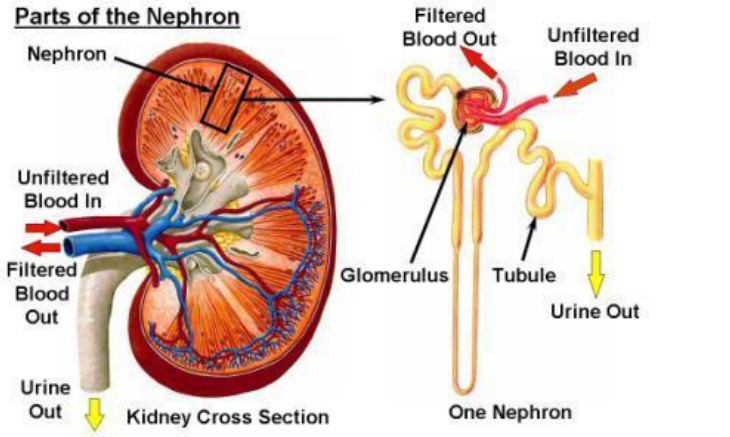
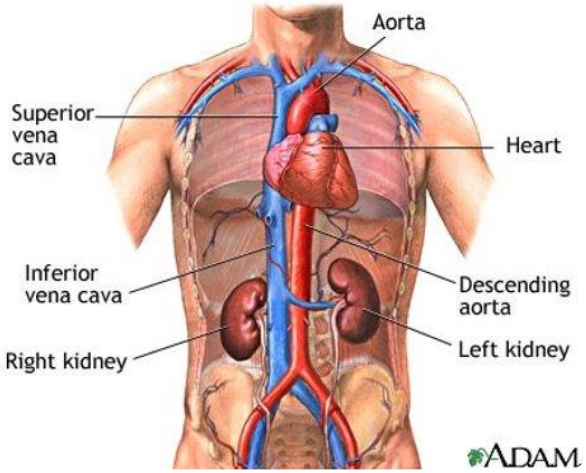
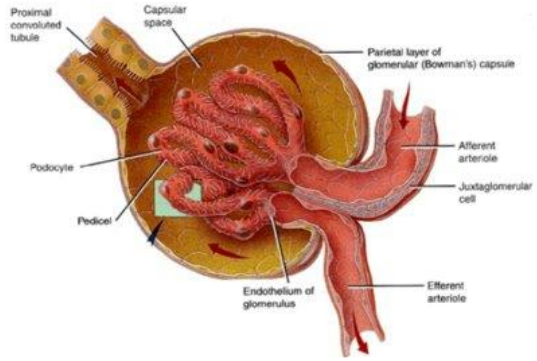


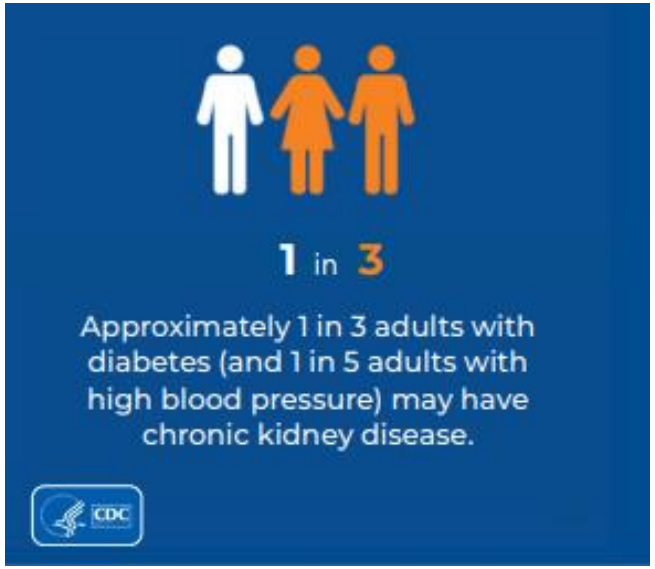




Diabetic Kidney Disease

Amy Mottl, MD MPH
Professor of Medicine
Division of Nephrology and Hypertension
amy_mottl@med.unc.edu

