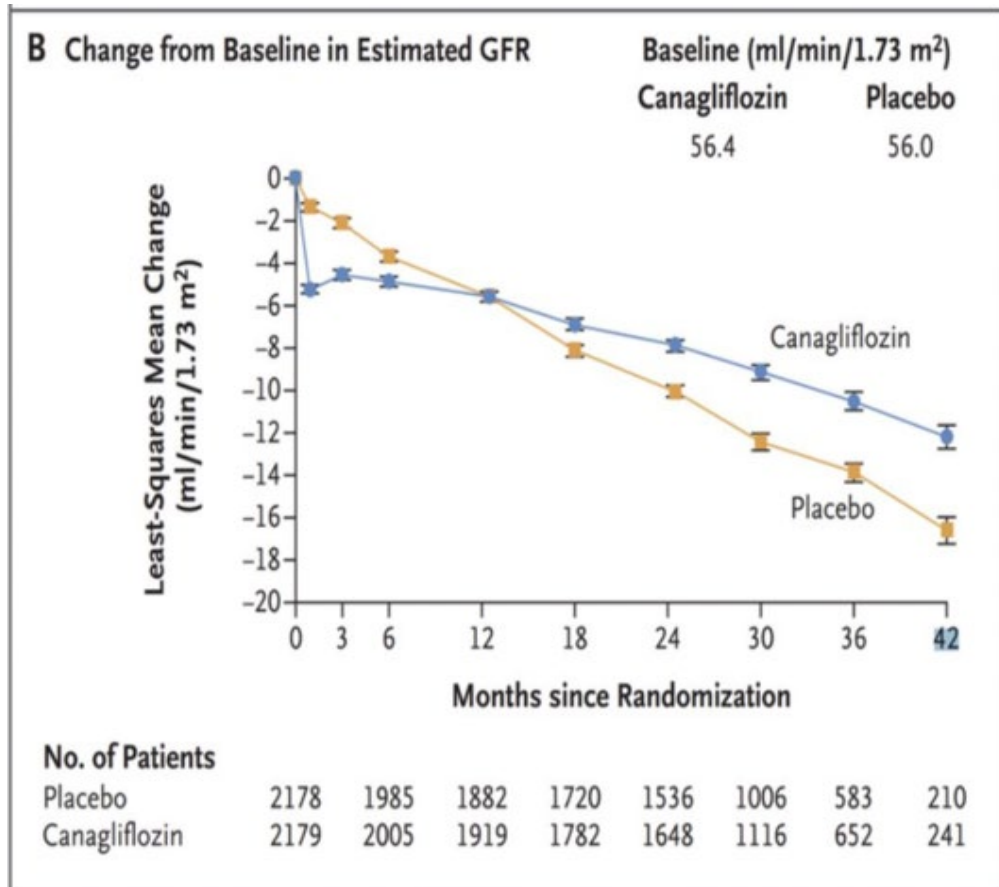
Heerspink H. *Nephrol Dial Transplant* 2019



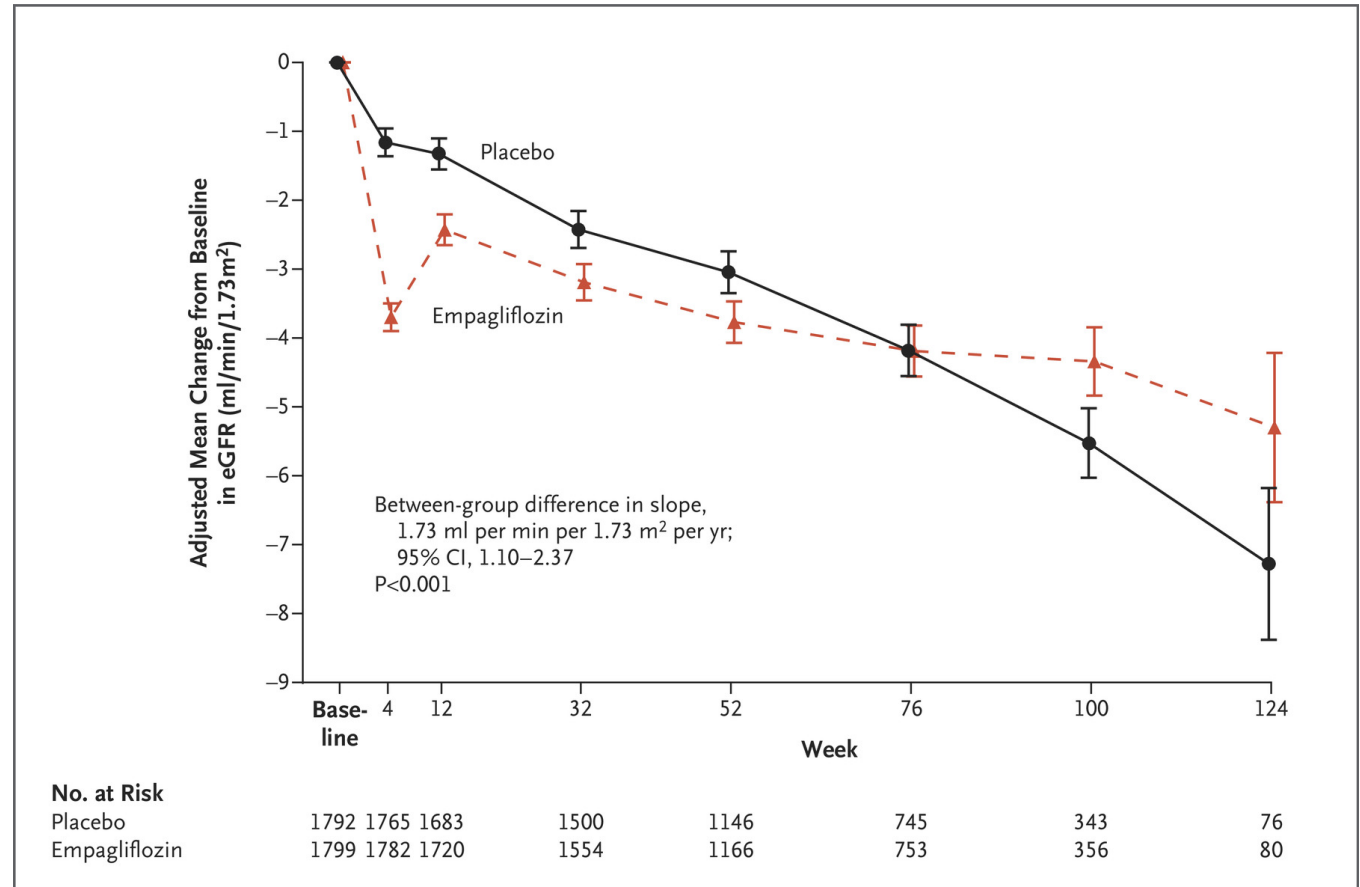
# Acute eGFR Decline After SGLT2 Inhibitors

## Cross-over and Better Trajectory Doesn't Occur until 12+ Months Later

CRENDENCE (NEJM 2019)



