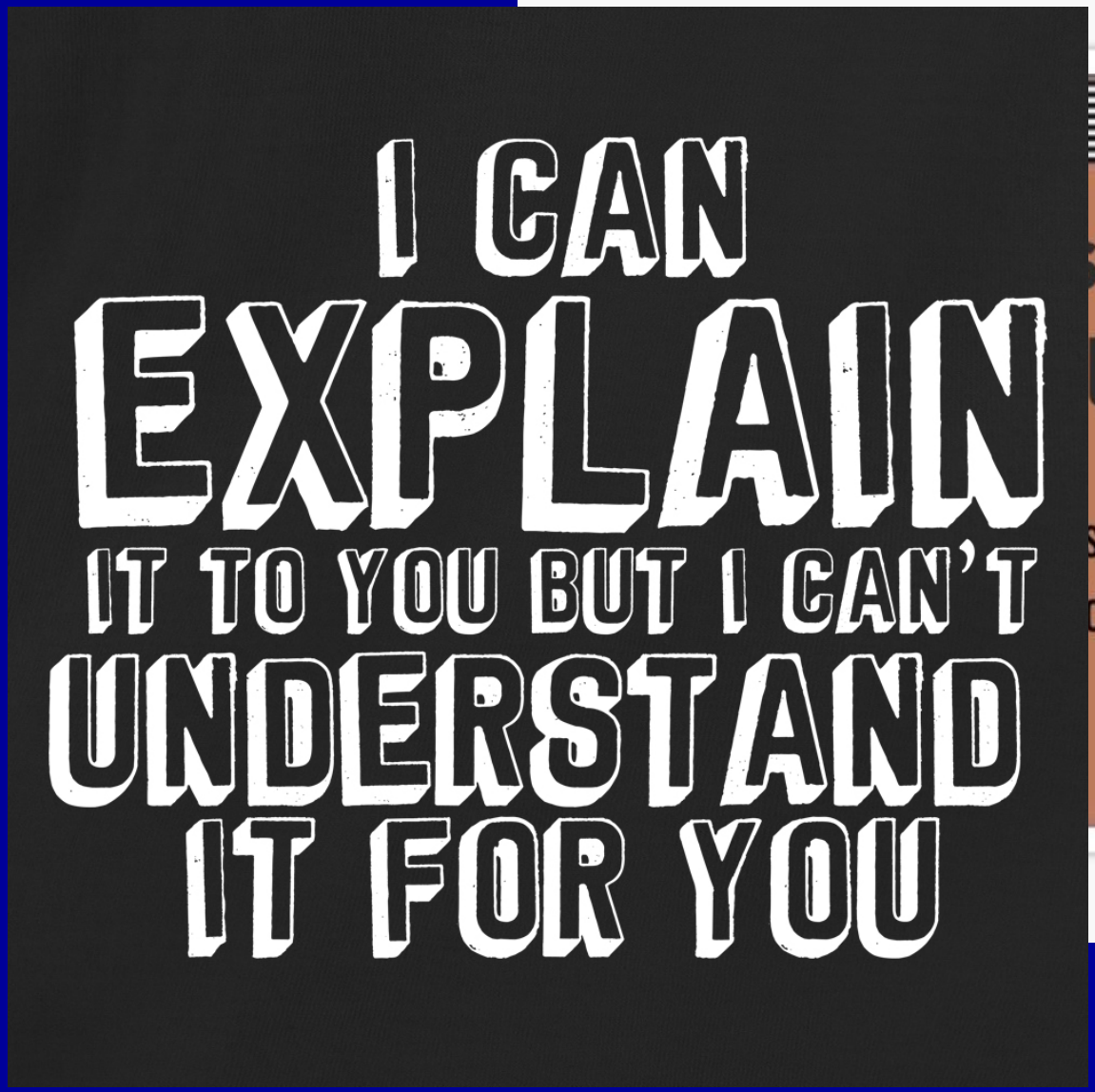
Nephrology:
(Everything you ever wanted to know, but were afraid to ask)

William J. Dahms, Jr., DO, FASN

3 June, 2026


I CAN
EXPLAIN
IT TO YOU BUT I CAN'T
UNDERSTAND
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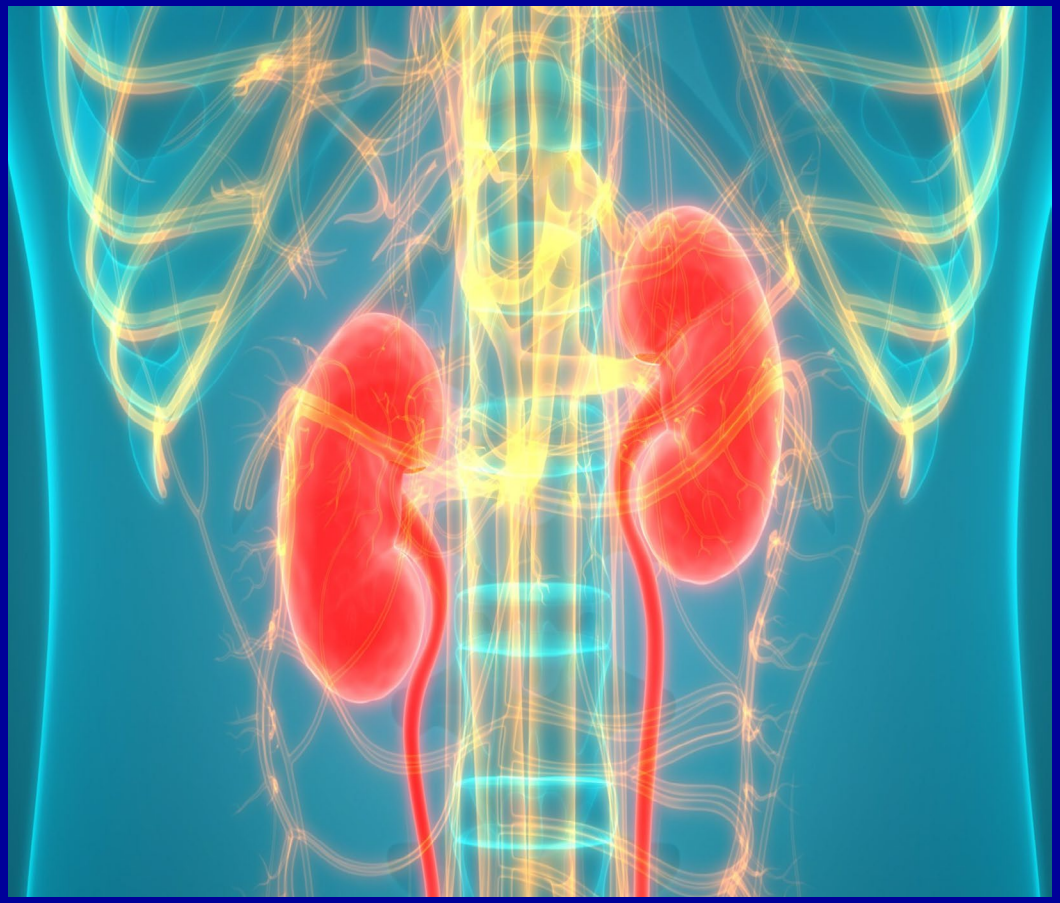
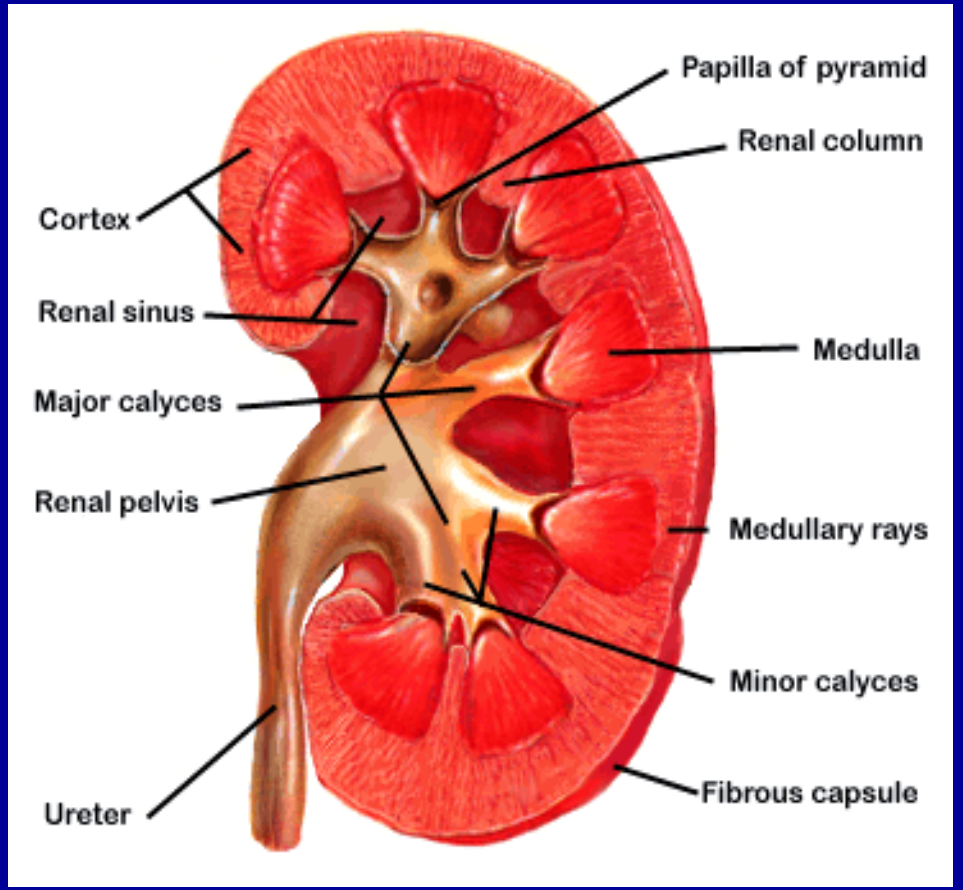
What Are Kidneys??

- Bean shaped organs
- About the size of a fist
- Located below the rib cage
- Either side of the spine



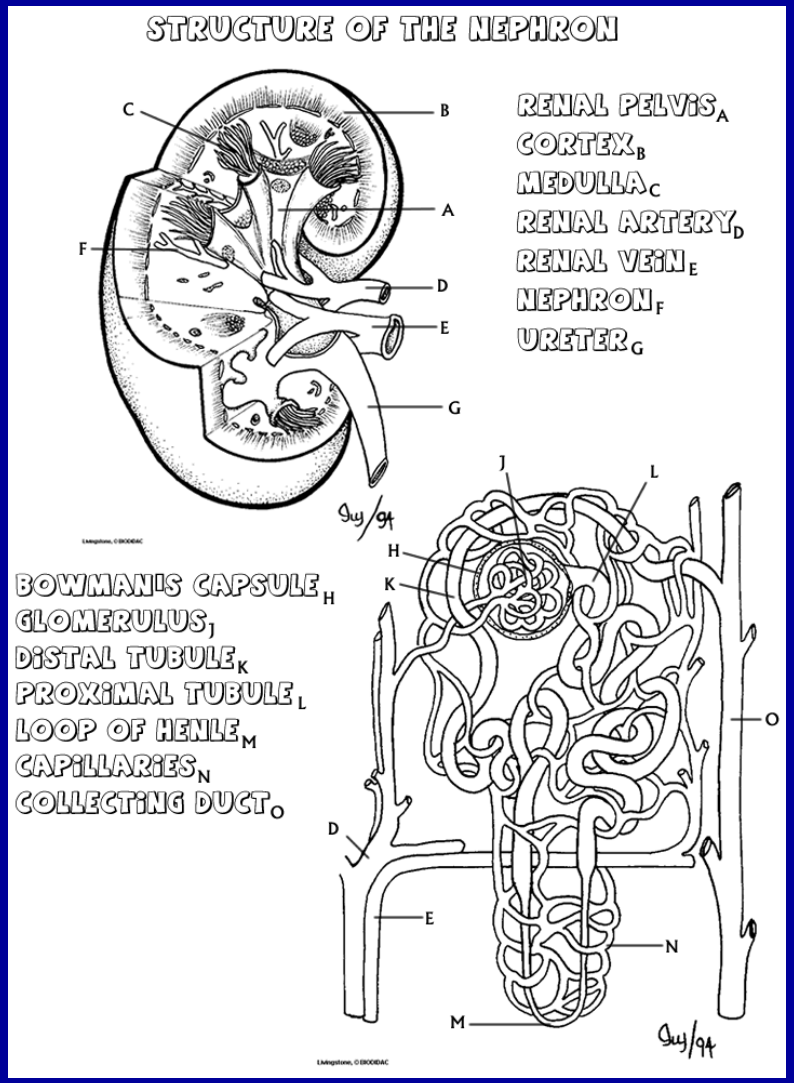
Normal Renal Function

- "Center of the human body"
- Filters > 200 quarts daily
- Maintains fluid and electrolyte homeostasis
  - Critical importance in BP regulation
- Excretes nitrogenous waste products
- Hormonally active
  - Bone health
  - RBC development