CKD Epidemiology

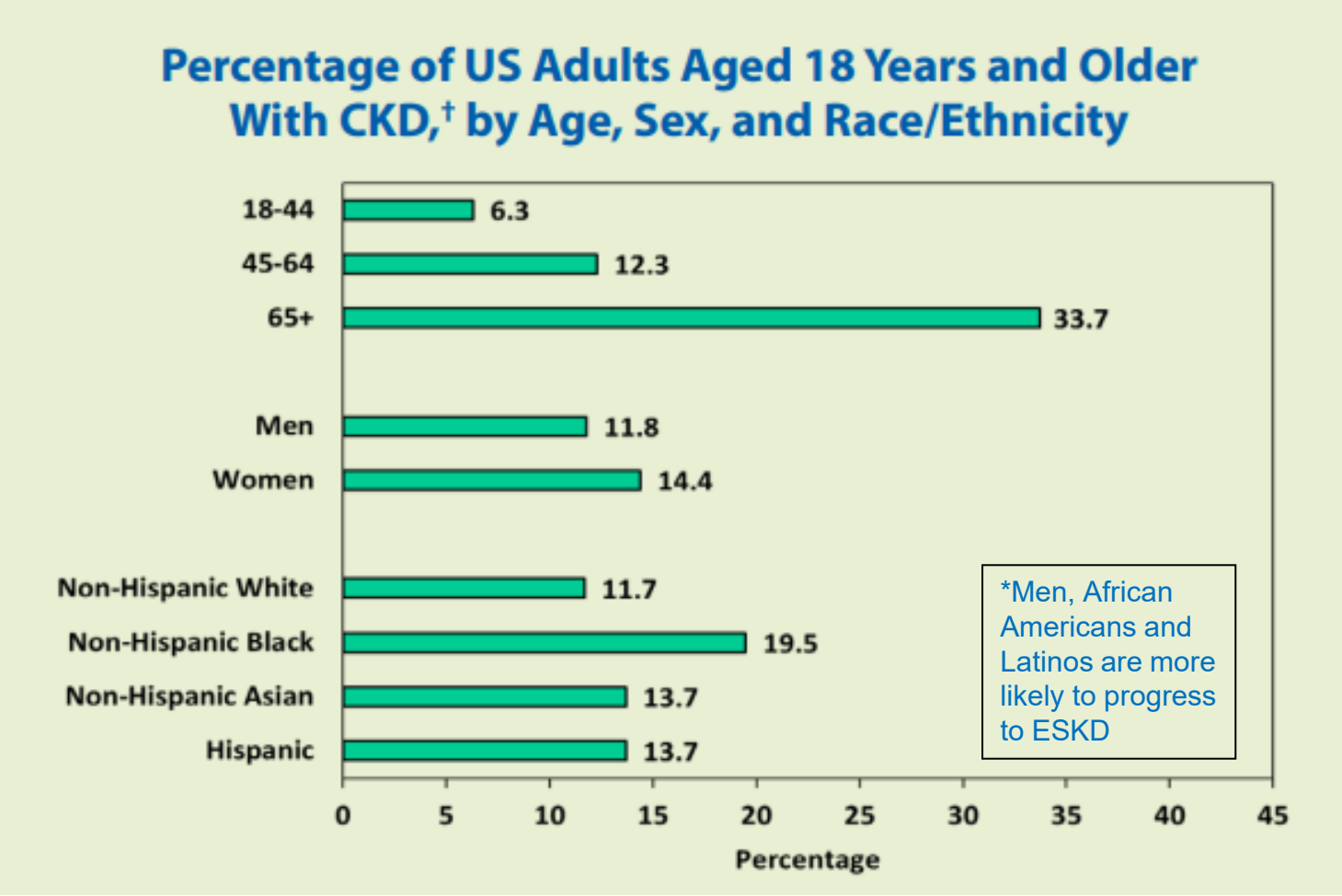


CKD is common

Only 10% of CKD patients are aware of their disease

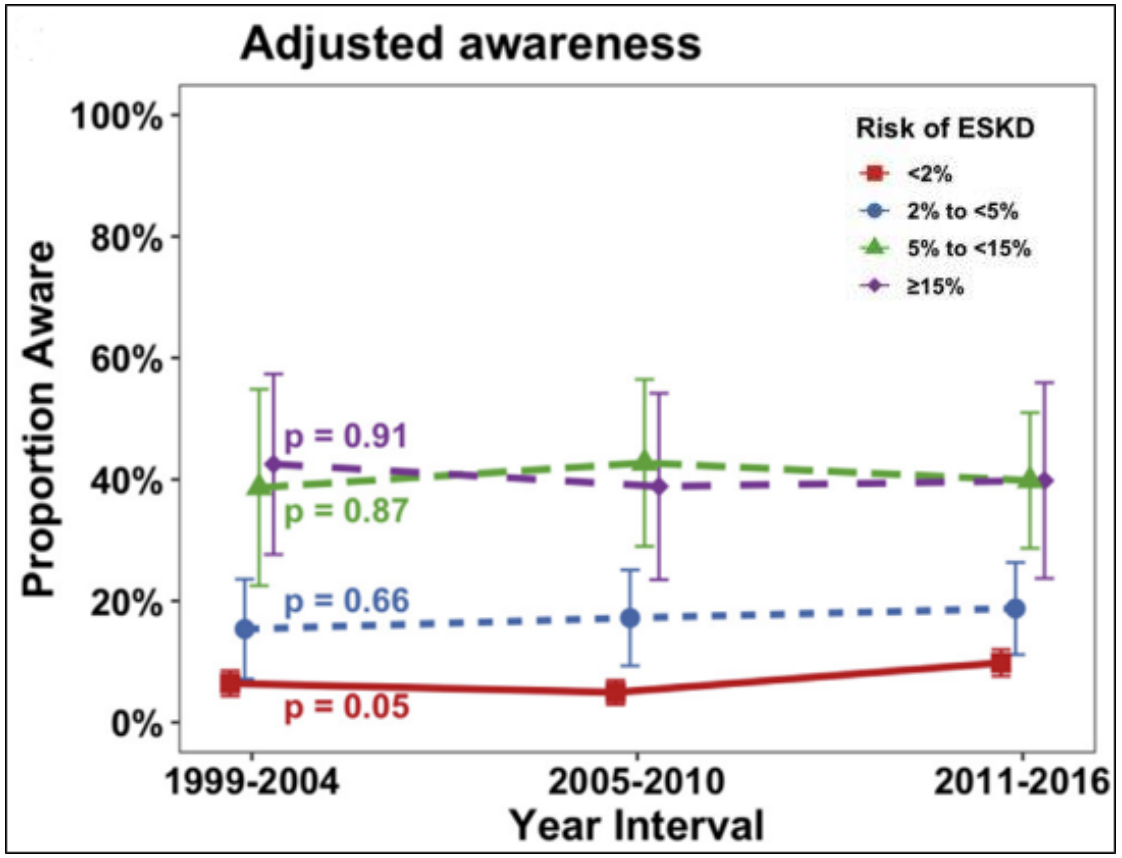
Referral to nephrology is often delayed until very late stages

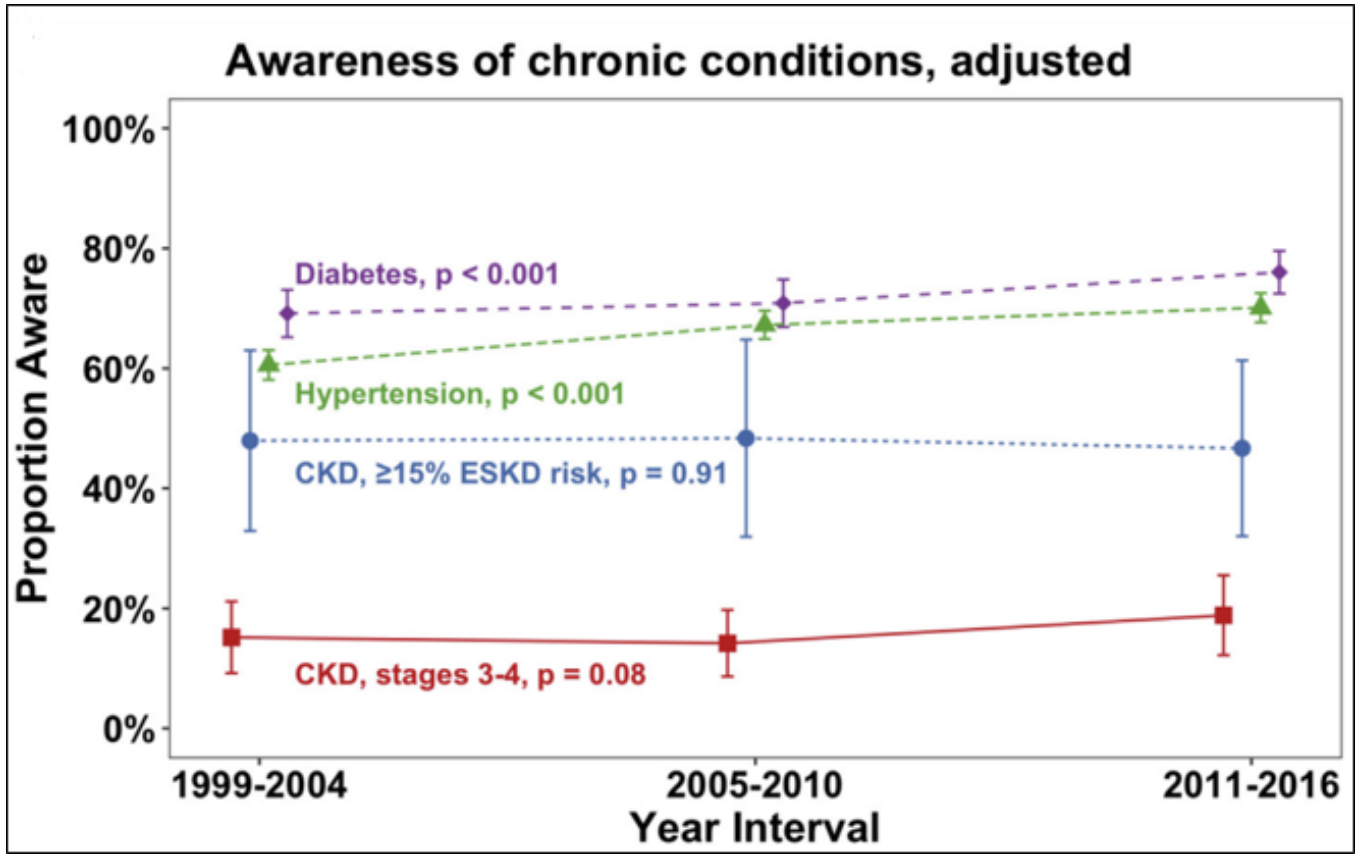
Vulnerable populations:
The elderly, minority Black and LatinX



African Americans comprise 12% of the total U.S. population, but 33% of all dialysis patients

