Approach to a case of Renal failure

Council Member
2011-2017

Champion
Asian Region

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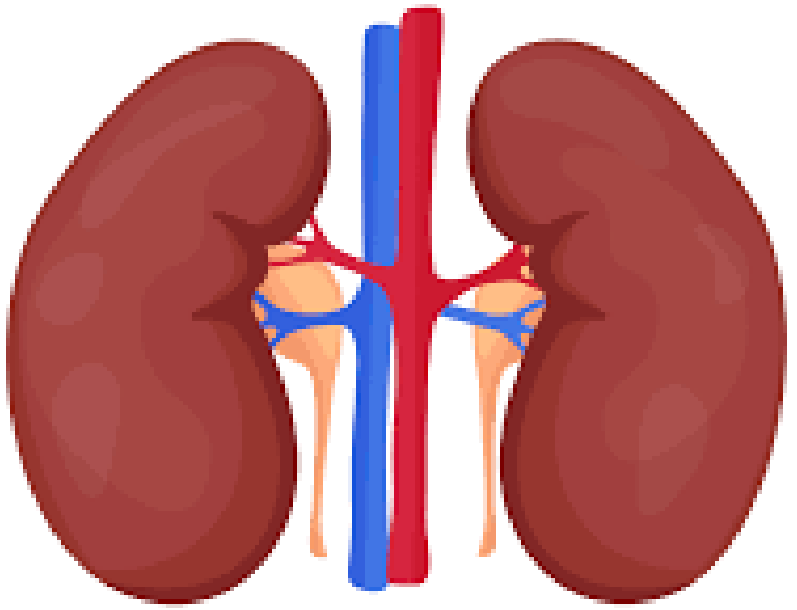
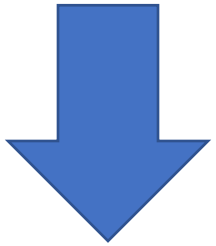
Outline of Talk

- Concept of renal failure
- Changing terminology
- Magnitude of problem
- Stages of disease
- Causes
- Clinical presentation
- Course of disease
- Management
- Prevention



Concept of Renal Failure



Loss of kidney function

Functions of Kidneys

Excretion of Waste

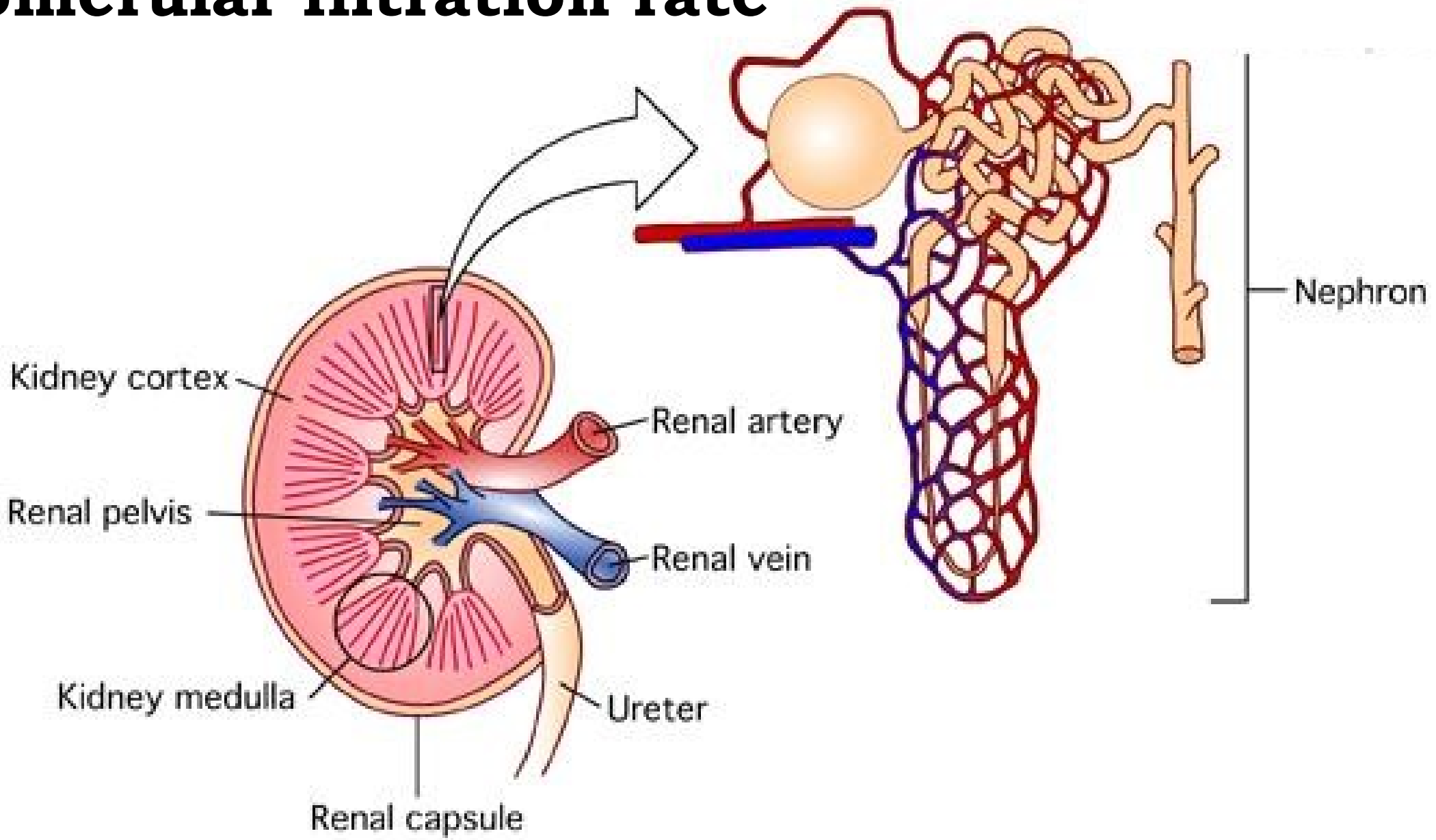
Maintenance of Internal Milieu

- Fluid
- Electrolyte
- Acid-base

Endocrine Function

- Erythropoetin
- Vit D 3
- Renin

Glomerular filtration rate



Basic Principle of GFR Measurement

Name	Equation	Units
Clearance	$\frac{U_x V}{P_x}$	mL/min
GFR	$\frac{U\ inulin \times V}{P\ inulin}$	mL/min
Clearance Ratio	$\frac{C\ x}{C\ inulin}$	None
Effective Renal Plasma Flow	$\frac{U\ (PAH) \times V}{P\ (PAH)}$	mL/min

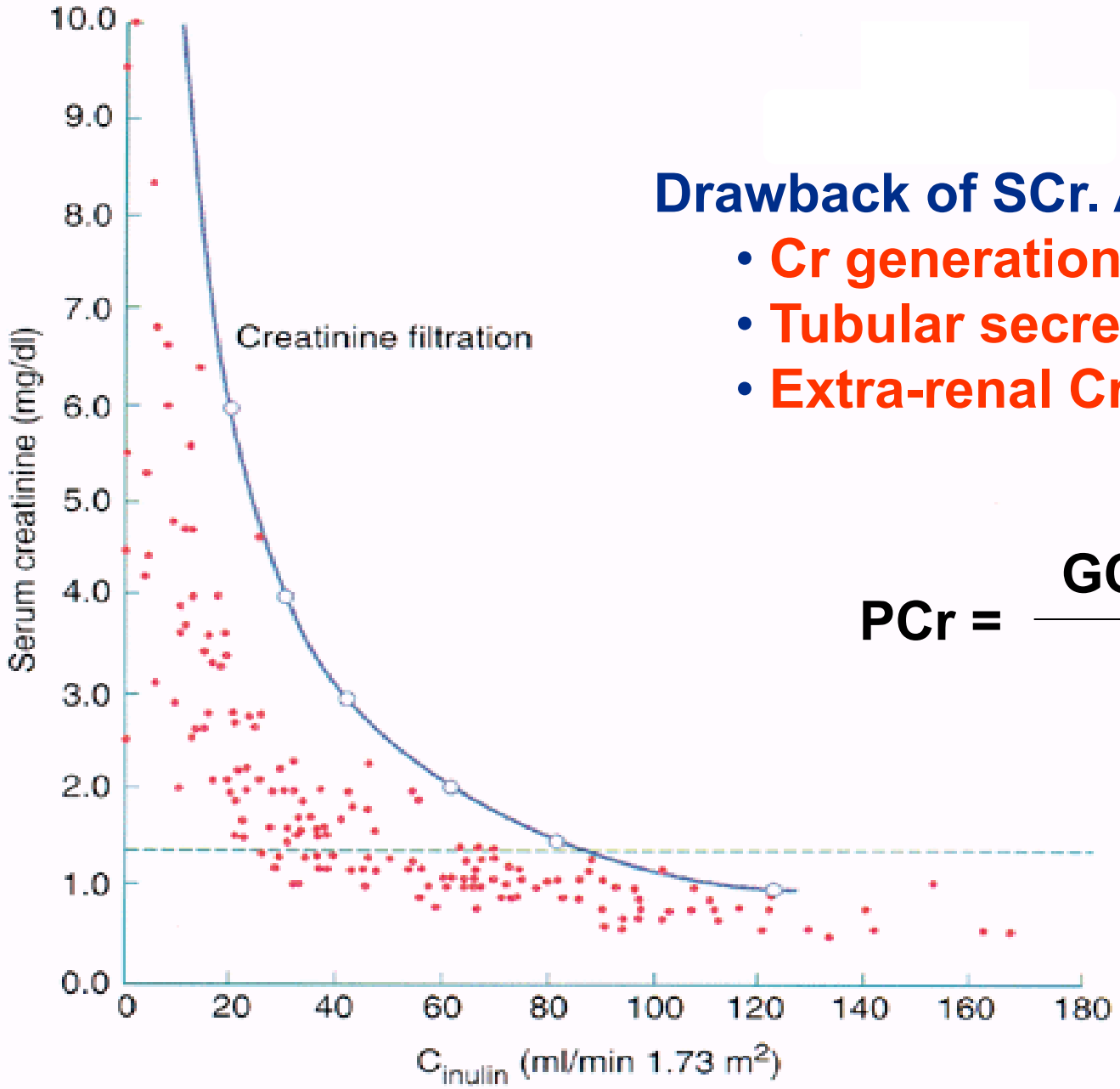
Method

Marker

Approach	Strengths	Limitations
Methods		
Urinary clearance		
Bladder catheter and continuous of marker	• Gold standard method	• Invasive
Spontaneous bladder emptying	• Patient comfort • Less invasive	• Possibility of incomplete bladder emptying • Low flow rates in people with low levels of GFR
Bolus administration of marker	• Shorter duration	• Rapidly declining plasma levels at high levels of GFR • Longer equilibration time in extracellular volume expansion
24 h urinary collection		• Cumbersome • Prone to error
Plasma clearance	• No urine collection required • Potential for increased precision	• Overestimation of GFR in extracellular volume expansion • Inaccurate values with 1-sample technique, particularly at lower GFR levels • Longer duration of plasma sampling required for low GFR
Nuclear imaging	• No urine collection or repeated blood samples required • Relatively short duration	• Less accurate
Markers		
Inulin	• Gold standard • No side effects	• Expensive • Difficult to dissolve and maintain into solution • Short supply
Creatinine	• Endogenous marker, no need for administration • Assay available in all clinical laboratories	• Secretion can vary among and within individuals
Iothalamate	• Inexpensive • Long half life	• Probable tubular secretion • Requirement for storage, administration, and disposal of radioactive substances when ^{125}I used as tracer • Use of non-radioactive iothalamate requires expensive assay • Cannot be used in patients with allergies to iodine
Iohexol	• Not radioactive • Inexpensive • Sensitive assay allows for low dose	• Possible tubular reabsorption or protein binding • Use of low doses requires expensive assay • Cannot be used in patients with allergies to iodine • Nephrotoxicity and risk for allergic reactions at high doses
EDTA	• Widely available in Europe	• Probable tubular reabsorption • Requirement for storage, administration, and disposal of radioactive substances when ^{51}Cr is used as tracer
DTPA	• Widely available in the US • New sensitive and easy to use assay for gadolinium	• Requirement for storage, administration, and disposal of radioactive substances when ^{99m}Tc used as tracer • Requires standardization for ^{99m}Tc • Dissociation and protein binding of ^{99m}Tc • Concern for NSF when gadolinium is used as the tracer

Abbreviations: DTPA, diethylenetriamine pentaacetic acid; EDTA, ethylenediamine tetraacetic acid; GFR, glomerular filtration rate; NSF, nephrogenic systemic fibrosis.

