

Chronic Kidney Disease and Renal Replacement update

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CAROLINA NEPHROLOGY

BC INTERNAL MEDICINE AND NEPHROLOGY

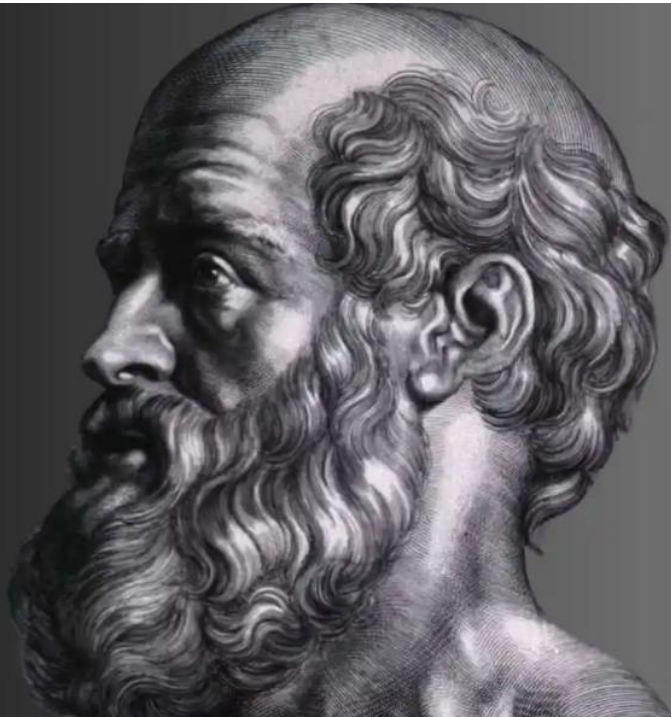
Disclosures

- ▶ No financial disclosures or ownership/investments in any products discussed



**“The
greatest
medicine
of all is
teaching
people
how not to
need it.”**

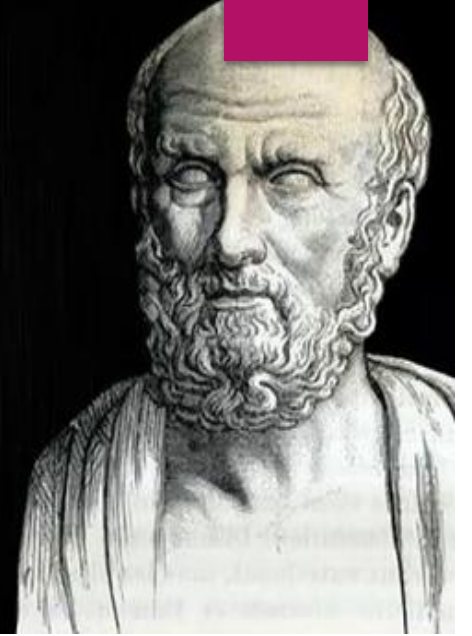
- Hippocrates



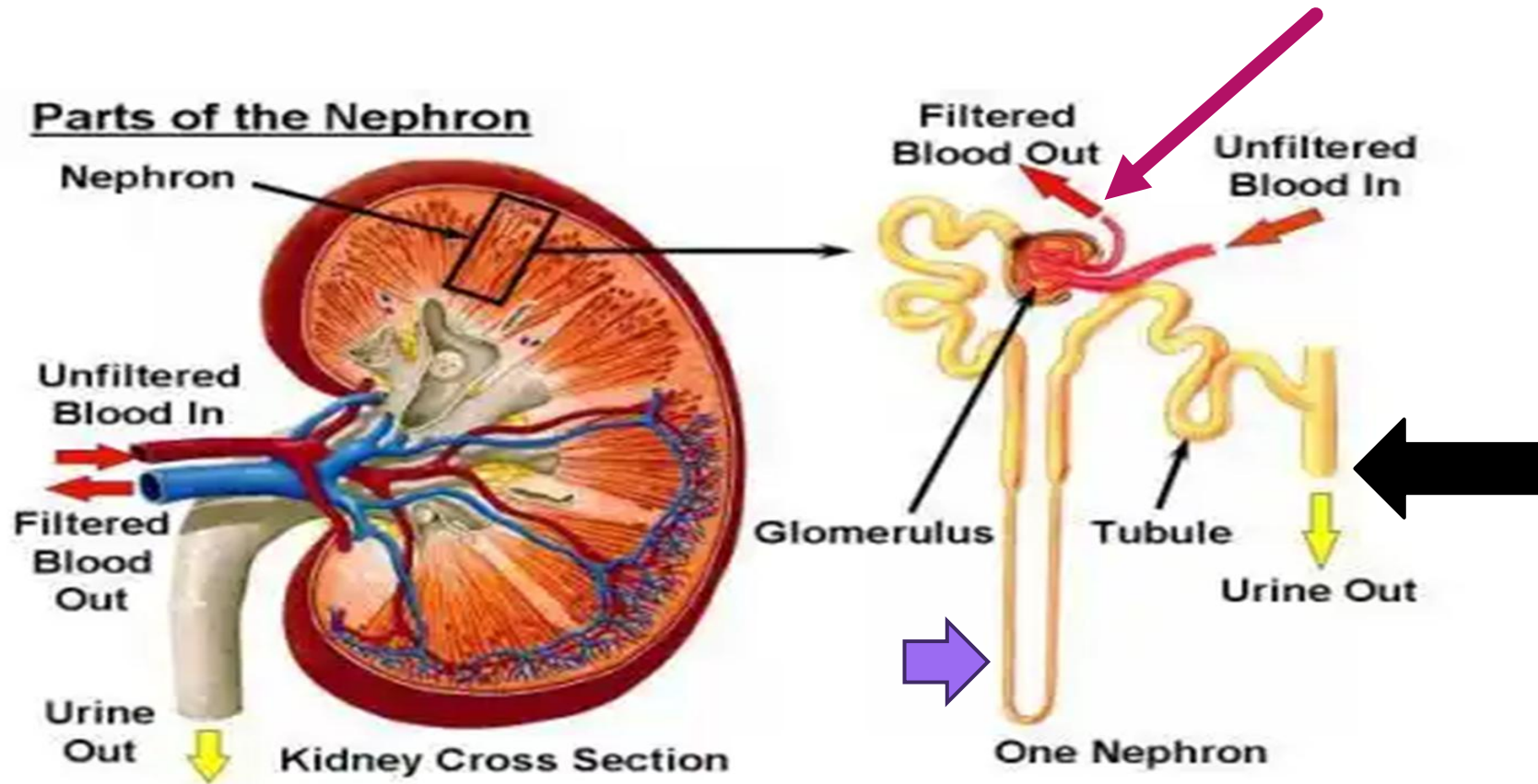
*“If we could give every individual
the right amount of nourishment and exercise,
not too little and not too much,
we would have found the safest way to health.”*

Hippocrates

Physician : 460 BC - 370 BC



Kidney Anatomy



Chronic Kidney Disease (CKD) Epidemic

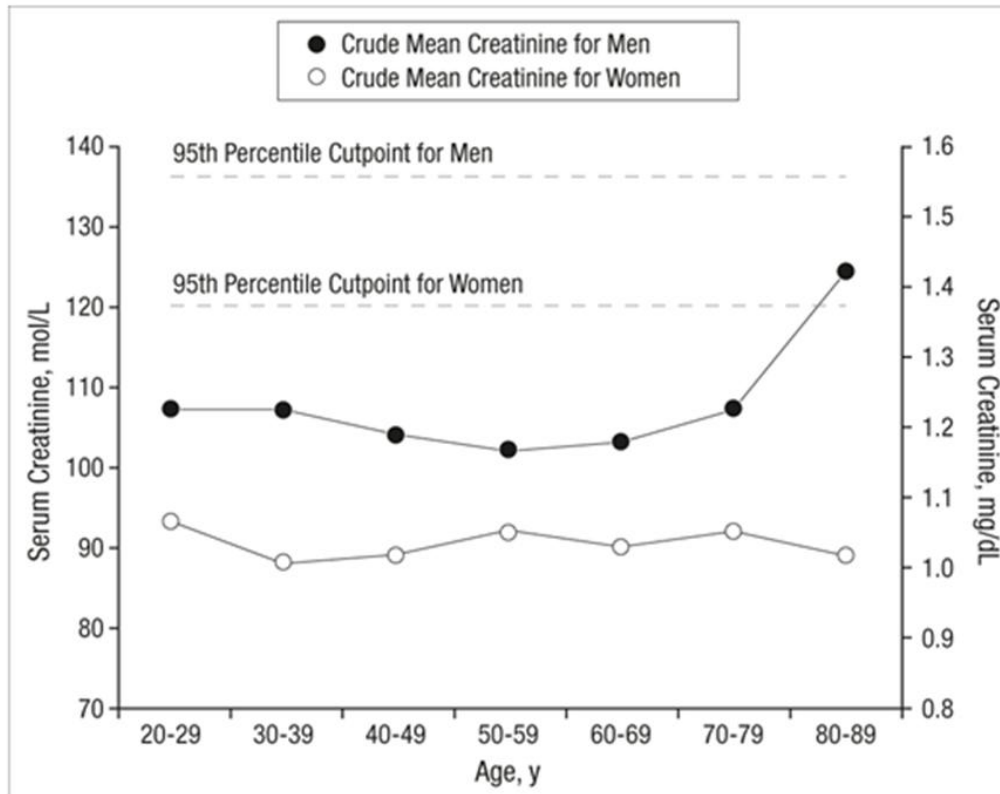
- ▶ ~38+ million Americans w/ CKD (10x AF), \$87+ billion/yr (2023 CDC)
- ▶ 1 in 7 adults will be diagnosis with chronic kidney disease, slightly more common in women than men
- ▶ CKD is most common in patients ≥ 65 yoa (+3x), 45-64 yoa (2x) and 18-44 yoa
- ▶ CKD is most common in non-Hispanic Black adults, affects equally non-Hispanic Asian adults and Hispanic adults
- ▶ 9 in 10 adults do not know or have not been told they have CKD
- ▶ 1 in 3 adults do not know or have been told that they have SEVERE CKD

| CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A) | | | | Albuminuria categories | | |
|--|-----|----------------------------------|-------|--|---|--|
| | | | | Description and range | | |
| | | | | A1 | A2 | A3 |
| | | | | Normal to mildly increased <30 mg/g <3 mg/mmol | Moderately increased 30–299 mg/g 3–29 mg/mmol | Severely increased ≥300 mg/g ≥30 mg/mmol |
| GFR categories (mL/min/1.73 m ²) Description and range | G1 | Normal or high | ≥90 | Screen 1 | Treat 1 | Treat and refer 3 |
| | G2 | Mildly decreased | 60–89 | Screen 1 | Treat 1 | Treat and refer 3 |
| | G3a | Mildly to moderately decreased | 45–59 | Treat 1 | Treat 2 | Treat and refer 3 |
| | G3b | Moderately to severely decreased | 30–44 | Treat 2 | Treat and refer 3 | Treat and refer 3 |
| | G4 | Severely decreased | 15–29 | Treat and refer* 3 | Treat and refer* 3 | Treat and refer 4+ |
| | G5 | Kidney failure | <15 | Treat and refer 4+ | Treat and refer 4+ | Treat and refer 4+ |

■ Low risk (if no other markers of kidney disease, no CKD) ■ High risk
■ Moderately increased risk ■ Very high risk

Chronic Kidney Disease and Microalbumin Stages

Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes care 2022



Reference sample: 95th percentile cutpoints for men and women (dashed lines) and crude mean serum creatinine levels for men (solid line, closed circles) and women (solid line, open circles) per decade of age.

• Serum Creatinine (mg/dl):age and gender

The Framingham Heart Study
 Bruce F. Culleton et al.
 Information
 Arch Intern Med.
 1999;159(15):1785-1790.
 doi:10.1001/archinte.159.15.1785

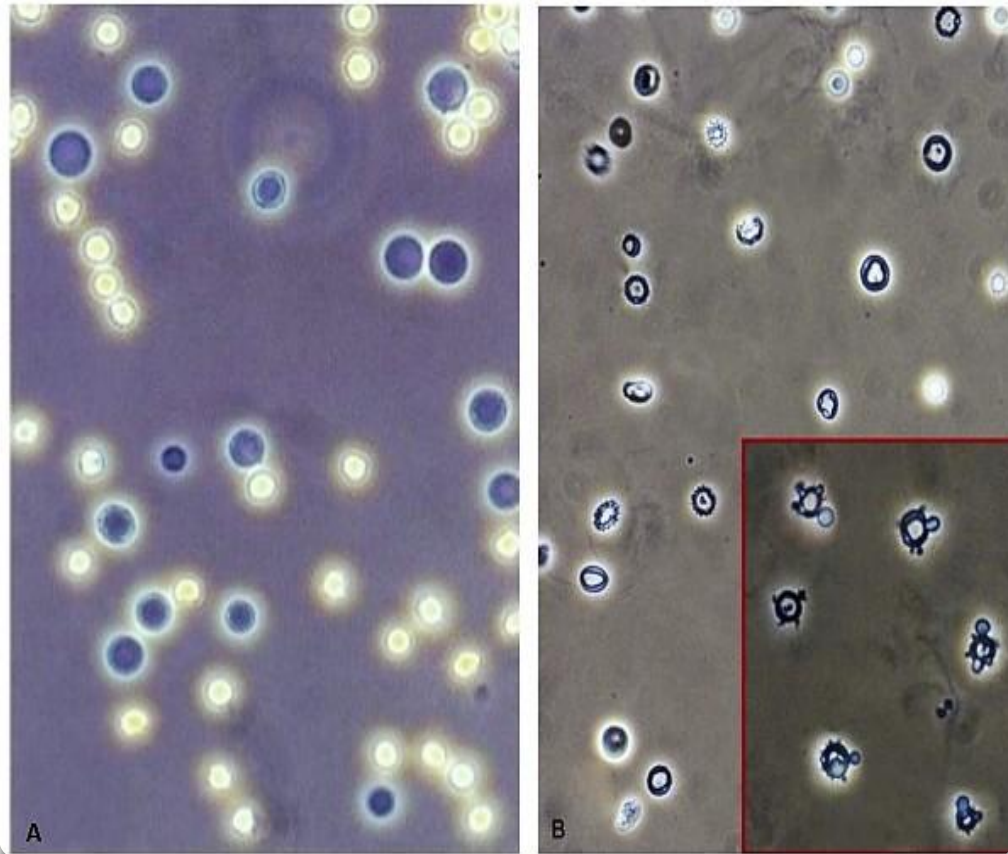
Evaluation

Balkan Nephropathy
Chinese Herb Nephropathy
(CHN)

- ▶ History and physical: Med Rec, BP, HX of foamy urine, weight gain, BLE swelling, fatigue LUTS, dysgeusia, sleep difficulties and cold intolerance
- ▶ **nephron endowment** (birth term and weight), maternal complications
- ▶ history of diabetes (70%), hypertension (20%), CAD/PVD, tobacco use, **obesity, OSA**, family HX of CKD/ESRD, autoimmune (ANA/SLE), vasculitis (ANCA, IgA)
- ▶ inherited diseases (ie ADPKD, Alport Syndrome, Thin Basement Membrane Nephropathy, APOL1 Mediated Kidney Disease)
- ▶ history of nephrolithiasis, nephrectomy, OB/GYN or urologic surgeries
- ▶ infections/STIs , chronic antibiotic use (beta-lactams)
- ▶ antineoplastic medications: cisplatin, cyclophosphamide, immune checkpoint inhibitors
- ▶ NSAID use (combined w/+RF), PPIs, contrast exposure, supplements (**creatinine, weight loss supplements, heavy metals**)
- ▶ environmental -**climate, water source, diet**

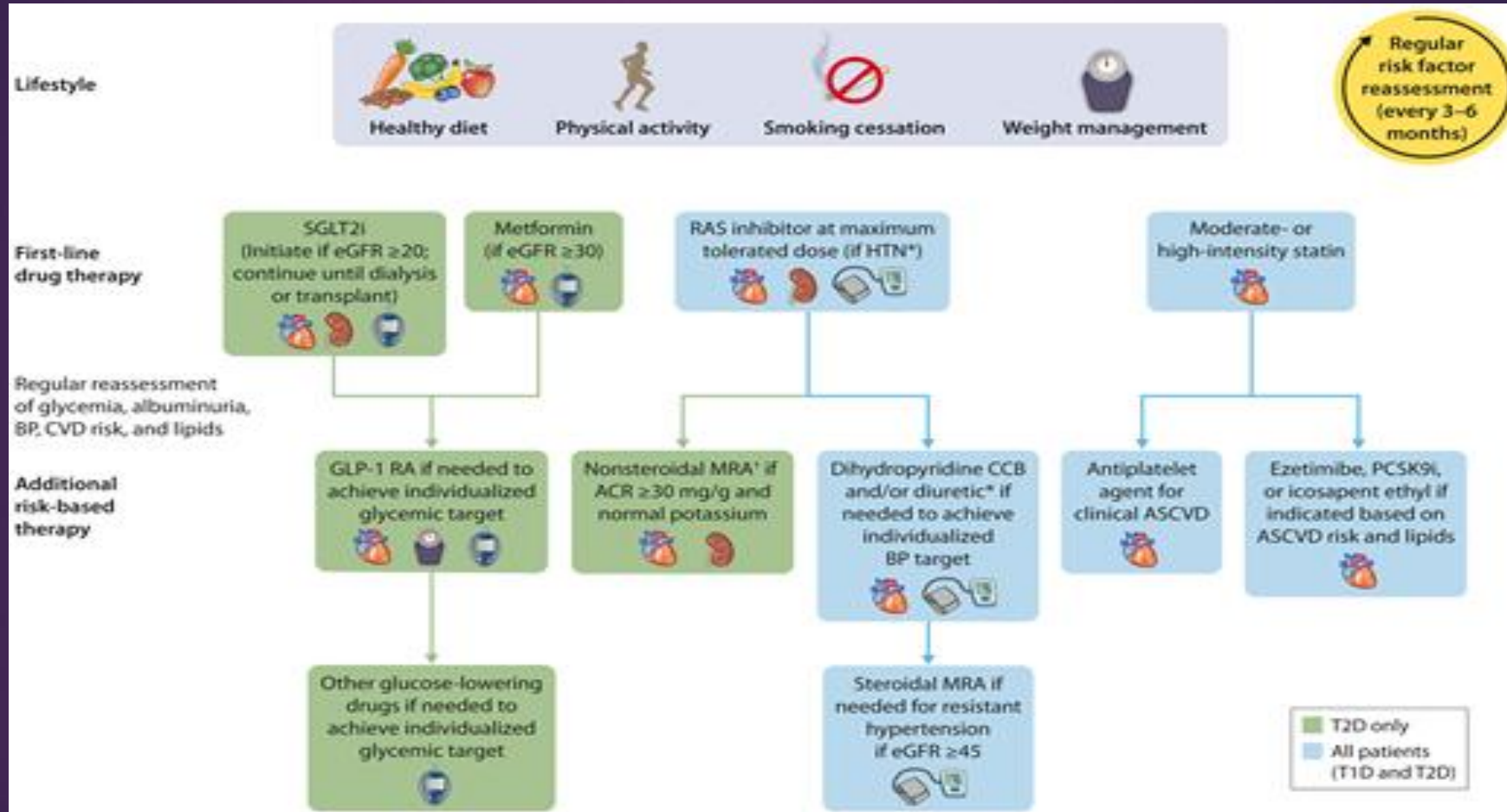
Mesoamerican Nephropathy (MeN)