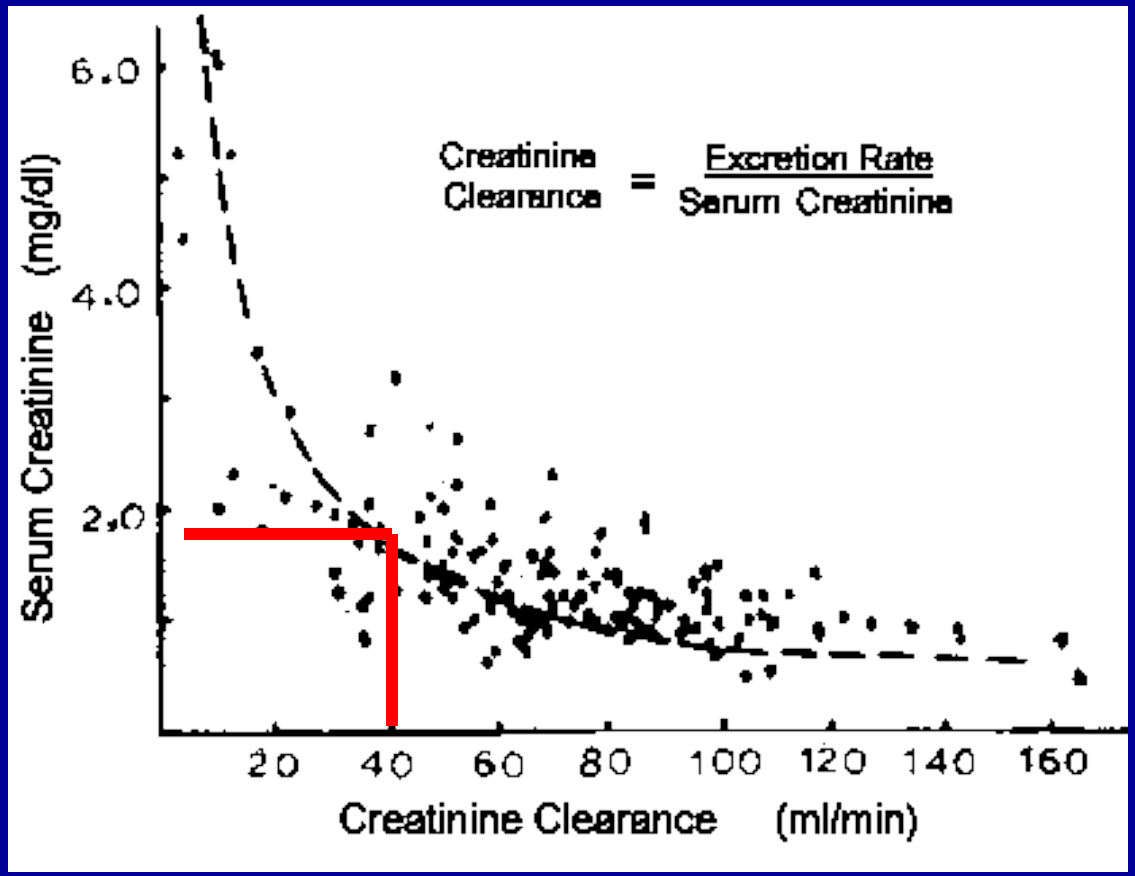


The Kidneys Are Complex!!

- Usually, we all have TWO
  - Each with an average of 1M nephrons
    - Filtering units
- Assessment of function
  - Estimated GFR (blood)
  - Urinalysis
  - Structural evaluation
- If all of the above are normal, no concerns!!

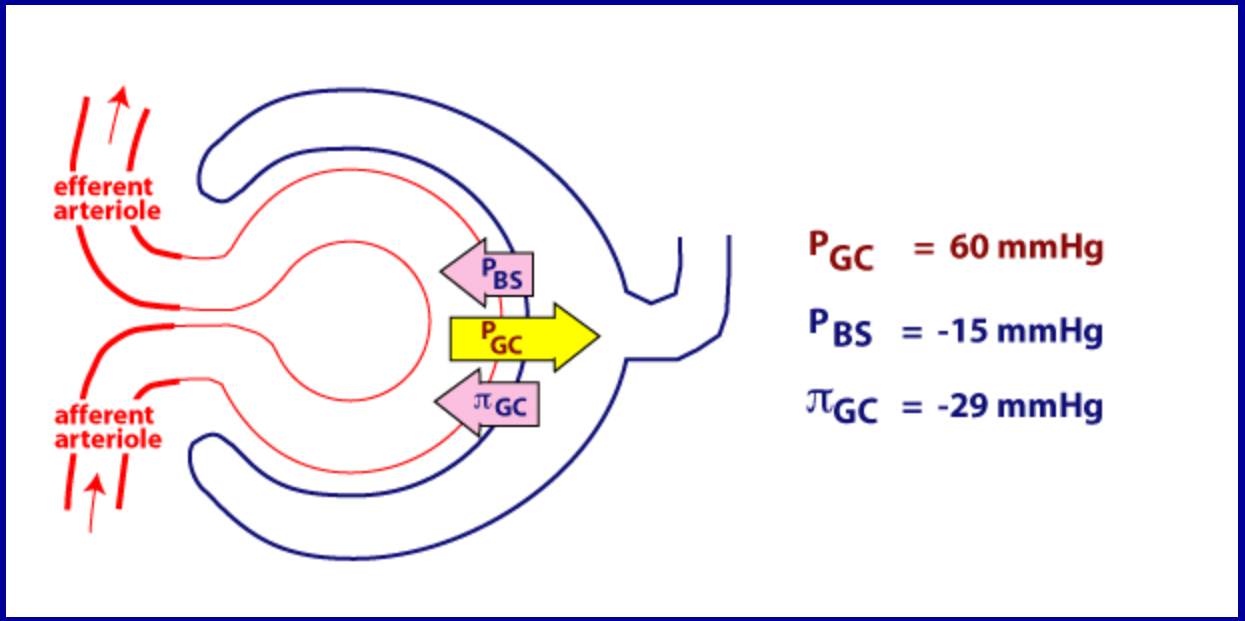


Serum Creatinine



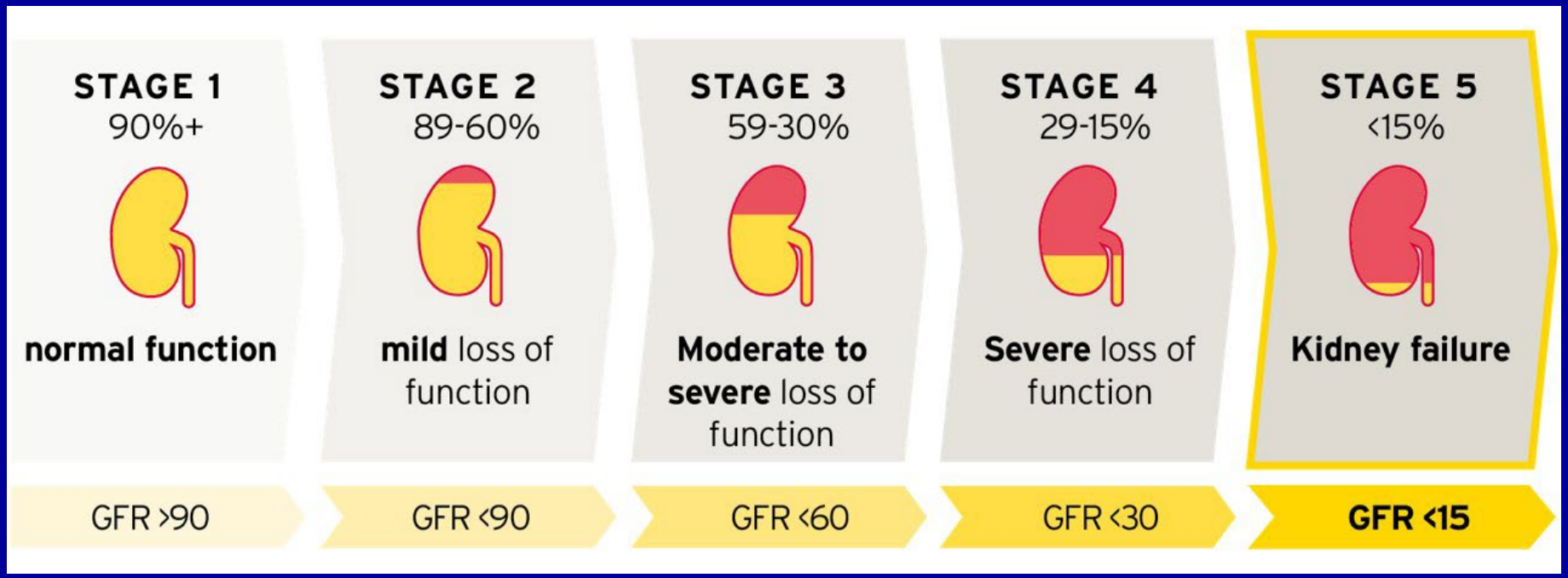
What is GFR?

- Rate *(at which the)* Glomeruli Filter *(plasma)*



- *Measured in mL/min/1.73m^2 BSA*

Chronic Kidney Disease (CKD)



850 million people worldwide!! (NIH 2022)
In the US, it's about 37 million cases (1 out of 7 Americans)!!

Kidney Disease Outcomes Quality Initiative (K/DOQI)

- Clinical Practice Guidelines on CKD

  American Journal of Kidney Disease Feb 2002

Table 2. Definition of Chronic Kidney Disease

Criteria
1. Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*: • Pathological abnormalities; or • Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR <60 mL/min/1.73 m^2 for ≥3 months, with or without kidney damage

Abbreviation: GFR, glomerular filtration rate

"The level of glomerular filtration rate (GFR) is widely accepted as the best overall measure of kidney function in health and disease."

Table 33. Stages of Chronic Kidney Disease: A Clinical Action Plan

Stage	Description	GFR (mL/min/1.73 m^2)	Action*
1	Kidney damage with normal or ↑ GFR	≥90	Diagnosis and treatment, Treatment of comorbid conditions, Slowing progression, CVD risk reduction
2	Kidney damage with mild ↓ GFR	60–89	Estimating progression
3	Moderate ↓ GFR	30–59	Evaluating and treating complications
4	Severe ↓ GFR	15–29	Preparation for kidney replacement therapy
5	Kidney failure	<15 (or dialysis)	Replacement (if uremia present)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m^2 for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

* Includes actions from preceding stages.

Abbreviations: CVD, cardiovascular disease

AJKD, 39 (2) Sup 1:S25, Feb 2002

GFR categories (ml/min/ 1.73 m^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 >30 mg/mmol
	G1	Normal or high	≥90		Monitor	Refer*
	G2	Mildly decreased	60–89		Monitor	Refer*
	G3a	Mildly to moderately decreased	45–59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30–44	Monitor	Monitor	Refer
	G4	Severely decreased	15–29	Refer*	Refer*	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

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http://www.kidney-international.org

CAUSES OF CKD

- Diabetes (Type 1 & Type 2)
- High Blood Pressure (Hypertension)
- Glomerular Diseases
- Genetic and Inherited Diseases
- Autoimmune Disorders
- Structural or Urinary Tract Issues
- Medications
- Cardiovascular Disease and Obesity

“Once CKD is recognized
-Look for complications!
-Look to prevent progression
(kidney protective meds)”

complications of kidney disease

file:///C:/Users/WilliamDahms/OneDrive%20-%20Nephrology%20Associates,%20P.A/Desktop/complications%20of%20kidney%20disease%20-%20Google%20Search.html

complications of kidney disease

Complications of CKD

From sources across the web

- Anemia
- Heart Disease
- Metabolic acidosis
- Hypertension
- Mineral and bone disorder
- Hyperkalemia
- Gout
- Kidney failure
- Bone weakness
- Fluid buildup
- Fluid retention
- Infection
- Reduced immune response
- Chest pain
- Colon problems
- Dehydration
- Liver failure
- Malnutrition
- Pregnancy complications
- Secondary hyperparathyroidism
- Stroke
- Uremia
- Vomiting

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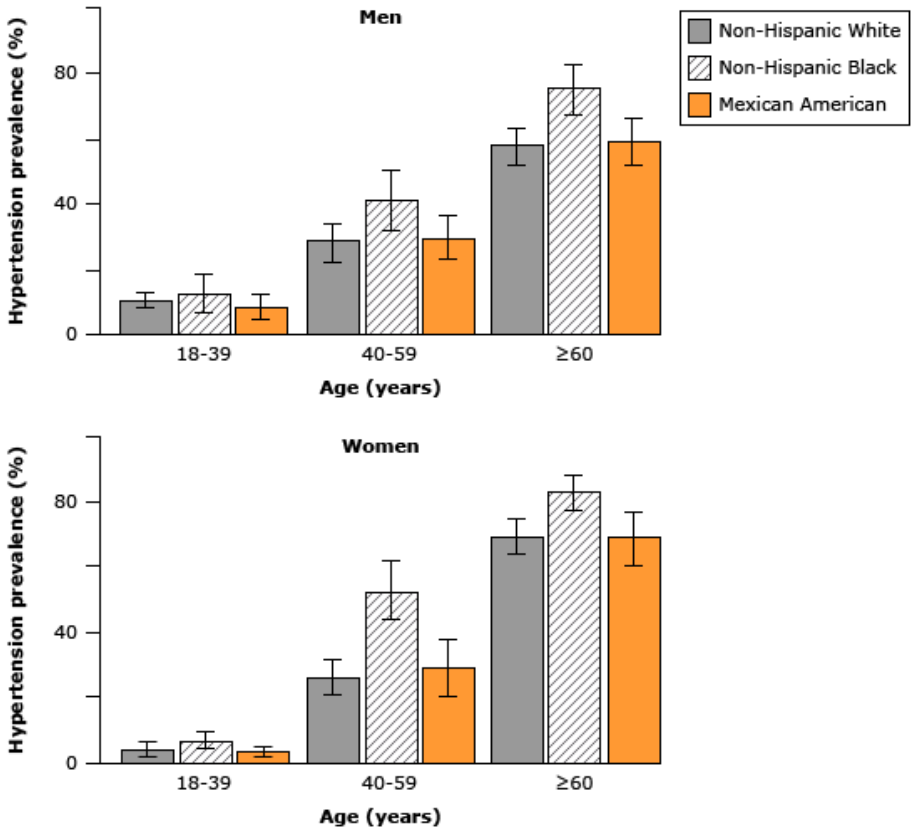
Hypertension

- Estimated prevalence of 30% in the United States
- Treatment of hypertension is the most common reason for office visits of non-pregnant adults to clinicians in the United States and for use of prescription drugs

Prevalence of hypertension in the United States



Prevalence of hypertension in men (upper graph) and women (lower graph) according to age and race/ethnicity in the United States from the NHANES survey. Hypertension occurs earlier and more frequently in non-Hispanic blacks.