Serum Cr. And GFR Correlation



Drawback of SCr. As marker of GFR

- **Cr generation**
- **Tubular secretion**
- **Extra-renal Cr. excretion**

$$PCr = \frac{GCr - TSCr - ERCr}{GFR}$$

Same serum creatinine & different GFR

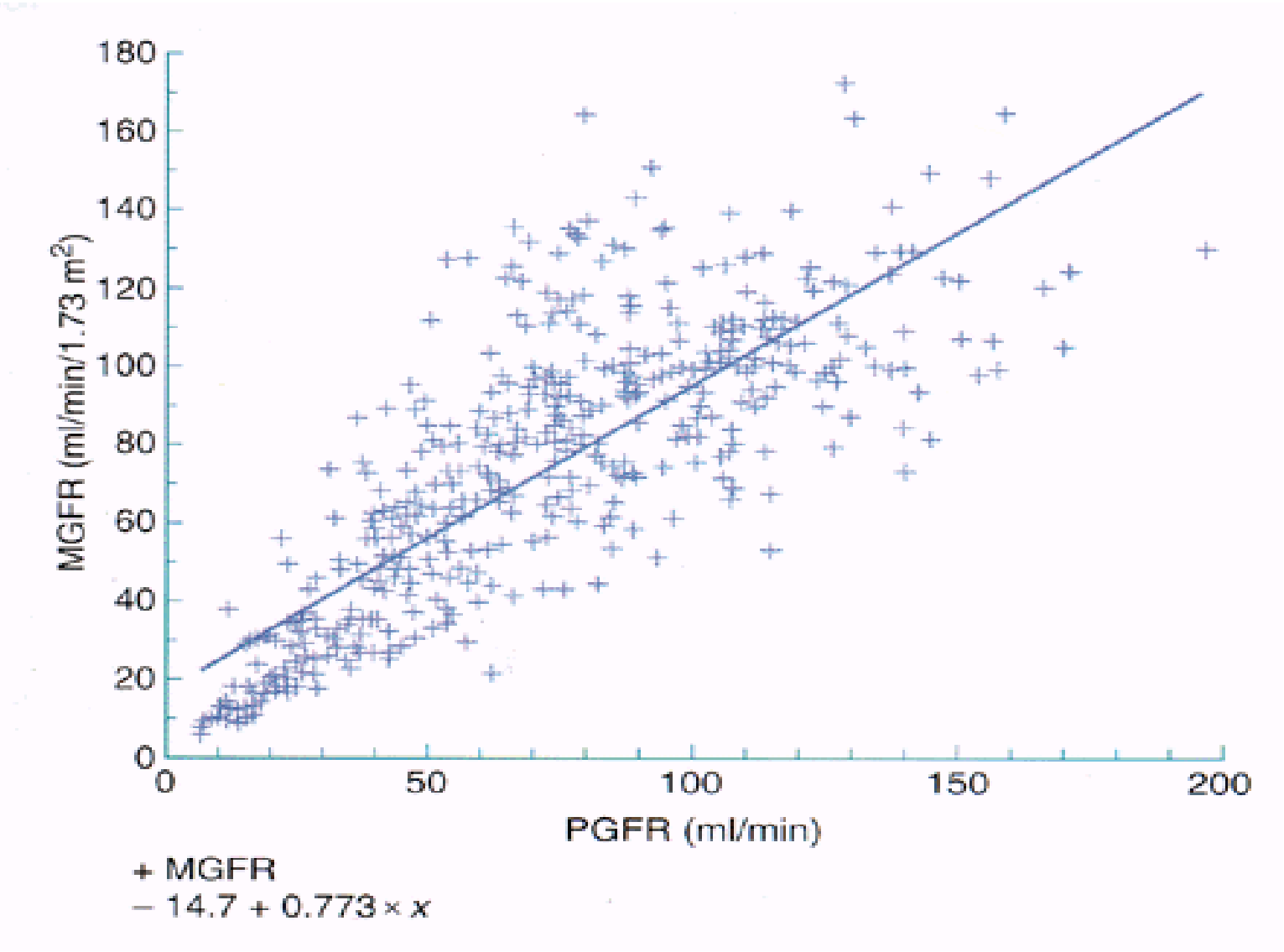
	Serum Creatinine = 1.3	
Gender	Male	Female
Weight	80	40
GFR	90 ml	45 ml

GFR estimation: eGFR Equations

- **Cockroft-Gault:** (140 - age) x weight/72 x S cr (x 0.85 if female)
- **MDRD 1:** 170 x Scr -0.999 x age -0.176 x (0.762 if female) x (1.180 if black) x Su -0.170 x Alb +0.318
- **MDRD 2:** [4v] 186 x S cr -1.154 x age -0.203 x (1.212 if black) x (0.742 if female)
- **Jelliffe 1**: 98 - 0.8 x (age - 20)/S cr (x 0.90 if female)
- **Jelliffe 2:** ♂: 100/S cr - 12 Female: 80/S cr - 7
- **Mawer:** Male: Wt x [29.3 - (0.203 x age)] x [1 - (0.03 x S cr)]/(14.4 x S cr) x (70/Wt)
- Female: Wt x [25.3 - (0.175 x age)] x [1 - (0.03 x S cr)]/(14.4 x S cr) x (70/Wt)
- **Bjornsson:** : [27 - (0.173 x age)] x Wt x 0.07/Scr : [25 - (0.175 x age)] x Wtx 0.07/Scr
- **Gates:** ♂: (89.4 xScr -1.2) + (55 - age) x (0.447 xScr -1.1) ♀ : (60 xScr -1.1) + (56 - age) x (0.3 xScr -1.1)

- **CKD-EPI:** GFR = 141 x $\min(Scr/k,1)^{\alpha}$ x $\max(S.cr/k,1)^{-1.209}$ x 0.993^{Age} x 1.018 [if female] x 1.159 [if black],

Measured and Estimated GFR Correlation



Renal Failure

Decrease in GFR < 60 ml/mt

Acute Renal Failure (ARF)

- Recent onset
- Mostly reversible

Chronic Renal Failure (CRF)

- > 3 months
- No reversibility
- Tendency of progression

Changing terminology

Renal Failure → Kidney Disease

Decrease in GFR < 60 ml/mt

Acute Renal Failure (ARF)

↓

Acute Kidney Injury (AKI)

- Recent onset
- Mostly reversible

Chronic Renal Failure (CRF)

↓

Chronic Kidney Disease(CKD)

- > 3 months
- No reversibility
- Tendency of progression

Definition of Disease

Acute Kidney Injury

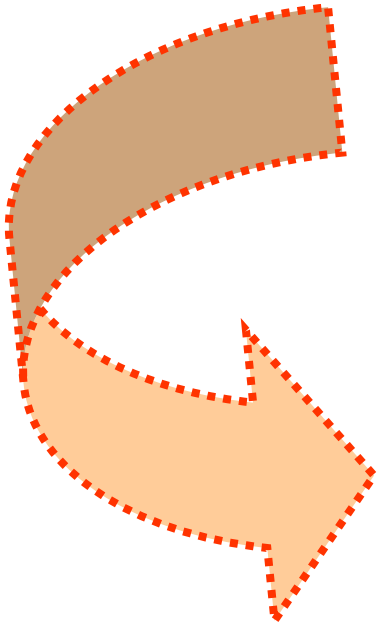
Sudden, fall in GFR in hours to days

+ + +

- **Azotemia**
- **Fall in urine output**
- **Potentially reversible**

Chronic Kidney Disease

Kidney Disease or GFR < 60 ml / mt / 1.73 sqm



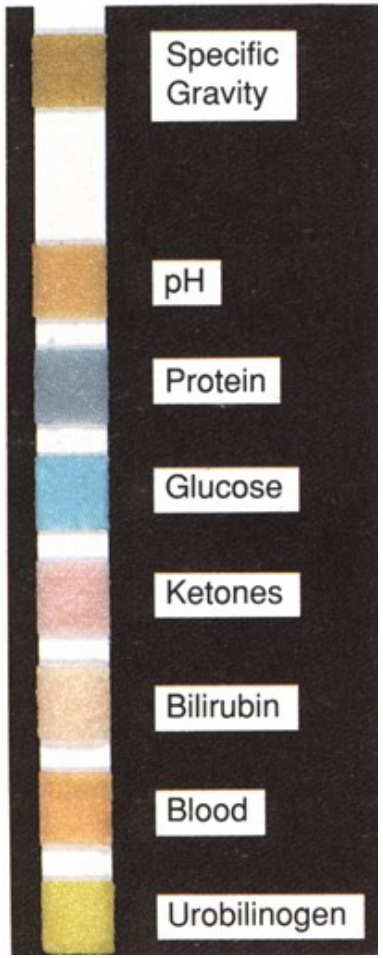
For > 3 months

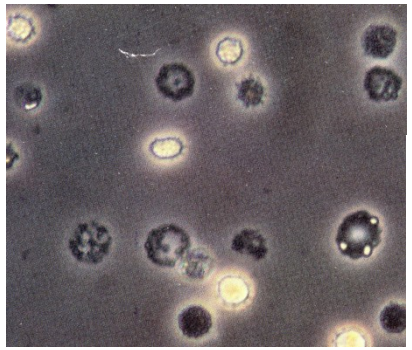
- Pathological abnormality or
- Marker of kidney damage

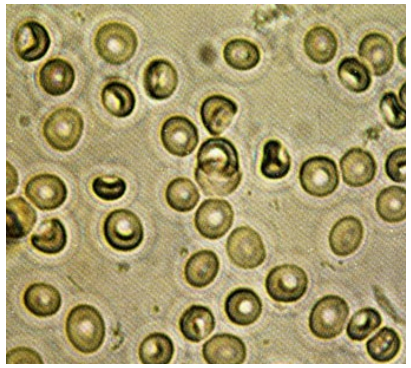
- Blood or urinary abnormality
- Abnormal imaging test

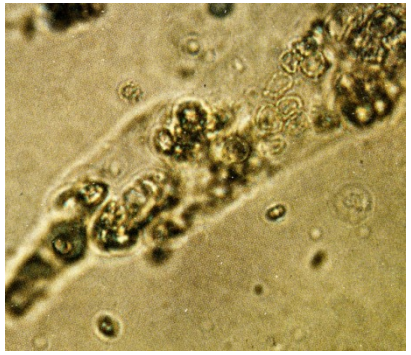
K/DOQI

CKD Diagnosis: Serum creatinine + Urine abnormality

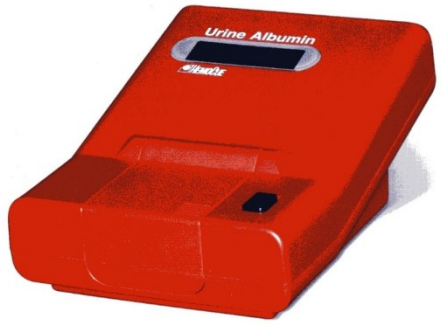






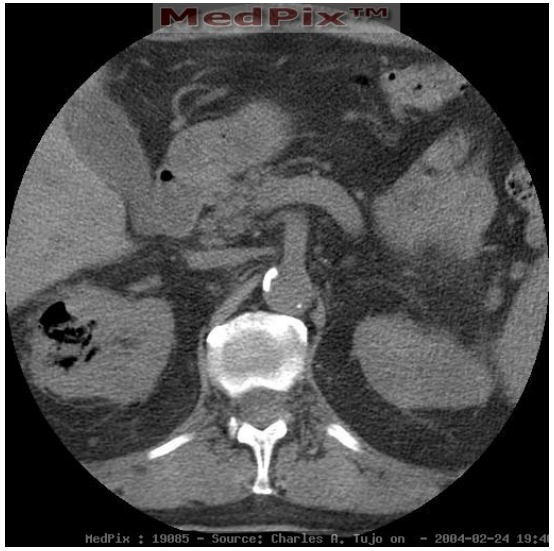


HemoCue® Urine Albumin
makes life easier for you

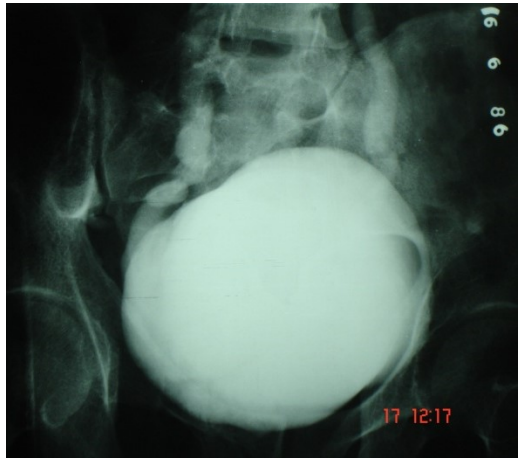


Blood Creatinine = eGFR

Abnormal Imaging



CPN



VUR

PKD

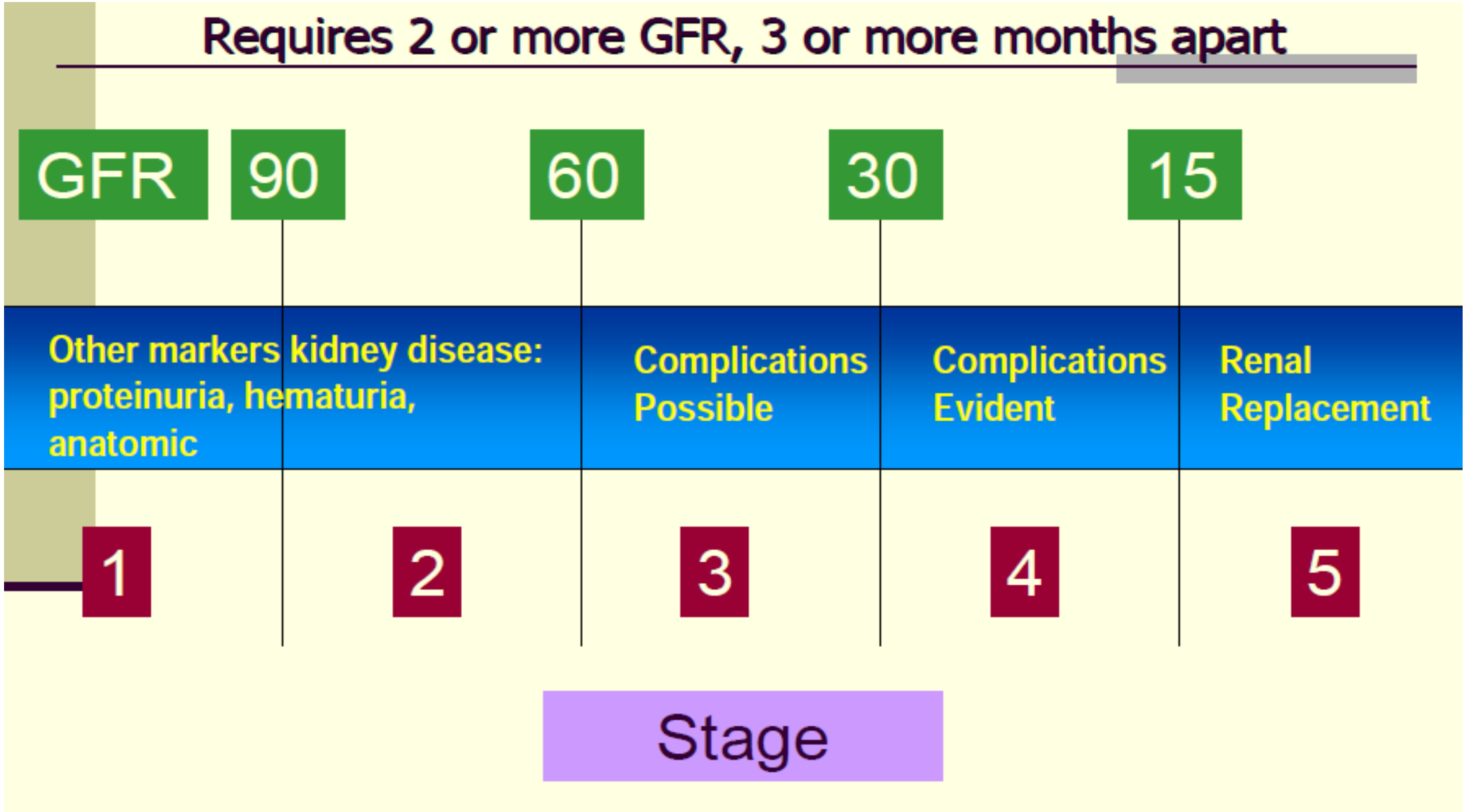
Multiple Stones

Stages of Disease

Acute Kidney Injury: Stages

Stages	Creatinine	Urine Output
1	▪ ≥ 1.5 times baseline or ▪ ≥ 0.3 mg/dL	▪ ≤ 0.5 mL/Kg for 6-12 hrs.
2	▪ ≥ 2 times baseline	▪ ≤ 0.5 mL/Kg for ≥ 12 hrs.
3	▪ ≥ 3 times baseline or ▪ Increase ≥ 4.0 mg/dL	▪ ≤ 0.3 mL/Kg for ≥ 24 hrs.