CKD Awareness is extremely low

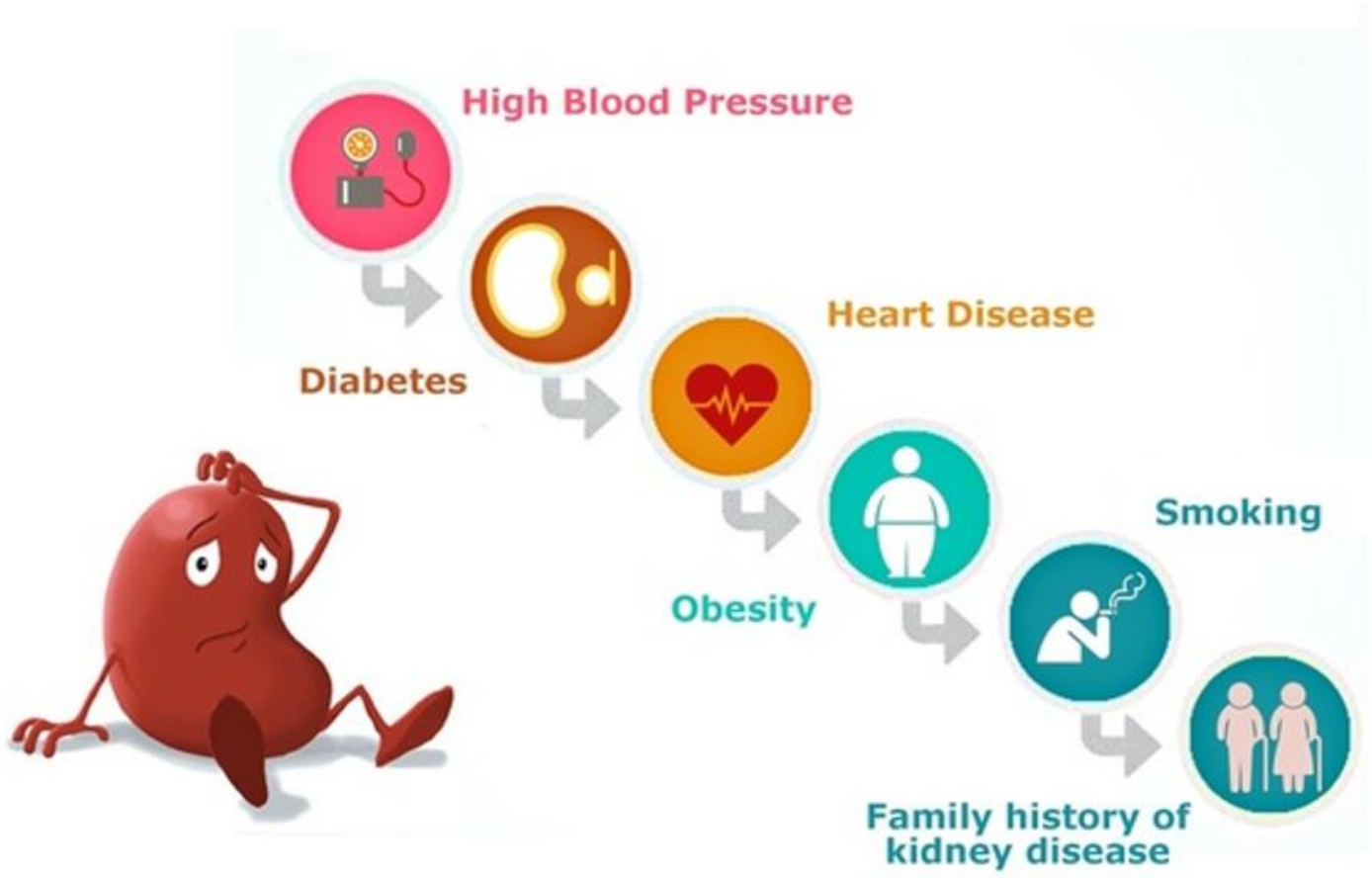




Chi et al. AJKD 2020; 76(2): 174-183

Risk Factors for CKD

The two most common causes of CKD are Diabetes (type 2) and Hypertension, accounting for roughly two-thirds of CKD!

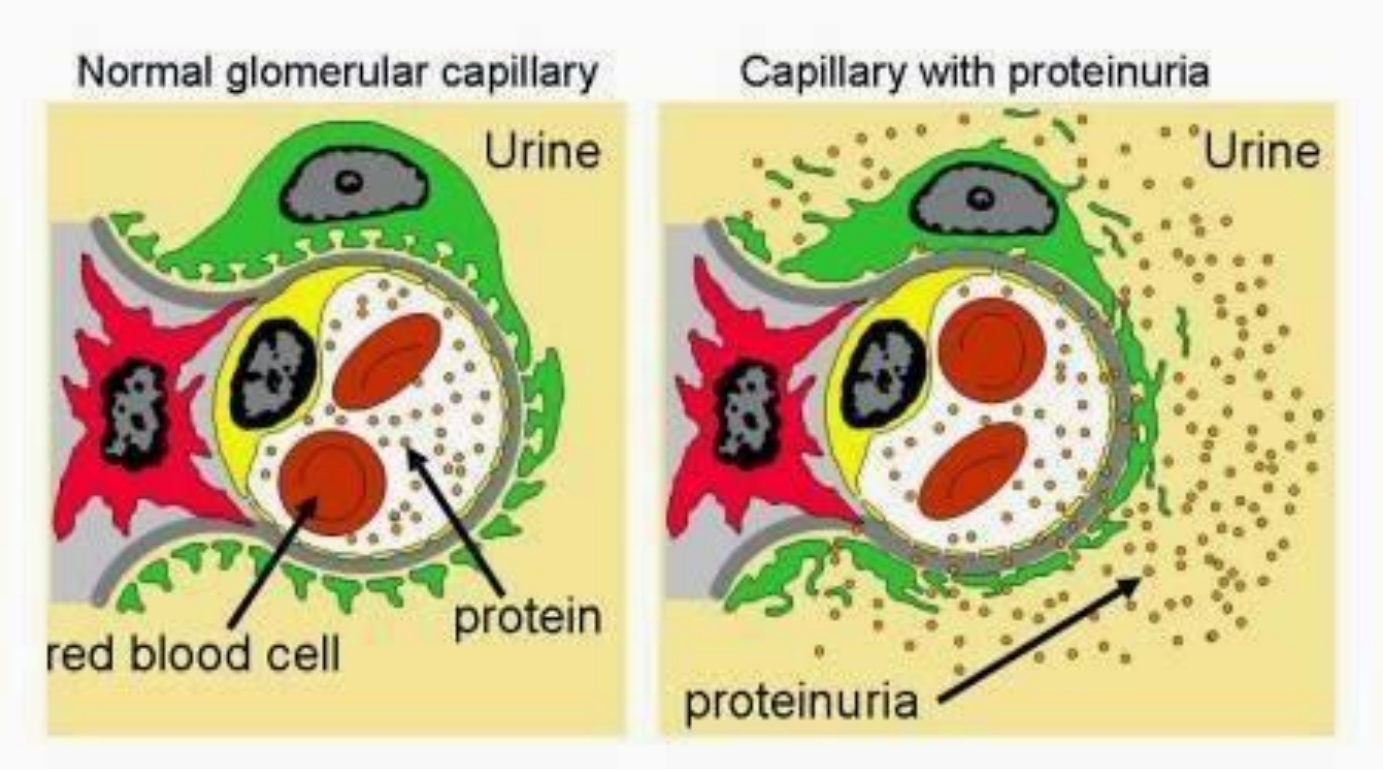


Job #1: Clean the Blood Assessing Kidney Function

- How well the kidney cleans the blood is typically reflected by the Glomerular Filtration Rate (GFR)
- Estimated by measuring creatinine in the blood and using an equation (eGFR)
  - CKD-Epi (race free) for adults
  - U25 for adolescents and children
- "Normal" 100-120 ml/min/1.73 m^2
- https://www.kidney.org/professionals/kdoqi/gfr_calculator

STAGES OF CHRONIC KIDNEY DISEASE		GFR*	% OF KIDNEY FUNCTION
Stage 1	Kidney damage with **normal** kidney function	90 or higher	90–100%
Stage 2	Kidney damage with **mild loss** of kidney function	89 to 60	89–60%
Stage 3a	**Mild to moderate** loss of kidney function	59 to 45	59–45%
Stage 3b	**Moderate to severe** loss of kidney function	44 to 30	44–30%
Stage 4	**Severe** loss of kidney function	29 to 15	29–15%
Stage 5	Kidney **failure**	Less than 15	Less than 15%

* Your GFR number tells you how much kidney function you have. As kidney disease gets worse, the GFR number goes down.