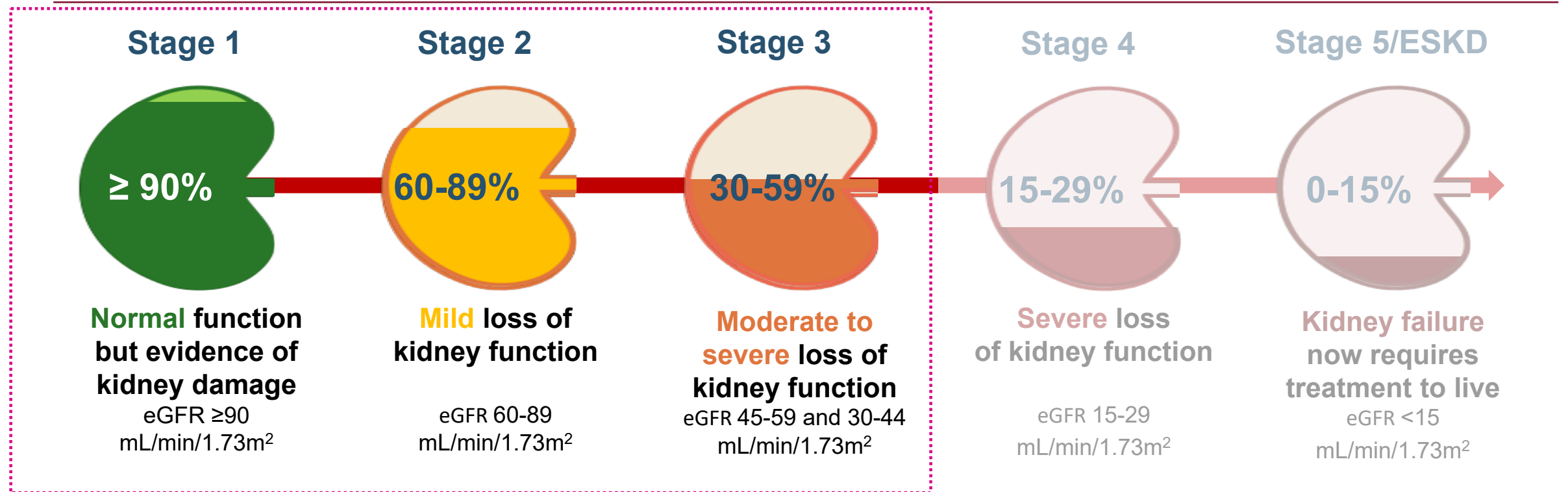
EMPEROR-Reduced (NEJM 2020)



# Outline

- ❑ CKD Burden in the general population is underappreciated
- ❑ Correct Classification Using Urine Albumin to Creatinine Ratio (UACR)
- ❑ **Risk stratify early in course of CKD (beyond GFR) and take action to prevent progression**
- ❑ Options include Blood Pressure Management (<120/80), use ACE/ARB to max dose if possible, use SGLT2i
  - ❑ This will also save the heart
- ❑ Use the Mount Sinai CKD Ambulatory Care Pathway and/or consider Nephrology referral

# There is Time to Intervene Prior to CKD Progression When It Is Irreversible



## OPPORTUNITY TO SHIFT DKD CARE UPSTREAM

**FUTURE: Earlier Intervention = Better Outcomes**

**CURRENT: Treat at costly end-stage**

# Outline

- ❑ CKD Burden in the general population is underappreciated
- ❑ Correct Classification Using Urine Albumin to Creatinine Ratio (UACR)
- ❑ Risk stratify early in course of CKD (beyond GFR) and take action to prevent progression
- ❑ **Options include Blood Pressure Management (<120/80), use ACE/ARB to max dose if possible, use SGLT2i**
  - ❑ **This will also save the heart**
- ❑ Use the Mount Sinai CKD Ambulatory Care Pathway and/or consider Nephrology referral

# Four Pillars of Diabetic Kidney Disease Management in 2022



# Metformin/Lifestyle + SGLT2i (ADA 2020 and KDIGO 2020)

## 2020 ADA Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes

**FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle**

**INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†**

**CONSIDER INDEPENDENTLY OF BASELINE A1C OR INDIVIDUALIZED A1C TARGET**

### HF OR CKD PREDOMINATES

- Particularly HF<sub>r</sub>EF (LVEF <45%)
- CKD: Specifically eGFR 30-60 mL/min/1.73 m<sup>2</sup> or UACR >30 mg/g, particularly UACR >300 mg/g

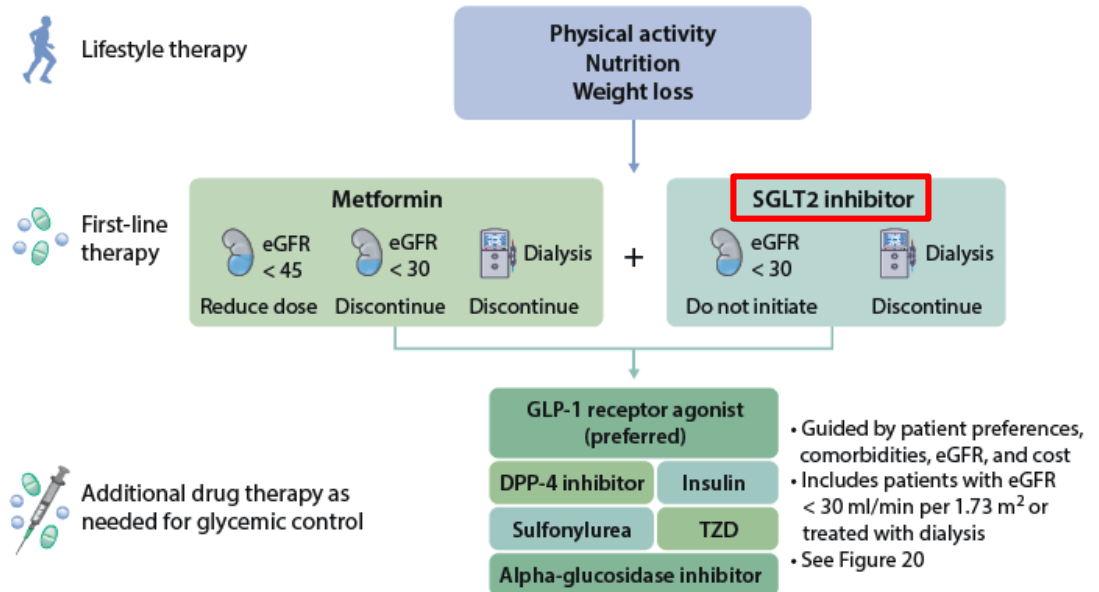
### PREFERABLY

**SGLT2i** with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate<sup>2</sup>

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate<sup>2</sup> add GLP-1 RA with proven CVD benefit<sup>1</sup>

## 2020 KDIGO Clinical Practice Guidelines for Diabetes Management in CKD



### 4.2 Sodium–glucose cotransporter-2 inhibitors (SGLT2i)

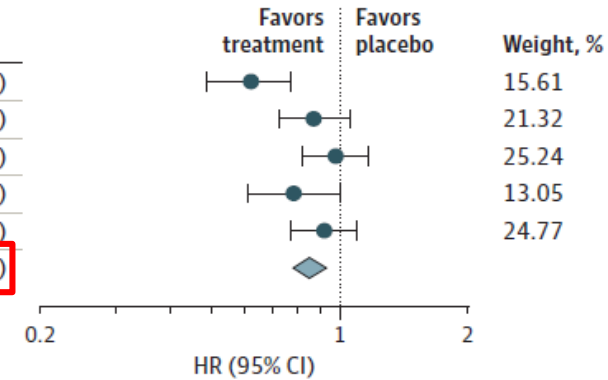
**Recommendation 4.2.1:** We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m<sup>2</sup> with an SGLT2i (1A).