Staging of chronic kidney disease



CKD Stages: GFR and Albuminuria

GFR category	GFR (ml/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Category	AER (mg/24 hours)	ACR (approximate equivalent) (mg/mmol)	ACR (approximate equivalent) (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.
*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 hours [ACR >2220 mg/g; >220 mg/mmol]).

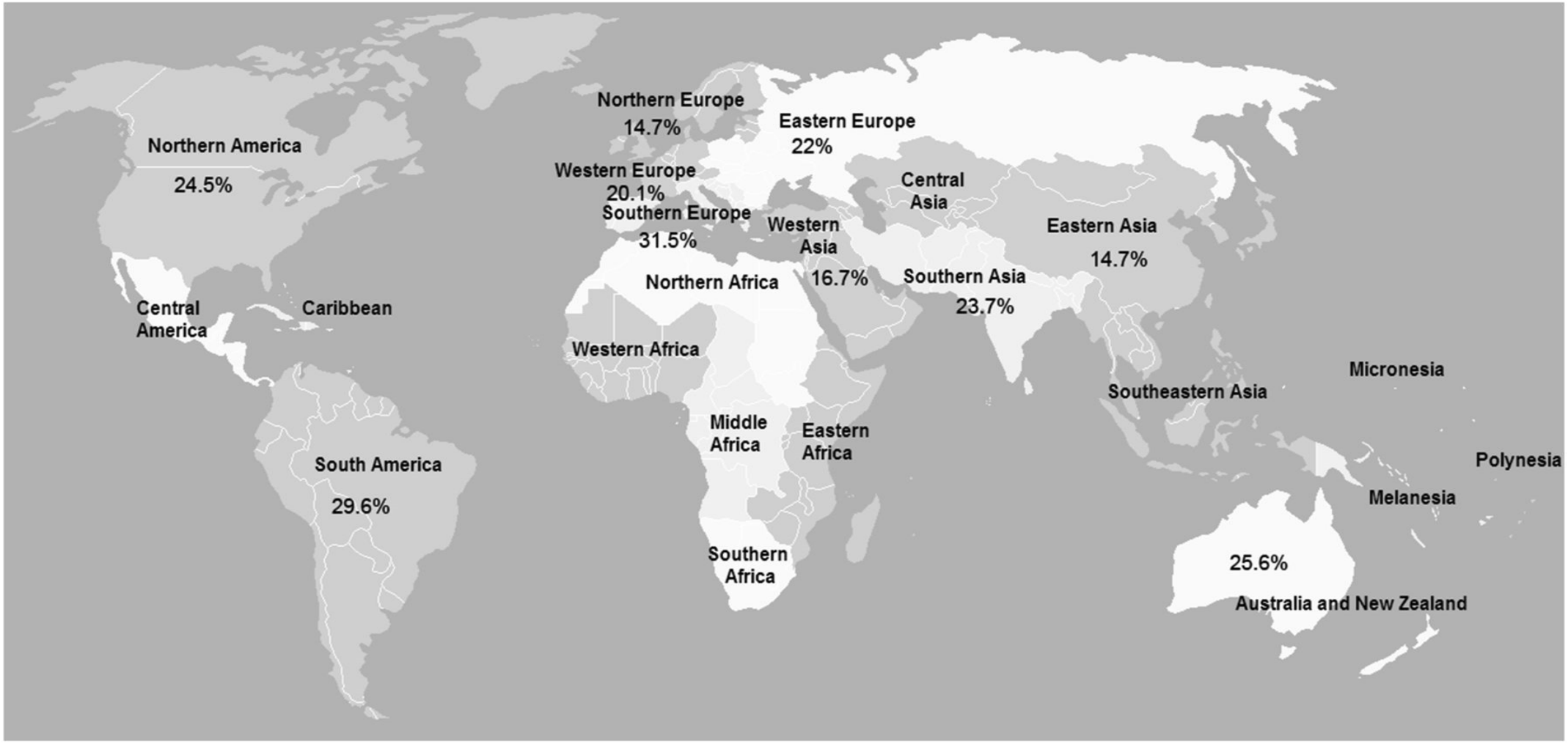
Assessing CKD

Percentage of US Population by eGFR and Albuminuria Category: KDIGO 2012 and NHANES 1999-2006

GFR categories (ml/min/ 1.73m^2) Description and range				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 >30mg/mmol	
	G1	Normal or high	≥90	55.6	1.9	0.4	57.9
	G2	Mildly decreased	60-89	32.9	2.2	0.3	35.4
	G3a	Mildly to moderately decreased	45-59	3.6	0.8	0.2	4.6
	G3b	Moderately to severely decreased	30-44	1.0	0.4	0.2	1.6
	G4	Severely decreased	15-29	0.2	0.1	0.1	0.4
	G5	Kidney failure	<15	0.0	0.0	0.1	0.1
				93.2	5.4	1.3	100.0

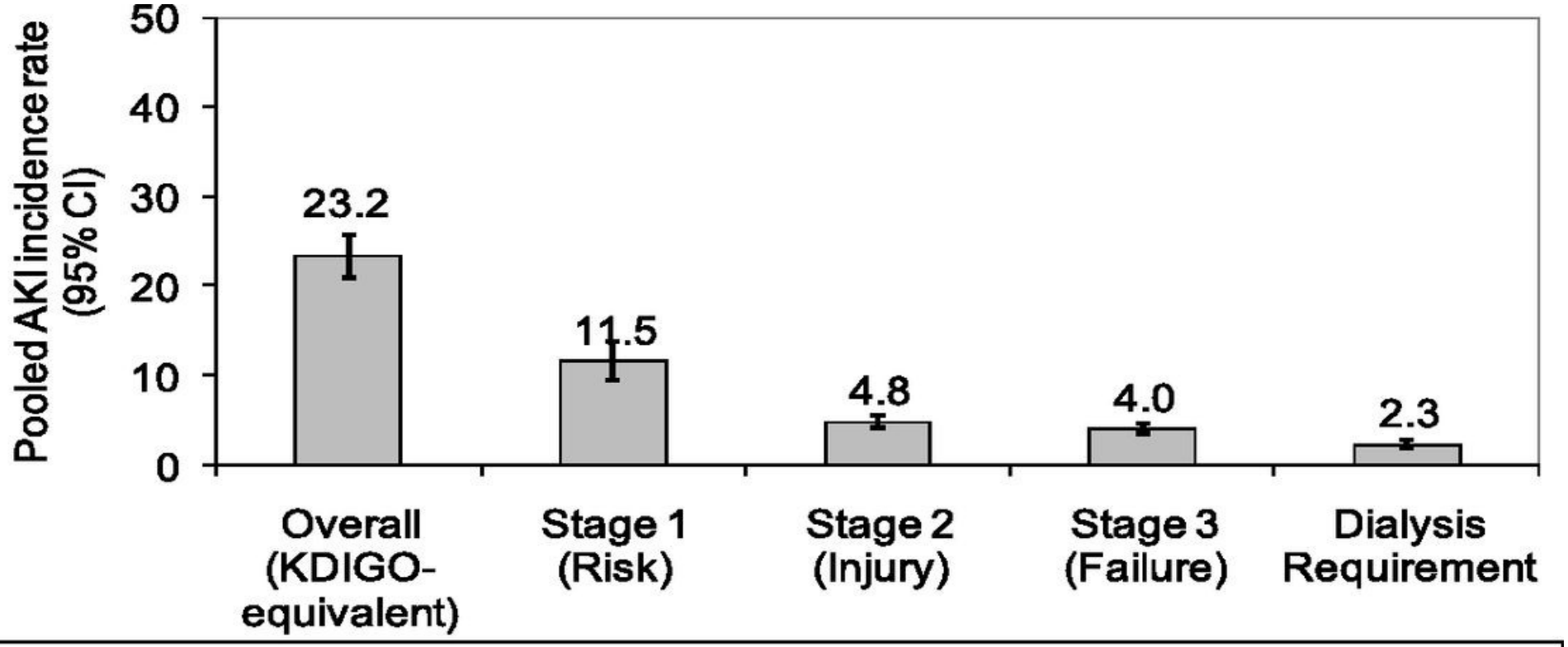
Magnitude of problem

Pooled incidence rate of AKI by world zones Of the Hospital Admission



Susantitaphong P et al. CJASN doi:10.2215/CJN.00710113

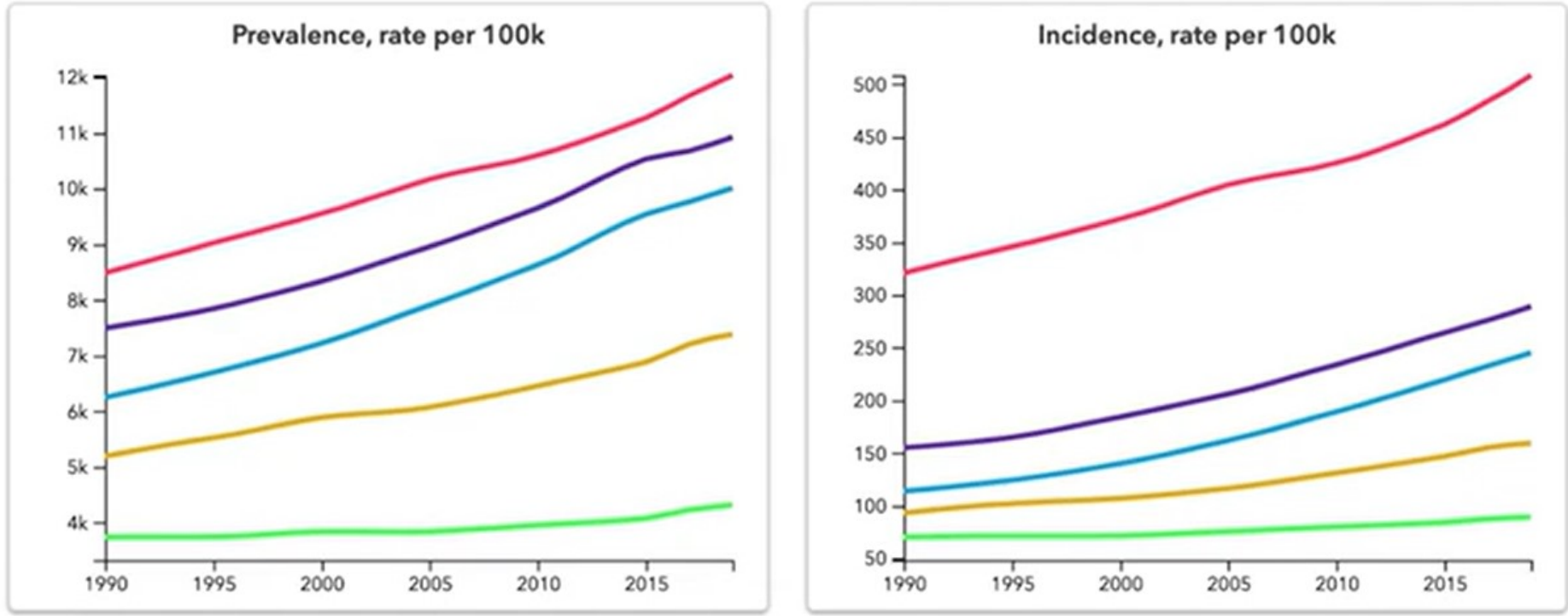
Pooled incidence rate of AKI by world zones



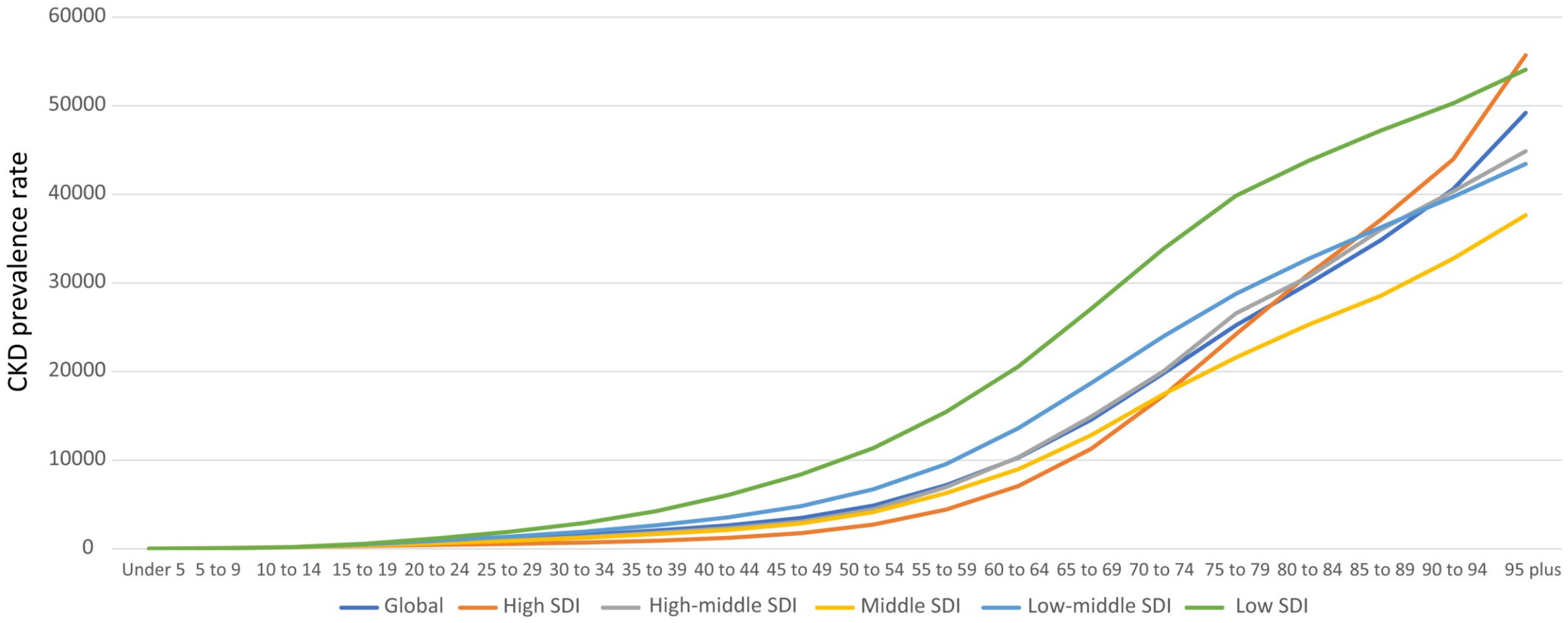
No. studies	154	112	108	108	189
No. patients	3,585,911	3,303,992	3,281,715	3,281,715	29,400,495