Job #2: Preventing loss of important nutritional factors

Proteinuria: the problem with leaky kidneys

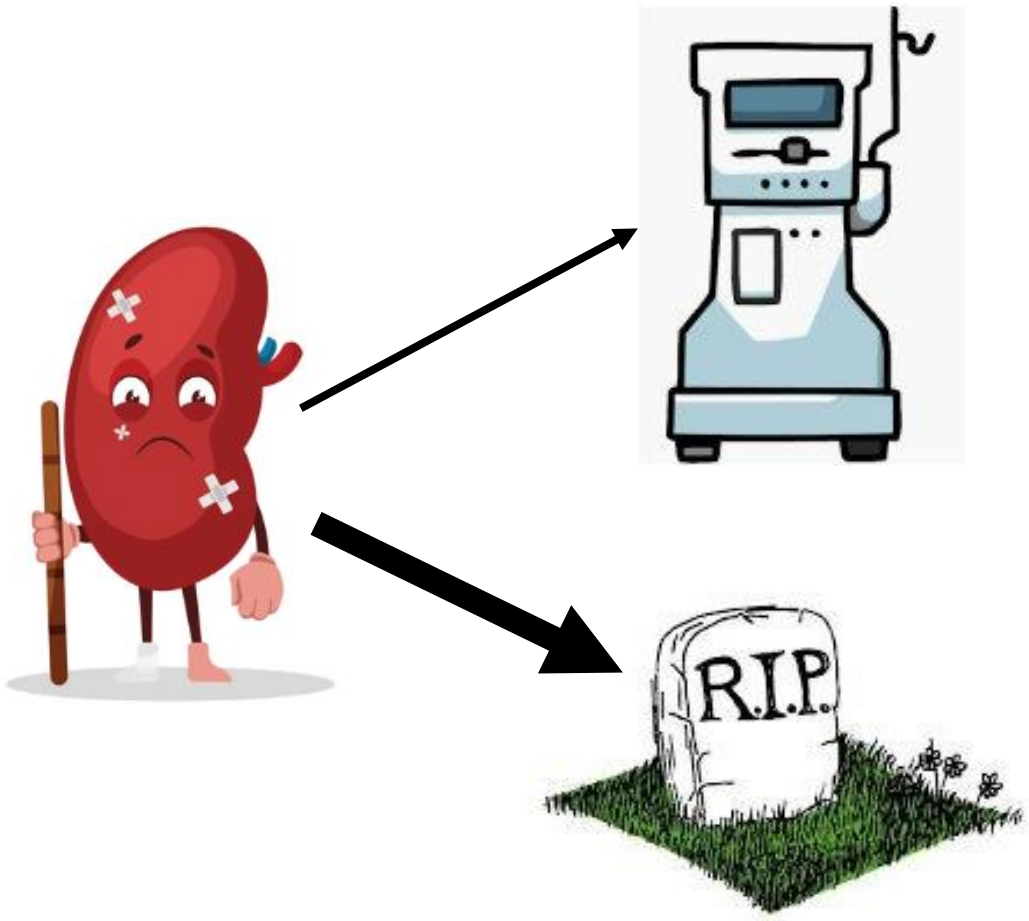
CKD Heat Map

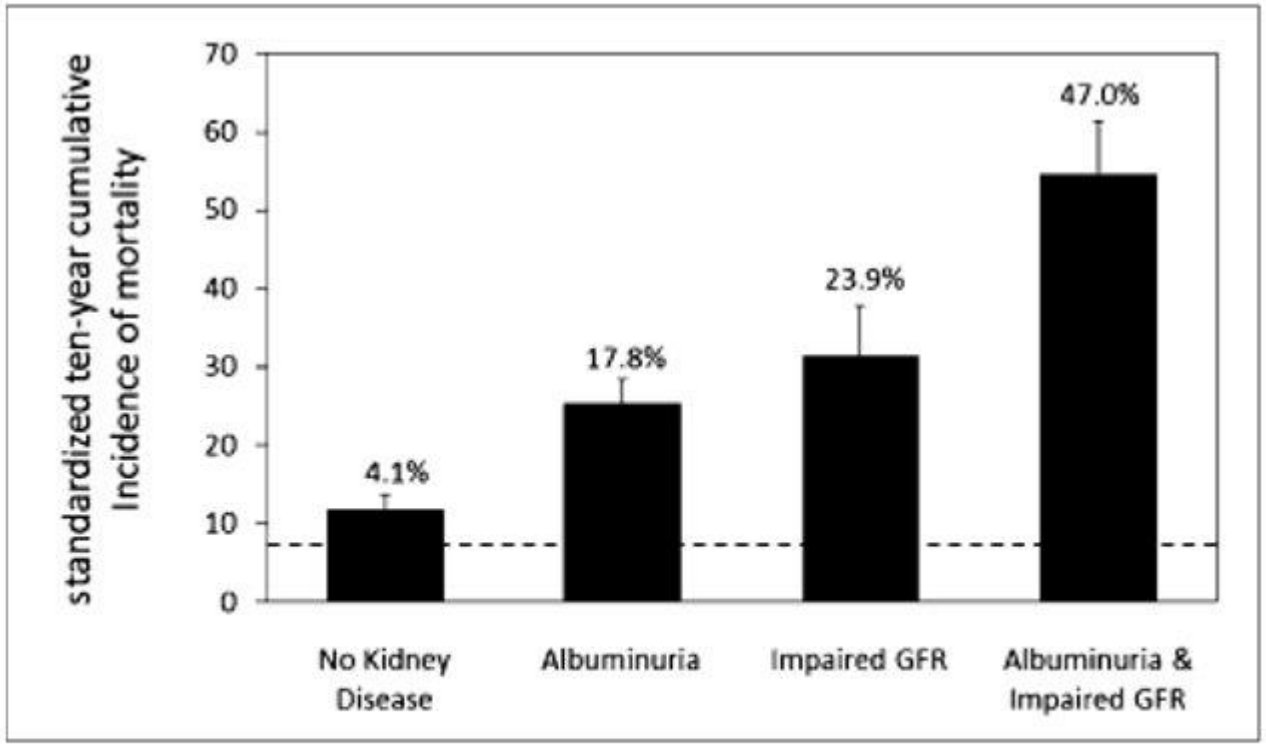
Prognosis of CKD by GFR and Albuminuria Categories

GFR categories (ml/min/1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-90			
	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.
KDIGO 2012