# SGLT2i Are Powerful Medications for Improved CV and Kidney Outcomes

Figure 2. Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Cardiovascular Death

**A** Overall CV death

	Treatment		Placebo		Hazard ratio (95% CI)
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	
EMPA-REG OUTCOME	172/4687	12.4	137/2333	20.2	0.62 (0.49-0.77)
CANVAS program	NA/5795	11.6	NA/4347	12.8	0.87 (0.72-1.06)
DECLARE-TIMI 58	245/8582	7.0	249/8578	7.1	0.98 (0.82-1.17)
CREDESCENCE	110/2202	19.0	140/2199	24.4	0.78 (0.61-1.00)
VERTIS CV	341/5499	17.6	184/2747	19.0	0.92 (0.77-1.10)
Fixed-effects model (Q= 11.22; df= 4; P= .02; I <sup>2</sup> = 64.3%)					<b>0.85 (0.78-0.93)</b>

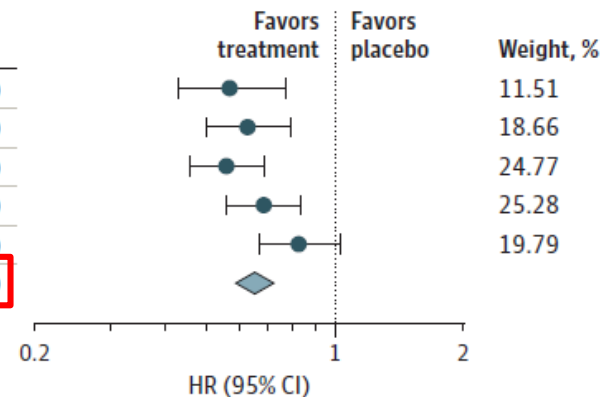


**15% Reduction in CV Death**

Figure 4. Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Kidney-Related Outcomes

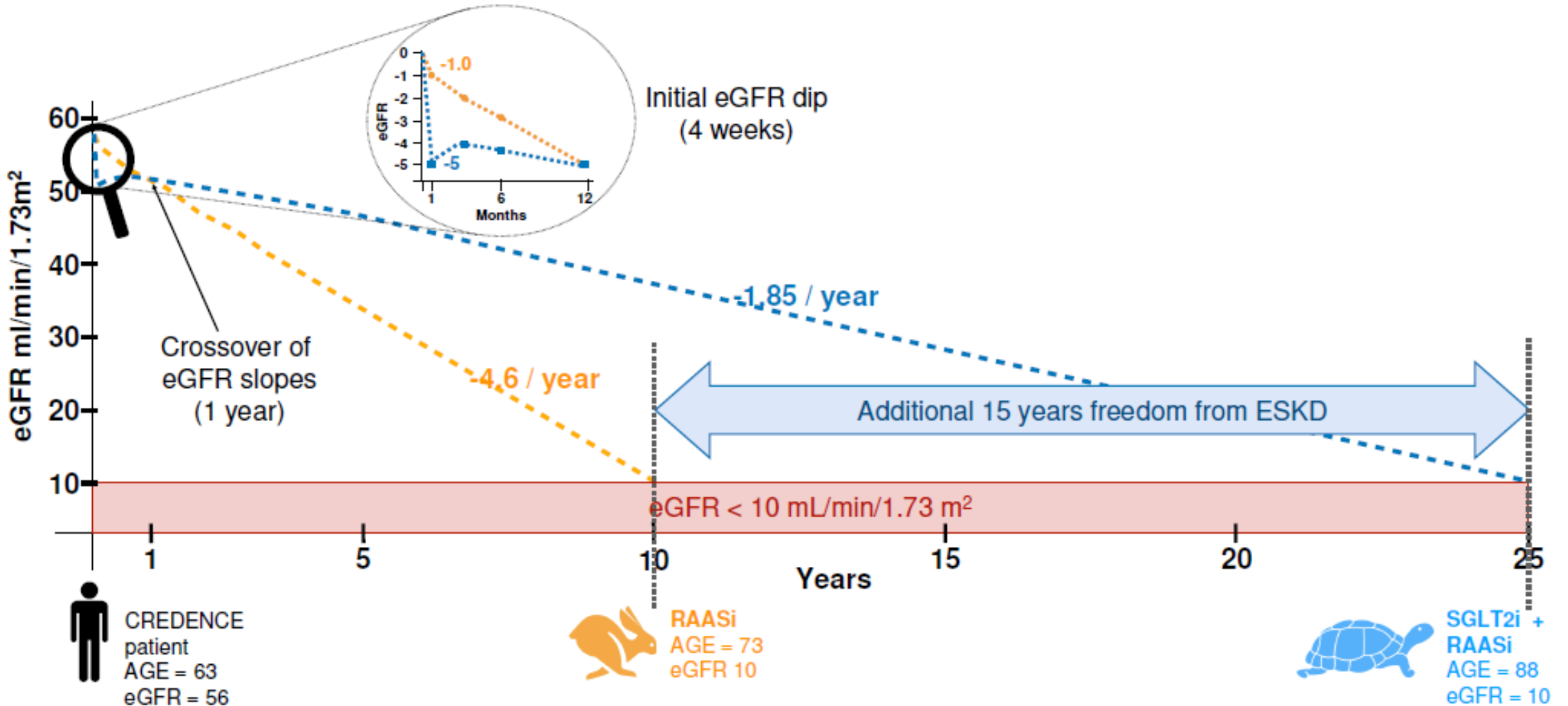
**A** Overall kidney outcomes

	Treatment		Placebo		Hazard ratio (95% CI)
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)
CANVAS program	NA/5795	5.5	NA/4347	9.0	0.60 (0.47-0.77)
DECLARE-TIMI 58	127/8582	3.7	238/8578	7.0	0.53 (0.43-0.66)
CREDESCENCE	153/2202	27.0	224/2199	40.4	0.66 (0.53-0.81)
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)
Fixed-effects model (Q= 7.96; df= 4; P= .09; I <sup>2</sup> = 49.7%)					<b>0.62 (0.56-0.70)</b>



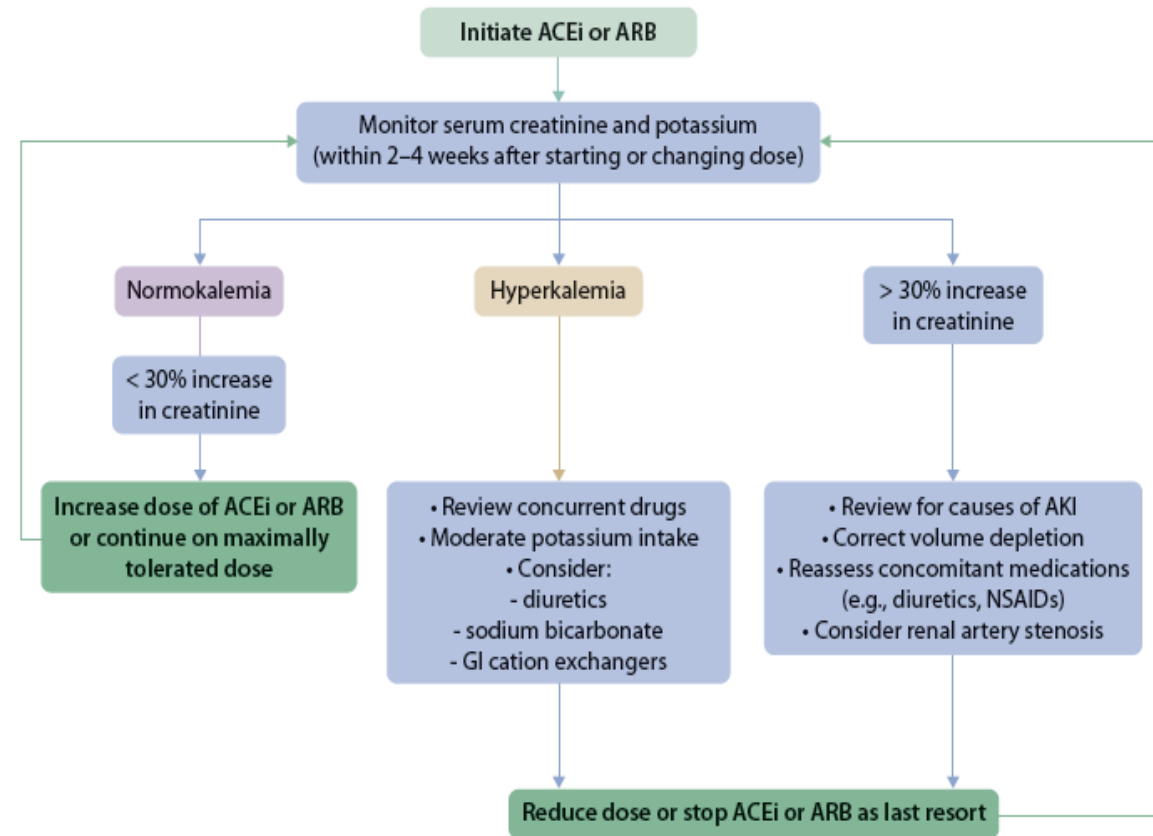
**38% Reduction in Kidney Outcomes**

# SGLT2i Inhibitors May Delay ESKD by 15 Years





# ACEi/ARB Initiation, Titration, and Mitigation Strategies for Hyperkalemia: KDIGO 2020



## 1.2 Renin–angiotensin system (RAS) blockade

**Recommendation 1.2.1:** We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (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).