Susantitaphong P et al. CJASN doi:10.2215/CJN.00710113

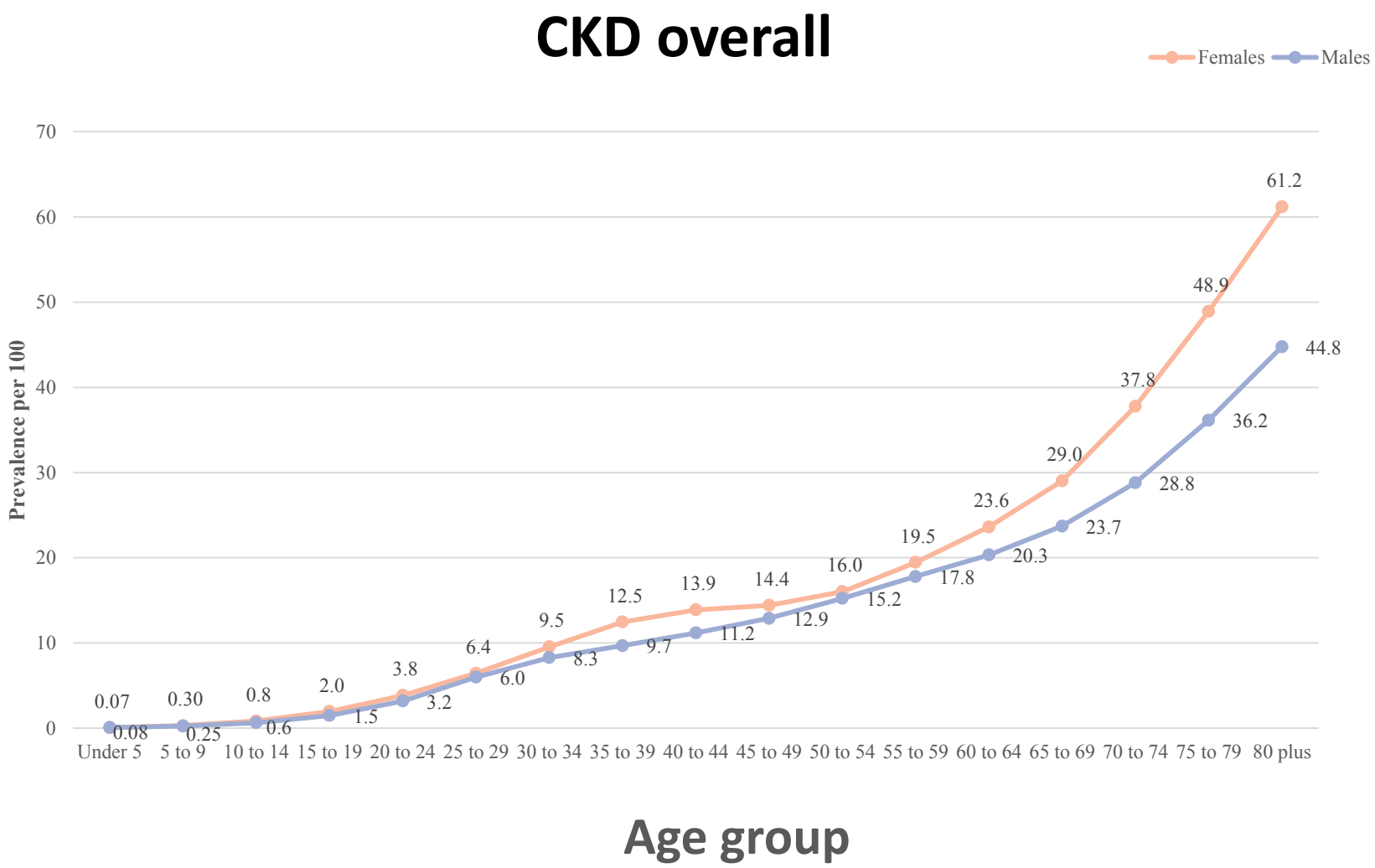
CKD TRAJECTORIES



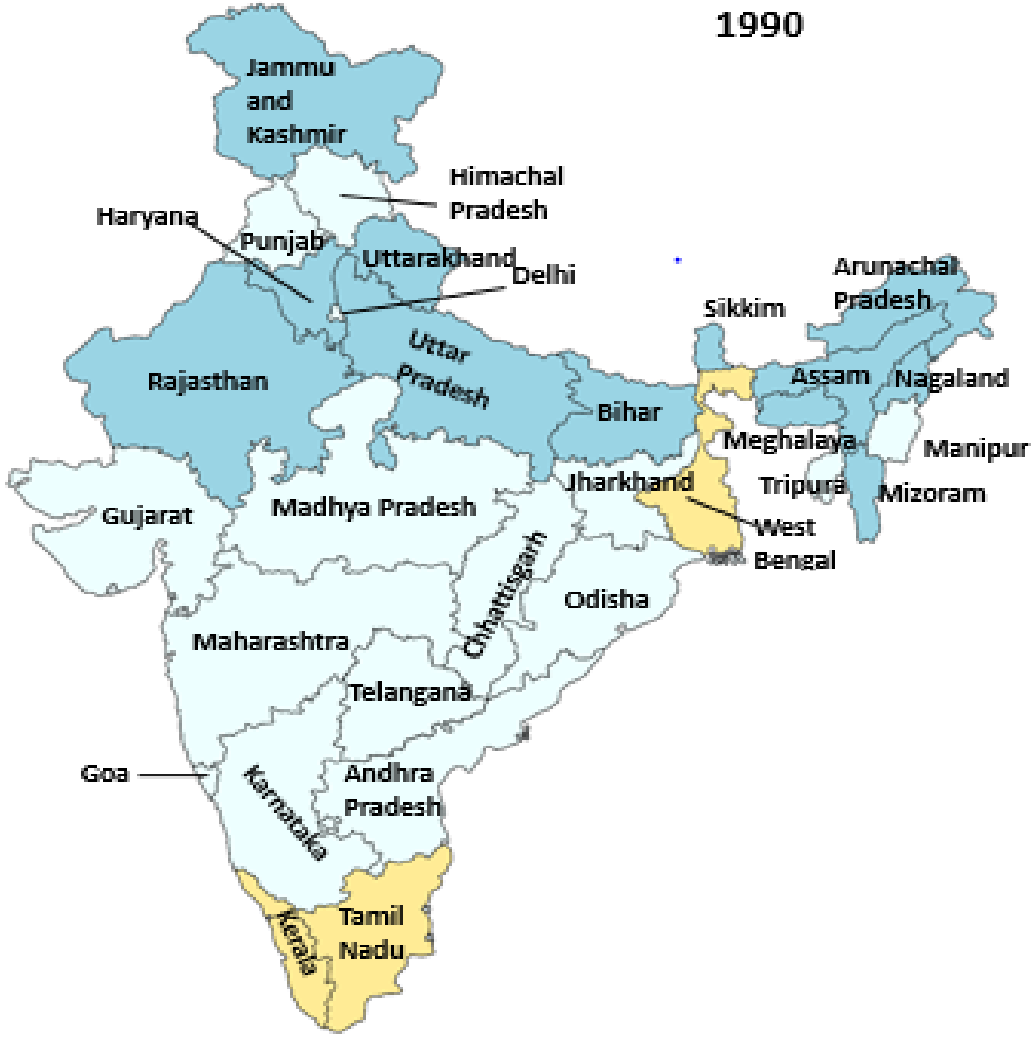
CKD prevalence rate by Age and SDI Sociodemographic Index (SDI) c
(per 100,000 population)