Evaluation continued



- ▶ metabolic panel, CBC
- ▶ renal ultrasound/ doppler vs CT vs MRI
- ▶ urinalysis with microscopy (dysmorphic RBCs and/or active sediment)
- ▶ *ANA, dsDNA, anti-Smith, C3, C4
- ▶ ANCA or anti GBM AB
- ▶ * proteinuria- UPCr (>0.5g/d>>> 24 hour urine protein)
- ▶ * UPEP, SPEP w/ immunization and SFLC
- ▶ HIV, Hep C and Hep B screen

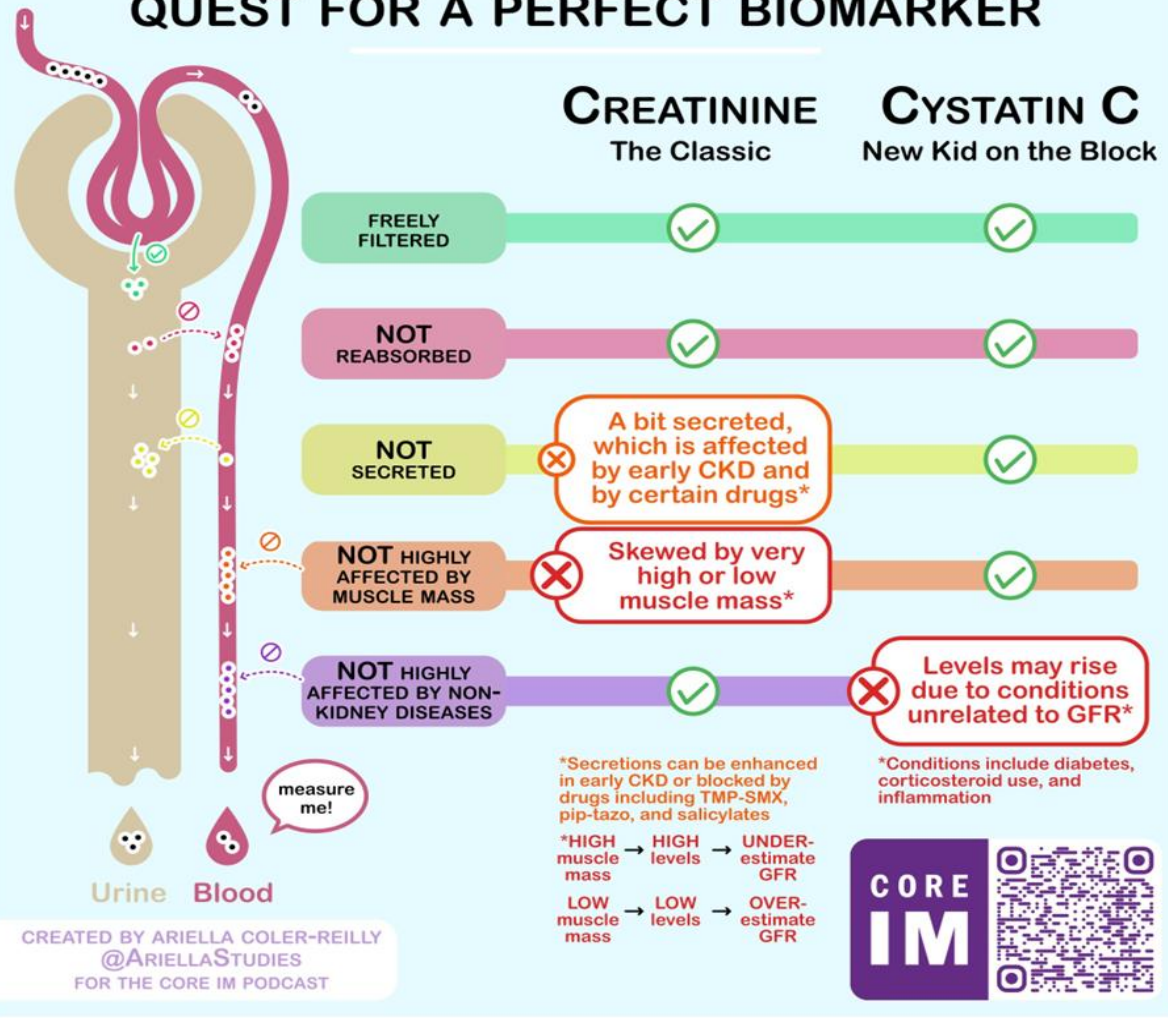
Goal Directed Management Diabetes Mellitus



Estimation of Renal Function

- ▶ **Basic metabolic panel**
- ▶ **24-hour urine creatine clearance ($\text{CrCl} = \text{Ucr mg/dl} \times 24\text{h L/d} / \text{Scr mg/dl}$),
eGFR = $\text{CrCl} + \text{Curea}/2$ (applicable eGFR < 45 ml/min)**
- ▶ **Iothalate and Iohexol (\$\$\$, radioactive, complicated)**
- ▶ **Inulin (\$\$\$ and accurate, complicated)**
- ▶ **Cystatin C**
 - ▶ **CKD-EPI creatinine-cystatin C equation (2021), NKF, ASN, KDIGO**
 - ▶ **https://www.kidney.org/professionals/kdoqi/gfr_calculator**
 - ▶ **<https://www.mdcalc.com/calc/3939/ckd-epi-equations-glomerular-filtration-rate-gfr>**