# Outline

- ❑ CKD Burden in the general population is underappreciated
- ❑ Correct Classification Using Urine Albumin to Creatinine Ratio (UACR)
- ❑ Risk stratify early in course of CKD (beyond GFR) and take action to prevent progression
- ❑ Options include Aggressive Blood Pressure Management (<120/80), use ACE/ARB to max dose if possible, use SGLT2i
  - ❑ This will also save the heart
- ❑ **Use the Mount Sinai CKD Ambulatory Care Pathway and/or consider Nephrology referral**

				Persistent Albuminuria Categories							
				A1	A2	A3					
				Normal-Mildly Increased	Moderately Increased	Severely Increased					
				<30 mg/g	30-300 mg/g	>300 mg/g	BMD*	NA Intake**	Diabetes Treatment***		
GFR Categories (ml/min/1.73m <sup>2</sup> )	Stage 1	Normal or High	≥90	1 visit/yr if CKD	1 visit/yr	2 visits/yr		<4 g (<2 g/d if HTN or DM)	Metformin	SGLT-2i	GLP-1 RA
	Stage 2	Mildly Decreased	60-89	1 if CKD	1	2					
	Stage 3a	Mild-Moderately Decreased	45-59	1	2	3					
	Stage 3b	Moderately-Severely Decreased	30-44	2	3	3	Assess for Bone Mineral Disorder				
	Stage 4	Severely Decreased	15-29	3	3	4+					
	Stage 5	Kidney Failure	<15	4+	4+	4+					
Hypertension without DM				ACE/ARB, CCB, Diuretic	ACE/ARB Suggested	ACE/ARB					
Hypertension-with DM, GFR>60				ACE, ARB, CCB, Diuretic	ACE/ARB						
Hypertension w DM, GFR<60				ACE/ARB							

Note: Risk of progression based on GFR and severity of albuminuria indicated by color (green-very low, yellow-low, orange-moderate, red-high, deep red-very high). Note: Frequency of follow-up based upon GFR and severity of albuminuria (visits per year)

\* Bone Mineral Disorder (BMD): Time to initiate monitoring for BMD, based on GFR

\*\* Daily sodium intake based on GFR

\*\*\* Appropriate use of SGLT-2, GLP-1 RA, and metformin based on GFR. SGLT-2 preferred. Use GLP-1 RA if SGLT-2 not tolerated or GFR <30

\*\*\*\* Recommended hypertension treatment based on severity of microalbuminuria and presence/absence of DM. Use highest tolerated dose

# Checklist for Chronic Kidney Disease Management for Front Line Providers

Screening/ Management	Clinical Targets	Frequency of Testing / Visits	Next Steps for Uncontrolled/Positive Findings
<b>Estimate GFR and albuminuria</b>	GFR $\geq$ 90 Urine ACR <30 mg/g	Stages 1-2: Annually Stage 3: Semiannual Stages 4/5: Quarterly	Determine if progressive Estimate risk for progression (Kidney Failure Risk Equation or KidneyIntelX in diabetics)
<b>Nutrition</b>	Protein Intake Stage 5: 0.6-0.8 g/kg/d Sodium intake Stages 3/4-5: <4g/<3 g d Stages 3-5 w Htn: <2 g/d	Annually and as needed	Provide dietary counseling (Nutritionist or CDE) Protein composition recommended: 50% High Biologic Value (foods that contain high protein includes poultry, fish, eggs), 50% plant-based (e.g. lentils, tofu, chickpeas)
<b>Blood Pressure Control</b>	Target Blood Pressure: <130/80	Monthly until controlled, then every 3-6 months	Lifestyle modification, Home BP monitoring Non-Diabetic: ACR <30 mg/g: Use ACE/ARB, CCB, Diuretic ACR 30-299 mg/g: Use of ACE/ARB suggested ACR >300 mg/d: Use ACE/ARB Diabetic: ACR<30: Use ACE/ARB, CCB, and/or Diuretic ACR >30 or GFR<60: Use ACE/ARB GFR <60: ACE/ARB
<b>Diabetes Mellitus Management</b>	HbA1c <7% (range <6.5-8%) Urine ACR <30 mg/g	Controlled: q 6 mon Poorly controlled: q 3 mon	Intensify medications to optimize control With CKD, both metformin and SGLT-2i as first line therapy Use GLP-1 RA if intolerant to SGLT-2i or GFR <30

Continued on next slide

Screening/ Management	Clinical Targets	Frequency of Testing / Visits	Next Steps for Uncontrolled/Positive Findings
Lipid Management	LDL <130 or <100 based on ASCVD risk	Annually	Lifestyle modification Statin therapy for Stage 3-5 (Non-Dialysis)
Metabolic Acidosis	Sodium Bicarbonate >22 meq/l	Stage 1-2: Annual Stage 3: q 6 mon Stages 4/5: q 3 mon	If bicarbonate <22 mEq/l, add sodium bicarbonate (650 mg TID) or sodium citrate (30 ml/d)
Anemia	Hgb level ≥13 mg/dl men, ≥12 women	Stage 3: Annual Stages 4-5: q 3 mon On ESA : q 3 mon	Replete iron orally or IV if iron deficient (FeSO4 325 mg TID, Fe gluconate 2-3 mg/kg/d BID-TID) Erythropoiesis Stimulating Agents if refractory
Bone Metabolic Disease	Normal Calcium and Phosphate concentrations	Screening at GFR <45 Stage 3A/3B: q 6-12mon Stage 4: q 3-6 mon Stage 5: q 1-3 mon	Correct hypocalcemia if <7.5 mg/dl (adjusted for albumen), symptomatic, or severe hyperPTH Treat hyperphosphatemia with diet (~900 mg/d) and phosphate binders if >6 mg/dl
	Vitamin D	Screening to establish baseline and as needed	Correct as without CKD, if Phosph/calcium normal. Calcitriol or synthetic vitamin D analogs if progressive hyperparathyroidism
	Parathyroid hormone level	Stage 3A/3B: Baseline Stage 4: q 6-12 mon Stage 5: q 3-6 mon	Correct modifiable factors Calcitriol/Vit D analogues for severe progressive disease
Hyperkalemia	Serum Potassium	Stage 1-2: Annual Stage 3: q 6 mon Stages 4/5: q 3 mon	Low potassium diet, Reduce or eliminate contributing meds, Correct acidosis Sodium polystyrene, Patiromer, or Sodium zirconium cyclosilicate
Behavioral Health	Depression Screen: PHQ 2/9	Annual Screening	Initiate treatment and/or refer
Immunizations	<ul style="list-style-type: none"> <li>PPSV 23</li> <li>Hepatitis B</li> <li>Influenza</li> </ul>	Once if GFR <30 or at higher risk, repeat in 5y Complete Hep B series when GFR <30 and at risk of progression. Annual	Consider administration of PV 13 at 65yrs  Check HepBs Ab to confirm immunity