Data from: Egan BM, Zhao Y, Axon RN. JAMA 2010; 303:2043.

Hypertension

- With the aging population and rise of obesity, HTN will become more common!
- Data from the 2005-2008 NHANES survey show that only 50.1 % of persons with hypertension have their blood pressure under control
  - < 140/90 mmHg

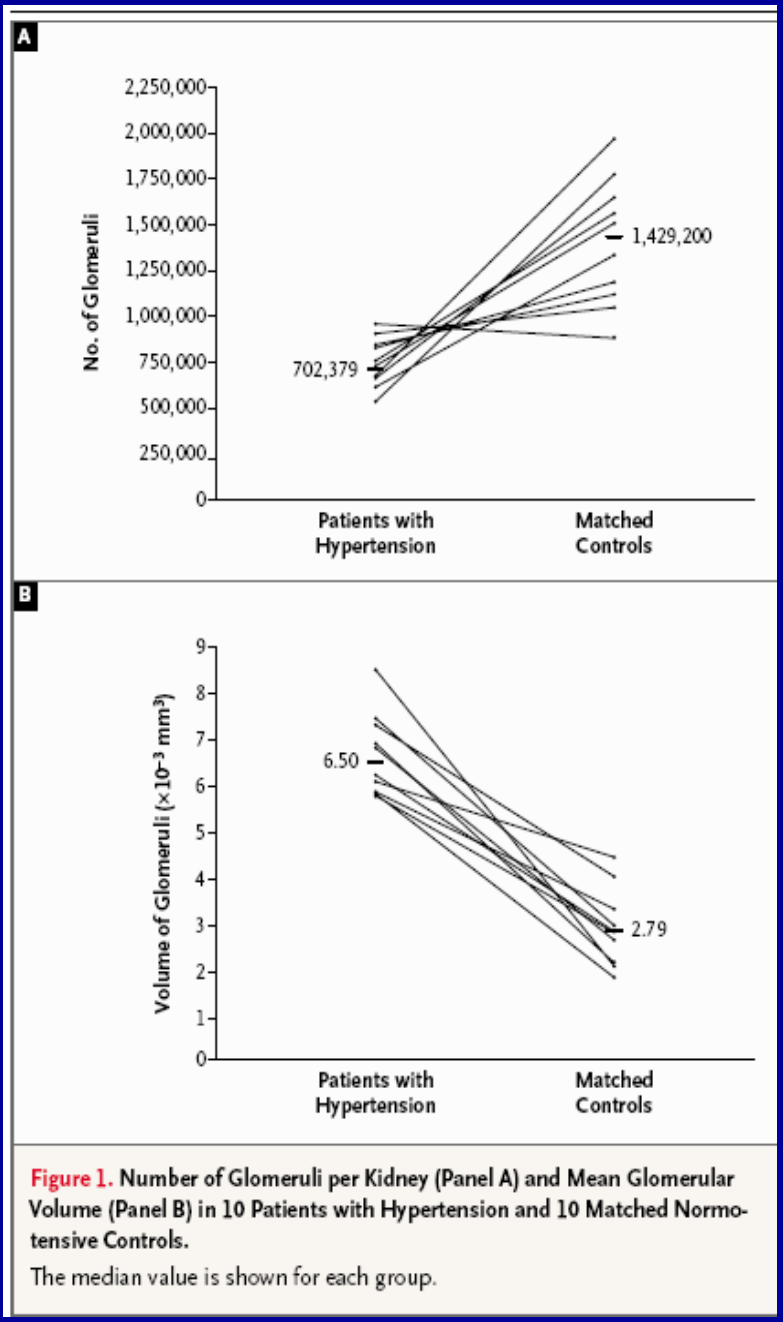


Figure 1. Number of Glomeruli per Kidney (Panel A) and Mean Glomerular Volume (Panel B) in 10 Patients with Hypertension and 10 Matched Normotensive Controls.

The median value is shown for each group.

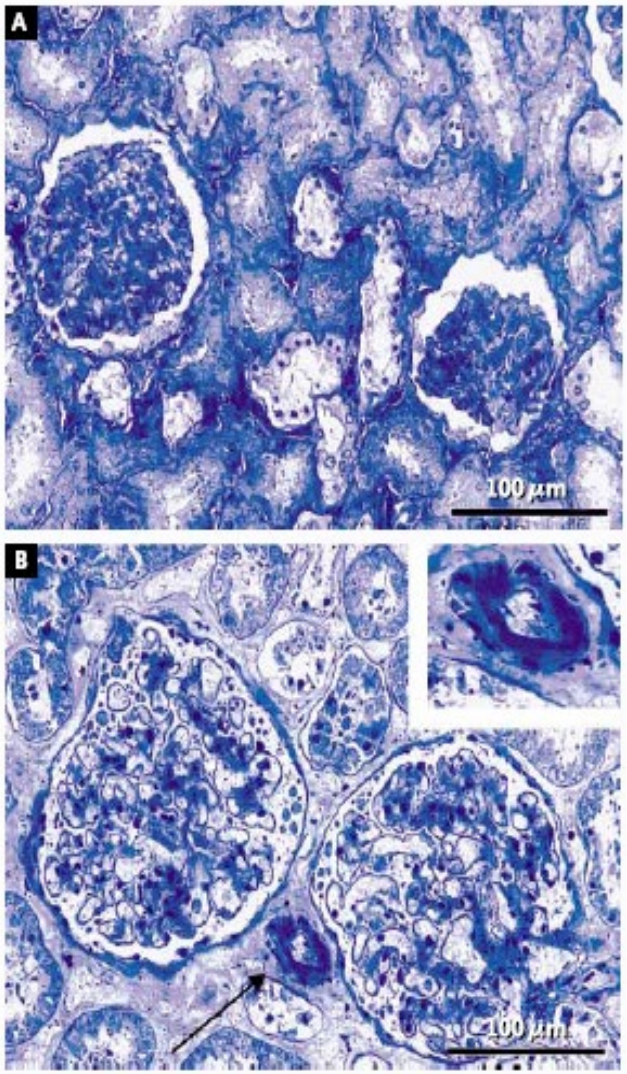
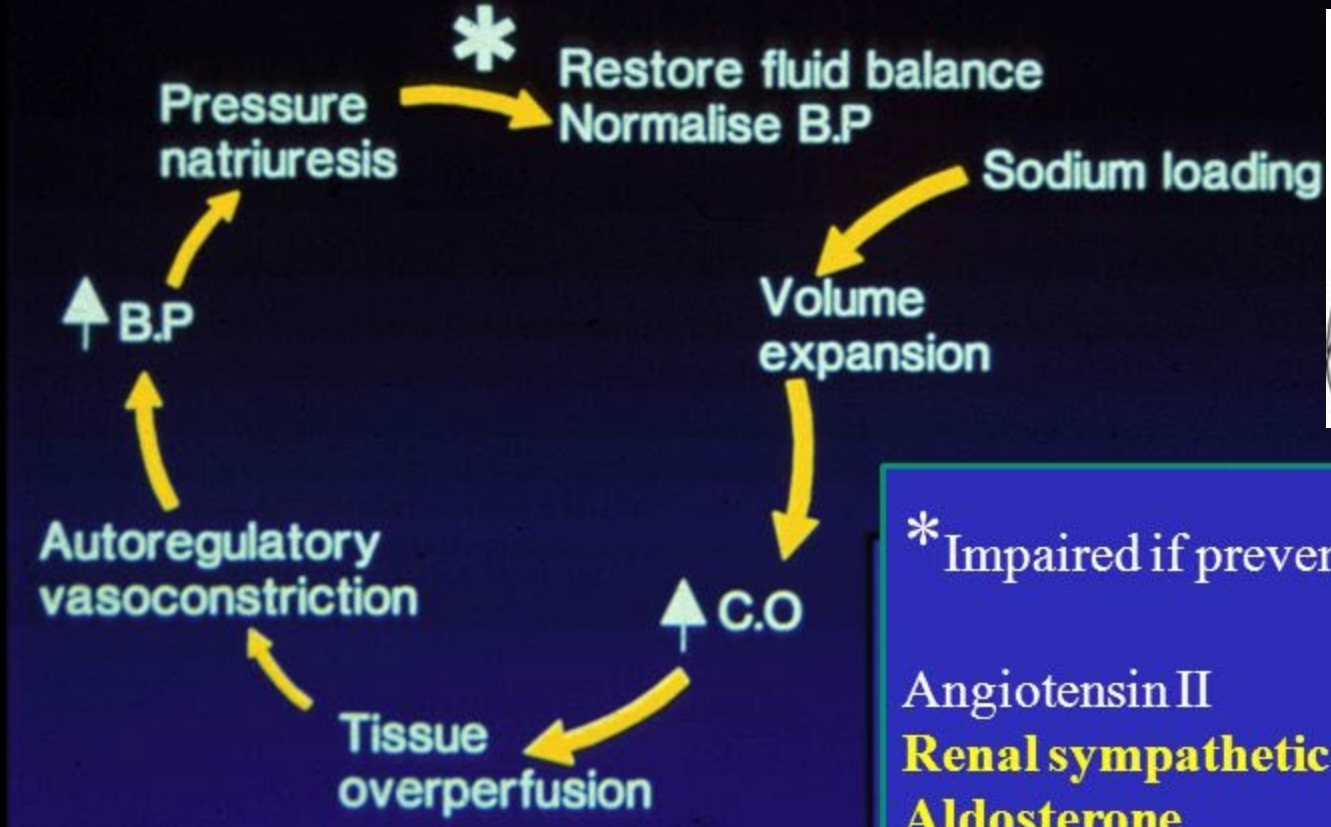


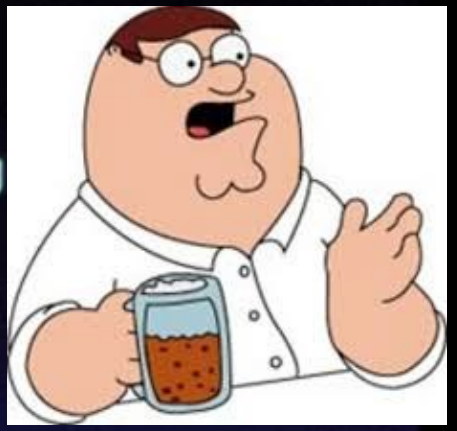
Figure 2. Representative Light Micrographs of Renal Cortex from a Normotensive Control (Panel A) and a Patient with Hypertension (Panel B).

The patient with hypertension has larger glomeruli and typical arteriolar changes with hyalinosis (arrow and inset).