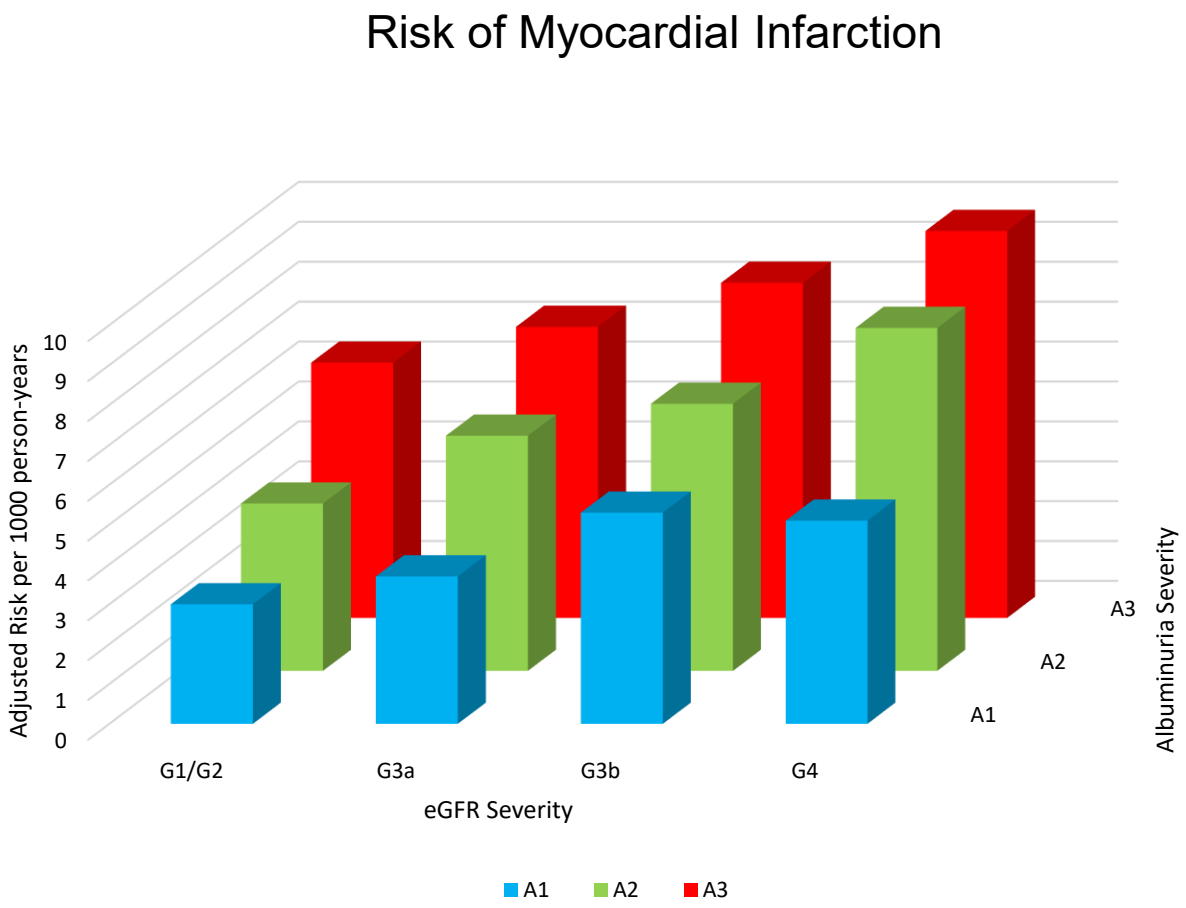
There are only 2 outcomes for CKD

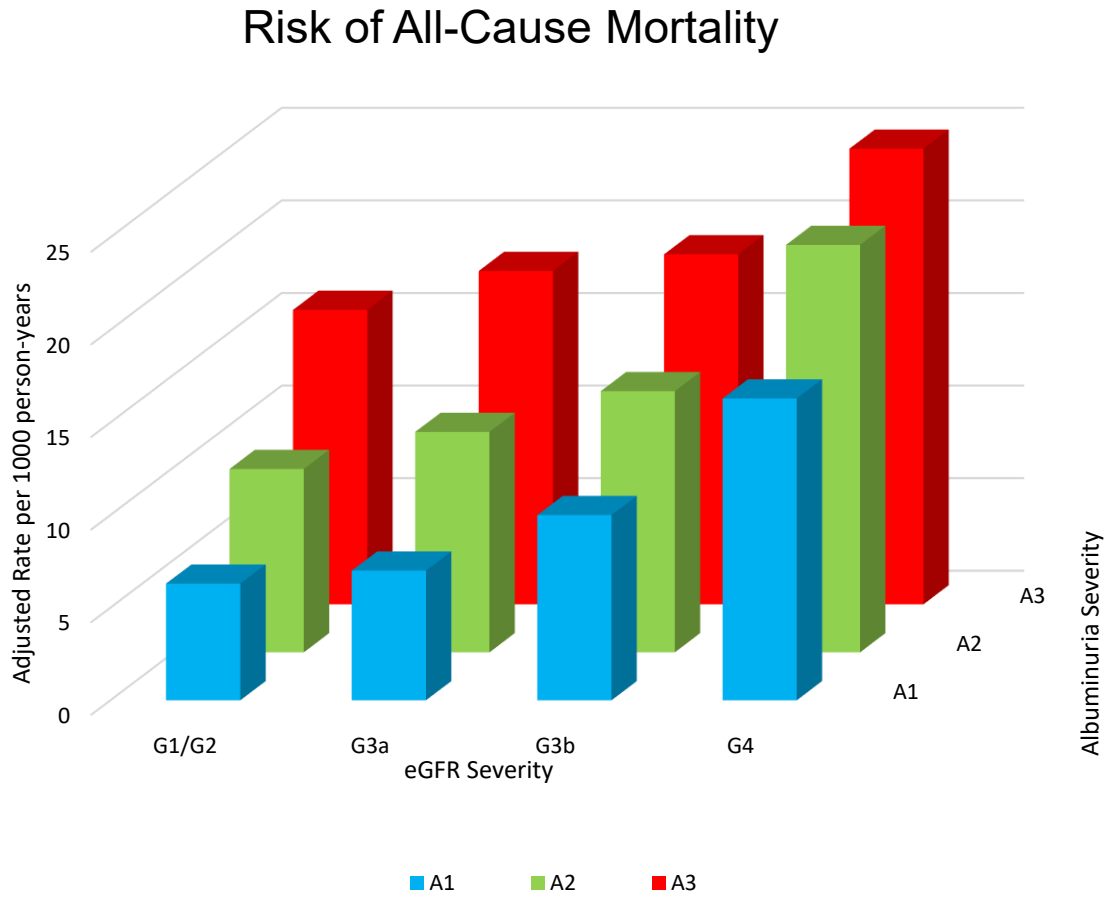




Ten-year mortality in type 2 diabetes by kidney disease manifestation, adjusted for age, sex and race in NHANES III.The dashed line indicates mortality in persons without diabetes or kidney disease. The numbers above error bars indicate excess mortality above the reference group.

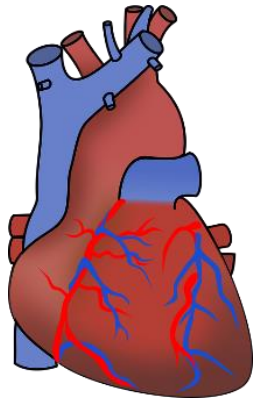
Cardiovascular Risk from CKD

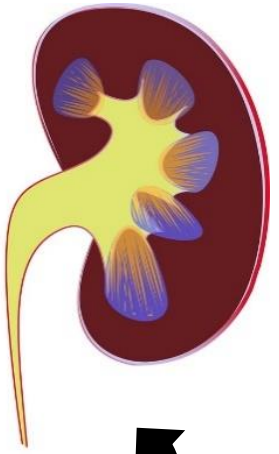




Adapted from: Hemmelgarn BR et al. *JAMA.* 2010;303(5):423-429.

Interaction between CVD and CKD





Fluid retention
vasoconstriction

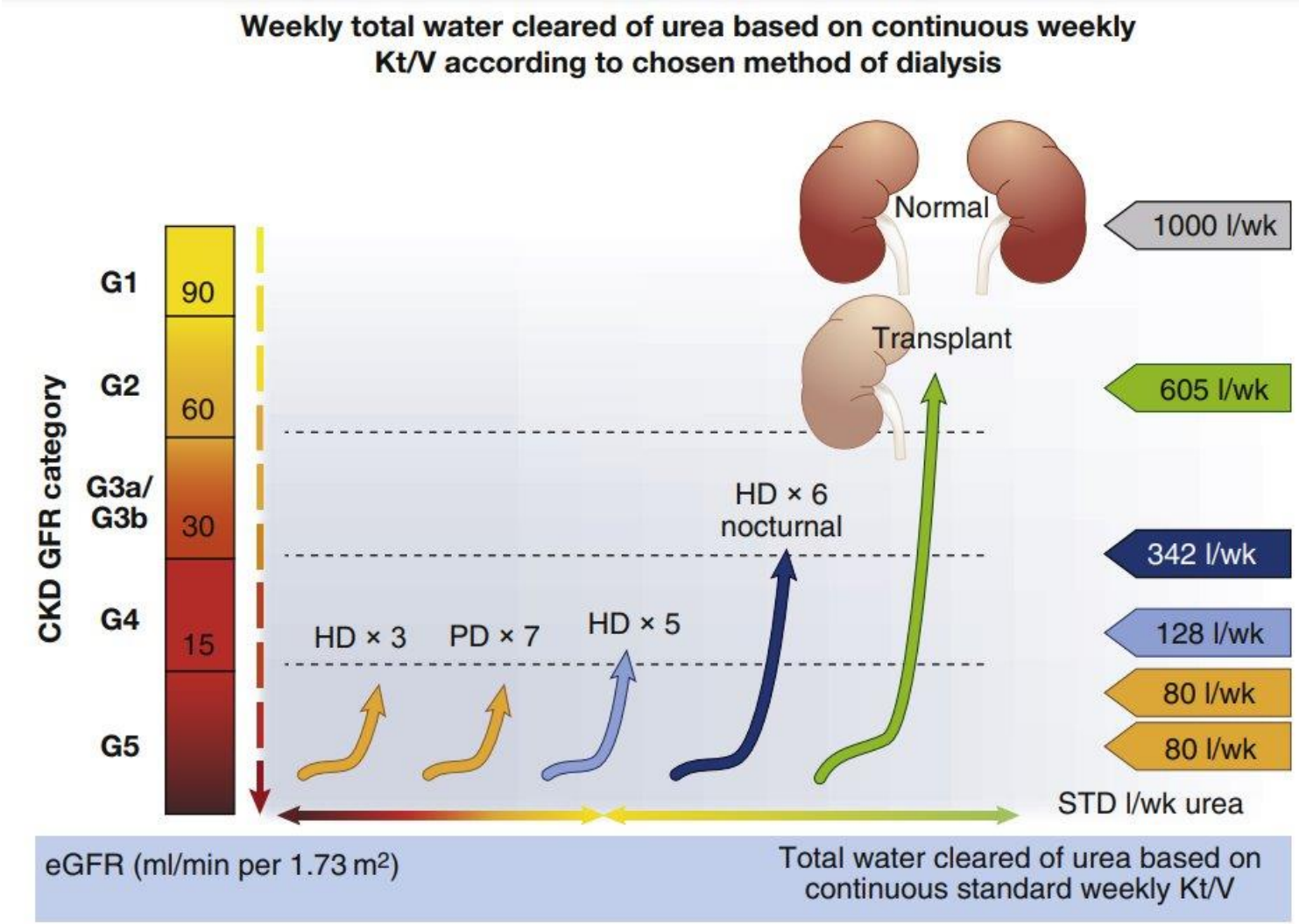
Hypertension
Inflammation
Oxidative Stress
RAAS activation
SNS activation
Myocardial disease
Valvular disease
Dyslipidemia
Heart Failure

Cardiovascular Disease Progressive Disease & Death

Hypertension
Inflammation
Oxidative Stress
RAAS activation
SNS activation
Vascular Calcification
Uremic toxins
Fluid retention
Anemia

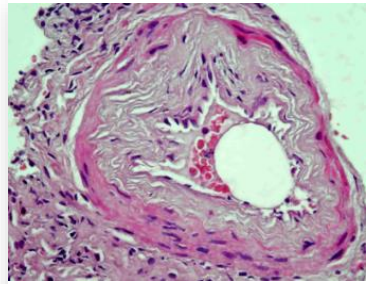
Genetics
Environmental Exposures
Diabetes
Age