### Checklist for Chronic Kidney Disease Management for Front Line Providers

Screening/ Management	Benchmark	Frequency	Next Steps for Uncontrolled/ Positive Findings
Estimate GFR and albuminuria	GFR $\geq$ 90 Urine ACR <30 mg/g	<b>Stages 1-2:</b> Annually <b>Stage 3:</b> Semiannual <b>Stages 4/5:</b> Quarterly	Determine if progressive Estimate risk for progression (Kidney Failure Risk Equation or KidneyIntelX in diabetics)
Nutrition	<b>PROTEIN INTAKE:</b> <b>Stage 5:</b> 0.6-0.8 g/kg/d <b>SODIUM INTAKE:</b> <b>Stages 3/4-5:</b> <4g/<3 g d <b>Stages 3-5 w Htn:</b> <2 g/d	Annually and as needed	Provide dietary counseling (Nutritionist or CDE) Protein: 50% High Biologic Value, 50% plant-based
Blood Pressure Control	<b>Target Blood Pressure:</b> <130/80	Monthly until controlled, then every 3-6 months	<b>Lifestyle modification, Home BP monitoring Non-Diabetic:</b> • ACR <30 mg/g, GFR <60: Use ACE/ARB, CCB, Diuretic • ACR 30-300 mg/g: Use of ACE/ARB suggested • ACR >300 mg/d: Use ACE/ARB <b>Diabetic:</b> • ACR<30: Use ACE/ARB, CCB, and/or Diuretic • ACR >30 or GFR<60: Use ACE/ARB
Diabetes Mellitus	HbA1c <7% (range <6.5-8%) Urine ACR <30 mg/g	<b>Controlled:</b> q 6 mon <b>Poorly controlled:</b> q 3 mon	Intensify medications to optimize control Both metformin and SGLT-2i as first line therapy Use GLP-1 RA if intolerant to SGLT-2i/GFR <30
Lipid Management	LDL <130 or <100 based on ASCVD risk	Annually	Lifestyle modification Statin therapy for Stage 3-5 (Non-Dialysis)
Metabolic Acidosis	Sodium Bicarbonate >22 meq/l	<b>Stage 1-2:</b> Annual <b>Stage 3:</b> q 6 mon <b>Stages 4/5:</b> q 3 mon	If bicarbonate <22 mEq/l, add sodium bicarbonate (650 mg TID) or sodium citrate (30 ml/d)
Anemia	Hgb level $\geq$ 13 mg/dl men, $\geq$ 12 women	<b>Stage 3:</b> Annual <b>Stages 4-5:</b> q 3 mon <b>On ESA:</b> q 3 mon	Replete iron orally or IV if iron deficient (FeSO4 325 mg TID, Fe gluconate 2-3 mg/kg/d BID-TID) Erythropoiesis Stimulating Agents if refractory
Bone Metabolic Disease	Normal Calcium and Phopshate concentrations	<b>Screening at GFR</b> <45 <b>Stage 3b:</b> q 6-12 mon <b>Stage 4:</b> q 3-6 mon <b>Stage 5:</b> q 1-3 mon	Correct hypocalcemia if <7.5 mg/dl (adjusted for albumen), symptomatic, or severe hyperPTH Treat hyperphosphatemia with diet (-900 mg/d) and phosphate binders if >6 mg/dl

# Mount Sinai Health System Chronic Kidney Disease Program

- Mission: facilitate timely identification and ensure optimized management of CKD
  - Ensure high-quality, guideline-based CKD care
- Multi-Disciplinary Care Team:
  - Nurse Practitioners: coordinate care with treating clinicians, patient education
  - Pharmacists: review medications/dosing, assistance with obtaining prior authorization
  - Dietitians: CKD dietitian or in partnership with Diabetes Alliance
- CKD-ESRD Transition Planning
  - ESRD modality and transplant education
  - Conservative management (medical management, in conjunction with palliative care)
  - Coordination of care between primary care clinician, nephrologist, surgeon
  - Avoid unnecessary utilization (e.g hospitalization for initiation of HD)

[tamara.muller@mountsinai.org](mailto:tamara.muller@mountsinai.org)

[waiyin.leung@mountsinai.org](mailto:waiyin.leung@mountsinai.org)

## Back to our case...

Chief Complaint: Routine follow up

58 year old man with HTN, **T2DM**, asthma, elevated BMI, dyslipidemia, and **CKD Stage G2A2** seen for routine follow up in clinic. HTN has been reasonably well controlled. He has been compliant with medications but difficulty with dietary restriction and does not exercise regularly. Non-smoker.

- ▶ Type 2 Diabetes since 2015
  - Hemoglobin A1c in 7s, most recently **7.5%**
  - Microalbuminuria: **UACR 121mg/g**
  - Managed with **metformin 1000mg BID**
  - Does not have documented retinopathy
  - Diet and lifestyle changes have been difficult for him
- ▶ HTN with ambulatory blood pressure 124/84
  - On **Losartan 100mg daily** and Nifedipine ER 30mg daily



## Back to our case...

### ► Past Medical History

- HTN
- DM2
- CKD G2A2
- Asthma
- BMI 29
- Dyslipidemia

### ► Medications

- Losartan 100mg daily
- Nifedipine ER 30mg daily
- Metformin 100mg BID
- Atorvastatin 40mg daily
- Albuterol MDI PRN

### ► Examination

- VS: 128/86 75 19
- Gen: well appearing in NAD
- Neck: No JVD
- Pulm: Chest clear
- CV: regular, no MRG
- Abd: soft/NT
- Ext: no peripheral edema

140	108	23	8.6	eGFR 66ml/min
4.2	22	1.2	121	HbA1c 7.1-7.5%
			3.6	

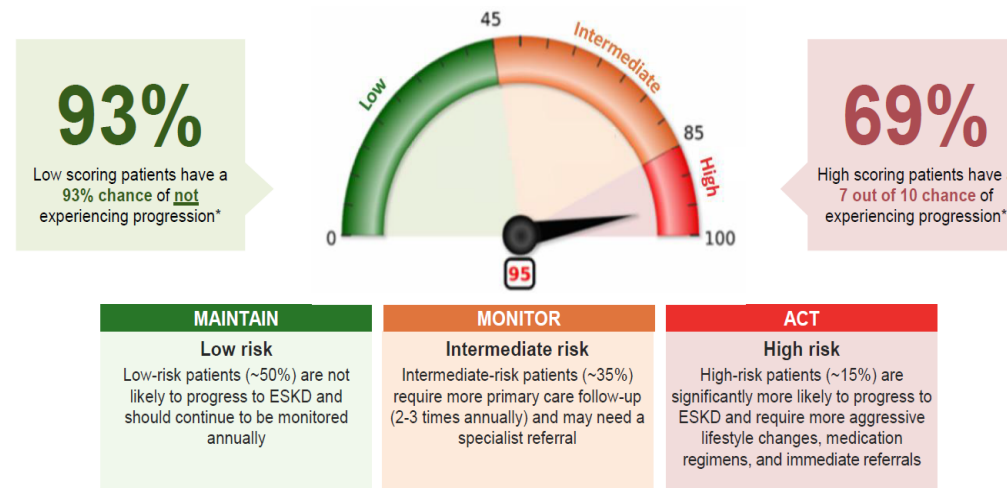
UA: no glucose, LE/nitrite, protein 100, no RBC/WBC  
UACR: 121mg/g

**KidneyIntelX Score: 88**

## Key Findings

58 year old man with HTN, T2DM, asthma, elevated BMI, dyslipidemia, and CKD Stage G2A2 with a KidneyIntelX score of **88**.