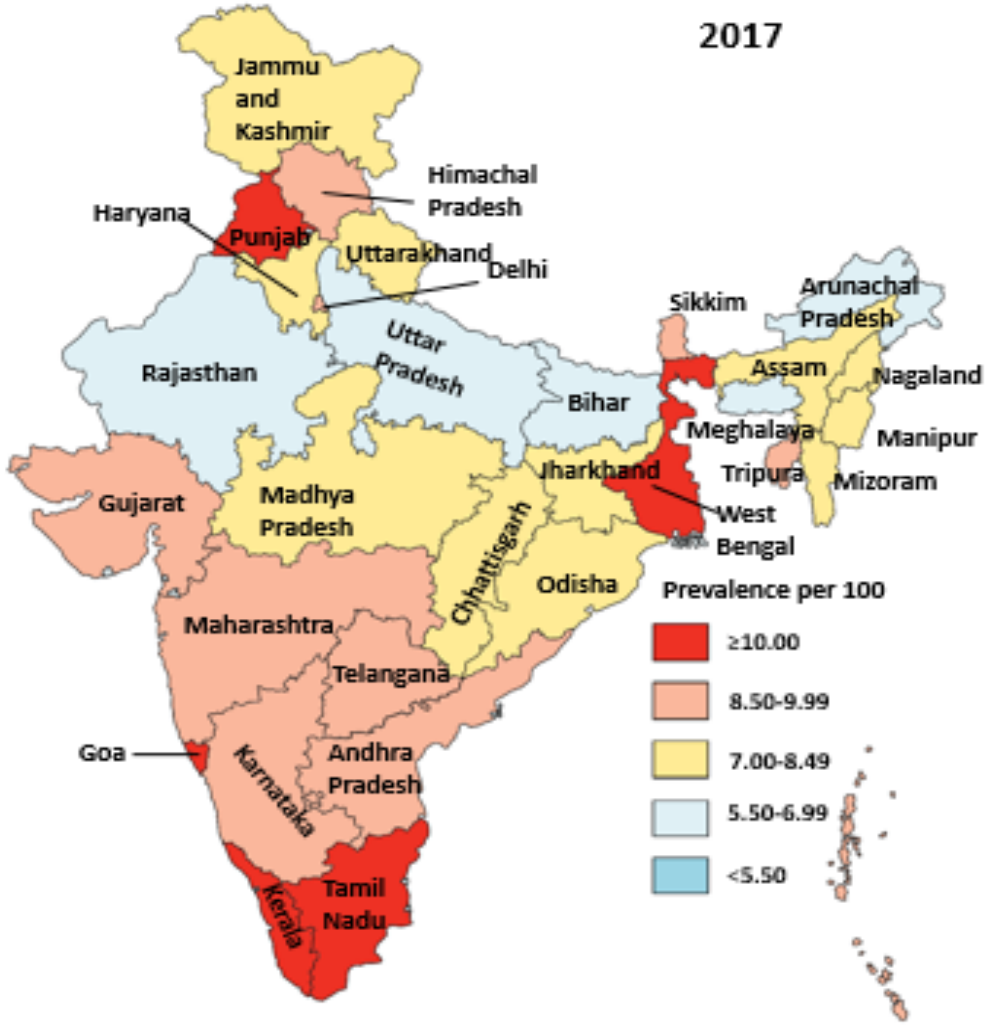


Age-specific prevalence of CKD in India by sex, 2017



Crude prevalence CKD in the states of India 1990 and 2017





Causes

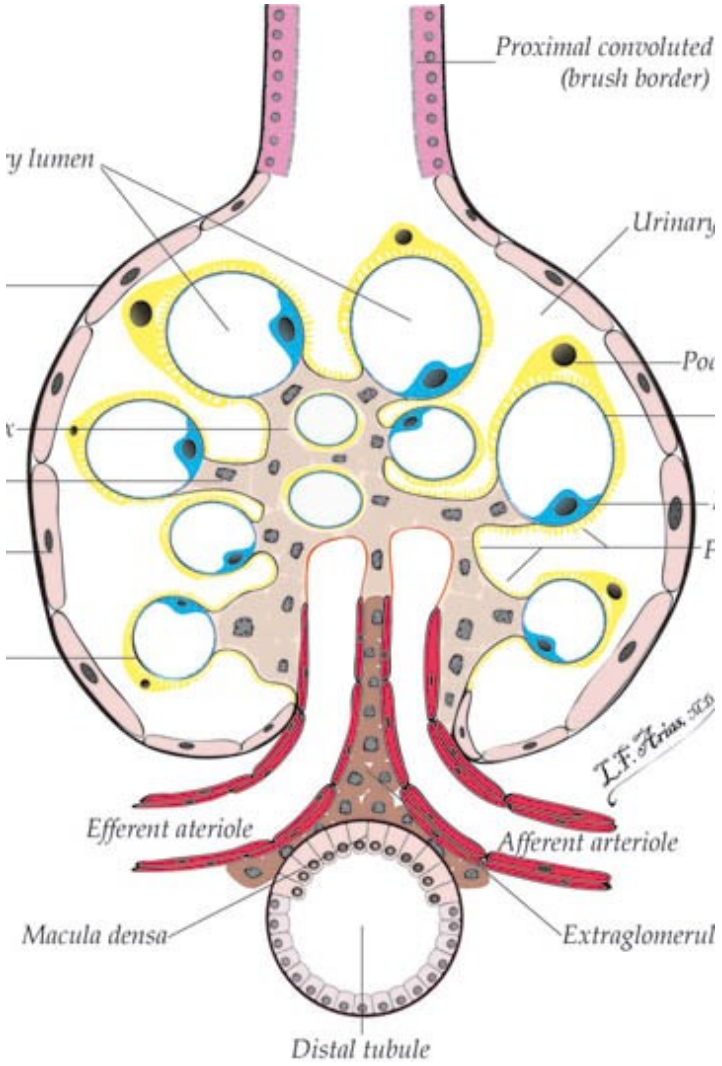
Causes of AKI

Post Renal

- Inside lumen
- in wall
- Outside lumen

Renal

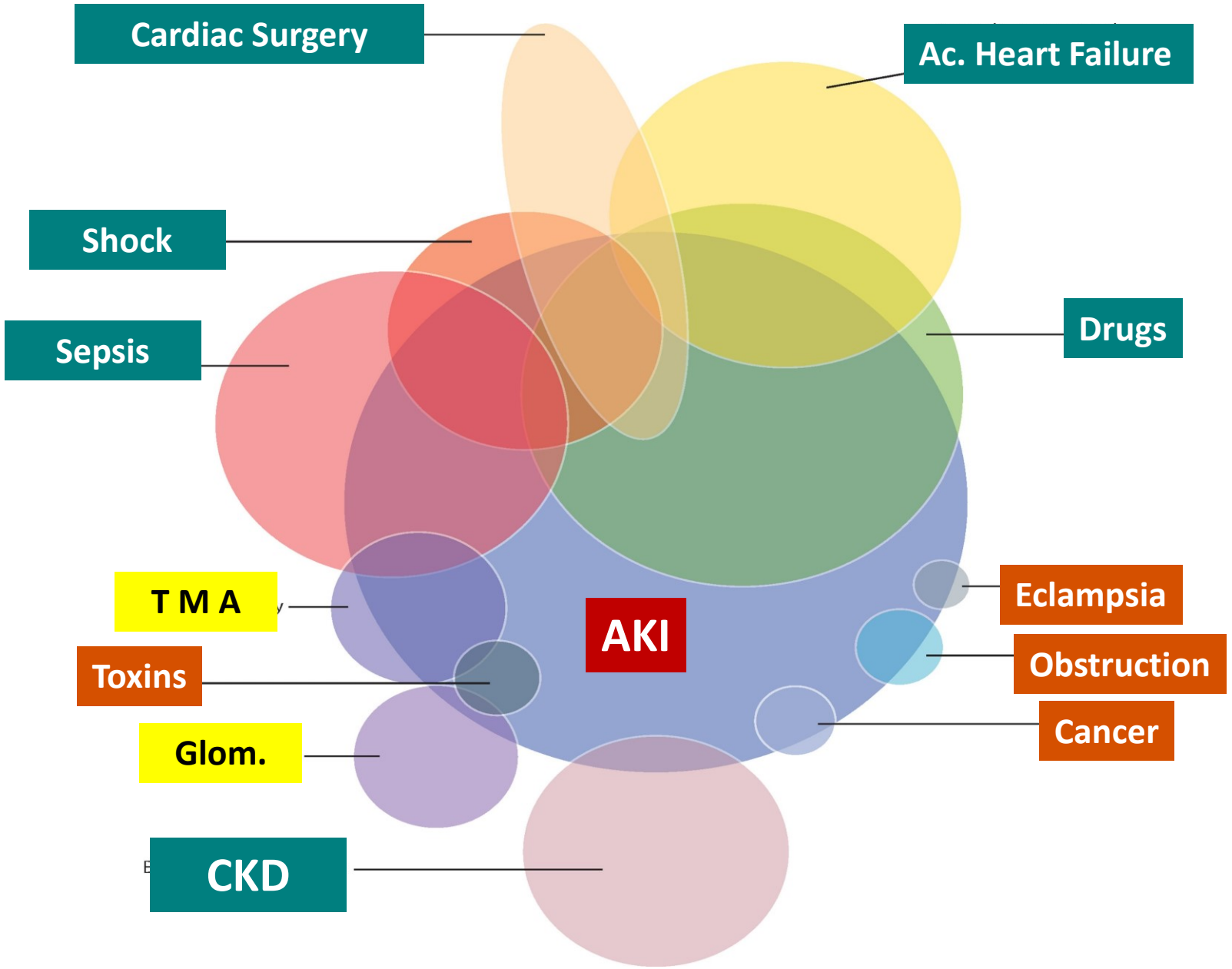
- ATN
- AGN
- AIN
- HUS / TTP
- Vascular



Pre-Renal

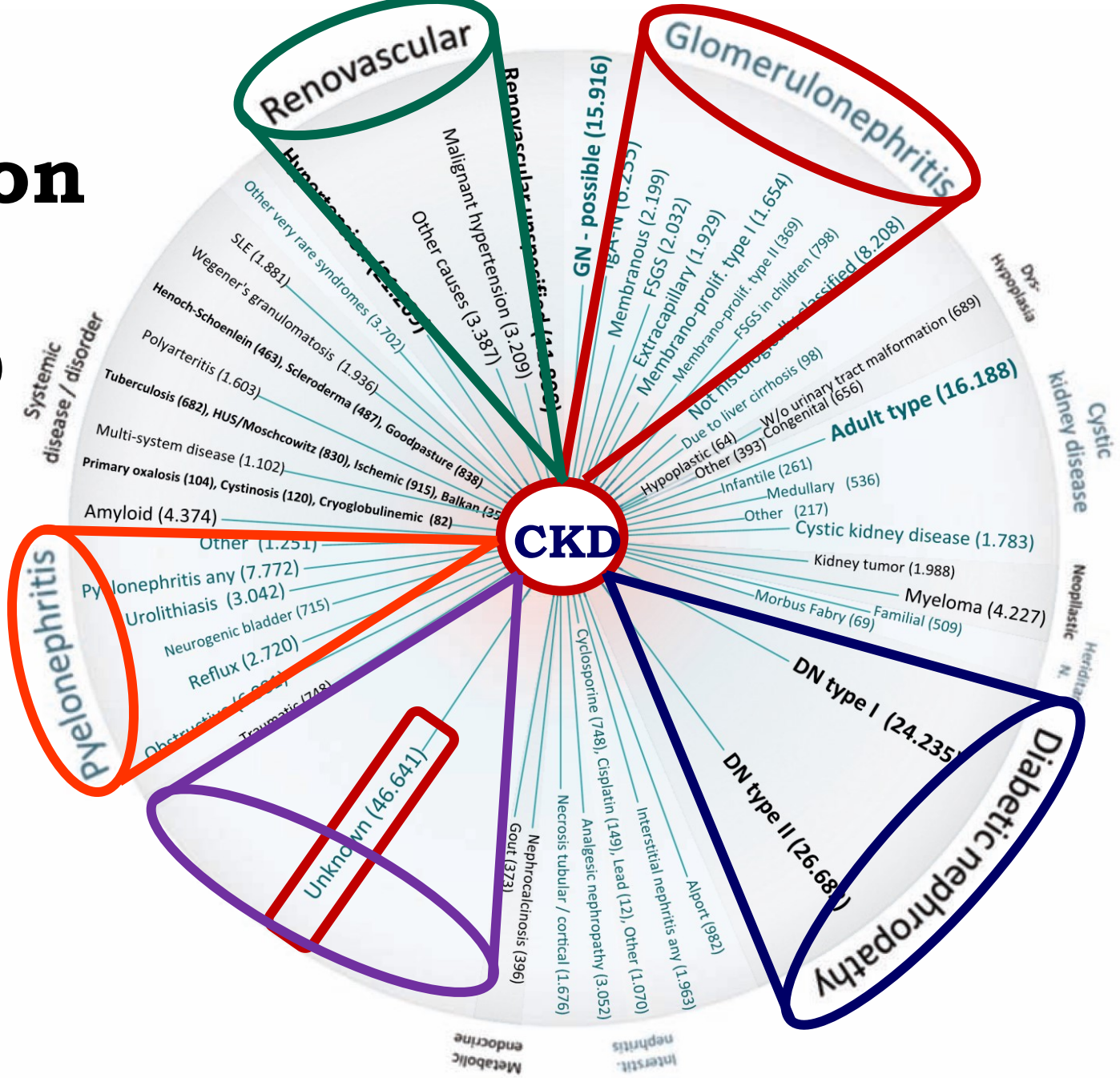
- Hypovolumia
- Hepatorenal
- Cardiac
- Anaesthesia

Common Causes of AKI



Lancet 2019

Common Causes of CKD



Numbers in parentheses represent number of patients

European Renal Association Data

Causes of Kidney Disease: AKI vs CKD

Group of causes	AKI	CKD
Pre-Renal		
	▪ **Hypovolemia**	▪ Cardio-renal syndrome
	▪ hypotension	▪ Hepato-renal syndrome
	▪ Post-surgery	▪ Ischemic Nephropathy
Renal		
	▪ **Acute Tubular Necrosis**	▪ **T2DM**
	▪ Acute Glomerulonephritis	▪ **Hypertension**
	▪ Acute interstitial Nephritis	▪ **TID**
	▪ HUS/TTP	▪ **Chronic Glomerulonephritis**
	▪ Vascular thrombosis	▪ **Polycystic Kidney**
Post Renal		
	▪ Intra-renal	▪ Intra-renal
	▪ In the wall	▪ In the wall
	▪ Outside wall	▪ Outside wall

Clinical Presentation

AKI: Predisposing Factors

- Advanced Age
- Volume Depletion
- Diuretic Use
- Proteinuria
- Myeloma
- Diabetes Mellitus
- Previous cardiac failure
- Previous Renal failure

AKI: History

Drugs

- NSAID
- Aminoglycoside
- Rifampicin
- ACEI
- Cyclosporine
- Chemotherapeutics
- Radio contrast
- Penicillin

Low Renal Perfusion

- Altered consciousness
- Gastroenteritis
- Heart Failure
- Chronic Liver Disease
- Excessive diuretics
- Antihypertensives
- Recent surgery

Systemic Disease

- Fever
- Alopecia
- Joint Pain
- Skin rash
- Oral ulcer
- Raynaud's
- Hypertension

AKI: Examination

Obstruction

- Renal lump
- Percussible bladder
- P/R examination
- External genitalia

Low Renal Perfusion

- Dry skin
- Tachycardia
- Hypotension
- Low JVP
- Signs of heart failure
- Signs of liver failure

Systemic Disease

- Rash, echymosis
- Episcleritis, Uveitis
- Purpura
- Edema
- Hypertension
- Oral ulcer, alopecia
- Vasculitis
- Arthritis

CKD: High-risk groups

- Diabetes
- Hypertension
- F/H of CKD
- Age > 60
- Past history of AKI

CKF: Pattern of Presentation

Asymptomatic

- Medical check-up
- Preoperative

Uremic Symptoms

- Edema
- Nausea, vomiting

Acute Kidney Failure

- With acute factors

Uremic Complications

- Pericarditis
- Chest infection
- Pulmonary edema

Sudden Death

CKD: Clinical Presentation

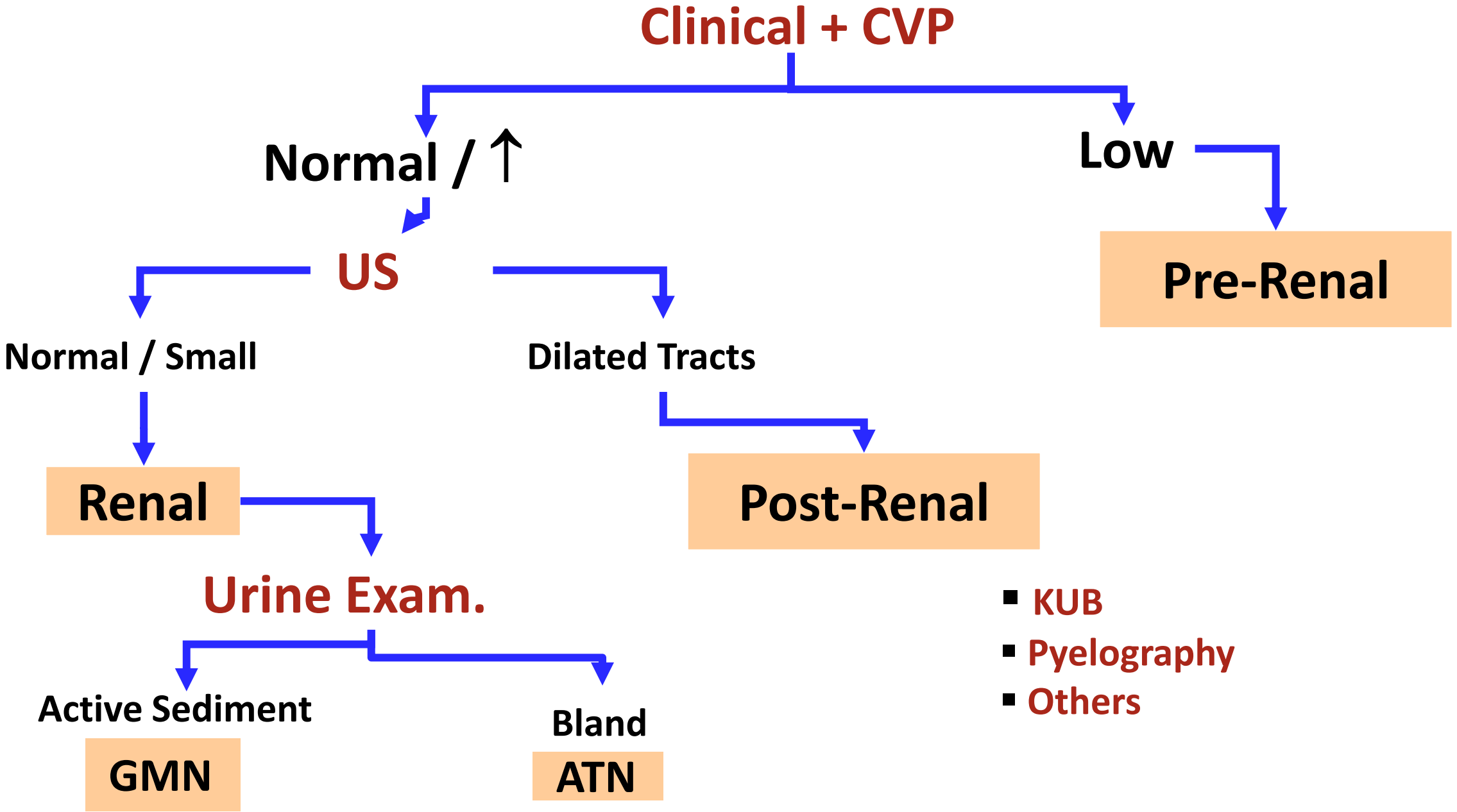
System	Symptoms	Sign
General	▪ Fatigue, ↓ well being	▪ Wasted sallow look
Skin	▪ Dryness, itching	▪ Pallor, ↑ pigmentation, bruise marks, Frost
GIT	▪ Anorexia, nausea, vomiting	▪ GI bleed, uremic tongue
CVS	▪ Edema, dyspnea, chest pain	▪ Hypertension, cardiomegaly, rub
Lung	▪ Fever, dyspnea	▪ Crept
Musculo-SS	▪ Growth failure, bone pain	▪ Deformities, rickets
Misc.	▪ Cramps, insomnia, numbness	▪ Neuropathy, myopathy, tremors, acidosis