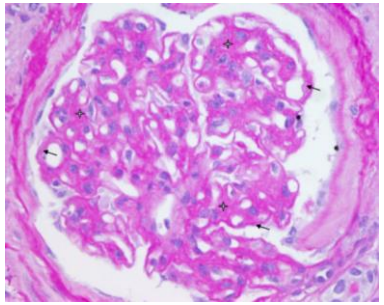
CKD and water clearance

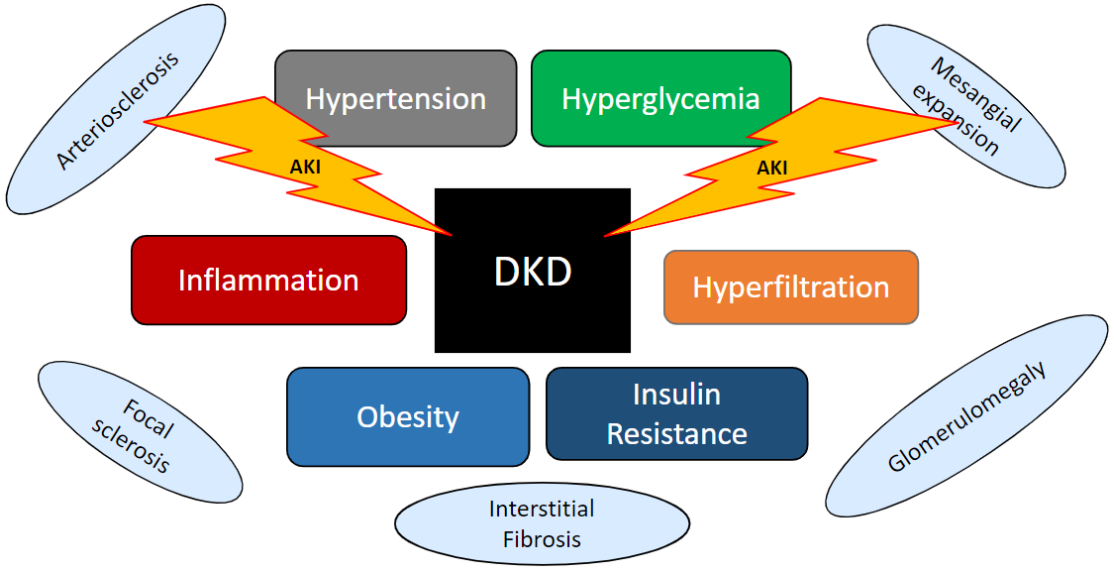


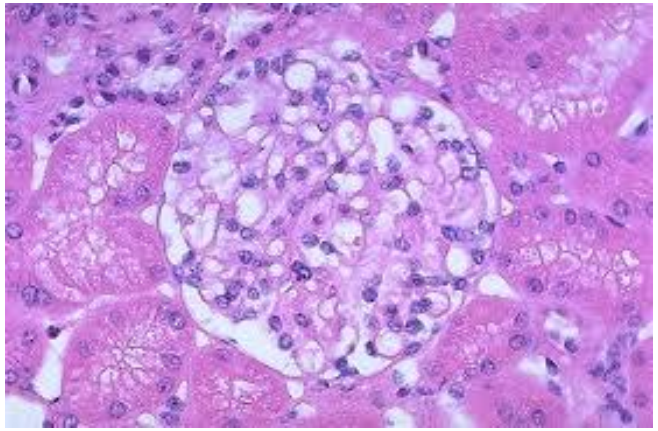
60% of people afflicted with congestive heart failure have concurrent CKD

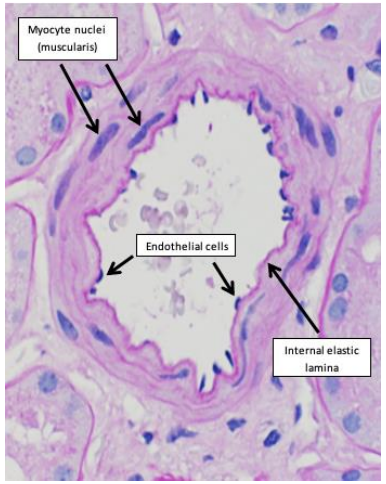
Pathogenetic factors in CKD and its progression