Keller et al, NEJM Jan 2003

Guyton hypothesis





*Impaired if prevented by:

Angiotensin II
Renal sympathetic nerve activity
Aldosterone
Reduced renal mass

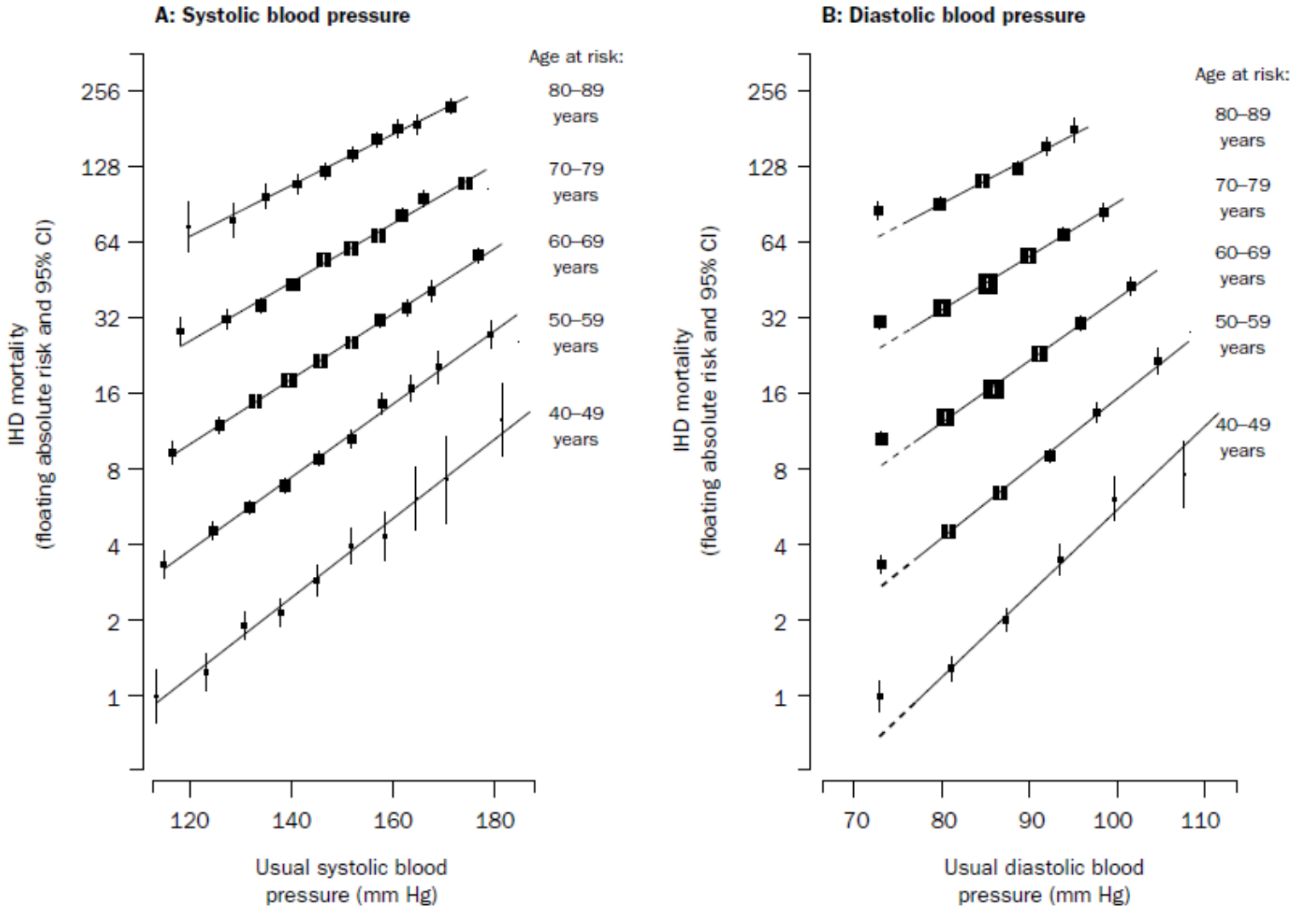
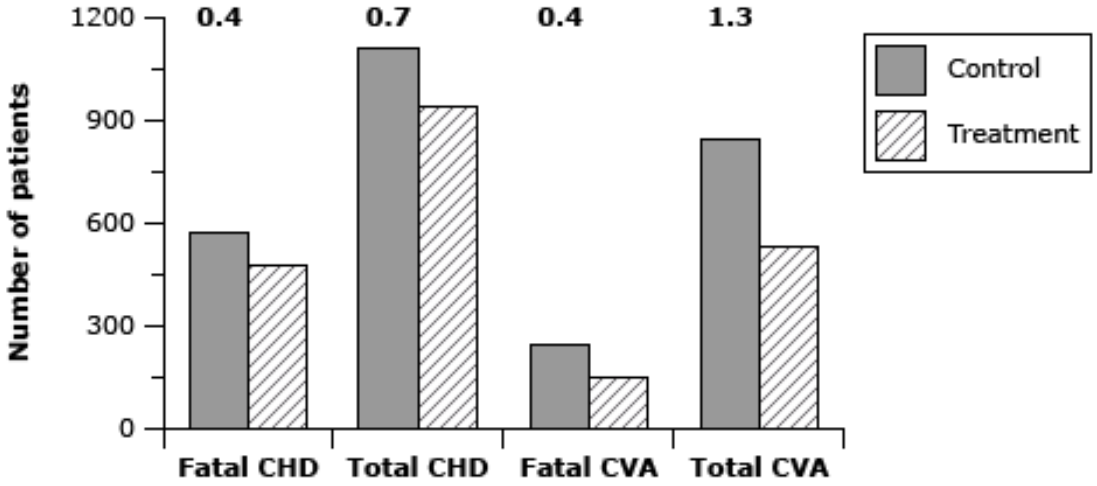


Figure 4: **Ischaemic heart disease (IHD) mortality rate in each decade of age versus usual blood pressure at the start of that decade**
Conventions as in figure 2.

Lewington et al, Lancet, Dec, 2002

Cardiovascular benefit of treating mild hypertension



Reduced incidence of fatal and total coronary heart disease (CHD) events and strokes following antihypertensive therapy in 17 controlled studies involving almost 48,000 patients with mild to moderate hypertension. The number of patients having each of these events is depicted, with active treatment lowering the incidence of coronary events by 16 percent and stroke by 40 percent. However, the absolute benefit – as shown, in percent, by the numbers at the top of the graph – was much less. Treatment for approximately four to five years prevented a coronary event or a stroke in 2 percent of patients (0.7 + 1.3), including prevention of death in 0.8 percent.

CVA: cerebrovascular accident (stroke).

Data from: Hebert PR, Moser M, Mayer J, et al. Recent evidence on drug therapy of mild to moderate hypertension and decreased risk of coronary heart disease. Arch Intern Med 1993; 153:578.

HOW TO TREAT?

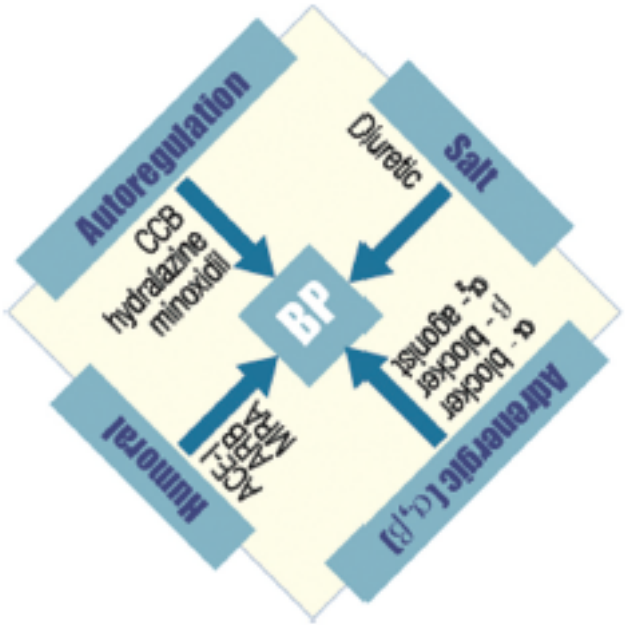


Figure 3. | This diagram emphasizes four basic physiologic processes that regulate BP and situates common antihypertensive drug classes along the side belonging to the process thought to be associated with the drug class's primary antihypertensive effect (adapted from Townsend and Cirigliano [13]). CCB = calcium channel blocker; ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; MRA = mineralocorticoid receptor antagonist.

Townsend, CJASN, 2011

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

The JNC 7 Report

JAMA, 289(19):2560-2572, May 21, 2003

Table 3. Lifestyle Modifications to Manage Hypertension*

Modification	Recommendation	Approximate Systolic BP Reduction, Range
Weight reduction	Maintain normal body weight (BMI, 18.5-24.9)	5-20 mm Hg/10-kg weight loss[23,24]
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8-14 mm Hg[25,26]
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)	2-8 mm Hg[25-27]
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4-9 mm Hg[28,29]
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks per day (1 oz or 30 mL ethanol [eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey]) in most men and no more than 1 drink per day in women and lighter-weight persons	2-4 mm Hg[30]

Abbreviations: BMI, body mass index calculated as weight in kilograms divided by the square of height in meters; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension.

*For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals.

Table 6. Clinical Trial and Guideline Basis for Compelling Indications for Individual Drug Classes

High-Risk Conditions With Compelling Indication*	Recommended Drugs						Clinical Trial Basis†
	Diuretic	β-Blocker	ACE Inhibitor	ARB	CCB	Aldosterone Antagonist	
Heart failure	•	•	•	•		•	ACC/AHA Heart Failure Guideline,[40] MERIT-HF,[41] COPERNICUS,[42] CIBIS,[43] SOLVD,[44] AIRE,[45] TRACE,[46] ValHEFT,[47] RALES[48]
Post–myocardial infarction		•	•			•	ACC/AHA Post-MI Guideline,[49] BHAT,[50] SAVE,[51] Capricorn,[52] EPHESUS[53]
High coronary disease risk	•	•	•		•		ALLHAT,[33] HOPE,[34] ANBP2,[36] LIFE,[32] CONVINCE[31]
Diabetes	•	•	•	•	•		NKF-ADA Guideline,[21,22] UKPDS,[54] ALLHAT[33]
Chronic kidney disease			•	•			NKF Guideline,[22] Captopril Trial,[55] RENAAL,[56] IDNT,[57] REIN,[58] AASK[59]
Recurrent stroke prevention	•		•				PROGRESS[35]

Abbreviations: AASK, African American Study of Kidney Disease and Hypertension; ACC/AHA, American College of Cardiology/American Heart Association; ACE, angiotensin-converting enzyme; AIRE, Acute Infarction Ramipril Efficacy; ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; ANBP2, Second Australian National Blood Pressure Study; ARB, angiotensin-receptor blocker; BHAT, β-Blocker Heart Attack Trial; CCB, calcium channel blocker; CIBIS, Cardiac Insufficiency Bisoprolol Study; CONVINCE, Controlled Onset Verapamil Investigation of Cardiovascular End Points; COPERNICUS, Carvedilol Prospective Randomized Cumulative Survival Study; EPHESUS, Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study; HOPE, Heart Outcomes Prevention Evaluation Study; IDNT, Inbesartan Diabetic Nephropathy Trial; LIFE, Losartan Intervention For Endpoint Reduction in Hypertension Study; MERIT-HF, Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure; NKF-ADA, National Kidney Foundation–American Diabetes Association; PROGRESS, Perindopril Protection Against Recurrent Stroke Study; RALES, Randomized Aldactone Evaluation Study; REIN, Ramipril Efficacy in Nephropathy Study; RENAAL, Reduction of Endpoints in Non–Insulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan Study; SAVE, Survival and Ventricular Enlargement Study; SOLVD, Studies of Left Ventricular Dysfunction; TRACE, Trandolapril Cardiac Evaluation Study; UKPDS, United Kingdom Prospective Diabetes Study; ValHEFT, Valsartan Heart Failure Trial.

*Compelling indications for antihypertensive drugs are based on benefits from outcome studies or existing clinical guidelines; the compelling indication is managed in parallel with the blood pressure.

†Conditions for which clinical trials demonstrate benefit of specific classes of antihypertensive drugs.

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

JNC 8, JAMA 2014

Box. Recommendations for Management of Hypertension

Recommendation 1

In the general population aged ≥60 years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP) ≥150 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg. (Strong Recommendation – Grade A)

Corollary Recommendation

In the general population aged ≥60 years, if pharmacologic treatment for high BP results in lower achieved SBP (eg, <140 mm Hg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted. (Expert Opinion – Grade E)

Recommendation 2

In the general population <60 years, initiate pharmacologic treatment to lower BP at DBP ≥90 mm Hg and treat to a goal DBP <90 mm Hg. (For ages 30-59 years, Strong Recommendation – Grade A; For ages 18-29 years, Expert Opinion – Grade E)

Recommendation 3

In the general population <60 years, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg and treat to a goal SBP <140 mm Hg. (Expert Opinion – Grade E)

Recommendation 4

In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

Salt Restriction

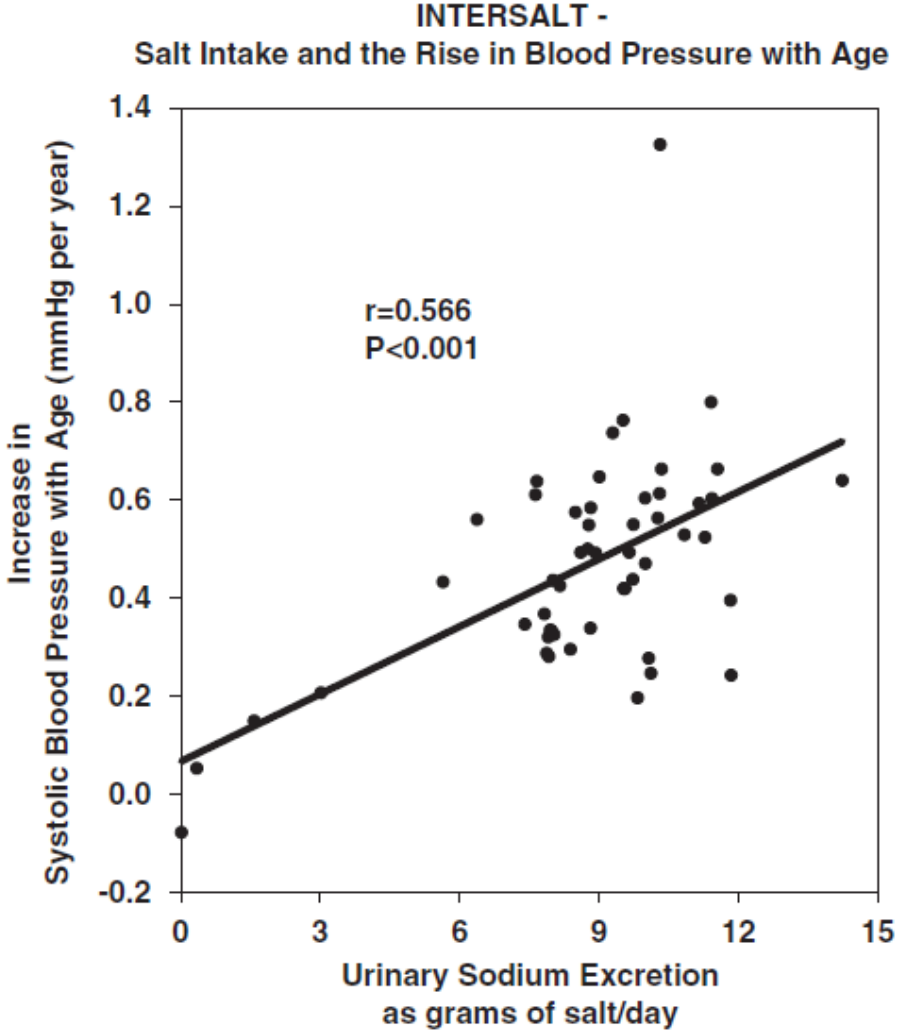


Figure 2 Relationship between salt intake and the slope of the rise in systolic blood pressure with age in 52 centres in the INTERSALT study. Adapted from Intersalt Cooperative Research group.[1]