ESTIMATED GLOMERULAR FILTRATION RATE: QUEST FOR A PERFECT BIOMARKER



CREATED BY ARIELLA COLER-REILLY
@ARIELLASTUDIES
FOR THE CORE IM PODCAST

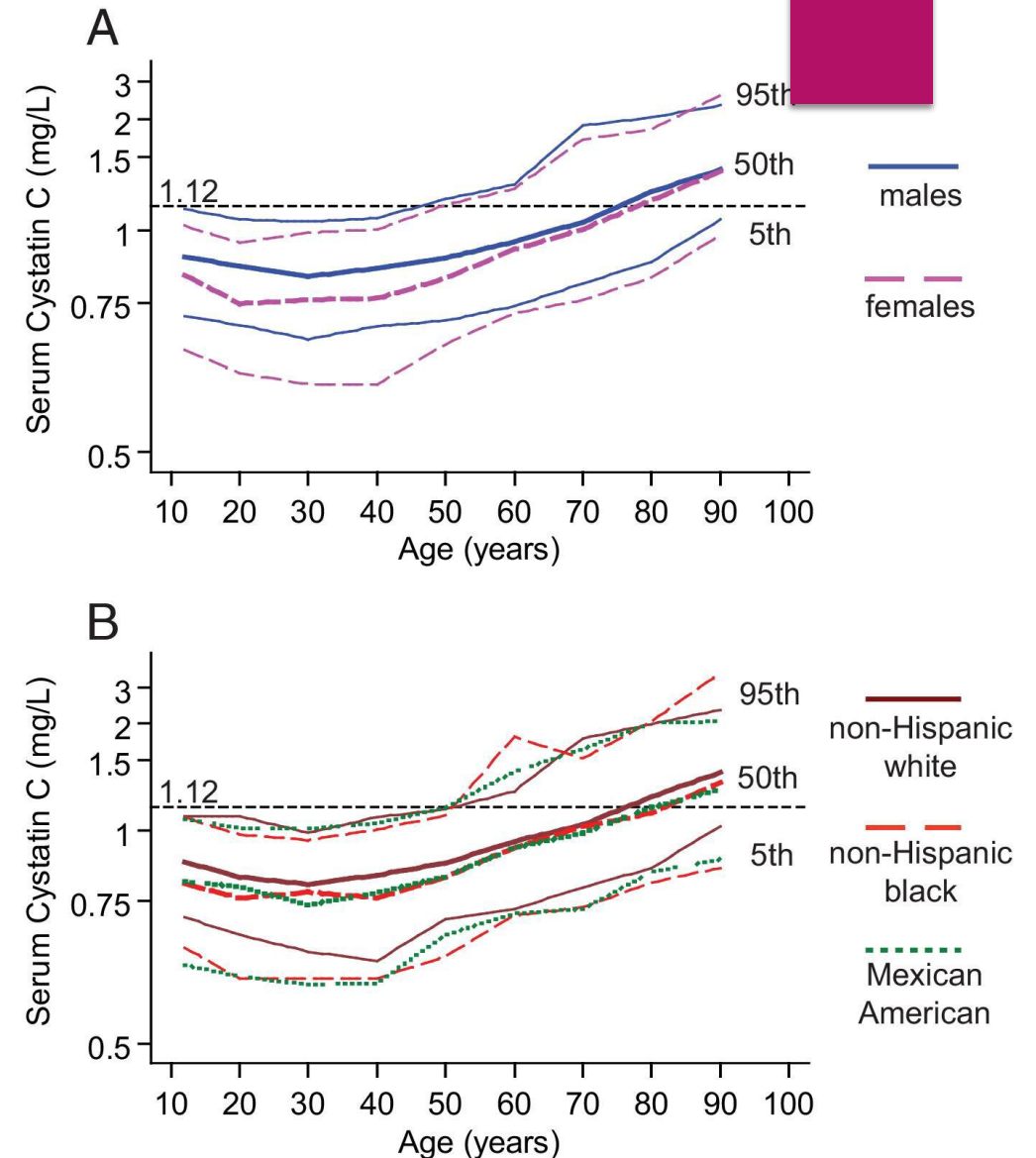
Serum Creatinine and Cystatin C

Cystatin C: age, gender, race

► Serum Cystatin C in the United States: The Third National Health and Nutrition Examination Survey (NHANES III)

Anna Köttgen MD, MPH, et al

American Journal of Kidney Diseases, 2008-
03-01, Volume 51, Issue 3, Pages 385-394



Cystatin C application

- ▶ High muscle mass ****
- ▶ Creatine supplements ****
- ▶ Low muscle mass (eg, children, chronic heart failure, amputations, neuromuscular disease)
- ▶ High animal protein diet ****
- ▶ Vegetarian diet ****
- ▶ Liver disease/ hypoalbuminemia
- ▶ Extreme frailty
- ▶ Drug dosing>>>> Antibiotics

Case

- ▶ 45 yo **Hispanic male** AD5M (1SG) 20+ yrs service with multiple mobilizations, no profiles, presents for SRP EUCOM
- ▶ PMHX- w/ **CKD 3(eGFR ~50), HX of nephrotic range proteinuria (4.5g/d), HX of FSGS (BX proven APR2010, sCr 3.8 mg/dl)**, HTN, HLD, BPH, SAR and multiple arthralgias (back, shoulder, ankle, neck), vitamin D def
- ▶ PSHX- wrist, **kidney BX with FSGS (Nephrology /MAMC recommend SM for retention OCT2010)**
- ▶ Meds: **Telmisartan 80mg**/ HCTZ 25mg daily, atorvastatin 40mg daily, D2 50000u qwk, finasteride 5mg daily, fluticasone NS BID, montelukast 10mg daily, cetirizine 10mg daily, lidocaine patch daily, APAP prn
- ▶ Family HX- non-contributory
- ▶ Social HX- no tobacco, ETOH or supplements
- ▶ Allergies: NKDA, cough documented with ACEi/Lisinopril

Case continued

- ▶ BP 116/76 HR 58, BMI 27.1
- ▶ Physical exam unremarkable
- ▶ SEP 2023 CHOL 207 LDL 143 HDL 49 TRIG 76
- ▶ OCT 2022 **Scr 1.4**, eGFR 64 ml/min/1.73, K 4.5 A1c 5.5, UPCR 0.1 g/g
 - ▶ Hgb 16, Hct 48.2, Plt 230, WBC 6.7
- ▶ SEP 2023 **Scr 1.7**, **eGFR 50 ml/min/1.73**, K 4.3, A1c 5.5, UPCR 0.1 g/g
 - ▶ Hgb 15.2, Hct 45.6, Plt 225, WBC 4.9
- ▶ JAN 2024 **Scr 1.7**, **eGFR 50 ml/min/1.73**, **K 5.1**, **UA bland**
- ▶ GO or TEMP NO GO????

Case continued

- ▶ FEB 2024 **Renal US/doppler: medical renal disease, no hydronephrosis, masses or calculi, normal size and RI WNL**
- ▶ SEP 2023 **Cystatin C 0.78**
- ▶ SEP 2023 **Scr 1.7, eGFR 50 ml/min/1.73**, K 4.3, a1c 5.5, UPCR 0.1 g/g
 - ▶ Hgb 15.2, Hct 45.6, Plt 225, WBC 4.9
- ▶ JAN 2024 **Scr 1.7, eGFR 50 ml/min/1.73, K 5.1, UA neg protein/blood**

kidney.org/professionals/kdoqi/gfr_calculator

MODS Home - MO... Body Mass Index (... DynaMed DFAS myPay | Onli... Defense Travel Syst... Army f

Serum Creatinine: 1.7 mg/dL $\mu\text{mol/L}$

Serum Cystatin C: 0.78

Age: 45 Years

Gender: Male Female

Standardized Assays: Yes No Not Sure

Adjust for body surface area: Yes No Not Sure

Calculate

Results

CKD-EPI creatinine equation (2021) 50 mL/min/1.73m²

CKD-EPI creatinine-cystatin equation (2021) 81 mL/min/1.73m²

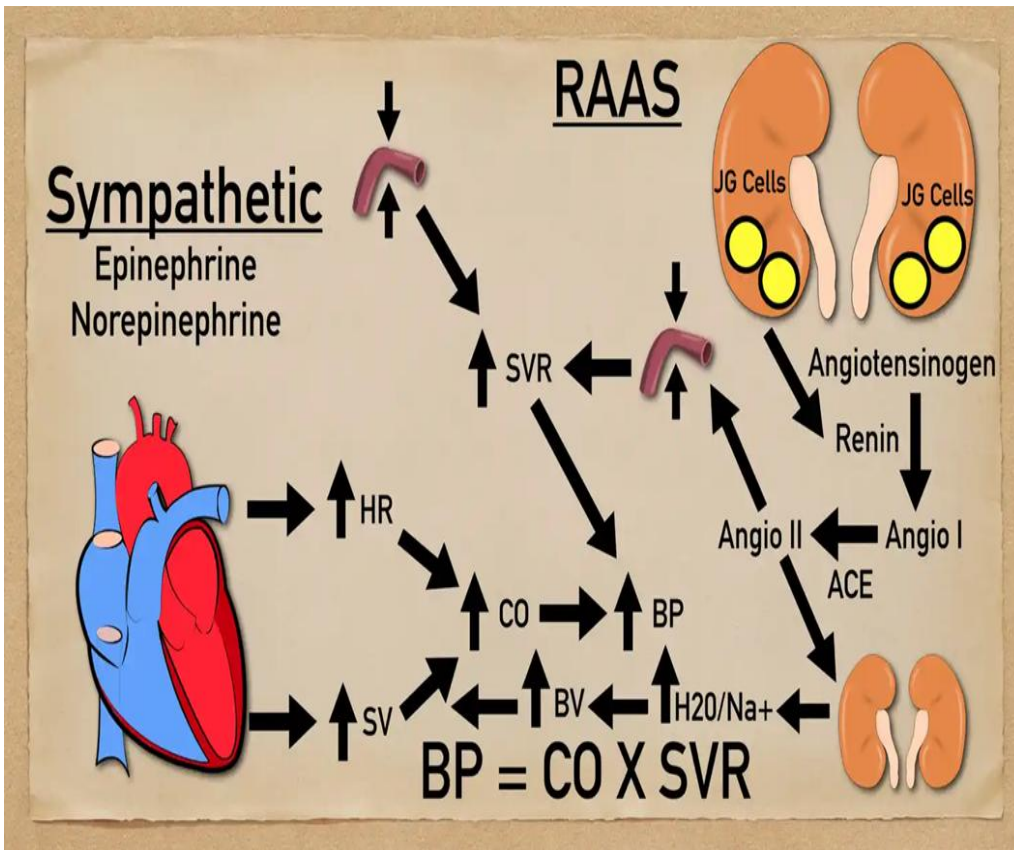
Case continued

Table 1: Target Blood Pressure Goals in Nonpregnant Adults With Diabetes and Hypertension