Clinical Presentation of Kidney Disease

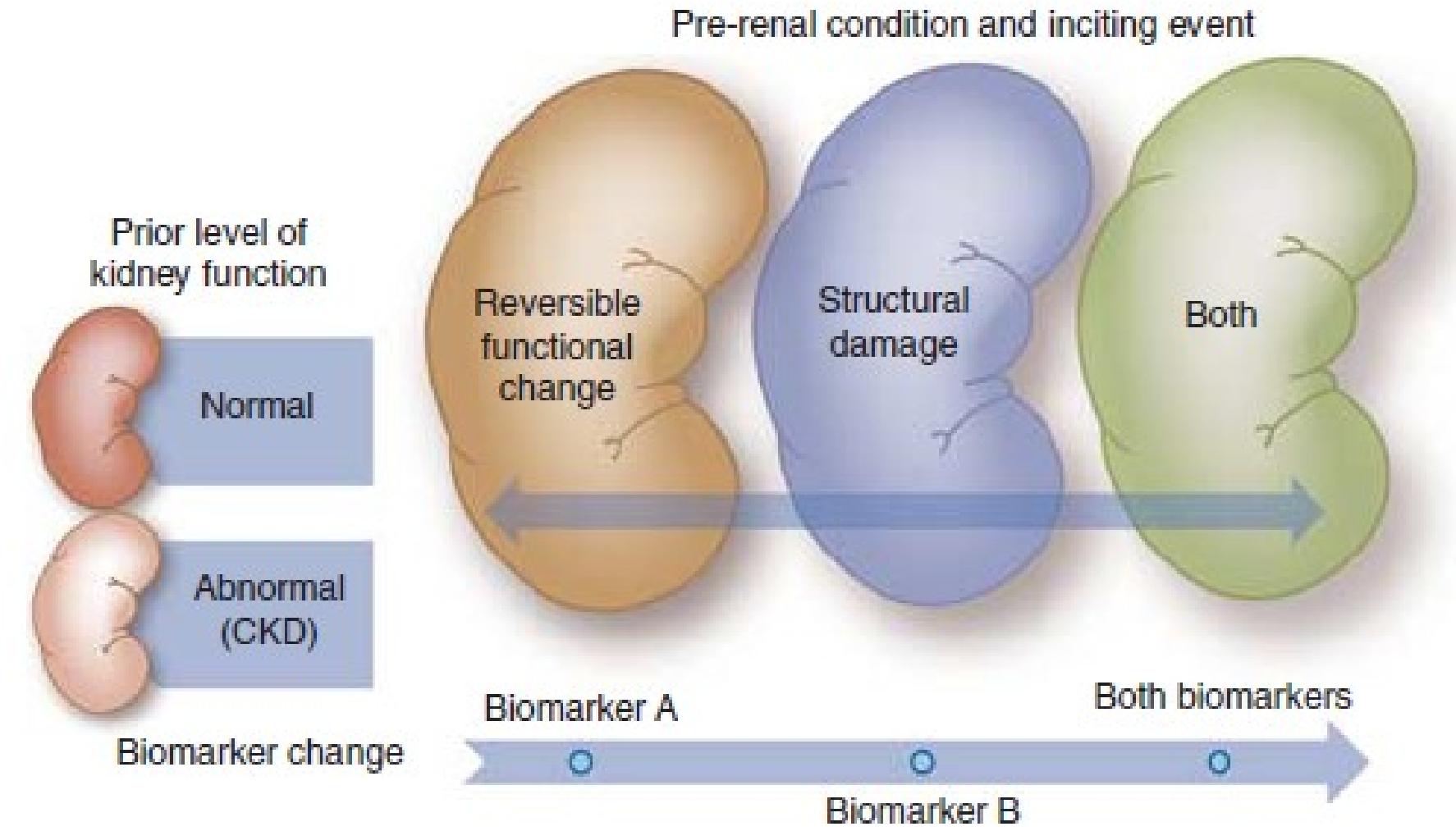
Group of causes	AKI	CKD
Asymptomatic	+	++++
H/0 Drugs + Sepsis	++++	++
Hospital Acquired	++++	±
Diabetes	+	+++++
Connective Tissue	+	+++
Hypertension	+	++++
Hypotension	++++	±
Anemia	+	++++
Bone Disease	±	++++
Acidosis	++++	++
Infections	++++	++
CVD	+	+++

Diagnosis and approach

AKI: Diagnosis & Approach



Biomarkers and AKI



Kidney International (2011) 80, 332 – 334

CKD: Diagnosis and approach

- **Urinalysis** :
  - SG, PH, protein, blood, crystals
  - **Urine microscopy** : casts, cells (eosinophils)
- **Renal imaging** : USG, Xray KUB, IVP, RGP, CT
- **Cause for CKD**
- **Markers of CKD:**
  - Anemia
  - Renal bone mineral disorder
  - Blood gas analysis
- **Viral infection assessment**
- **Renal biopsy**

Management

Management of AKI

Prevent complications

Enhance renal recovery

AKI: Basic principles of management

- Early recognition & initiation of treatment
- Determine & manage primary cause of renal failure
- Identify & correct reversible factors
- Prevent further renal injury
- Ongoing evaluation of the patient
- Anticipate and prevent potential problems
- Supportive therapy till recovery

AKI Management: Components

- Electrolyte Homeostasis
- Volume homeostasis
- Acid-Base homeostasis
- Selecting and dose modification of drug
- Maintaining Nutrition
- Uremia by dialysis
- Newer therapies

ARF: Nutritional Management

Do not withheld Nutrition to decrease symptoms

Adequate nutrition	Improves survival in ICU.
Protein Intake	1.0 – 1.2 g/kg/day Higher in catabolic patients
Calories	30 to 35 Kcal/kg/day
Fluid	Minimum but adequate
Na	Restriction
K	Restriction
Anti-oxidants	supportive
Vitamins	supportive

AKI: Indication of dialysis

Biochemical

- Hyperkalemia > 6.5 meq/L
- Academia < 7.1
- Azotemia Urea > 180 mg%
- Dyselectrolytemia

  Na > 160 meq/L

  Na < 115 meq/L

Clinical

- Oliguria < 200 ml
- Resistant Pulmonary Edema
- Uremic Encephalopathy
- Hyperthermia

Early vs. Late dialysis ?
Conventional vs. CRRT ?

Management of CKD

Retard progression to ESRD

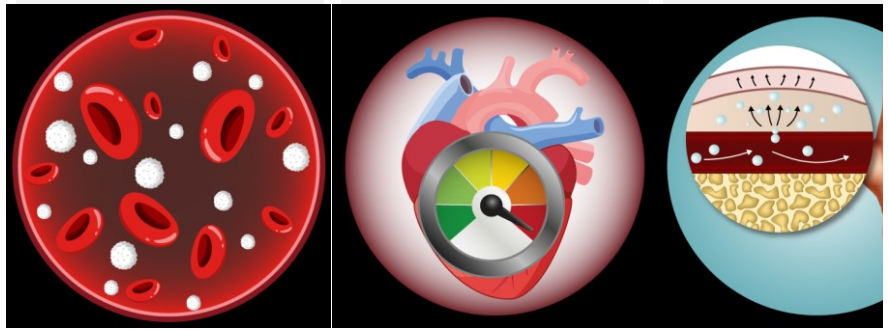
Keep patient asymptomatic

CKD Treatment: Direct and indirect approaches

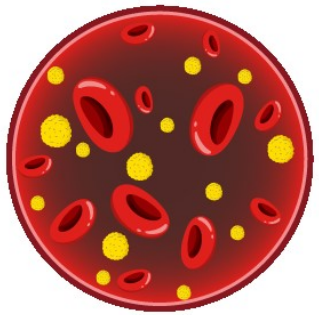
Hyperglycaemi

Hypertension

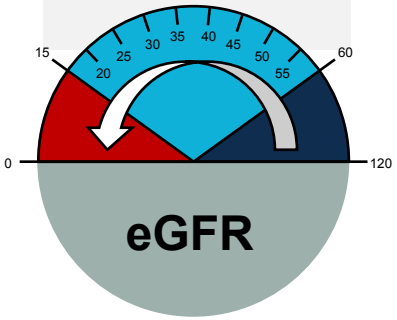
Hypervoler



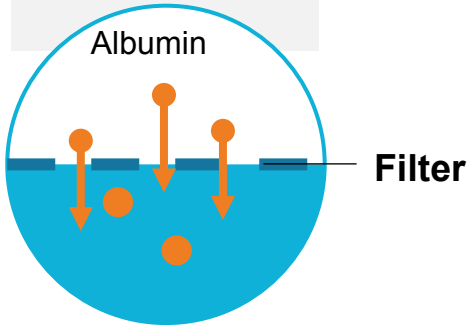
HBa1C > 7



Slowing down eGFR decline



Reducing albuminuria



CKD: Principles of treatment

- Detect & treat acute factors
- Avoid nephrotoxic drugs & further damage
- Adjust medications for degree of CKD

Early referral To Nephrologist

+++

Conservative Therapy

- Hepatitis B vaccination
- Diet & fluid restriction
- Hypertension
- Renal bone disease
- Anemia
- Acidosis
- Vascular access preparation

Renal Replacement Therapy

CKD: Dietary management

- **Calories** — 35 K Cal / Kg
- **Proteins** — Restrict when eGFR ≤ 30 ml
  0.6 G/Kg good quality
  Keto-analogues
- **Salt** — Restrict if Ht. And/or edema
- **Lipids** — 50% of diet
  Poly USA : SFA 2:1
- **K** — 40 - 60 meq/L
- **Vitamin supplementation**