Analysis of 177 Cases of Hypertensive Vascular Disease with Papilledema*

One Hundred Twenty-six Patients Treated with Rice Diet

BARBARA NEWBORG, M.D. *and* WALTER KEMPNER, M.D.
Durham, North Carolina

TABLE VI
RETINOPATHY IN 100 PATIENTS TREATED WITH RICE DIET*

	Disappeared Completely		Disappeared Partially		No Change	
	Number of Patients	Time in Months (averages)	Number of Patients	Time in Months (averages)	Number of Patients	Time in Months (averages)
Papilledema (100 patients)	92	5	3	2	5	4
Hemorrhages (90 patients)	69	8	16	8	5	4
Exudates (94 patients)	56	15	30	7	8	5

* Eyeground photographs available before and 1 to 121 months after treatment with the rice diet was started.

American Journal of Medicine, July 1955

Effects of Dietary Sodium Reduction on Blood Pressure in Subjects With Resistant Hypertension

Results From a Randomized Trial

Eduardo Pimenta, Krishna K. Gaddam, Suzanne Oparil, Inmaculada Aban, Saima Husain, Louis J. Dell'Italia, David A. Calhoun

(*Hypertension*. 2009;54:475-481.)

- 4 week randomized cross-over evaluation
- 12 patients with resistant HTN
  - SBP > 140 or DBP > 90 despite 3+ medications including thiazide
- High versus low salt diet
  - Low salt 50 mmol/day
  - High salt supplemented with NaCl tabs
  - Other portions of diet controlled

Table 1. Characteristics of Patients Entered in the Study

Characteristics	All Patients n=12
Male/female	4/8
Black/white	6/6
Age, y	55.5±9.4 (34–66)
BMI, kg/m^2	32.9±6.3
No. of antihypertensive medicines	3.4±0.5
Serum potassium, mEq/L	3.8±0.4
Serum creatinine, mg/dL	1.0±0.3
Brain natiuretic peptide, pg/mL	36.7±30.6
Plasma aldosterone, ng/dL	10.2±5.6
Plasma renin activity, ng/ml/h	1.1±0.8
Urinary aldosterone, mcg/24 hours	11.7±3.9
Urinary sodium, mmol/24 hours	194.7±68.6
Creatinine clearance, mg/min	132.8±36.0
Office BP, mm Hg	
Systolic	145.8±10.8
Diastolic	83.9±11.2

BMI, indicates body mass index; BP, blood pressure.

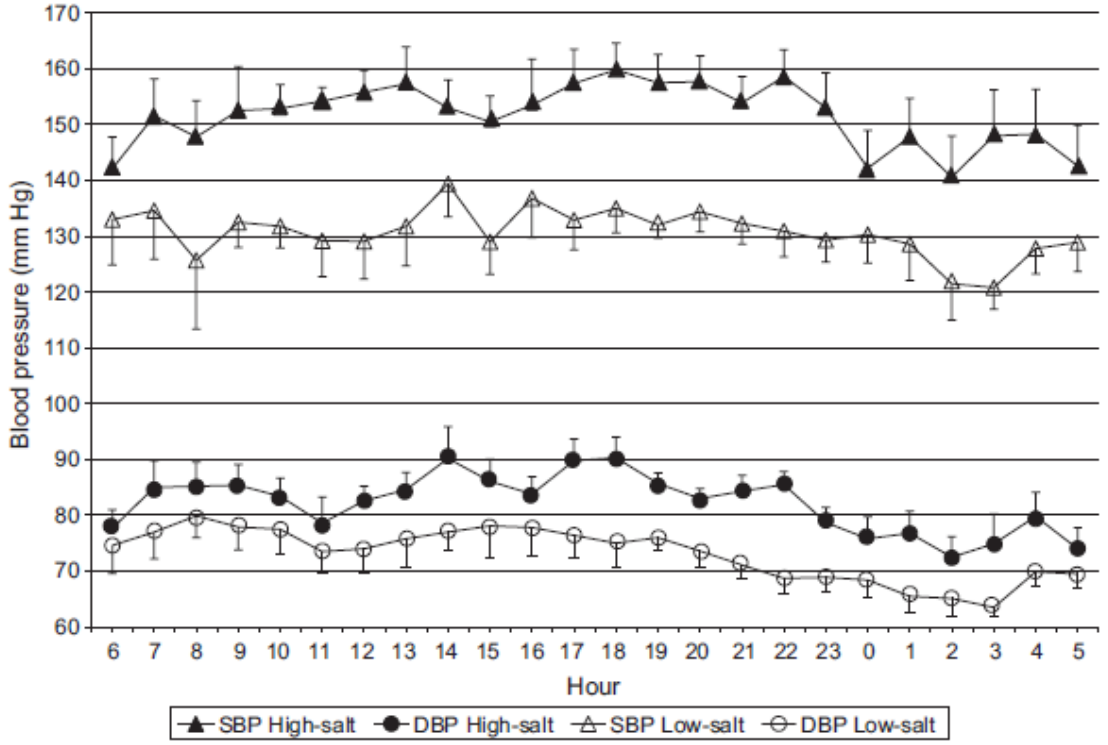


Figure. Comparison of 24-hour ambulatory blood pressure values during low- and high-salt diet. Data presented as mean±SE.

What is Diabetes?

- Diabetes- Increased urine production
  - Insipidus
    - Abnormal water regulation
  - Mellitus
    - From increased sugar in the urine

Diabetes Mellitus

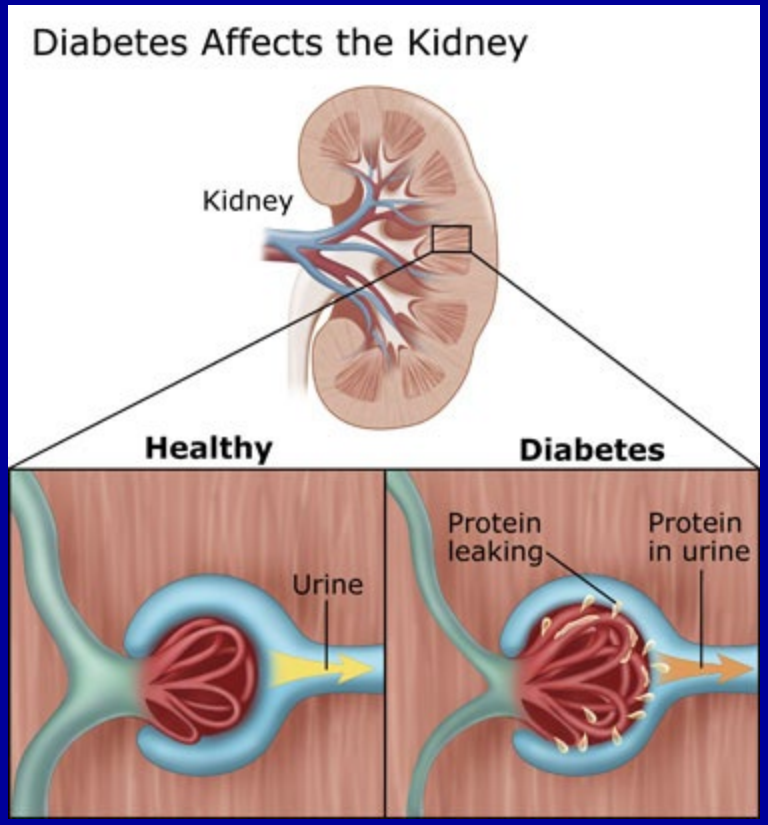
- Type 1
  - Lack of pancreatic production of insulin
    - Genetics
    - Viral infection(?)
  - Onset at young age
  - Thin body type
  - Abrupt onset
  - Polyuria, polydipsia
- Type 2
  - Middle age to elderly onset
  - Often no symptoms
  - Normal or increased insulin levels
    - “pancreatic burnout”
  - Genetic & dietary factors


TM

Diabetic Nephropathy is the Leading Cause of ESRD in the USA!

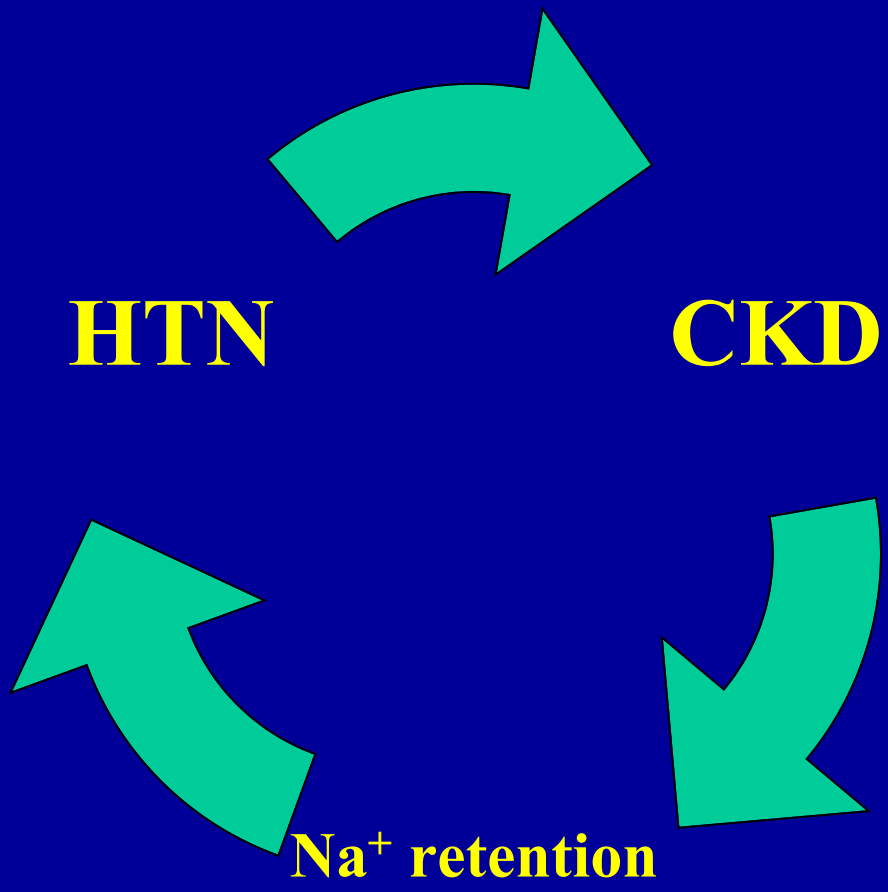
How Does Diabetic Kidney Disease Happen??