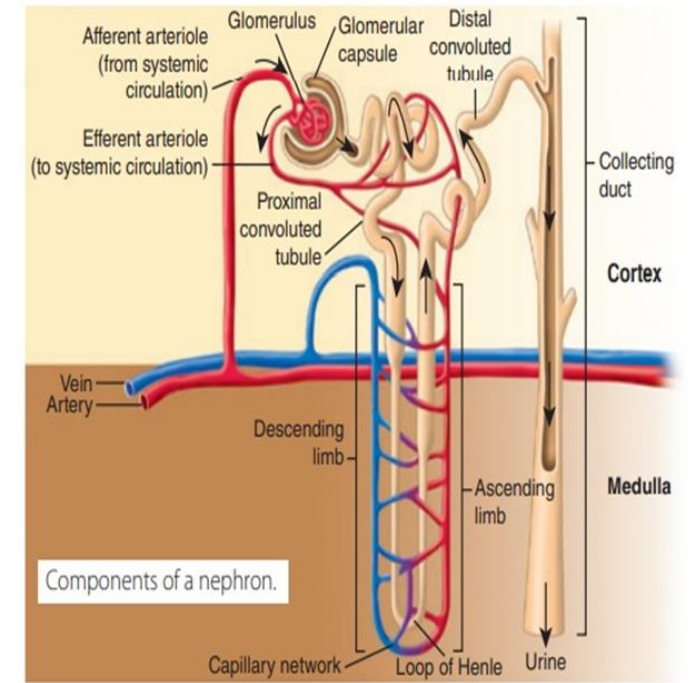
| Organization | Systolic Blood Pressure Goal | Diastolic Blood Pressure Goal | Reference |
|---|--|---|---|
| American College of Cardiology/American Heart Association (ACC/AHA) | < 130 mm Hg (ACC/AHA Class I, Level B-R) | < 80 mm Hg (ACC/AHA Class I, Level C-EO) | J Am Coll Cardiol 2018 May 15;71(19):e127 |
| American Diabetes Association (ADA)* | < 130 mm Hg (ADA Grade B) if safely attainable (on-treatment) <ul style="list-style-type: none"> individualize blood pressure targets through shared decision-making process that incorporates cardiovascular risk, possible adverse effects of anti-hypertensive medications, and patient preferences (ADA Grade B) | < 80 mm Hg (ADA Grade B) if safely attainable (on-treatment) <ul style="list-style-type: none"> individualize blood pressure targets through shared decision-making process that incorporates cardiovascular risk, possible adverse effects of anti-hypertensive medications, and patient preferences (ADA Grade B) | Diabetes Care 2024 Jan 1;47(Suppl 1):S1-S321 PDF |
| Eighth Joint National Committee (JNC 8) | < 140 mm Hg (JNC8 Expert opinion) | < 90 mm Hg (JNC8 Expert opinion) | JAMA 2014 Feb 5;311(5):507, |
| American College of Physicians (ACP) | < 135 mm Hg | < 80 mm Hg | Ann Intern Med 2003 Apr 1;138(7):587, systematic review in Ann Intern Med 2003 Apr 1;138(7):593 |
| European Society of Cardiology/European Society of Hypertension (ESC/ESH) | ≤ 130 mm Hg (ESC/ESH Class I, Level A) | < 80 mm Hg (ESC/ESH Class I, Level A) | Eur Heart J 2018 Sep 1;39(33):3021 |
| Hypertension Canada | < 130 mm Hg (Hypertension Canada Grade C) | < 80 mm Hg (Hypertension Canada Grade A) | Can J Cardiol 2020 May;36(5):596 |

Guideline Directed Blood Pressure Goals

122 M American Adults (2023)
 - ~30% are not on meds
 - ~22% < 130/80 mmHg



1. Lifestyle/DASH/EX/SC
2. ACEi/ARB-SVR
3. D-CCB-SVR
4. Thiazide-like-CO
-loop, CA-inhibitor
-SGLT2i
5. MRA-CO/SVR
6. Alpha blocker-SVR
7. csBB or non-csBB-
CO/SVR
8. Diltiazem/Verapamil-
CO/SVR
9. Vasodilators-SVR



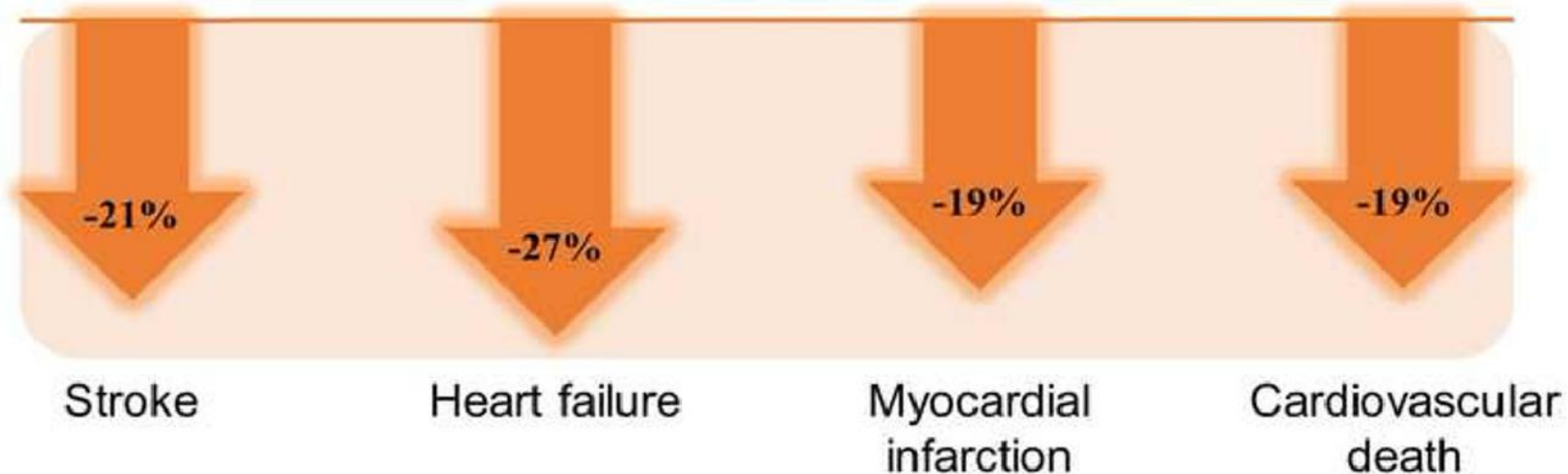
Hypertension $BP = CO \times SVR$

More vs less intensive BP control strategy

Cumulative trial sequential analysis of randomized studies

Included studies: HOT, UKPDS-38, ABCD (H), AASK, Schrier et al., ABCD (N), REIN-2, JATOS, Cardio-Sis, ACCORD BP, VALISH, HOMED-BP, Wei et al., SPS3, SPRINT, STEP

A more intensive BP control reduces the risk of:



Benefits of intensive control: 140/90 >> 120/80

European Journal of Internal Medicine, 2022-07-01, Volume 101, Pages 49-55

Polypharmacy in CKD

Kidney 360. Polypharmacy in Patients with Chronic Kidney Disease.2024 Apr
25; 5(4);

- ▶ Review of 127 studies: CKD (76), ESRD (38) and KTX (13)
- ▶ 484,915 patients (82% with CKD)
- ▶ Mean number of medications for CKD ~9.7 medications
- ▶ > 9.7 medications for ESRD and KTX patients
- ▶ Conclusion
 - ▶ Increased adverse drug reactions
 - ▶ Increased all cause mortality
 - ▶ Faster eGFR decline
 - ▶ Lower QoL

NSAID USE/ CKD

“systematic review of NSAID use in people with CKD in seven cross-sectional studies found that 8%–21% were currently taking NSAIDs”

“risk factors for NSAID-associated nephrotoxicity included higher drug doses, longer durations, concurrent use of renin-angiotensin system (RAS) inhibitors or diuretics, preexisting CKD, and advanced age”

“risk of hospitalization with GI bleeding is 50% higher in people with CKD stage 3, and seven times higher people with CKD stage 4 or 5”

“absolute risk of AKI is four times greater in people with CKD”

“AKI and hyperkalemia, respectively, for new NSAID use in older adults irrespective of renal function”

Kidney360. 2020 Nov 25; 1(11): 1189–1191.

Common medications and CKD

- ▶ 1. Fenofibrate- elevation in creatinine>>> gemfibrozil
- ▶ 2. Rosuvastatin- dose dependent increase in proteinuria, hematuria and CKD, maximum dose 10mg daily with eGFR<30
- ▶ 3. Topiramate- increase in non-anion gap acidosis
- ▶ 4. Gabapentin/ pregabalin- dose dependent increase in somnolence, lethargy, encephalopathy
- ▶ 5. Beta-lactams- cefepime increase in neurotoxicity/ encephalopathy
- ▶ 6. morphine/hydrocodone- cleared renally>> APAP, tramadol, oxycodone, hydromorphone, fentanyl

Referral to Nephrology

- ▶ acute kidney injury or abrupt sustained fall in glomerular filtration rate (GFR)
- ▶ GFR < 45 mL/minute/1.73 m² (GFR categories G3b, G4 and G5)
- ▶ consistent evidence of significant albuminuria (albumin to creatinine ratio ≥ 300 mg/g, protein to creatinine ratio ≥ 500 mg/g)
- ▶ Progression of CKD, calcium disorders
- ▶ urinary red cell casts, RBCs > 20 per HPF sustained or >5 per HPF dysmorphic RBCs and not readily explained
- ▶ WBCs casts/AIN
- ▶ hypertension refractory to treatment with ≥ 4 antihypertensive agents
- ▶ Persistent sodium, potassium, magnesium abnormalities; acid-base disturbances
- ▶ recurrent or extensive nephrolithiasis
- ▶ hereditary kidney disease ADPKD, Alport Syndrome, Thin Basement Membrane, APOL1 Mediated kidney Disease