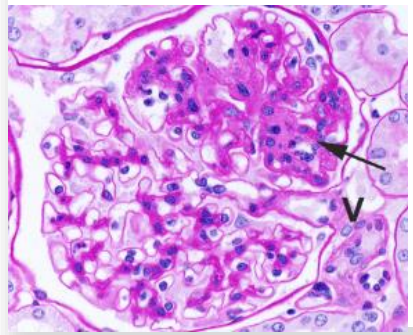


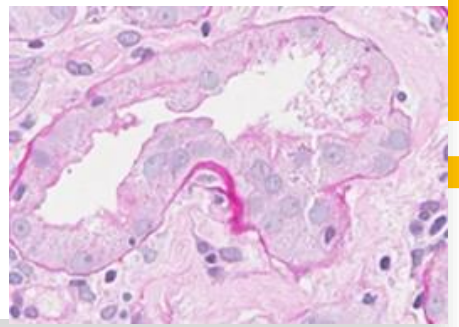


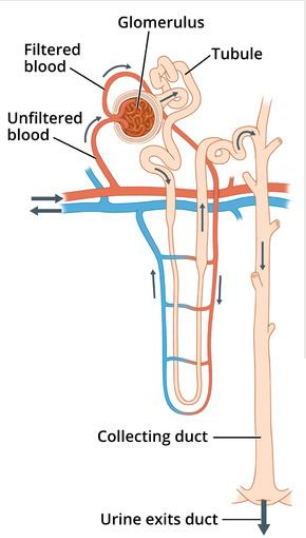




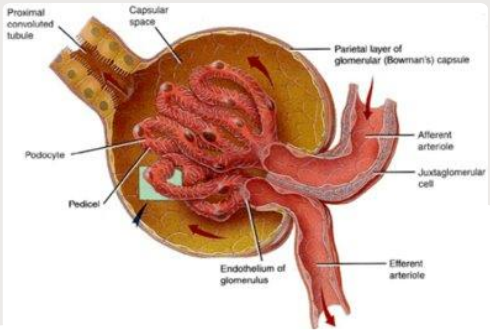








Sheer stress and vascular damage

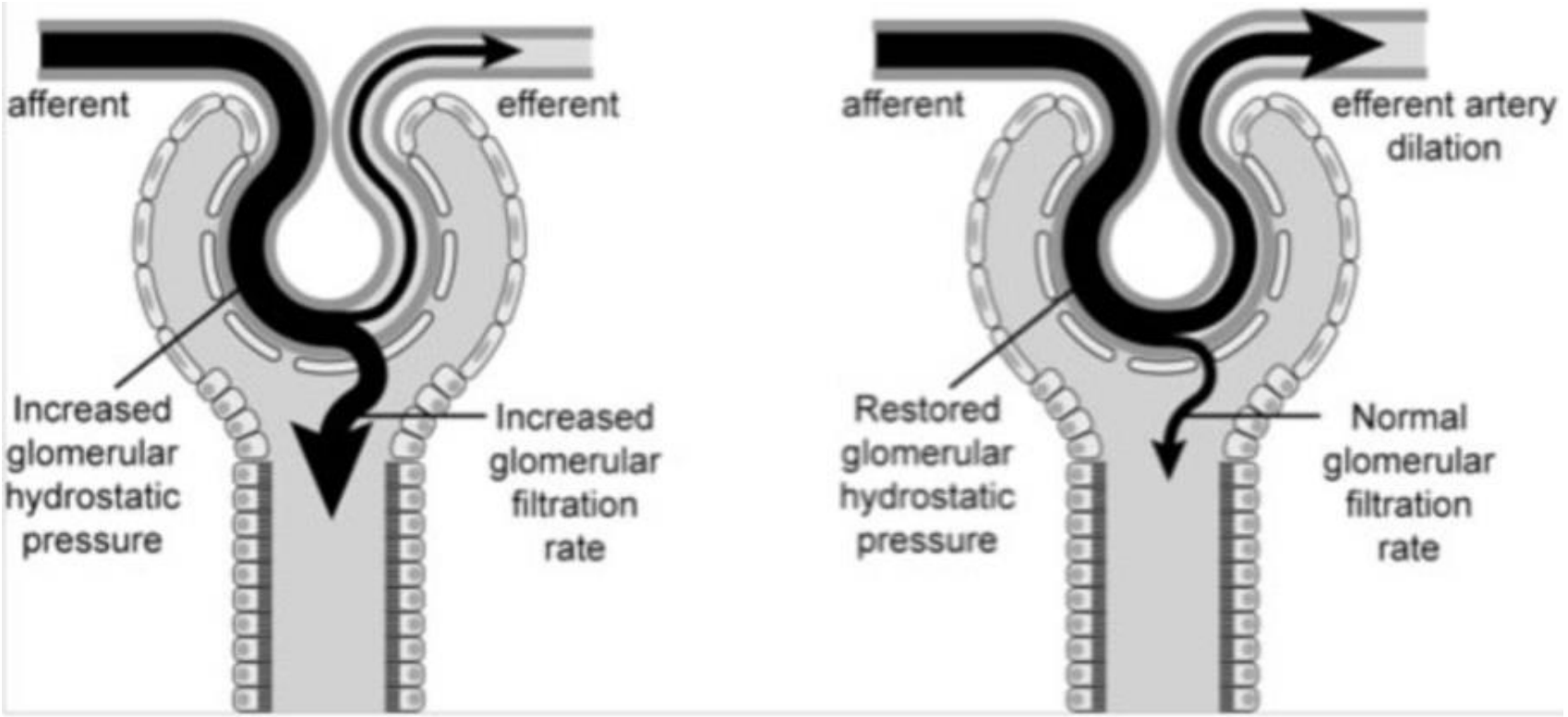


<u>Renin-Angiotensin-Aldosterone Inhibitors:</u>

ACEis

ARBs

MRAs



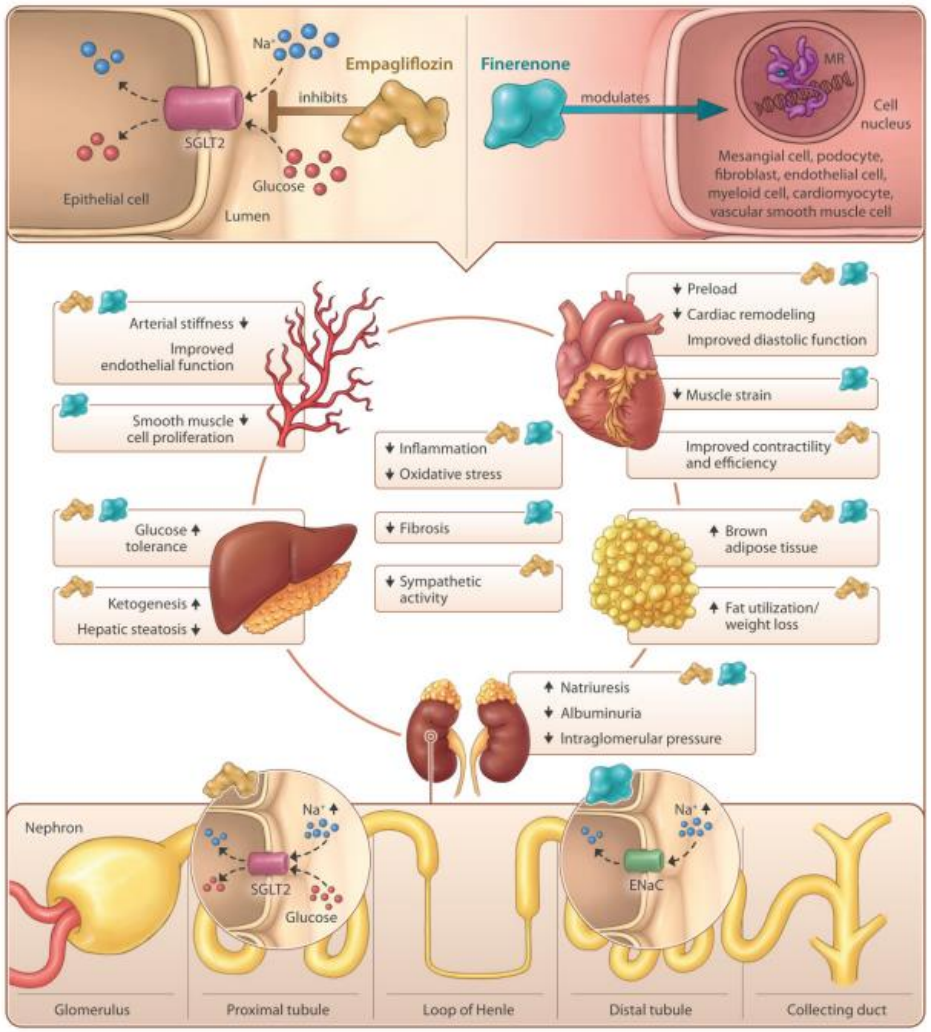
<u>SGLT2 inhibitors:</u>

Dapagliflozin

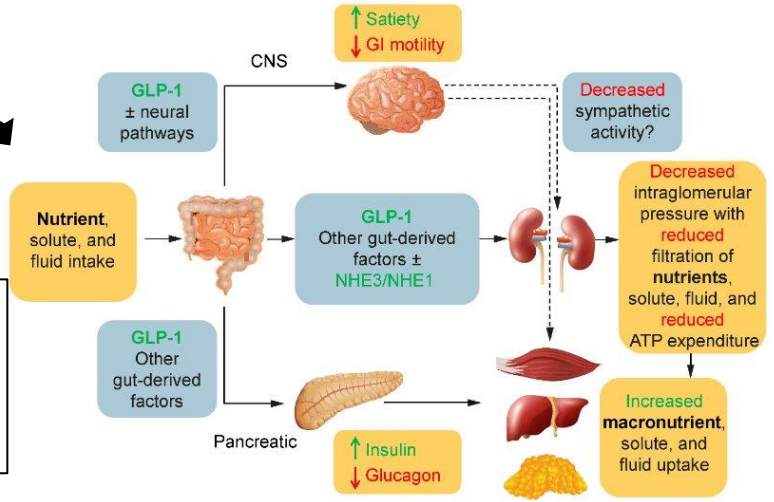
Empagliflozin

Cangliflozin

Inflammation, oxidative stress and fibrosis lead to CKD and its progressior

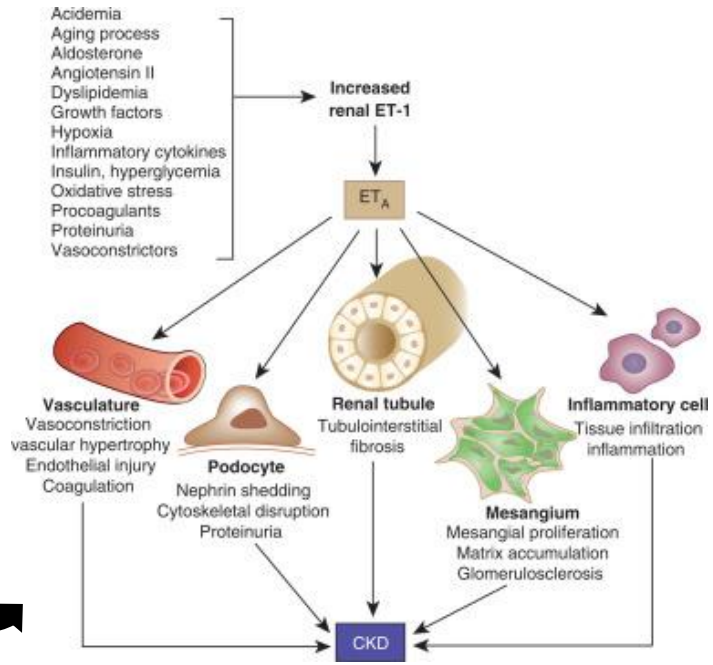


Glucagon-like peptide agonists

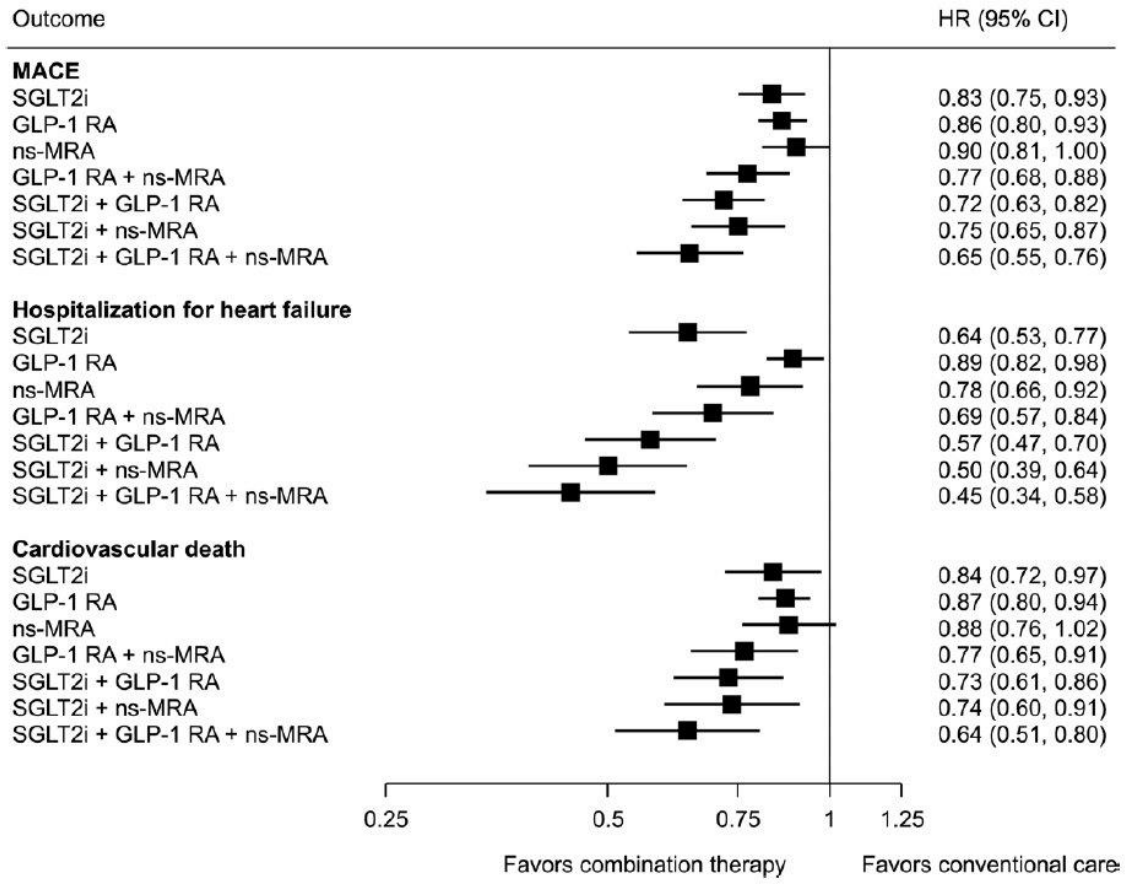


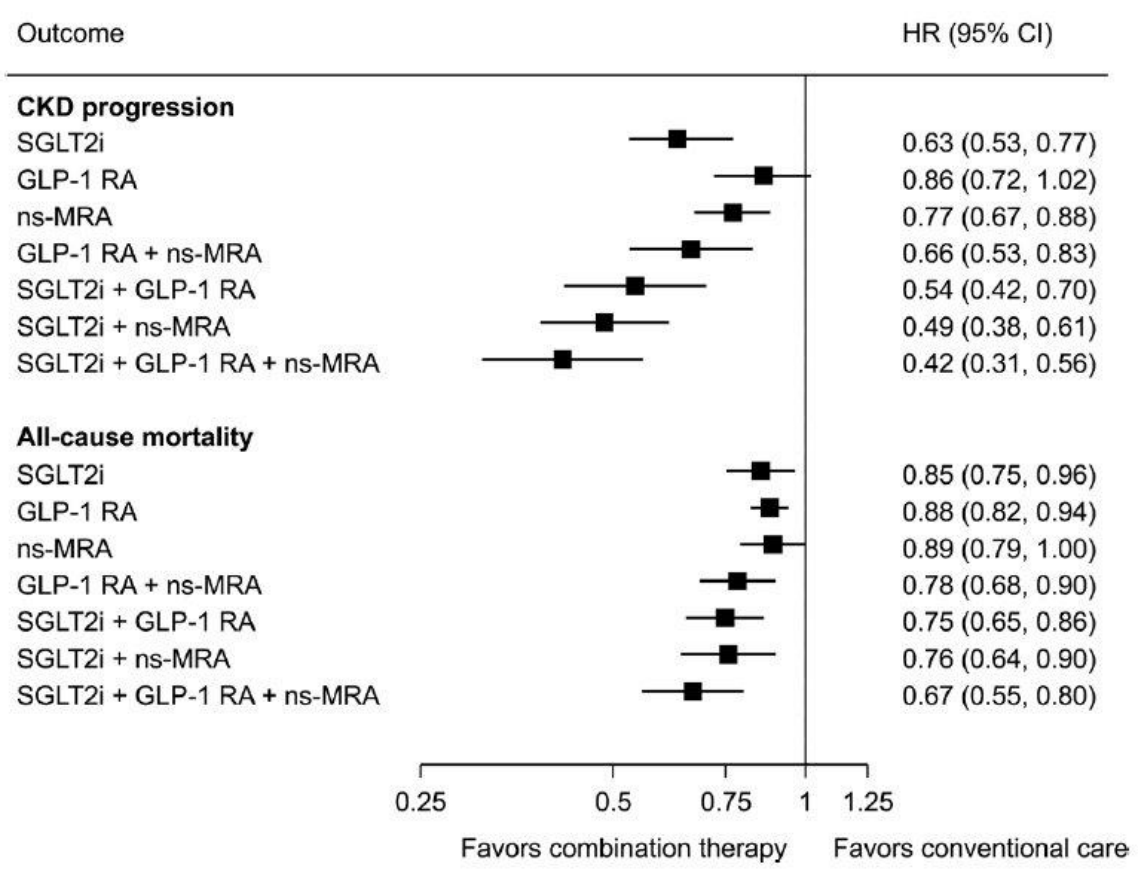
SGLT2i and mineralocorticoid receptor antagonists

Endothelin antagonism



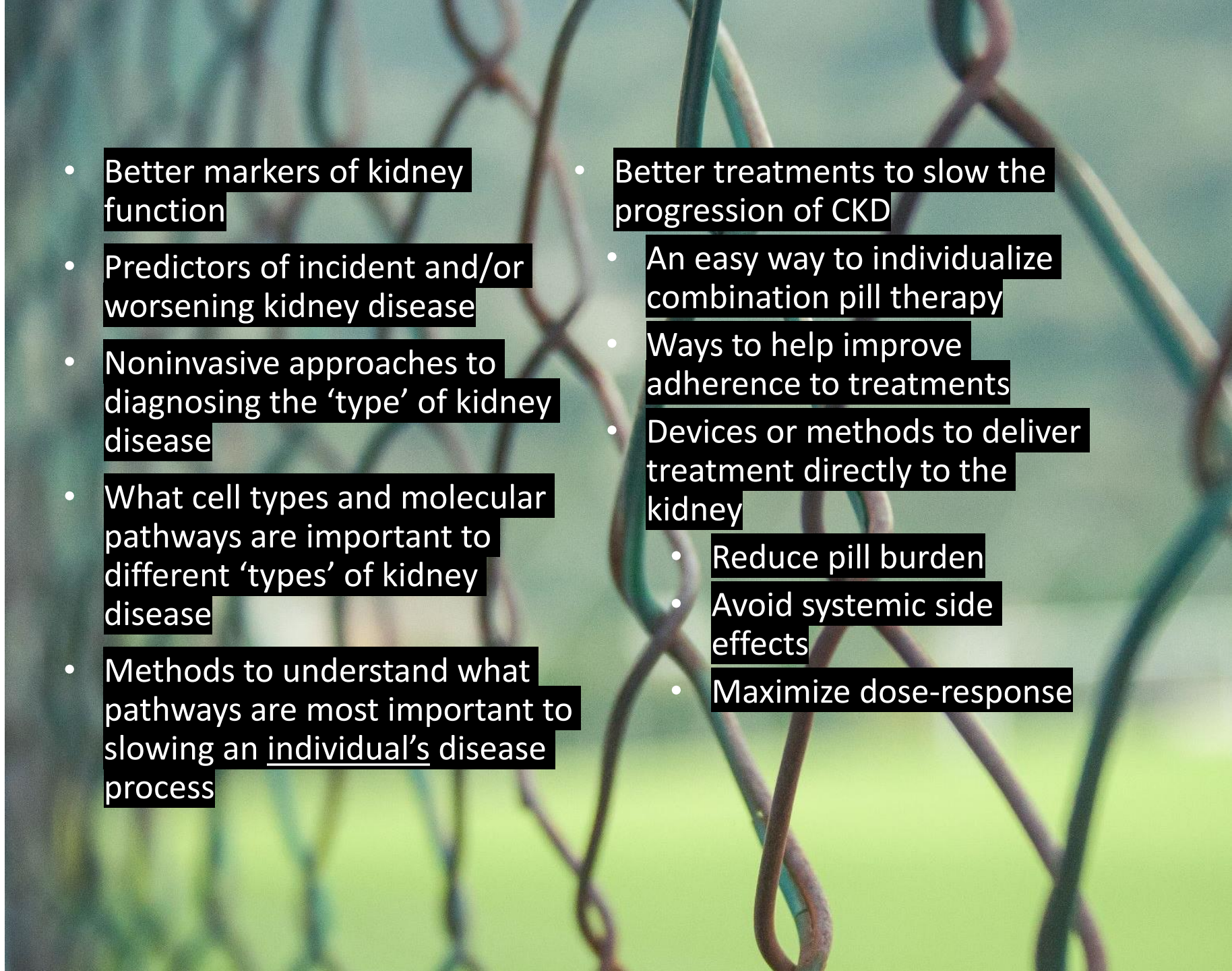
Multitargeted therapy is necessary to prevent ESKD, cardiovascular events and death





Neuen et al. Circulation 2024; 149: 450-462

Barriers to preventing CKD progression



- Better markers of kidney function
- Predictors of incident and/or worsening kidney disease
- Noninvasive approaches to diagnosing the ‘type’ of kidney disease
- What cell types and molecular pathways are important to different ‘types’ of kidney disease
- Methods to understand what pathways are most important to slowing an individual’s disease process

- Better treatments to slow the progression of CKD
  - An easy way to individualize combination pill therapy
  - Ways to help improve adherence to treatments
  - Devices or methods to deliver treatment directly to the kidney
    - Reduce pill burden
    - Avoid systemic side effects
    - Maximize dose-response