- High blood sugar causes hyperfiltration
  - Creat/GFR normal (or high!)
- Advanced glycosylation end-products (AGEs)
  - Effect the blood vessels (small and large)
  - Cause abnormal cell growth and proliferation
  - Damages important cells in the kidneys
    - Causes proteinuria

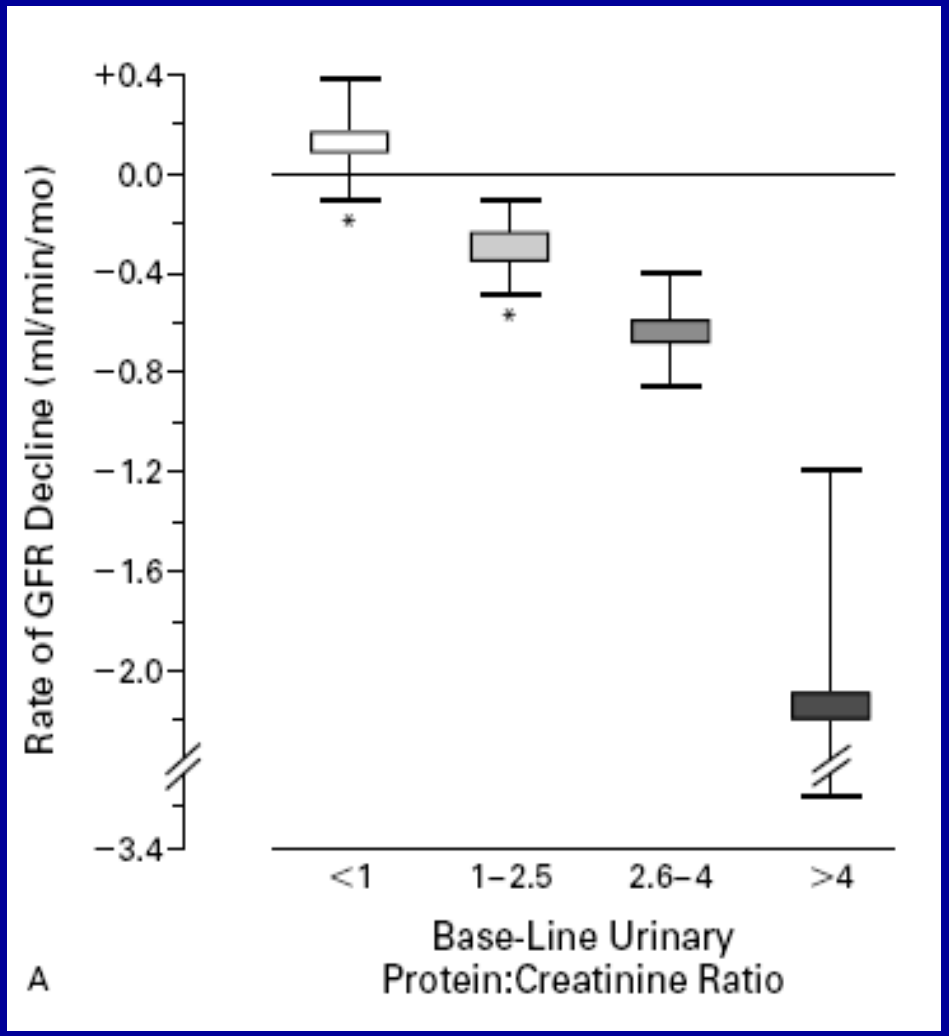


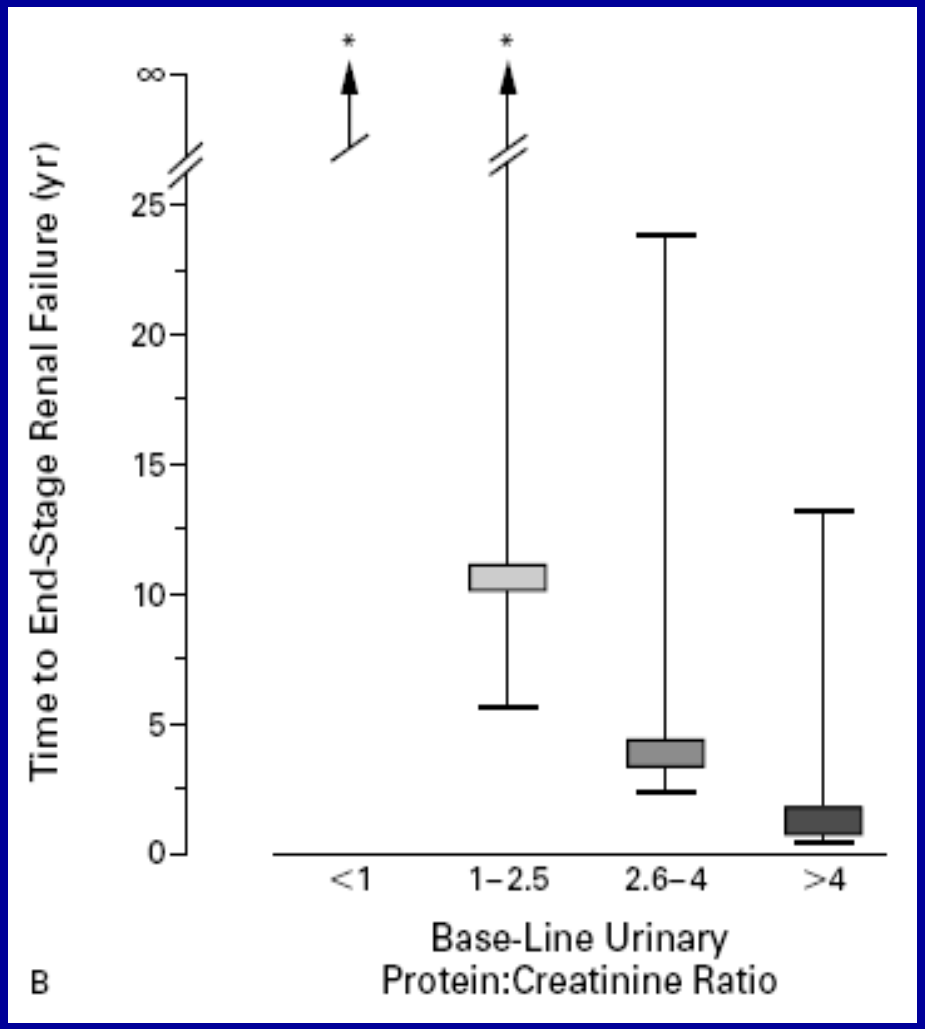
Proteinuria

- Early on it's "microalbuminuria"
  - 30 – 300 mg/24 hrs
  - Important screening test!!
- Diabetic Nephropathy
  - Macroalbuminuria (> 300 mg/24 hrs)
- Will lead to sodium retention and hypertension!
  - Vicious cycle that makes proteinuria worse!



Detrimental effects of proteinuria





Remuzzi & Bertani, NEJM Nov 1998

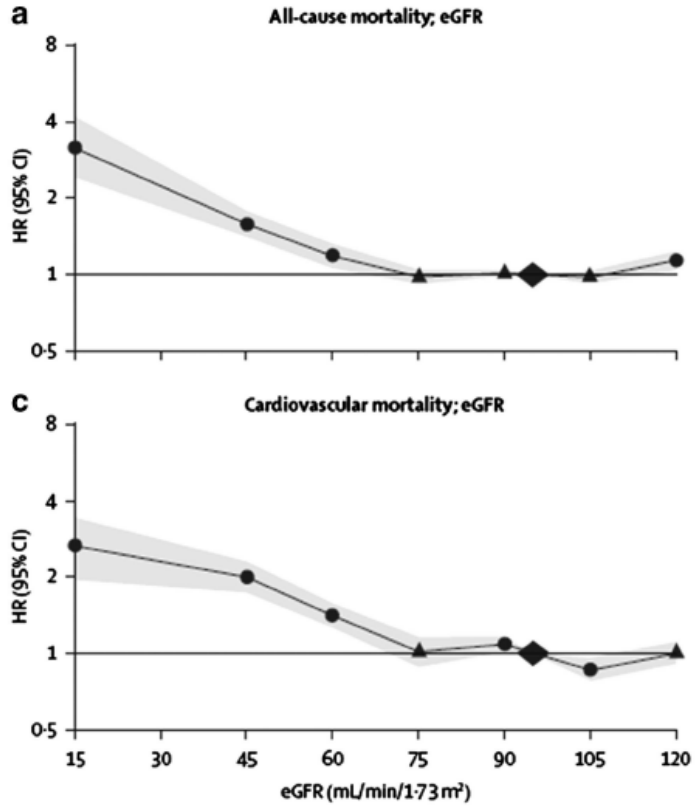


Figure 3 | Relationship of eGFR with mortality. HRs and 95% CIs for all-cause (**a**) and cardiovascular mortality (**c**) according to spline eGFR. HRs and 95% CIs (shaded areas) are adjusted for ACR, age, sex, ethnic origin, history of CVD, systolic BP, diabetes, smoking, and total cholesterol. The reference (diamond) was eGFR 95 ml/min/1.73 m^2 and ACR 5 mg/g (0.6 mg/mmol), respectively. Circles represent statistically significant and triangles represent not significant. ACR, albumin-to-creatinine ratio; BP, blood pressure; CI, confidence interval; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio. Reprinted from The Lancet, vol 375, Matshushita K, van de Velde M, Astor BC, et al.[4] Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis, p. 2073-2081, 2010, with permission from Elsevier; accessed http://download.thelancet.com/pdfs/journals/lancet/PIIS0140673610606745.pdf

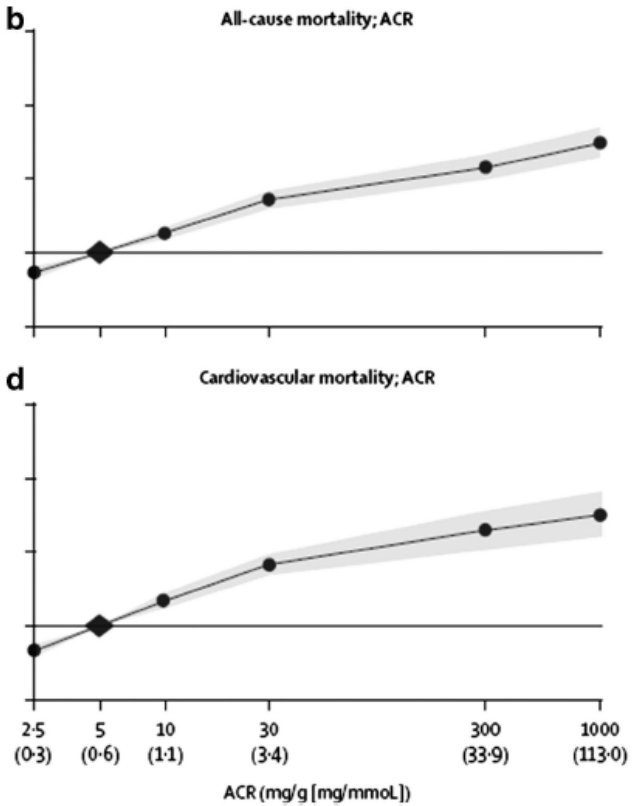


Figure 4 | Relationship of albuminuria with mortality. HRs and 95% CIs for all-cause (**b**) and cardiovascular mortality (**d**) according to ACR. HRs and 95% CIs (shaded areas) are adjusted for age, sex, ethnic origin, history of CVD, systolic BP, diabetes, smoking, and total cholesterol and spline eGFR. The reference (diamond) was ACR 5 mg/g (0.6 mg/mmol) and eGFR 95 ml/min/1.73 m^2, respectively. Circles represent statistically significant and triangles represent not significant. ACR plotted in mg/g. To convert ACR in mg/g to mg/mmol multiply by 0.113. Approximate conversions to mg/mmol are shown in parentheses. ACR, albumin-to-creatinine ratio; BP, blood pressure; CI, confidence interval; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio. Reprinted from The Lancet, vol 375, Matshushita K, van de Velde M, Astor BC, et al.[4] Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis, p. 2073-2081, 2010, with permission from Elsevier; accessed http://download.thelancet.com/pdfs/journals/lancet/PIIS0140673610606745.pdf

Diabetic Nephropathy

- The greater the proteinuria, the more rapid the decline in renal function
  - Many patients end up on dialysis!
- Time course of disease progression is variable
  - Depends on many factors
  - Genetics
  - Medications

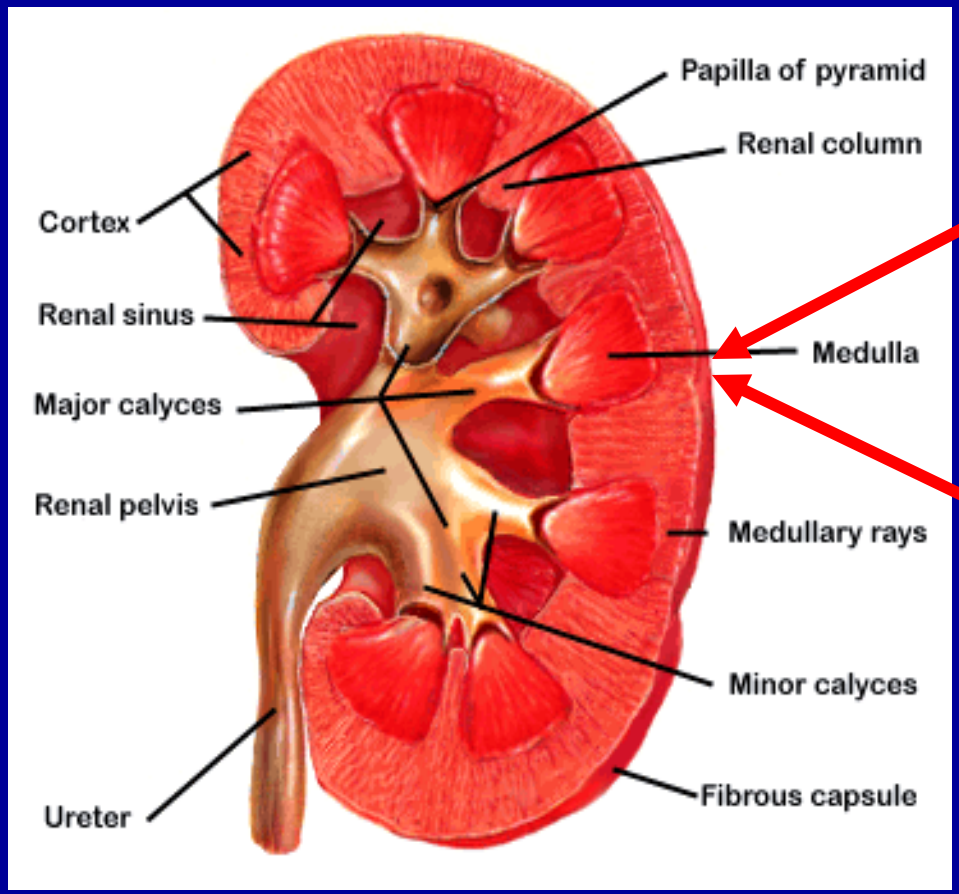
Treatment

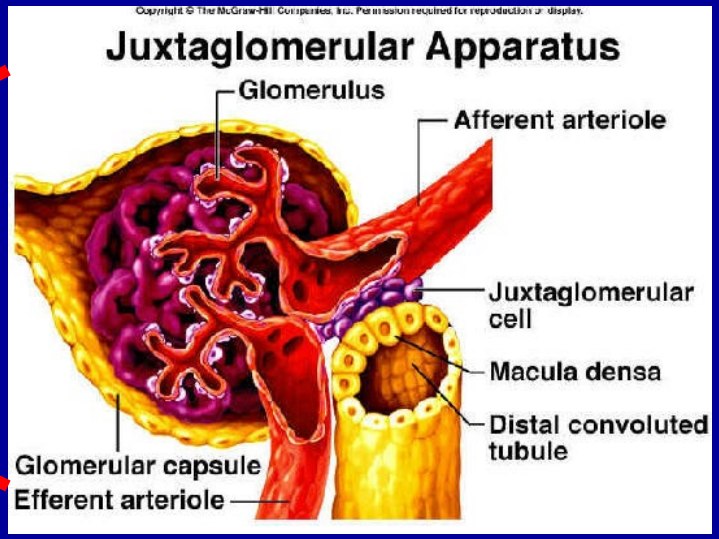
- Multifactorial risk factor reduction
  - Reduce dietary fat
  - Light to moderate exercise
  - Smoking cessation
  - Blood sugar control (A1C < 6.5%)
  - BP control (< 130/80)
  - ACE inhibitor therapy
  - Lipid-lowering therapy

CKD Treatment

It's all about protecting the glomeruli!