- ✘ “The practice of medicine is an *art*, not a *trade*; a *calling*, not a *business*: a calling in which your **heart** will be exercised equally with your **head**”

William Osler “Aequanimitas”



Transition from CKD 5 (eGFR <15) to ESRD Renal Replacement Therapies



Indications for Emergent or Urgent Renal replacement

A- Refractory Acidosis (pH<7.1)

E- Electrolyte Abnormalities: Refractory Hyperkalemia (K>6.5)

I- Intoxications: ASA, APAP, Isopropyl Alcohol, Methanol, Ethylene Glycol, Lithium, Barbiturates, Theophylline, Valproic acid

O- Volume overload in the setting of AKI/ CKD 5, refractory to diuresis

U- Uremia: uremic pericarditis, uremic encephalopathy

Renal Replacement Modalities

Continuous Renal Replacement Therapy (CRRT) 24 hours

Sustained Low Efficiency Dialysis (SLED) 6-10 hours

Hemodialysis

- **Incenter Hemodialysis 4+ hours thrice weekly**
- **Home Hemodialysis 2-3 hours 4-5 times week**

Peritoneal Dialysis

- **Continuous Ambulatory Peritoneal Dialysis (CAPD) nightly**
- **Continuous Cyclic Peritoneal Dialysis (CCPD) daily**

Absolute and Relative Contraindications for Hemodialysis

Lack of vascular access

**Cardiovascular instability: unstable angina,
hypotension, volume overload and large weight gains**

Distance from hemodialysis center

Unwillingness to tolerate

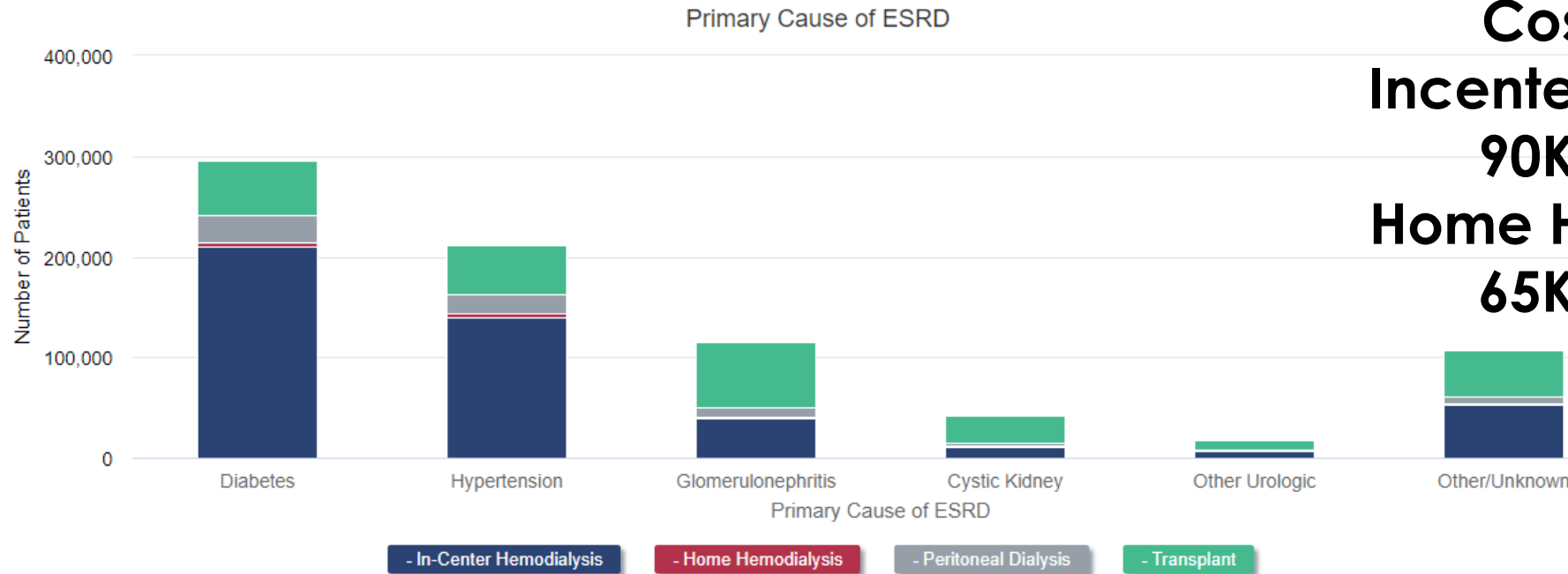
Dementia/ Failure to thrive/ Agitation >>Palliative?

Advance malignancy/ poor prognosis

Contraindications for Peritoneal Dialysis

- ▶ **Prior abdominal surgeries with adhesions**
- ▶ **Diverticular disease/ inflammatory bowel disease**
- ▶ **Chronic/ uncontrolled back pain**
- ▶ **COPD/emphysema**
- ▶ **Homelessness/ lack of space**
- ▶ **Hernias (diaphragmatic/ pleuroperitoneal leak)**
- ▶ **Colostomy/ileostomy/ ileal conduit**
- ▶ **Personal hygiene**
- ▶ **Recurrent peritoneal infections**
- ▶ **Peritoneal membrane dysfunction**

Primary Cause of ESRD 2023:USRDS ESRD

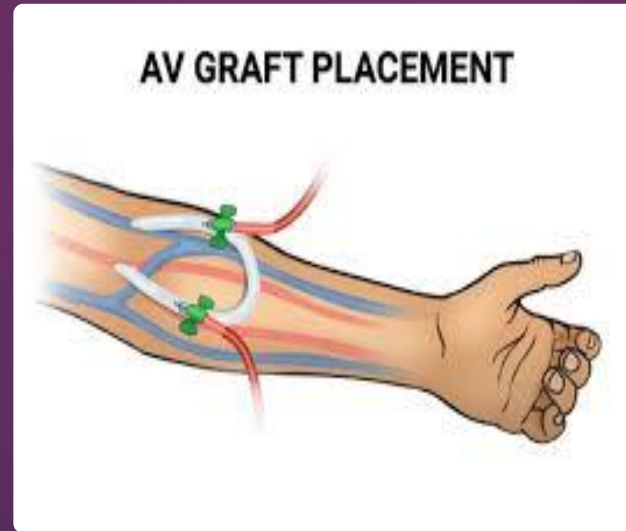
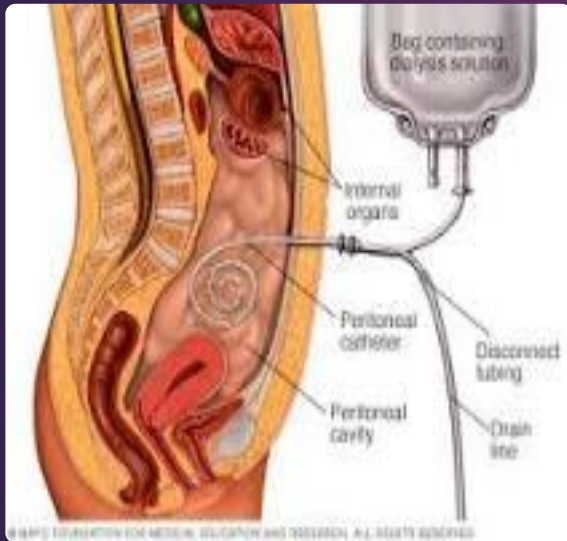
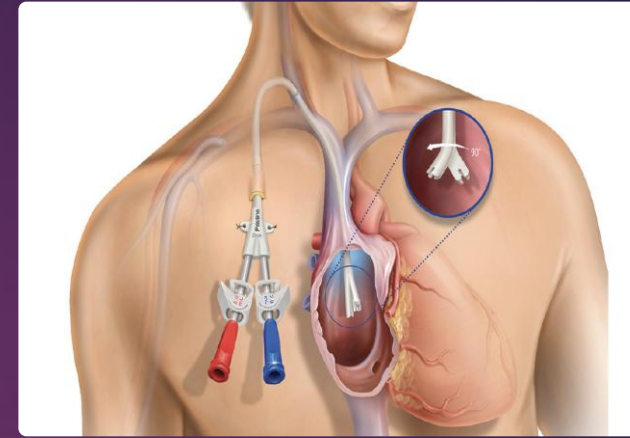
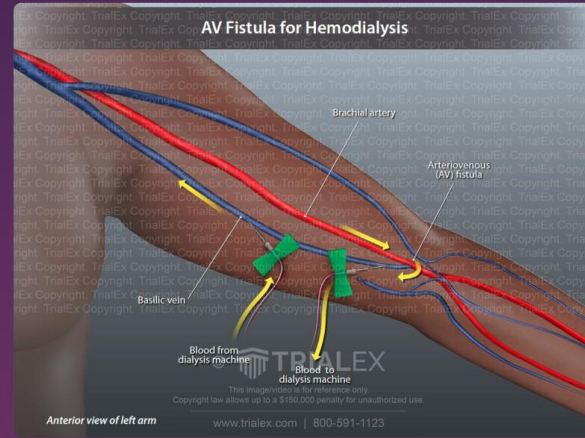
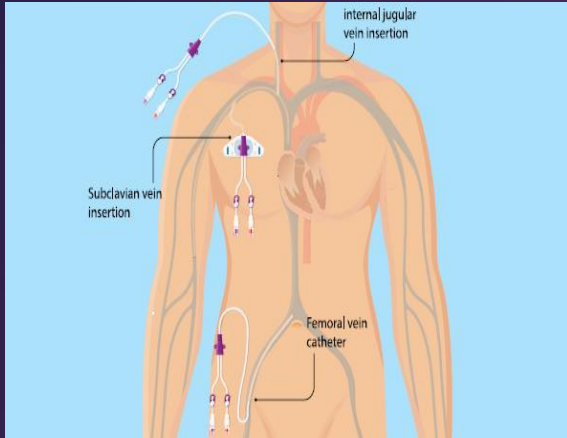


Cost 2024
Incenter HD \$72K-
90K/ pt/yr
Home HD/PD \$53-
65K/ pt/yr

Data Source: USRDS ESRD Database. U.S. and U.S. territories ESRD patients. Persons with "Uncertain Dialysis" type were excluded.