Course of Disease

Acute Kidney Injury: Mortality

- HI Countries 0.3 million/year
- LMI Countries 1.4 million/year

Lewington et al. Kidney Int. 2013

Course of AKI

Two groups of factors play a role

Factors affecting the patient

1. Previous health condition
2. Primary disease causing AKI
3. Severity of renal injury

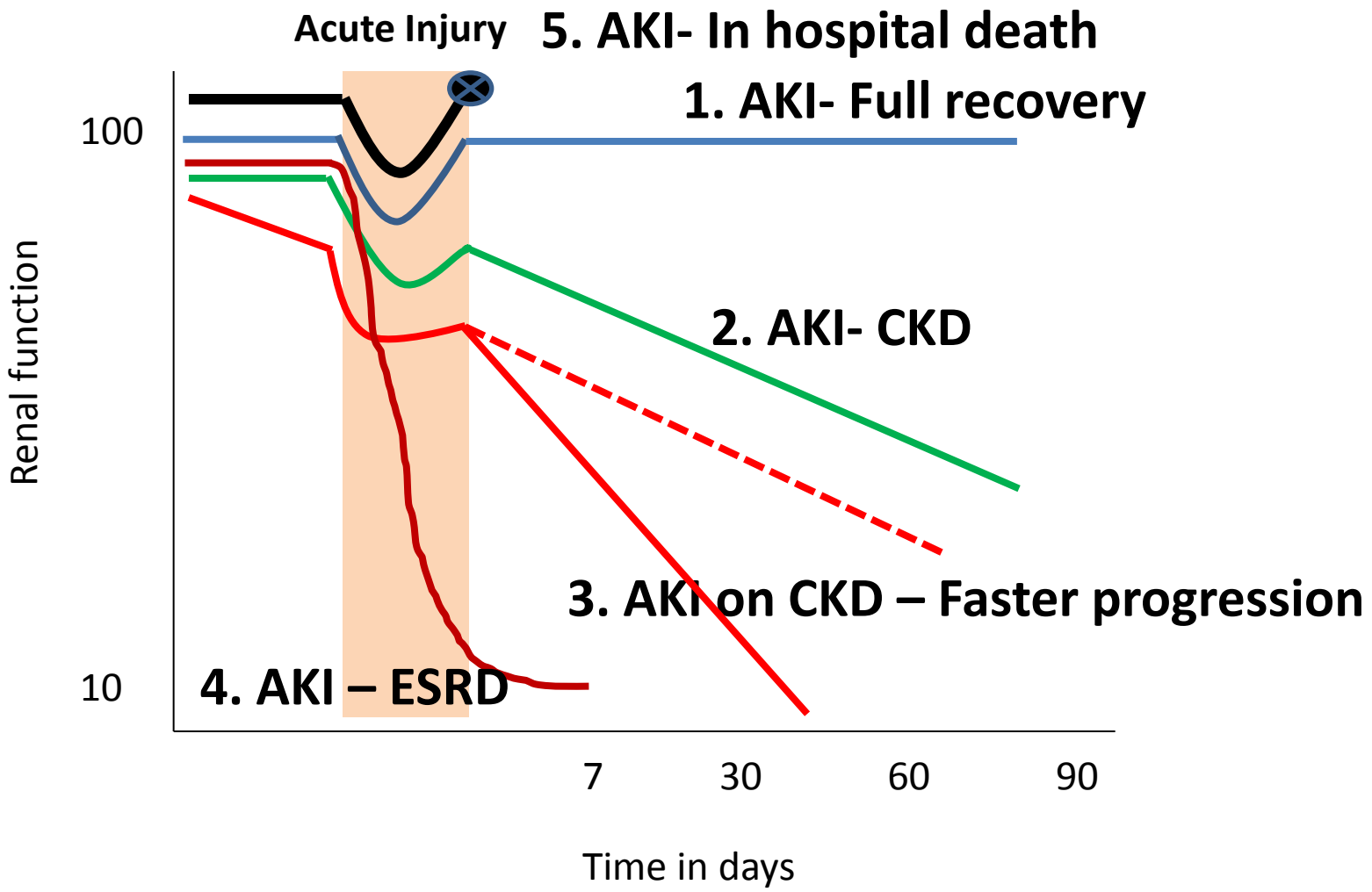
Response of the patient to the insult

1. Systemic Inflammatory Response Syndrome
2. MODS (Multi Organ Dysfunction)

AKI: Bad Prognostic Features

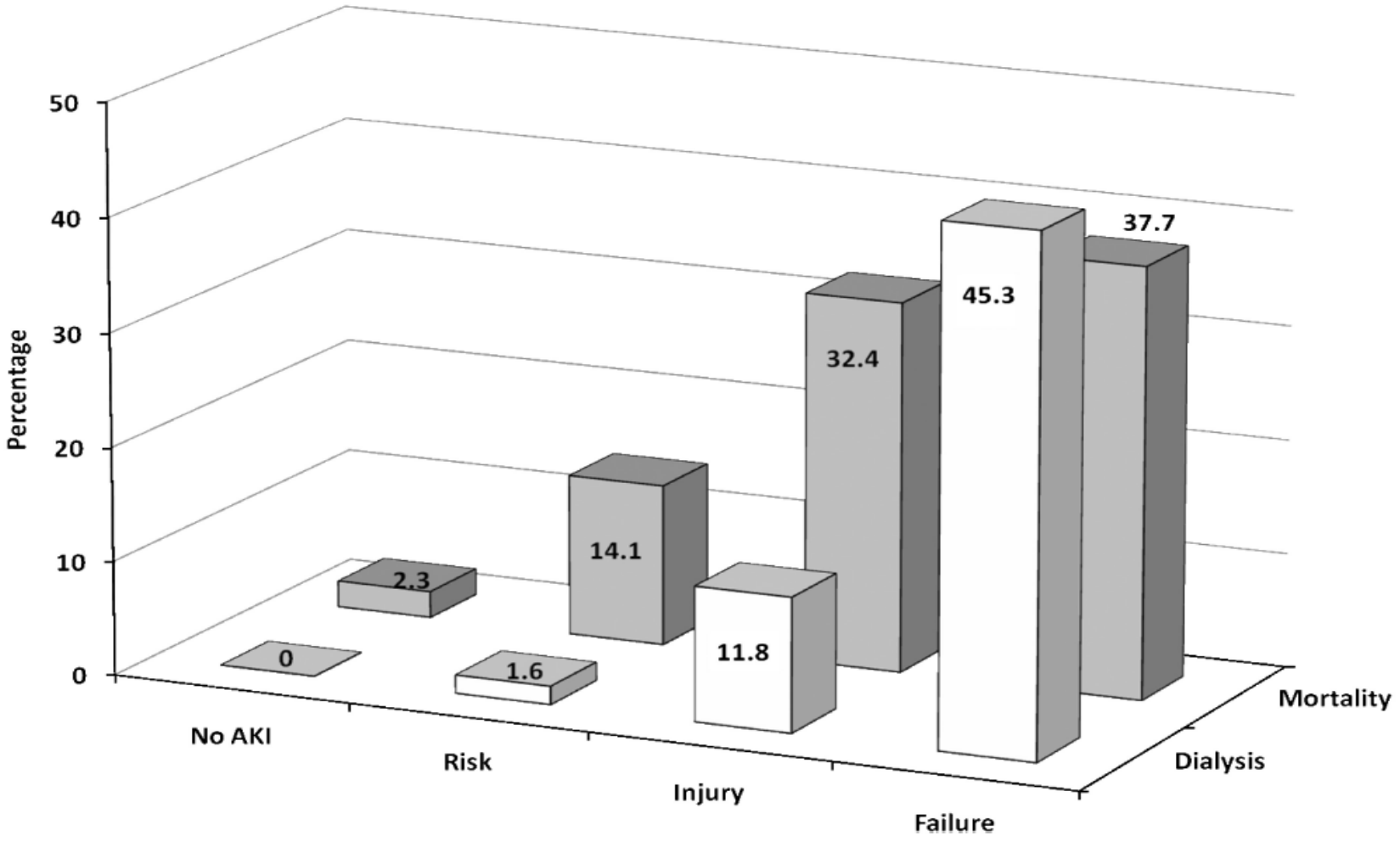
- Increasing age
- Prolonged oliguria
- Presence of sepsis
- A hyper catabolic state
- Need of ventilator support
- Multi-organ involvement especially ARDS

AKI: Outcome



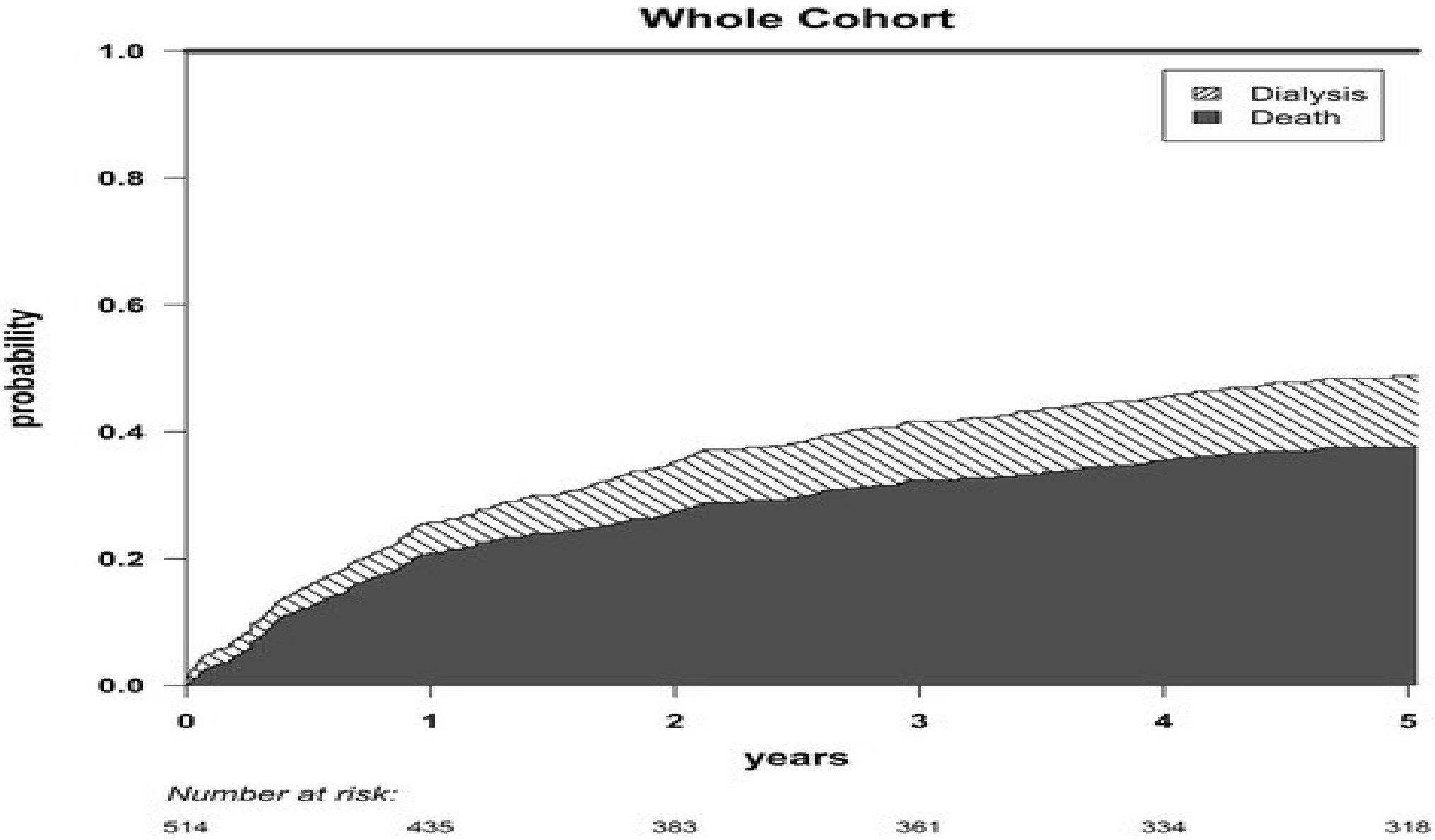
Cerdá J et al. CJASN 2008;3:881-886

Stage of AKI Predicts Mortality

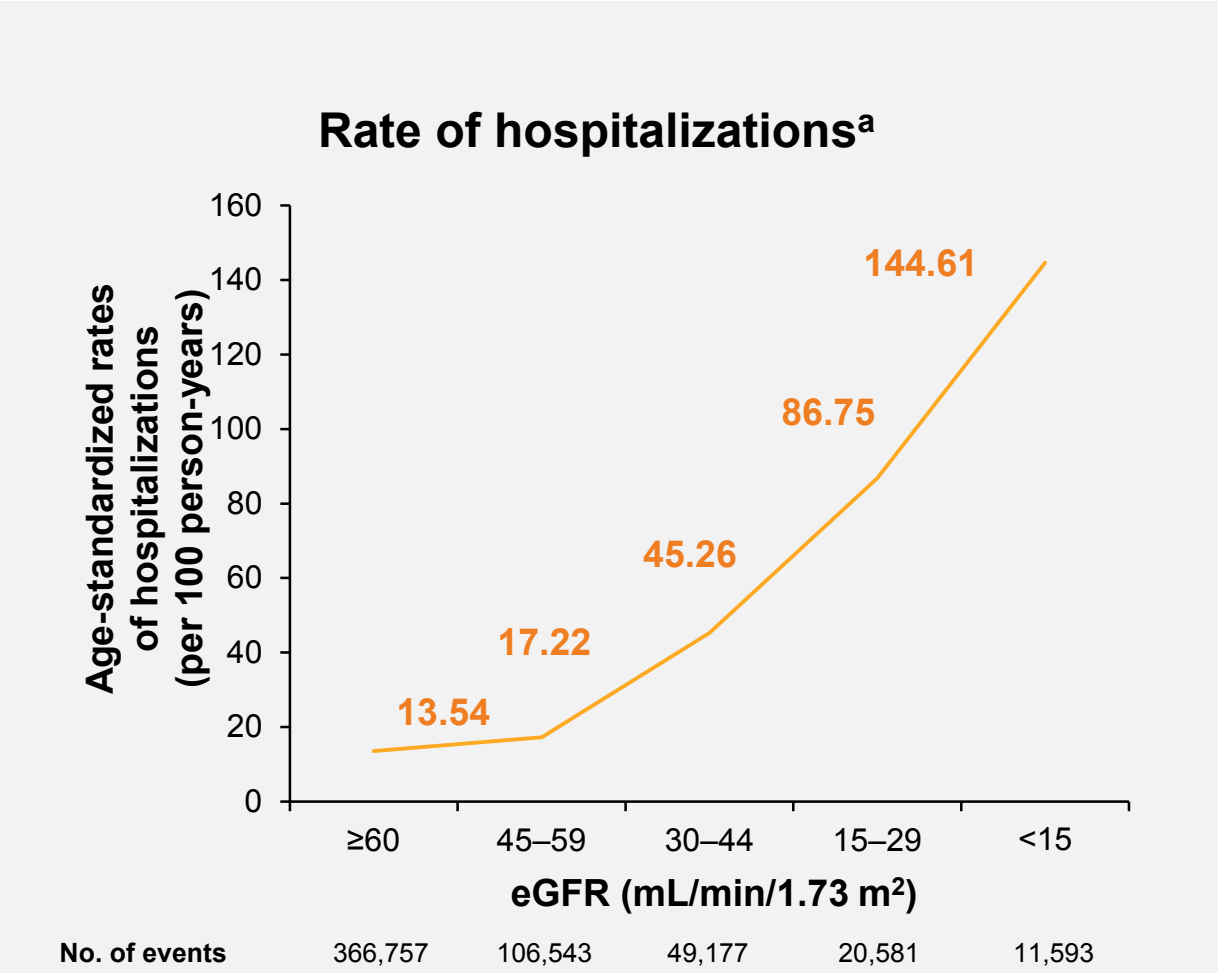


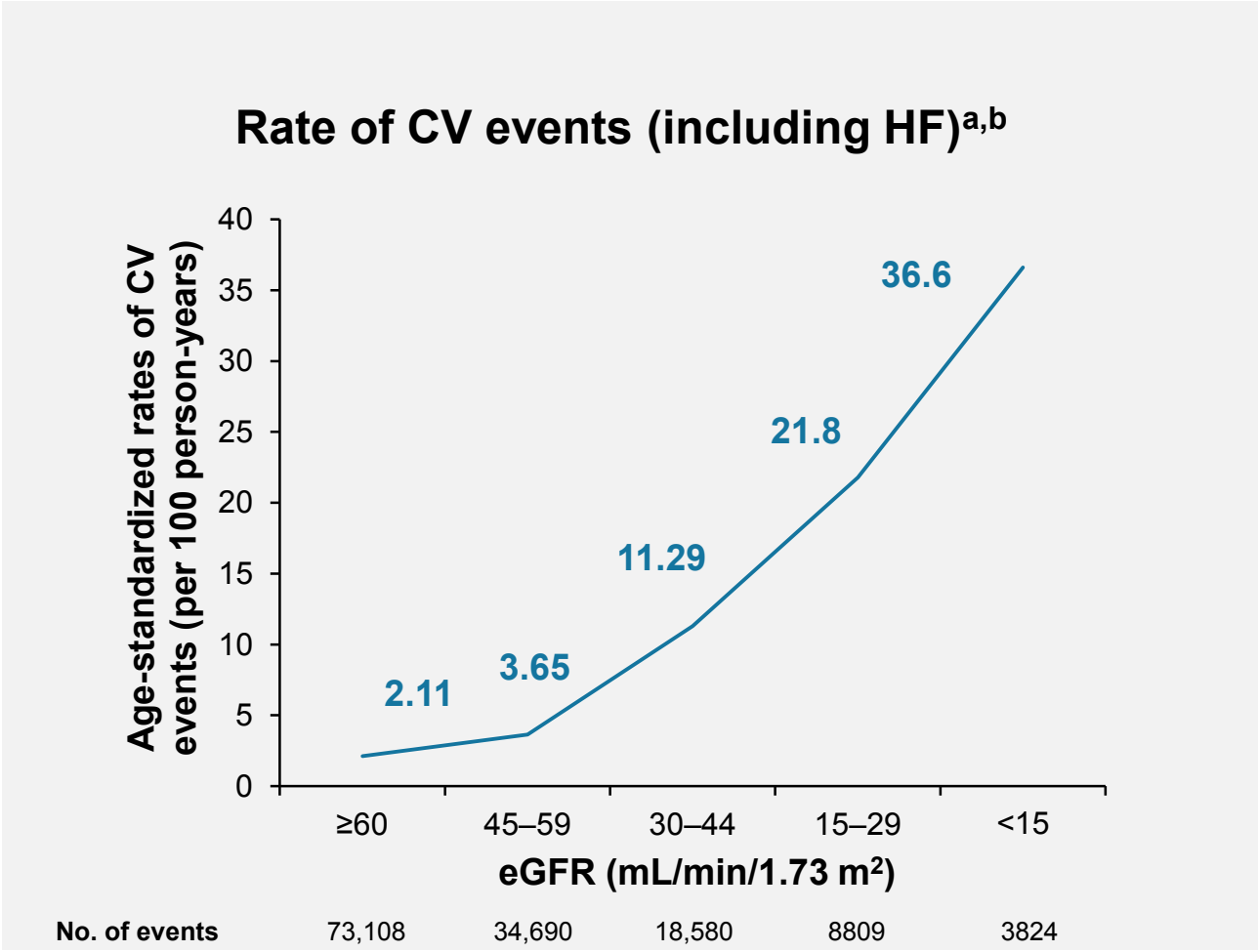
Basu G et al: AKI in tropical acute febrile illness in a tertiary care centre—RIFLE criteria validation: NDT. 2011.26: 524-531