1,000,000 glomeruli per kidney!

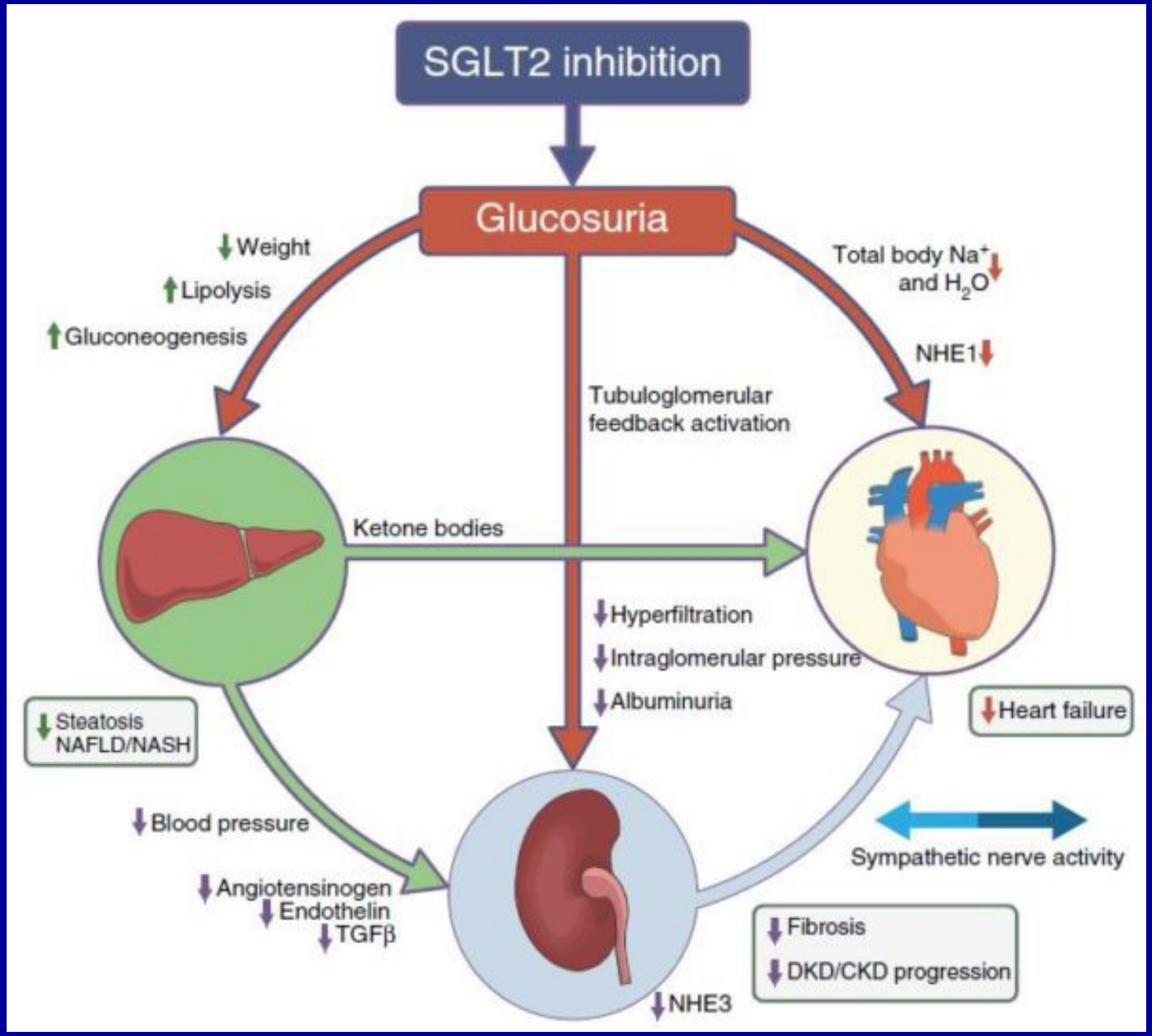


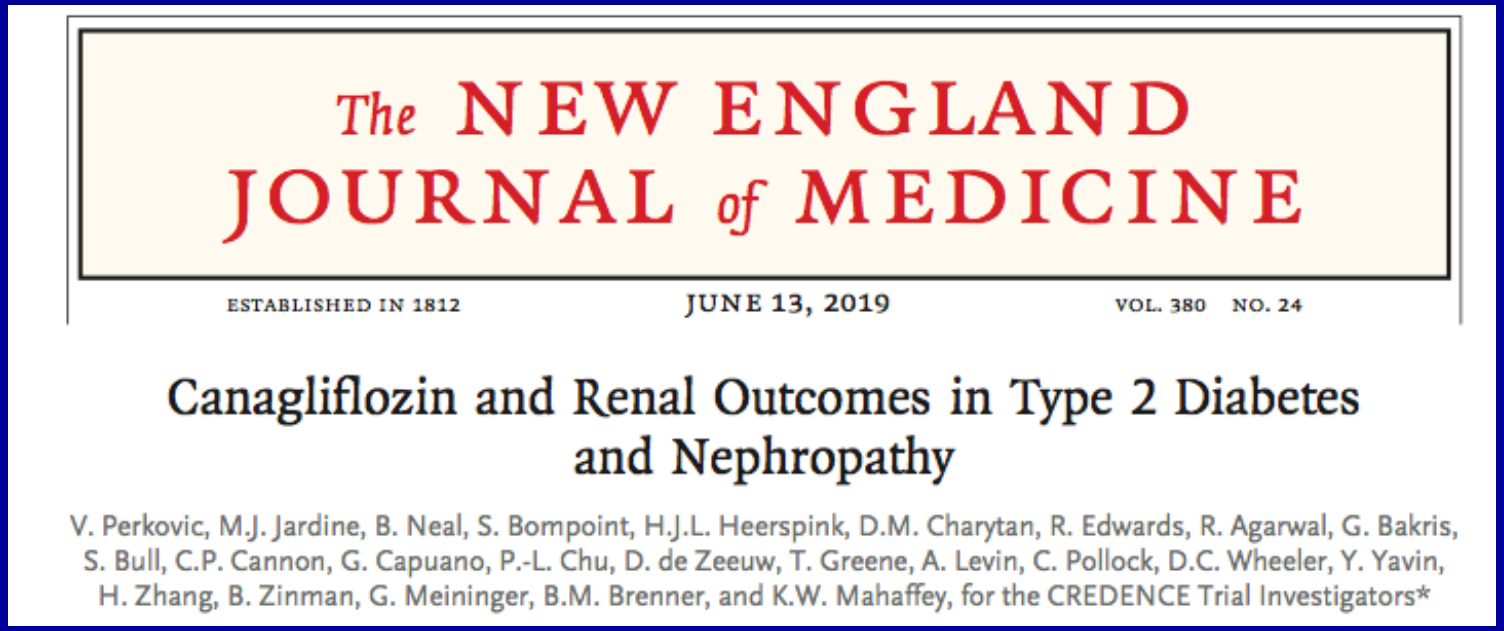


So, What Are The Mainstays of CKD Treatment?

- RAAS inhibition (BP reduction)
  - RENAAL (2001)
  - IDNT (2001)
- SGLT-2 inhibition
- Selective MRA treatment (finerenone)
  - FIDELIO DKD

More than just lowering blood sugar!





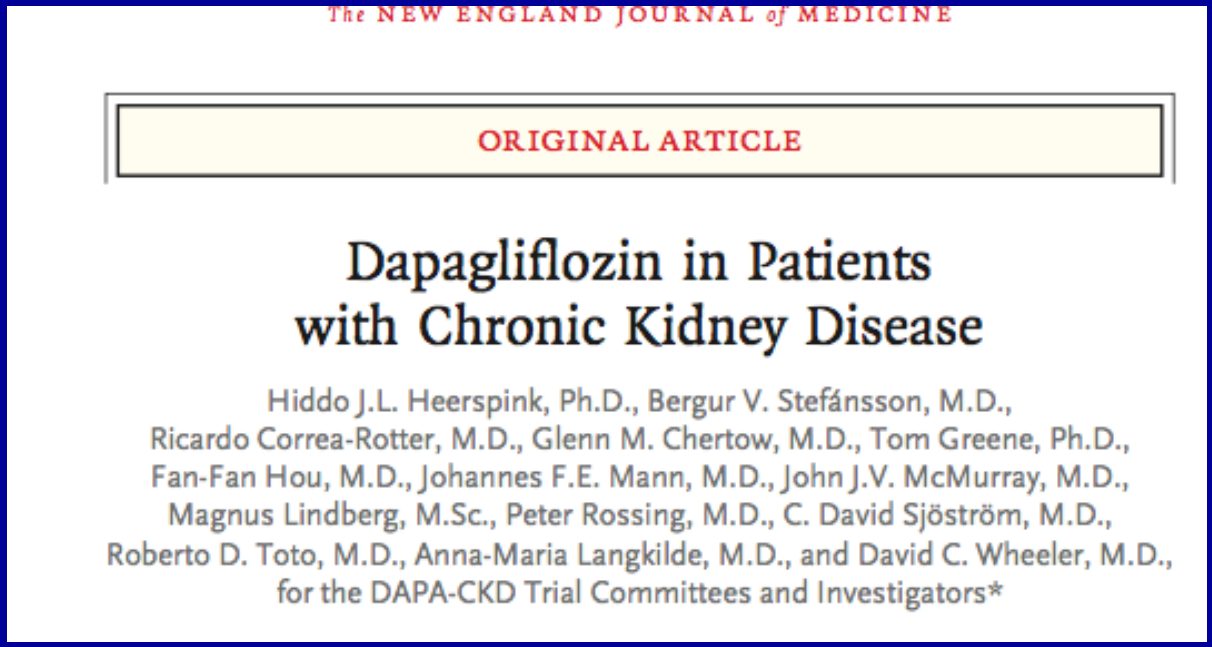
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 13, 2019 VOL. 380 NO. 24

Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

V. Perkovic, M.J. Jardine, B. Neal, S. Bompoint, H.J.L. Heerspink, D.M. Charytan, R. Edwards, R. Agarwal, G. Bakris, S. Bull, C.P. Cannon, G. Capuano, P.-L. Chu, D. de Zeeuw, T. Greene, A. Levin, C. Pollock, D.C. Wheeler, Y. Yavin, H. Zhang, B. Zinman, G. Meininger, B.M. Brenner, and K.W. Mahaffey, for the CREDENCE Trial Investigators*

-Patients with Type 2 DM and albuminuric CKD stage 2 & 3
    -Treated with 100 mg canagliflozin daily vs placebo
    -Already receiving RASi therapy (ACEi or ARB)
-At median follow up 2.62 years, treatment group had...
    -34% lower relative risk of ESRD, doubling of serum creat or death from renal causes
    -lower risk of CV death/MI/CVA



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dapagliflozin in Patients with Chronic Kidney Disease

Hiddo J.L. Heerspink, Ph.D., Bergur V. Stefánsson, M.D., Ricardo Correa-Rotter, M.D., Glenn M. Chertow, M.D., Tom Greene, Ph.D., Fan-Fan Hou, M.D., Johannes F.E. Mann, M.D., John J.V. McMurray, M.D., Magnus Lindberg, M.Sc., Peter Rossing, M.D., C. David Sjöström, M.D., Roberto D. Toto, M.D., Anna-Maria Langkilde, M.D., and David C. Wheeler, M.D., for the DAPA-CKD Trial Committees and Investigators*

N ENGL J MED 383;15 NEJM.ORG OCTOBER 8, 2020

-4304 albuminuric CKD patients with & WITHOUT DM (67/33)
  - -eGFR 25-75 mL/min
  - -98% of patients on RASi (ACEi or ARB)
  - -Assigned to dapa 10 mg daily vs placebo
  - -Median follow up 2.4 years
- -Risk of eGFR decline by 50%, ESRD, death from renal/CV causes significantly lower with dapa

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Empagliflozin in Patients with Chronic Kidney Disease

The EMPA-KIDNEY Collaborative Group*

N ENGL J MED 388;2 NEJM.ORG JANUARY 12, 2023

EMPA-Kidney Trial

-Enrolled 6609 patients to receive 10 mg empagliflozin versus placebo to assess effects on progression of CKD as well as death from CV causes

-Patients had either

-GFR 20-45 or…

-GFR 45-90 PLUS proteinuria

What Else???