Renal Replacement in the past



Dialysis
access

Renal Replacement Therapies

- Home Therapies

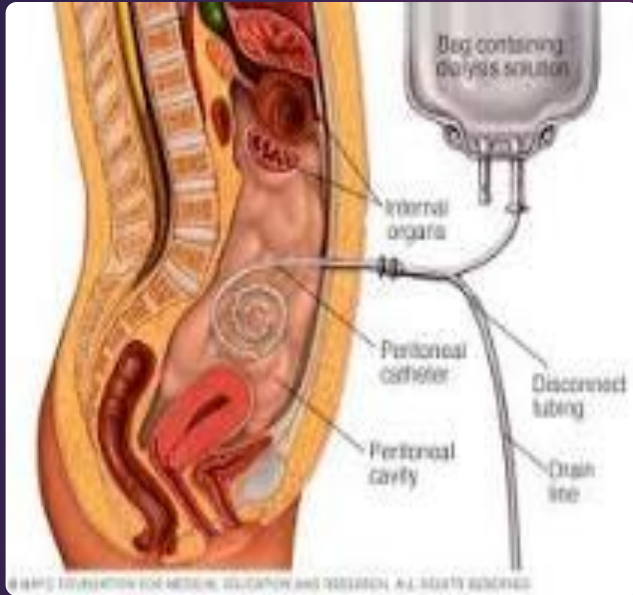
- -Peritoneal Dialysis (generally nightly)
- -Home Hemodialysis (4-5 nights/week)

-Incenter Therapies

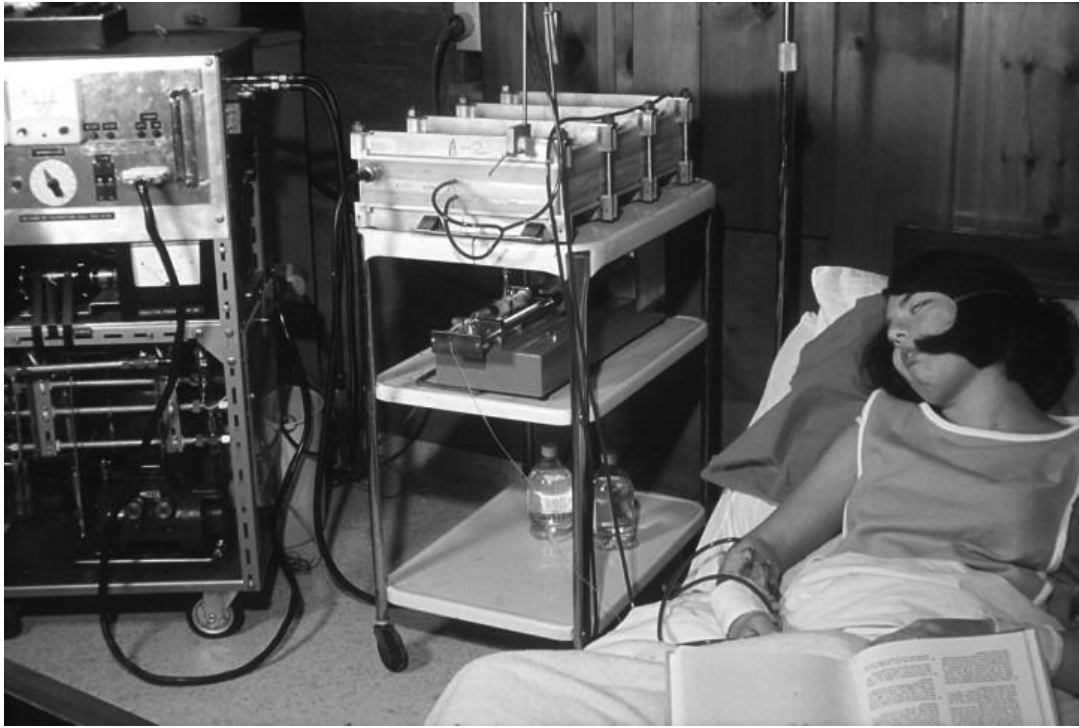
- -Hemodialysis

-Hospital Therapies

- -Peritoneal dialysis
- -Hemodialysis
- -SLED (Sustained Low-Efficiency Dialysis, 6-10 hours)
- -CRRT (continuous renal replacement therapy, 24 hours)



Peritoneal Dialysis



Home Hemodialysis

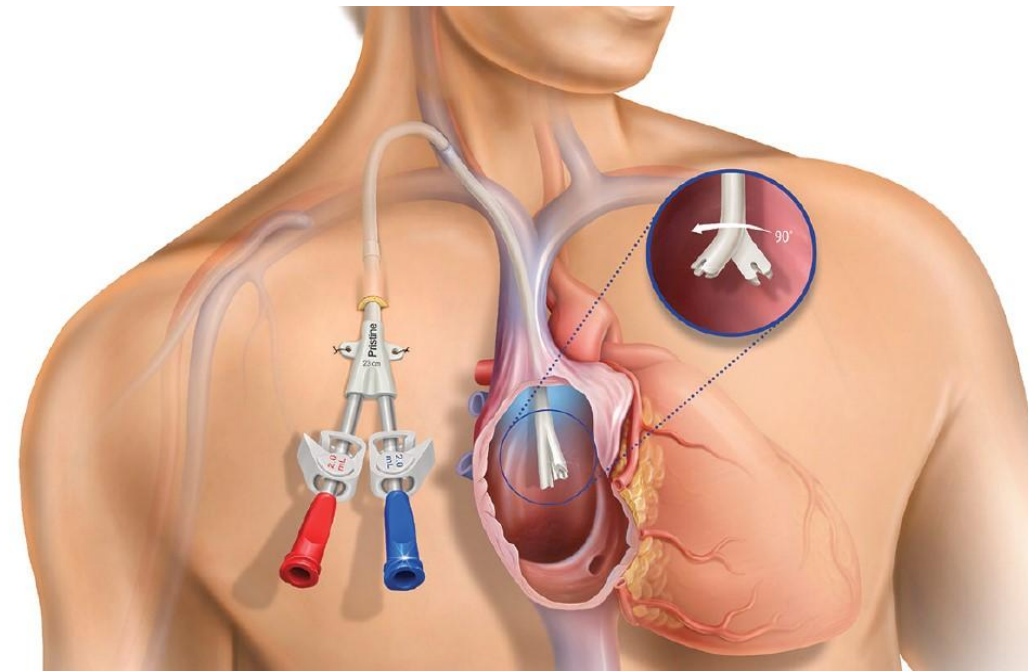
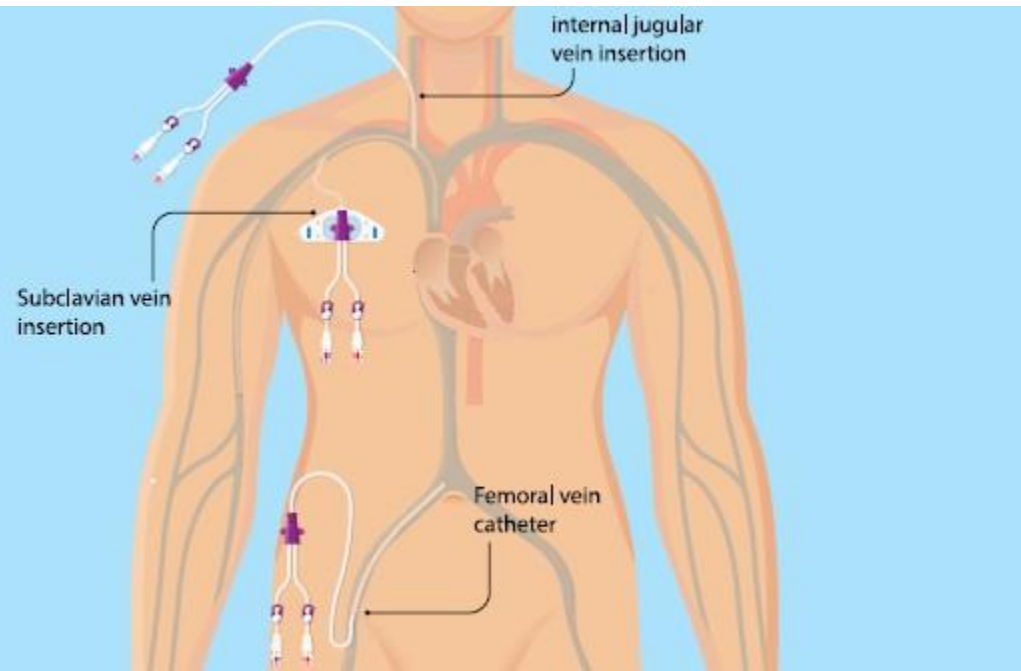