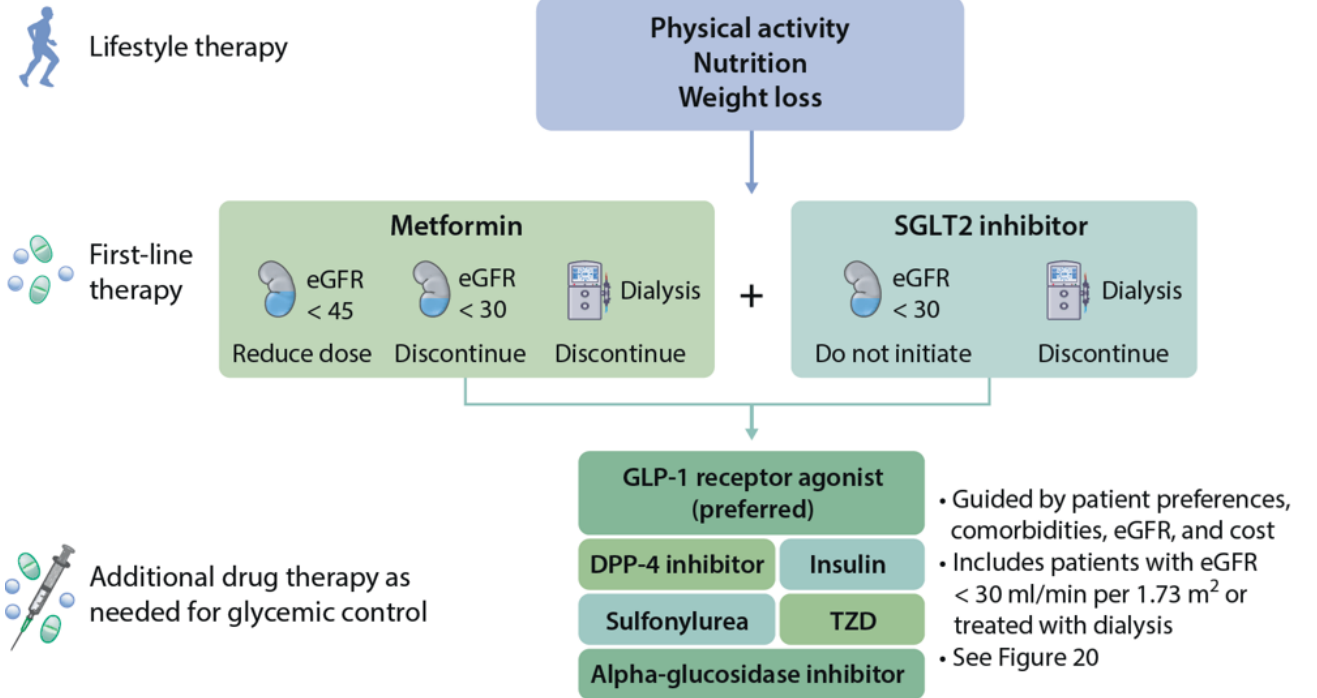
- ▶ Diet and lifestyle modifications have remained difficult for this patient
- ▶ Uncontrolled HTN, DM or other significant risk factors did not stand out
- ▶ Patient was previously unaware of CKD and potential long term consequences
- ▶ KidneyIntelX score increased patient and clinician awareness of condition



# 2020 KDIGO Diabetes in CKD Guideline

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1	A2	A3
				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 <sup>2</sup> ) Description and range	G1	Normal or high	≥ 90			
	G2	Mildly decreased	60–89		X	
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	< 15			



## Recommendations Made for This Patient

- ▶ Developed plan to address difficulties in diet and lifestyle modification
- ▶ Referral to CKD Program including consultation with dietitian
- ▶ Initiated discussion re: CKD including risk factors and possible long-term sequelae
- ▶ Medications reviewed
- ▶ Following discussion, he was started on **dapagliflozin** 5mg daily
- ▶ One month follow up arranged to assess tolerance and titrate dose

# Heart Failure (HF) and CKD

# Management of Heart Failure in CKD

## ► Epidemiology:

- In a large meta-analysis, approximately 50% of patients with HF had co-extant CKD
- Prevalence of HF increases as kidney function decreases
- Prognosis of patients with HF and CKD is poor with higher mortality (OR 2.34 95% CI 2.2-2.5, P<0.001)

### Box 1. Case discussion

#### Presentation

A 54-year-old man was referred to a joint cardiology-nephrology clinic presenting with progressive edema, increasing breathlessness (New York Heart Association class 3), decreased urine output, and stage 5 CKD. On examination, he had leg edema, his weight since the last hospital visit had increased by 9 kg, his BP was 158/70 mm Hg, his pulse rate was 74 beats/min, his jugular venous pressure was elevated, and bibasilar chest crepitations were audible. He had no ascites. Four years ago, he was diagnosed with biopsy proven, stage 3 diabetic nephropathy; multivessel, inoperable coronary artery disease; and heart failure with reduced ejection fraction. He suffered from hypertension and hypercholesterolemia.

#### Investigation

His echocardiogram showed reduced ejection fraction of 20%, and an electrocardiogram showed sinus rhythm with QRS duration of 100 ms. His blood tests showed sodium 130 mmol/L, potassium 5.7 mmol/L, creatinine 4.2 mg/dl (372  $\mu$ mol/L), eGFR 15 ml/min per 1.73 m<sup>2</sup>, and N-Terminal pro-B-type natriuretic peptide 2742 ng/L.

#### Management

He was previously treated with aspirin, clopidogrel, bisoprolol, ramipril, atorvastatin, metformin, and insulin; and hospital admissions were prevented using variable doses furosemide, with intermittent metolazone and careful monitoring of weight and electrolytes. In the joint clinic, his furosemide dose was increased, he was started on daily metolazone, his  $\beta$ -blocker dose increased, intravenous iron was administered, and metformin was stopped. He was informed about long-term KRT and visited the peritoneal dialysis unit. All of this was only possible because he was seen in a joint CKD-heart failure clinic with access to specialist nurses.

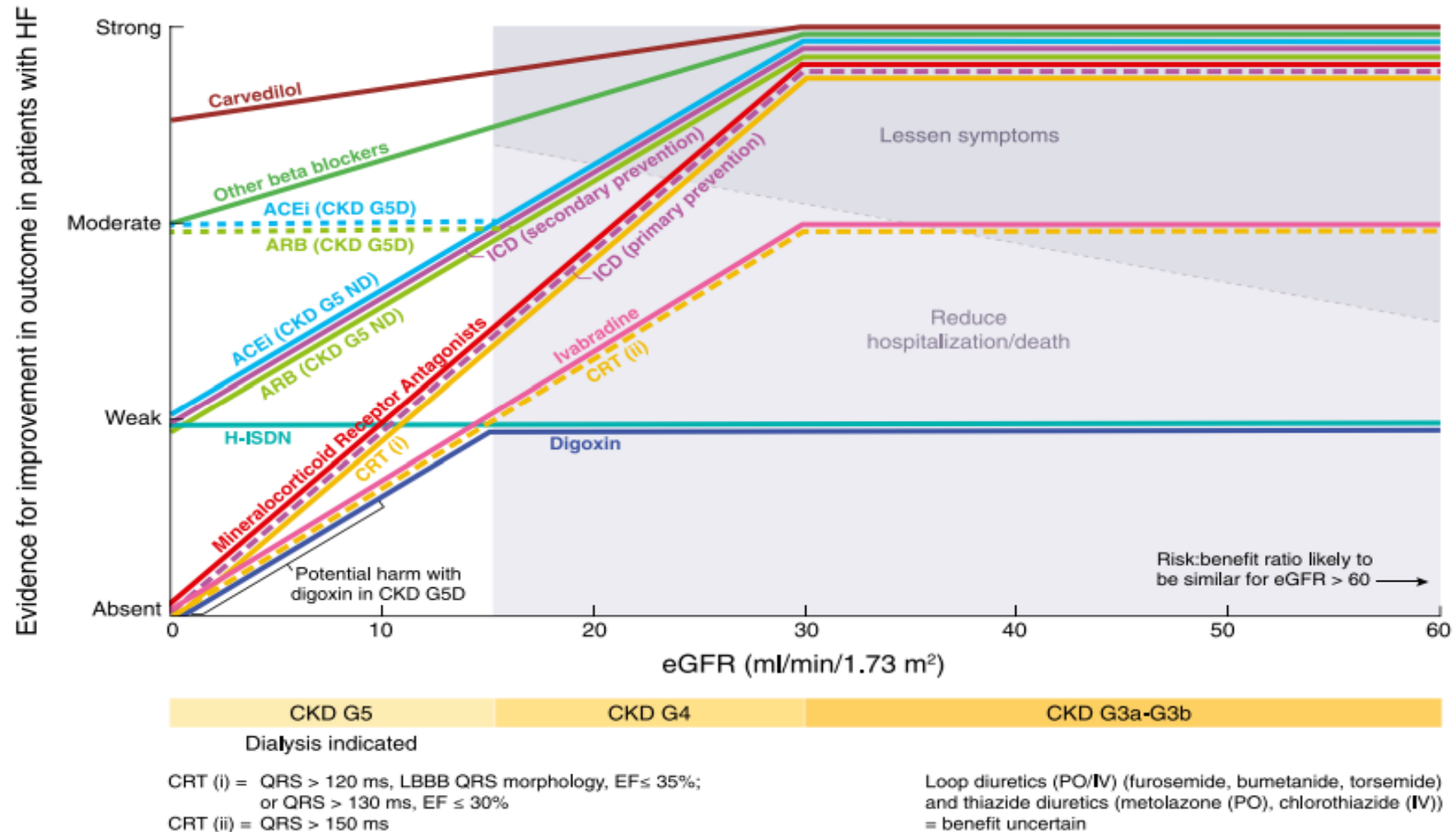
# Pharmacotherapy of HF in Patients with CKD