Outcome of CKD: Mortality

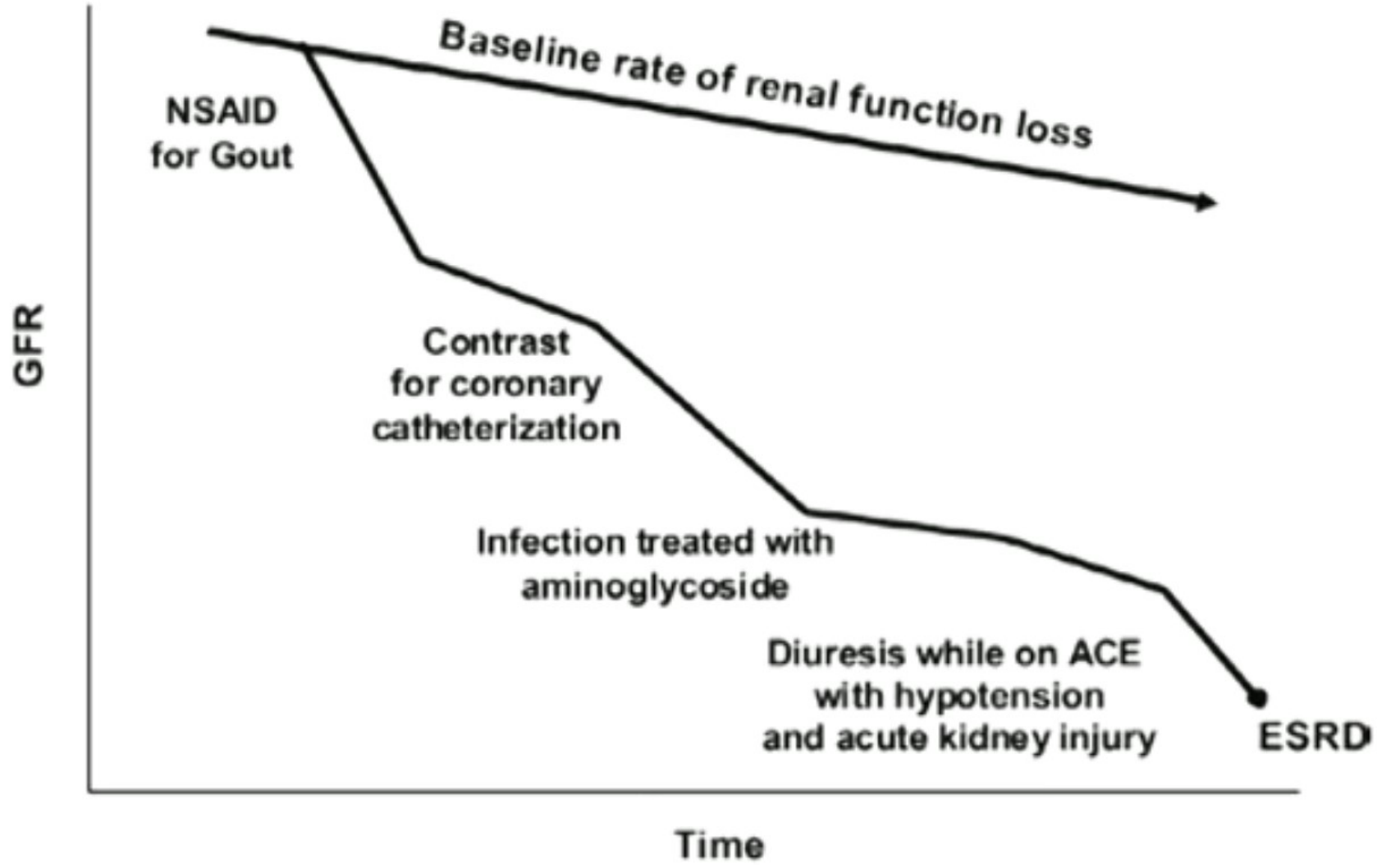


Outcome of CKD: Morbidity



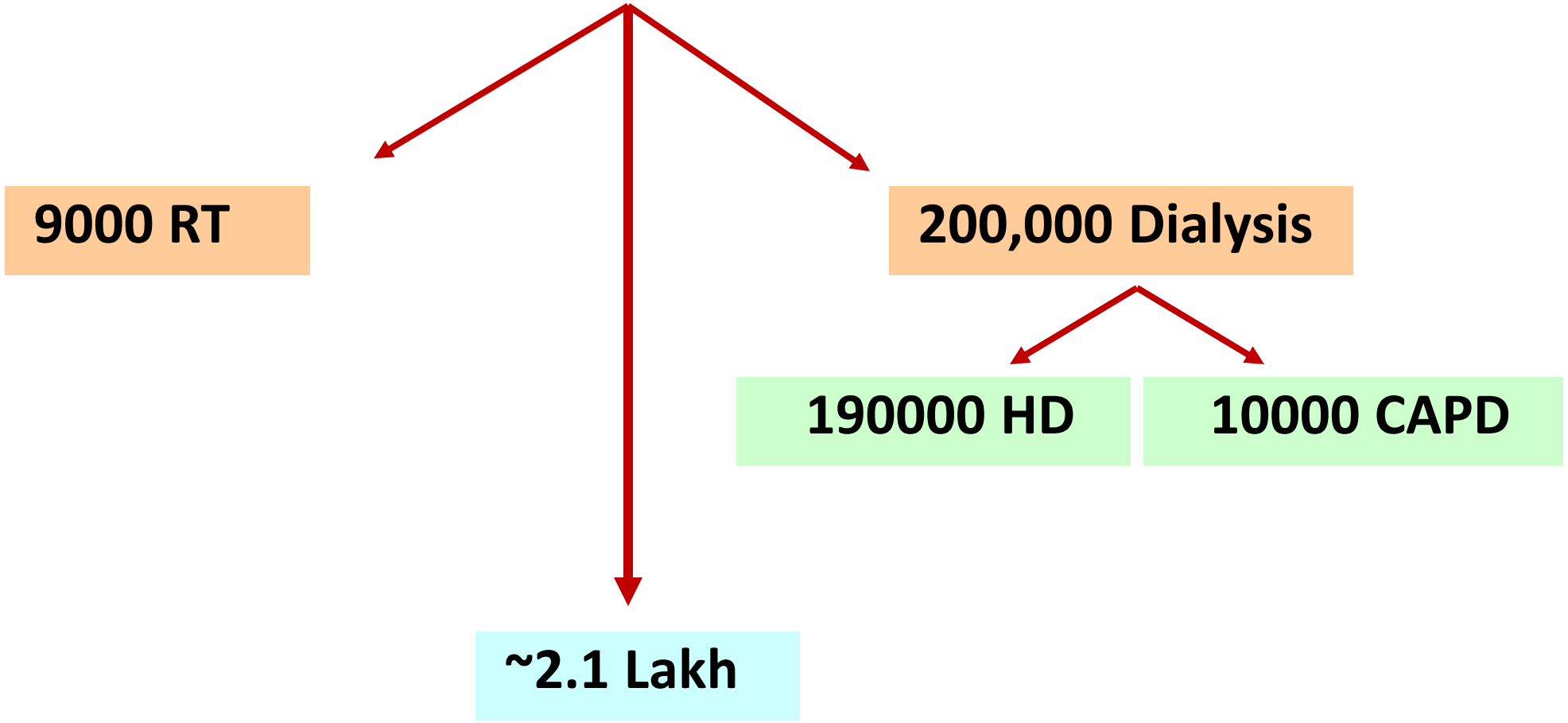


Avoid AKI: Responsible of Primary Care Physician



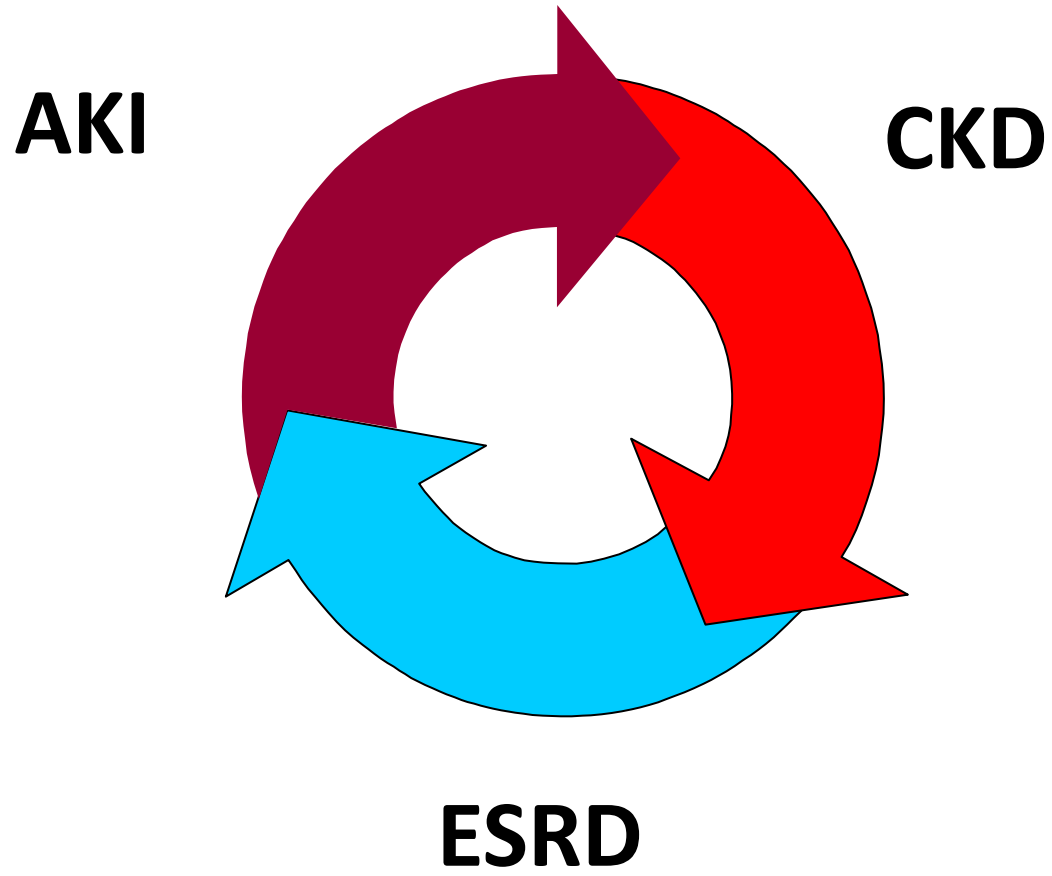
Outcome of ESRD in India (2022)

4.0 Lakh at any time in India requires RRT



Death without appropriate Treatment

AKI- CKD - ESRD Link



Prevention

AKI: Prevention

- Prevention of sepsis
- No drug on own
- Early detection and treatment of acute factors
- Drug dosing adjustment in CKD

Acute Factors for Kidney Injury

- Uncontrolled Hypertension
- Infection
- Dehydration
- Hypovolumia
- Nephrotoxic drugs
- Obstruction
- Hypo- K
- Hyper - Ca

Prevention of CKD: High-risk group

- Diabetes
- Hypertension
- Family h/o of CKD
- Age. 60
- Past history of AKI
- Any specific group
  - African-american in USA
  - Aborginals in Australia

Other than Screening Whom to look for CKD?

1. Edema
2. Unexplained anemia
3. Bone pains and pathological #
4. Family history of CKD
5. Anorexia and vomiting

Earlier intervention: Significant impact

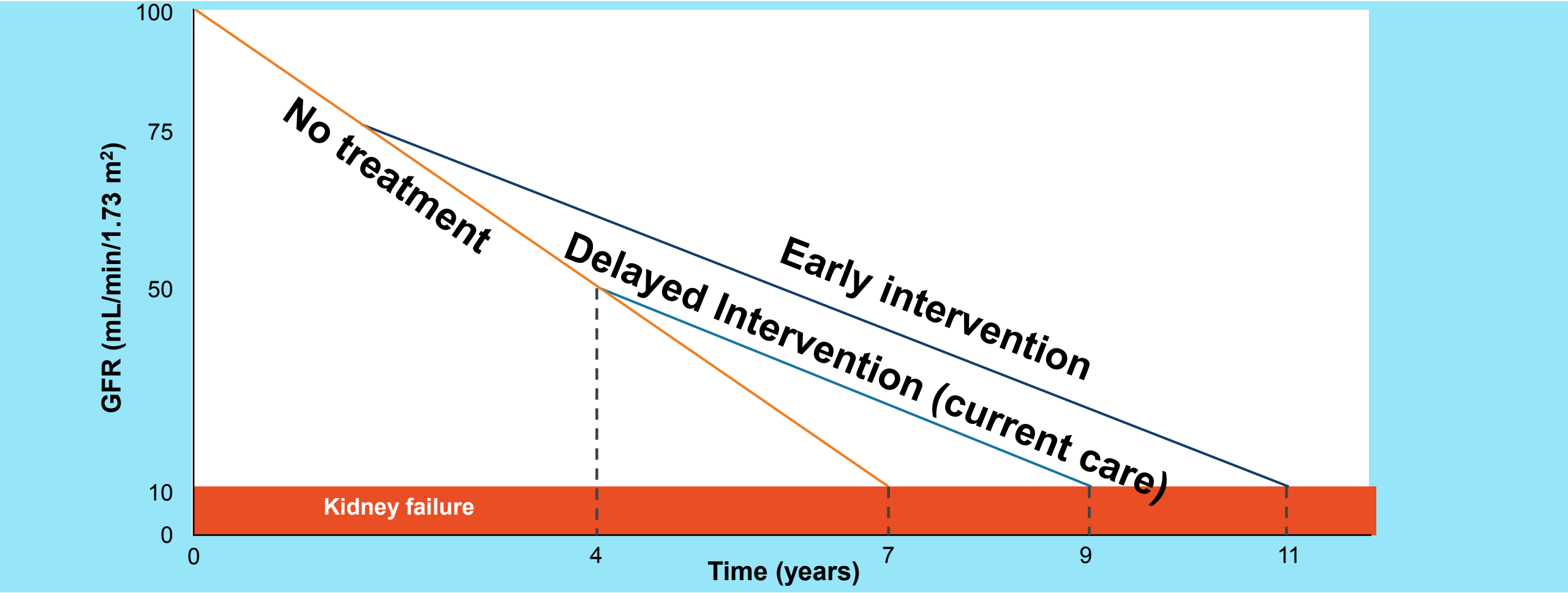


Image adapted from Alabama Department of Public Health
GFR, glomerular filtration rate
Alabama Department of Public Health. Available at https://www.alabamapublichealth.gov/publications/assets/kidneydiseasereport.pdf (Accessed September 2021)

Prevention of CKD: What is required?

- Few Questions
- BP Measurement

Urine Protein Testing

Blood Creatinine + Sugar

- Rs. 100-200 in Pvt. Clinic
- Free in Govt. Hospital

Intervention Possible at detection

1. Life style modifications
2. Blood pressure control
3. Glycemic control
4. Reduction in proteinuria, ACE inhibitors
5. Dietary protein modification
6. Lipid control
7. Avoiding nephrotoxic drugs
8. Early referral to nephrologist

Take home message