In-Center Hemodialysis

In Hospital Urgent Renal replacement



- ▶ **Continuous renal replacement**
 - ▶ **Temporary dialysis catheter**
 - ▶ **Tunnel dialysis catheter**



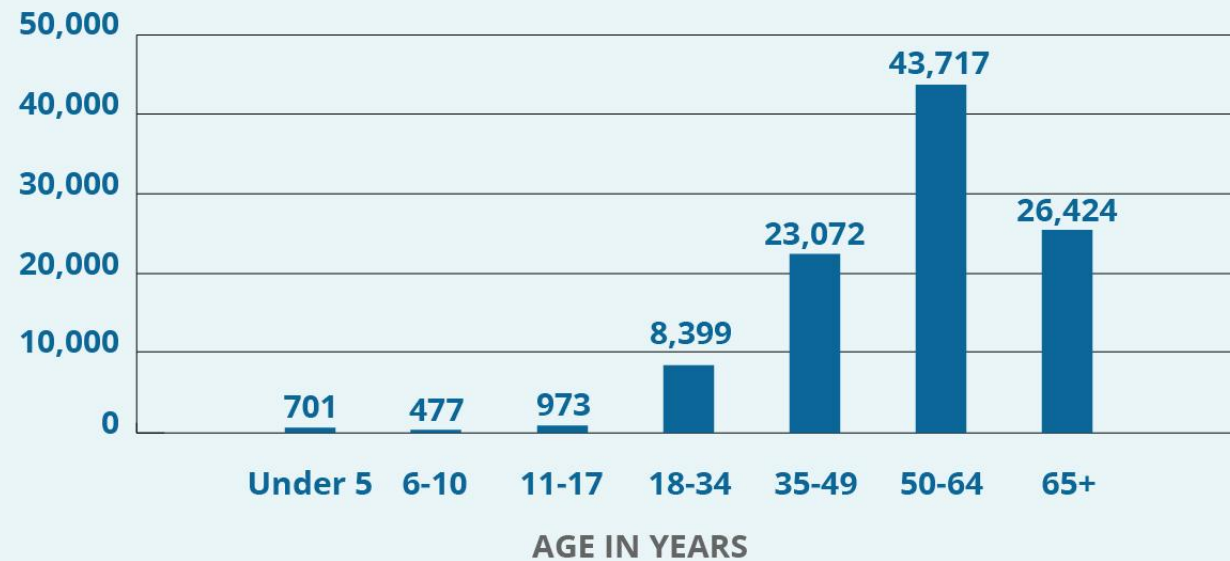


Continuous Renal Replacement Therapy-CRRT Persistent Intermittent Renal Replacement therapy (PIRRT)

Organ transplant waiting list by age March 2024

Waiting List by Age

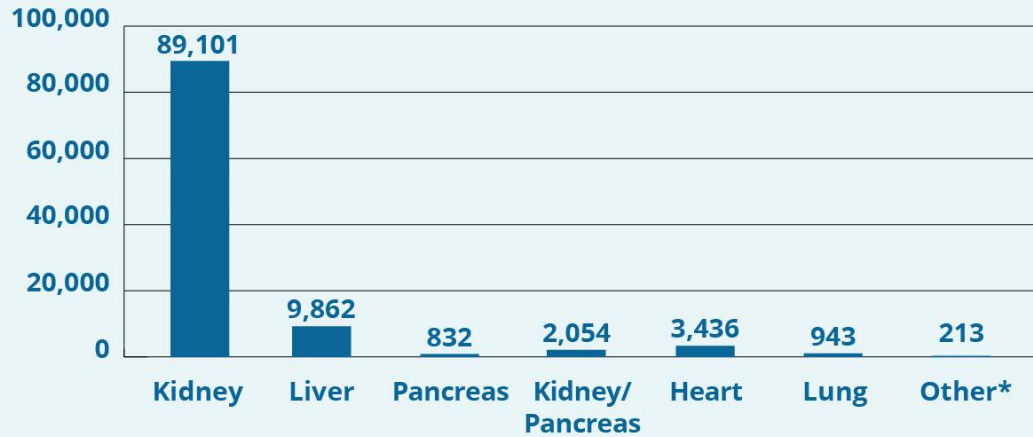
As of March 2024



Based on OPTN data as of March 21, 2024.

Patients on the Waiting List by Organ

As of March 2024

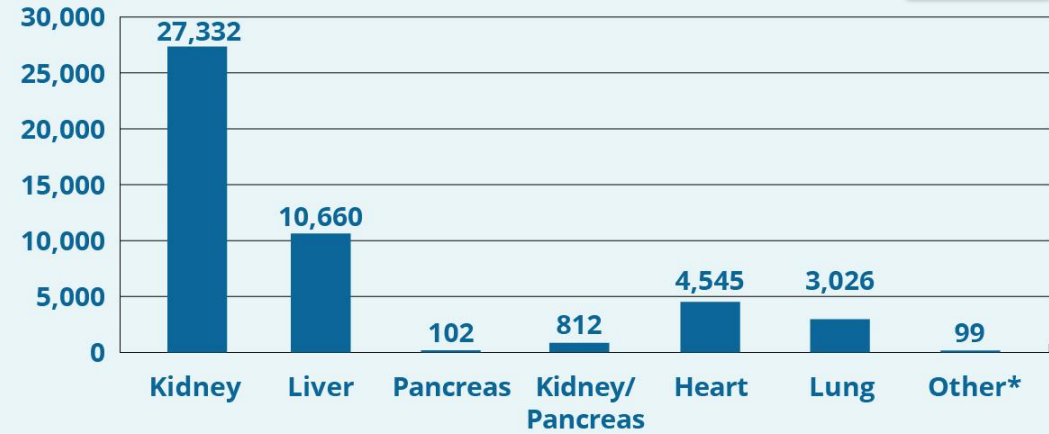


*Other includes kidney/pancreas and allograft transplants like face, hands, and abdominal wall.

Based on OPTN data as of March 21, 2024. Data subject to change based on future data submission or correction. Totals may be less than the sums due to patients included in multiple categories.

Transplants Performed by Organ

As of March 2024



*Other includes kidney/pancreas and allograft transplants like face, hands, and abdominal wall.

Based on OPTN data as of March 21, 2024. Data subject to change based on future data submission or correction. Totals may be less than the sums due to patients included in multiple categories.

Organ transplant in US: March 2024

Closing thoughts

- ▶ CKD is growing and costly epidemic, this disease does NOT discriminate !!
- ▶ Be resilient through **motivational interviewing** and **shared decision making**
- ▶ Embrace the 3 As of Success: **Ability, Available and Affable**
- ▶ Hyperfocus on screening polypharmacy, eliminate OTC NSAIDS and supplements, encourage compliance with GDMT/medications, low Na diet, smoking cessation, aerobic activity and adequate hydration
- ▶ Prevention thru aggressive weight management with nutritional referrals, early start of GLP1* and Bariatric referral
- ▶ Guideline directed therapy for management of blood pressure/CHF (RASi/ SGLT2i), Diabetes (CGMS, SGLT2i/GLP1/metformin/insulin) and lipids (high intensity statins/ezetimibe/ PCSK9i)
- ▶ Routine monitoring renal function and urinalysis, baseline imaging, BP < 130/80, glucose control
- ▶ Refer eGFR <45, for proteinuria and/or hematuria, start the workup and refer early!!

Thank you



References

- ▶ **CDC: Chronic Kidney Disease in the United States-2023**
- ▶ **Kidney360. 2020 Nov 25; 1(11): 1189–1191.**
- ▶ **<https://kdigo.org/guidelines/ckd-evaluation-and-management/>**
- ▶ **The Framingham Heart Study, Bruce F. Culeton et al. Arch Intern Med. 1999;159(15):1785-1790.**
- ▶ **European Journal of Internal Medicine, 2022-07-01, Vol 101, pp 49-55.**
- ▶ **American Journal of Kidney Diseases, 2008-03-01, Vol 51, Issue 3, Pages 385-394**
- ▶ **Kidney 360. Polypharmacy in Patients with Chronic Kidney Disease.2024 Apr 25; 5(4)**
- ▶ **Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO); Diabetes Care 2022; 45 (12): 3075-3090**
- ▶ **Association of Rosuvastatin Use with Risk of Hematuria and Proteinuria. JASN 33(9):p 1767-1777, September 2022. | DOI: 10.1681/ASN.2022020135**
- ▶ **Type II Renal Tubular Acidosis Secondary to Topiramate: A Review. Cureus 10(11): e3635. doi:10.7759/cureus.3635**