Agents	CKD Stages 1– 3	CKD Stages 4 and 5
ACEis	Should be used in all patients with HFrEF, with monitoring of creatinine and potassium	May be used in HFrEF, with monitoring of creatinine and potassium. Dose modification may be necessary
$\beta$ -Blockers	Should be used in all patients with HFrEF	May be used in HFrEF
Mineralocorticoid receptor antagonists	Should be used in HFrEF, with careful monitoring of potassium	May be used in HFrEF, with caution and monitoring of potassium
ARBs	Should be used in all patients with HFrEF with caution	May be used in HFrEF, with monitoring of creatinine and potassium
Ivabradine	May be used in patients with HFrEF with sinus rhythm and who are stable on $\beta$ -blockers	Unknown effects
Angiotensin receptor and neprilysin inhibitor	May be used in patients with HFrEF instead of ACEis/ARBs	Unknown effects
Sodium-glucose cotransporter 2 inhibitor	Can be used in patients with HFrEF with or without diabetes	Unknown effects
Hydralazine and isosorbide dinitrate	Should be considered in patients with HFrEF who are intolerant to ACEis/ARBs	May be considered in patients with HFrEF who are intolerant to ACEis/ARBs

ACEi, angiotensin-converting enzyme inhibitor; HFrEF, heart failure with reduced ejection fraction; ARB, angiotensin receptor blocker.



# Evidence for HF Management in Patients with CKD with Different Levels of Kidney Function





# Blood Pressure Management with CKD



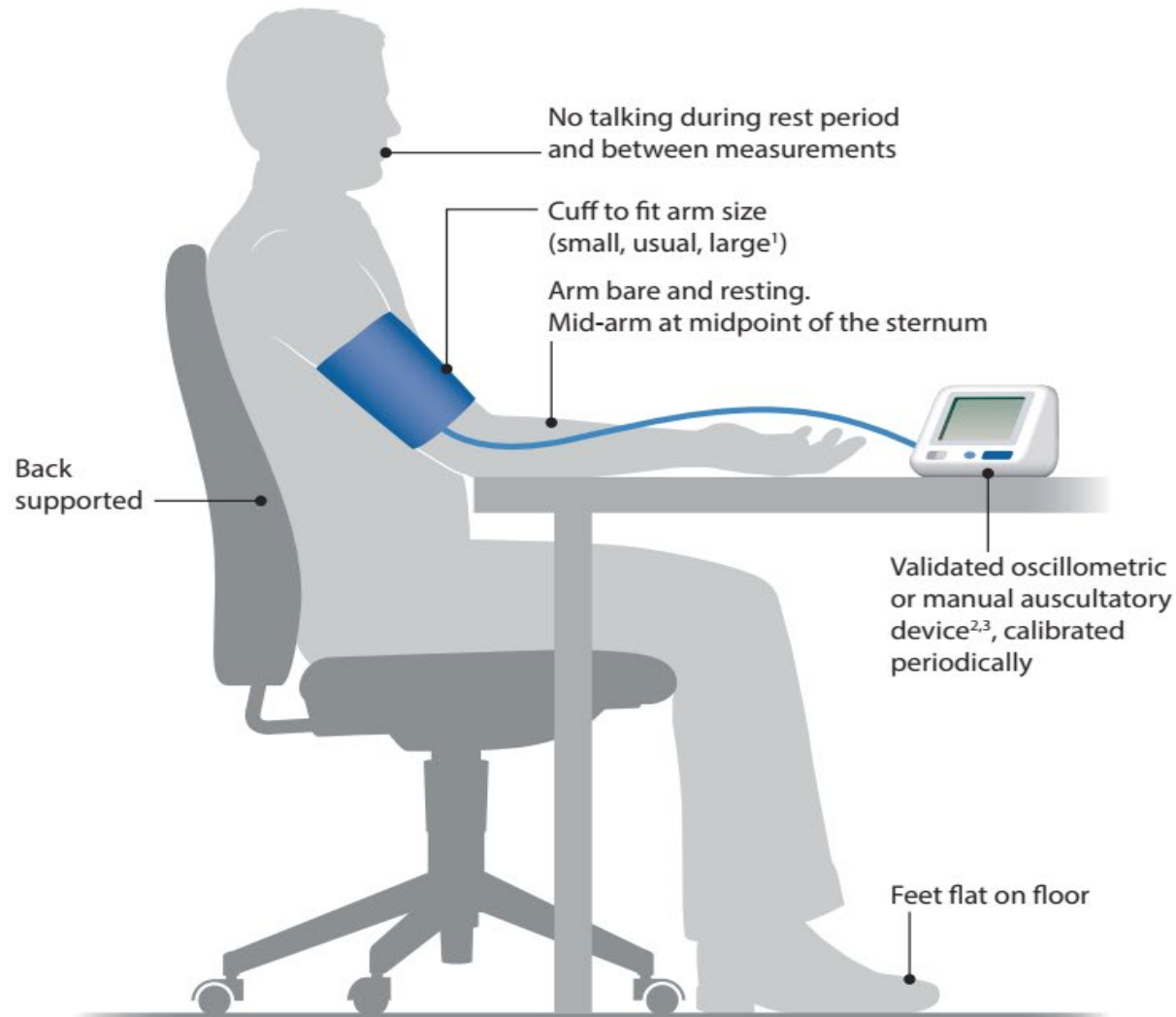
# KDIGO 2021 CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF BLOOD PRESSURE IN CKD

KDIGO Guideline Co-Chairs:  
Alfred K. Cheung, MD  
Johannes F.E. Mann, MD

Guideline: Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney Int.* 2021;99(3S):S1–S87

Executive Summary: Cheung AK, Chang TI, Cushman WC, *et al.* Executive summary of the KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney Int.* 2021; 99(3): 559–569

# Blood Pressure Measurement



- Quiet room (no talking by patient or observer)
- No smoking, caffeine, or exercise for  $\geq 30$  min before measurement
- Empty bladder
- Note the time of most recent BP medication taken before measurements
- Relax for  $> 5$  min
- At first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings
- Separate repeated measurements by 1–2 minutes
- Use an average of  $\geq 2$  readings obtained on  $\geq 2$  occasions
- Provide patients with the SBP/DBP readings verbally and in writing

<sup>1</sup>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

<sup>2</sup>See validated electronic devices lists at [www.stridebp.org](http://www.stridebp.org)

<sup>3</sup>For auscultatory readings, either the stethoscope diaphragm or bell may be used. Use a palpated radial pulse obliteration pressure to estimate SBP, then inflate the cuff 20–30 mm Hg above this level for auscultatory determination of BP level. Deflate the cuff pressure 2 mm Hg per second, and listen for Korotkoff sounds

# Blood Pressure Management in Patients with CKD, with or without DM, Not Receiving Dialysis

- ▶ Recommendation 3.1.1: We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120mm Hg, using standardized office BP measurement (2B).
- ▶ This recommendation is weak according to GRADE because there is less certainty that the benefits outweigh the harms in the following scenarios:
  - ▶ CKD G4 and G5
  - ▶ Diabetes
  - ▶ Individuals with SBP 120-129 mm Hg
  - ▶ Patients with very low baseline diastolic BP, particularly in the presence of coronary artery disease
  - ▶ Specific etiology of CKD
  - ▶ Severely increased proteinuria
  - ▶ Older age
  - ▶ Younger age
  - ▶ Very frail
  - ▶ White coat hypertension
  - ▶ Severe hypertension

# Lifestyle Interventions for Lowering BP in Patients with CKD not Receiving Dialysis

## ► Key Recommendations:

- Target a sodium intake of <2gm of sodium per day (<90mmol of sodium per day, or <5gm of sodium chloride per day) in patients with high BP and CKD (2C)
- The Dietary Approaches to Stop Hypertension (DASH)-type diet or use of salt substitutes that are rich in potassium may not be appropriate for patients with advanced CKD or those with hyporeninemic hypoaldosteronism or other causes of impaired potassium excretion because of the potential for hyperkalemia
- Patients with high BP and CKD should be advised to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance (2C).
  - Consider the CV fitness status, physical limitations, cognitive function, and risk of falls when deciding on the implementation and intensity of physical activity interventions in individual patients



# Blood Pressure Management in Patients with CKD, with or without DM, NOT receiving Dialysis

## ► Key Guideline Practice Points:

- It may be reasonable to treat people with high BP, CKD, and no albuminuria with or without DM with RASi
- RASi should be administered to the highest approved dose that is tolerated
- Changes in BP, serum creatinine, and serum potassium should be checked within 2-4 weeks of initiation or titration of dose
- Hyperkalemia associated with use of RASi can often be managed by measures to reduce serum potassium levels rather than decreasing the dose or stopping RASi
- Continue ACEi or ARB therapy unless serum creatinine rises by more than 30% within 4 weeks following initiation of treatment or an increase in dose
- At low GFR (i.e. near or less than 15ml/min per 1.73m<sup>2</sup>), consider reducing the dose or discontinuing ACEi or ARB in the setting of either symptomatic hypotension or uncontrolled hyperkalemia despite medical treatment, or to reduce uremic symptoms
- **We recommend avoiding any combination of ACEi, ARB, and direct renin inhibitor therapy in patients with CKD, with or without DM**

# Visit MSHP's Chronic Condition Management Hub

## Download Chronic Condition Management Resources

### Chronic Condition Quick Reference Guides

- COPD
- Heart Failure
- CKD
- Hypertension
- Diabetes
- PAD

### Mount Sinai Ambulatory Pathways

- COPD
- Heart Failure
- Hypertension
- Diabetes

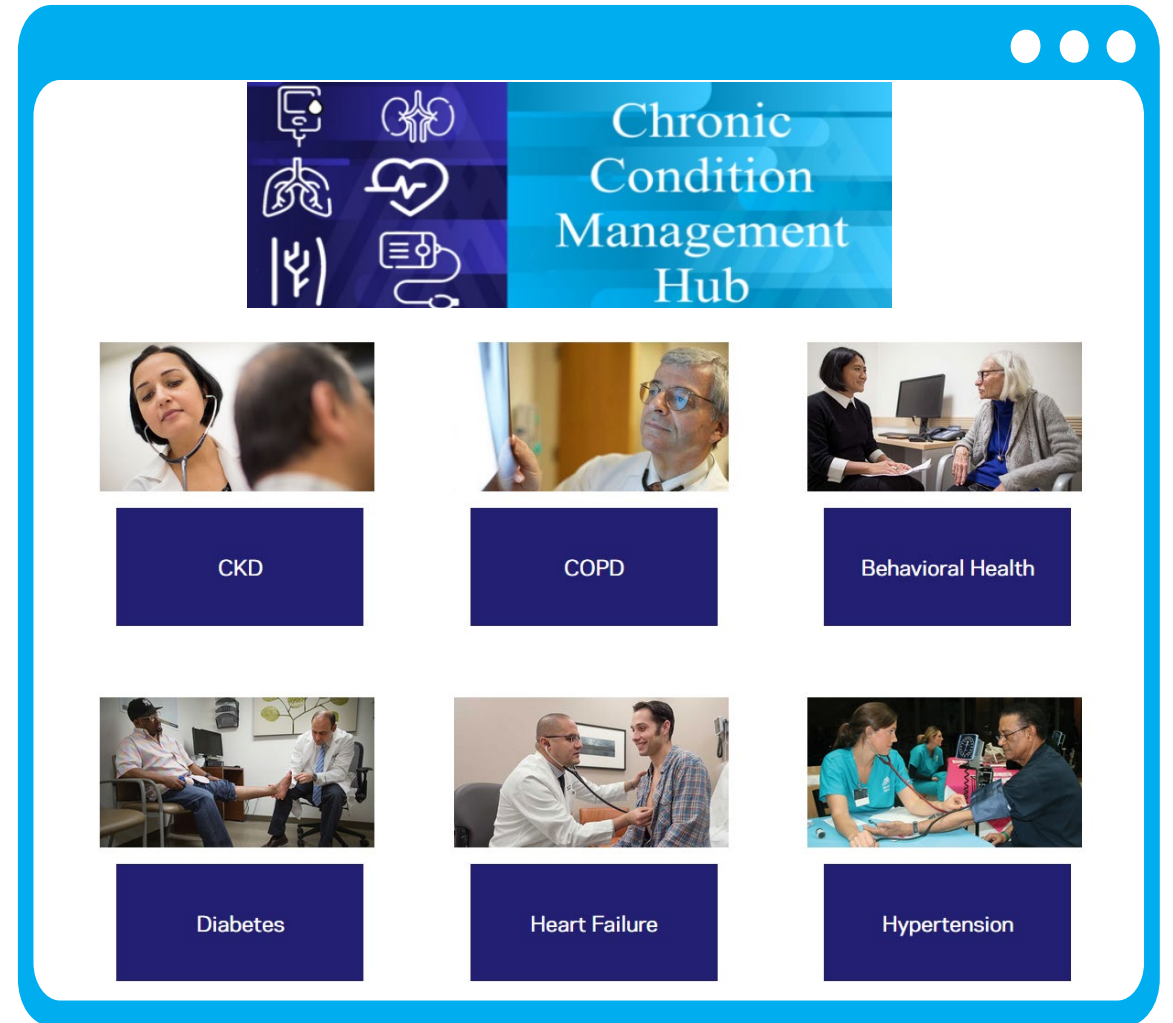
### *Find more!*

Find A Specialist Search Tool

Team Based Care

Behavioral Health Resources

Patient Materials



<https://bit.ly/conditionmanagement>

**THANK YOU**