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

Vlado Perkovic, M.B., B.S., Ph.D., Katherine R. Tuttle, M.D.,
Peter Rossing, M.D., D.M.Sc., Kenneth W. Mahaffey, M.D.,
Johannes F.E. Mann, M.D., George Bakris, M.D., Florian M.M. Baeres, M.D.,
Thomas Idorn, M.D., Ph.D., Heidrun Bosch-Traberg, M.D.,
Nanna Leonora Lausvig, M.Sc., and Richard Pratley, M.D.,
for the FLOW Trial Committees and Investigators*

FLOW Trial

- 3533 diabetic CKD patients
  - Maximal doses of RAS inhibitors
  - Randomized to weekly semaglutide 1 mg vs placebo
  - Median follow up of 3.4 years
  - Trial was stopped early due to significant benefit in the treatment group
    - 24% risk reduction of achieving the primary composite end point
      - Kidney failure, 50% drop in eGFR, or death from renal/CV causes

This article was published on May 24, 2024, at NEJM.org.

DOI: 10.1056/NEJMoa2403347

What is NOT part of the plan?

- “So Doc, you’re
  kidneys... That n
  more water, righ

JAMA | Original Investigation

Effect of Coaching to Increase Water Intake on Kidney Function Decline in Adults With Chronic Kidney Disease
The CKD WIT Randomized Clinical Trial

William F. Clark, MD; Jessica M. Sontrop, PhD; Shih-Han Huang, MD, PhD; Kerri Gallo, RN; Louise Moist, MD, MSc; Andrew A. House, MD; Meaghan S. Cuerden, MSc; Matthew A. Weir, MD, MSc; Amit Bagga, MD; Scott Brimble, MD; Andrew Burke, MD; Norman Muirhead, MD; Sanjay Pandeya, MD; Amit X. Garg, MD, PhD

JAMA. 2018;319(18):1870-1879. doi:10.1001/jama.2018.4930

RCT conducted at 9 centers in Canada

-Approximately 600 patients

- -CKD stage 3
- -Micro/macroalbuminuria
- -Total urine volume < 3 L

-Randomized to “coaching” to drink more water vs standard intake

Table 3. Primary Outcome: 1-Year Change in Estimated Glomerular Filtration Rate[a]

eGFR, mL/min per 1.73 m^2	Mean (95% CI)		Adjusted Between-Group Difference in Change[b] (95% CI)	*P* Value
	Hydration Group (n = 311)	Control Group (n = 308)		
Prerandomization	43.3 (42.1 to 44.4)	43.6 (42.6 to 44.7)		
12 Months	41.0 (39.5 to 42.6)	41.7 (40.3 to 43.1)		
Change	−2.2 (−3.3 to −1.1)[c]	−1.9 (−2.9 to −0.9)[c]	−0.3 (−1.8 to 1.2)	.74

CKD-REIN Study, NDT 2021

Prospective cohort study

Water intake and progression of chronic kidney disease (CKD): the CKD-REIN cohort study

Background

General population studies suggest that higher water intake may reduce CKD prevalence and kidney function decline

Cohort studies in CKD are inconclusive, but some suggest that higher fluid intake may not be appropriate

Methods

Multi-centre study (n=40)
CKD-REIN cohort (France)

Adult patients with CKD 3–4 (eGFR 15–60 ml/min/1.73 m²)

Urine volume and osmolarity by 24 h urine collection

Interview to evaluate total and plain water intake

Outcomes:
- eGFR slope
- Progression to kidney failure

N=1265
with water intake and 24 h urine collection

Results

Plain water intake (litres/day)	Kidney failure hazard ratio	eGFR slope (ml/min/1.73 m²/year)
> 2	1.55 (95% CI 1.03–2.32)	−2.48 (95% CI −3.15 to −1.81)
1.5–2	1.76 (95% CI 0.95–3.24)	−2.12 (95% CI −2.61 to −1.62)
1–1.5	Ref	−1.79 (95% CI −2.16 to −1.42)
0.5–1	1.59 (95% CI 1.06–2.38)	−2.34 (95% CI −2.76 to −1.93)
< 0.5	1.88 (95% CI 1.02–3.47)	−1.43 (95% CI −2.14 to −0.71)

Conclusion

In patients with CKD, the relationship between plain water intake and progression to kidney failure appears to be U-shaped. Both low and high intake may not be beneficial in CKD

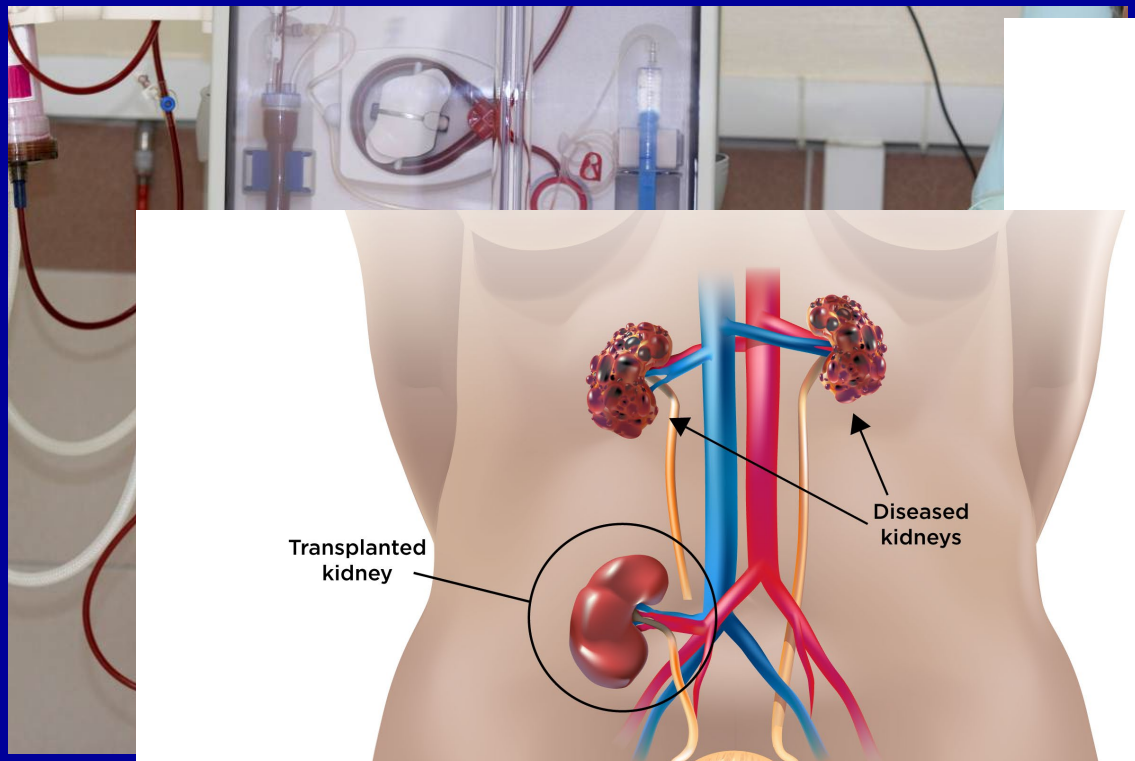
ndt NEPHROLOGY DIALYSIS TRANSPLANTATION

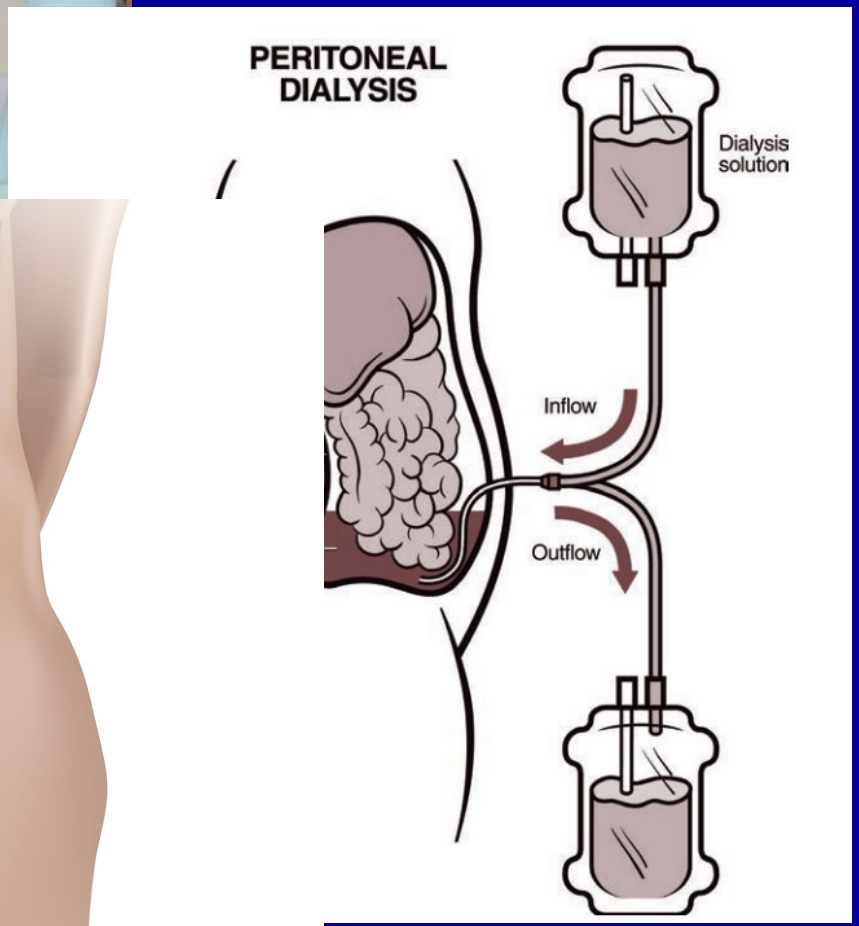
Wagner, S. et al. NDT (2021)
@NDTSocial

CKD-WIT & CKD-REIN

- Conclusion?
  - In patients with CKD, “forced hydration” is NOT a reliable part of the treatment plan!

What About When Kidneys Fail??





End-Stage Renal Disease

- About 550,000 Americans on dialysis currently
- More than 260,000 Americans are living with a kidney transplant

1.U.S. Renal Data System Annual Data Report ESRD Chapter 1, Incidence, Prevalence, Patient Characteristics and Treatment Modalities (**Annual Data Report | USRDS**)

Dialysis

Hemodialysis

- The patient's blood is cleaned directly through an artificial kidney
- Can be done in a center or at home
- Needs durable access to the blood stream
  - Preferably though an AV shunt/fistula/graft
- Takes time…..

Peritoneal Dialysis

- The patient uses his/her own peritoneal membrane to clean the blood
- Fluid infused via an abdominal catheter and is "cycled" over the course of hours
- Usually done at home, preferably overnight

Kidney Transplant

- Surgical procedure where a new kidney is implanted into a patient with kidney failure
- About 27,500 per year in the US
- Living donor (25%)
  - Preferred
- Deceased donor (75%)
  - Usual wait time of 4-7 years depending on blood type

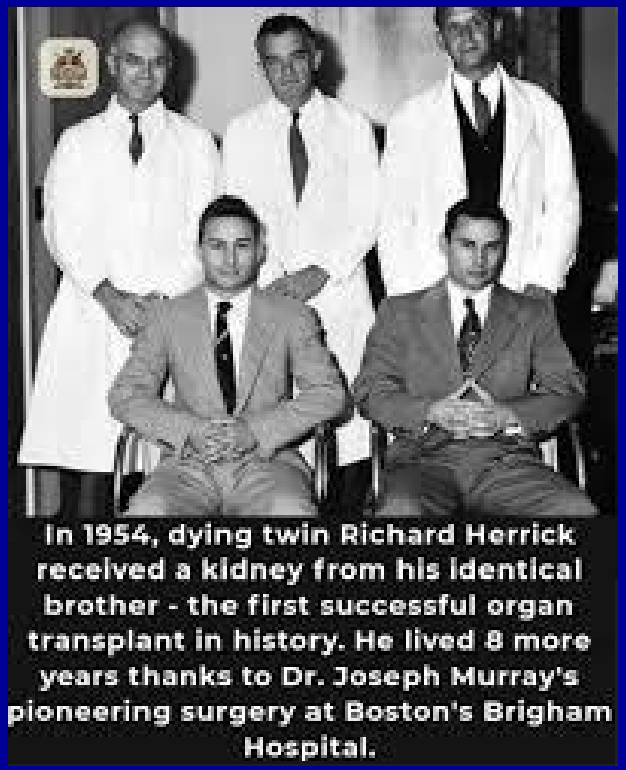
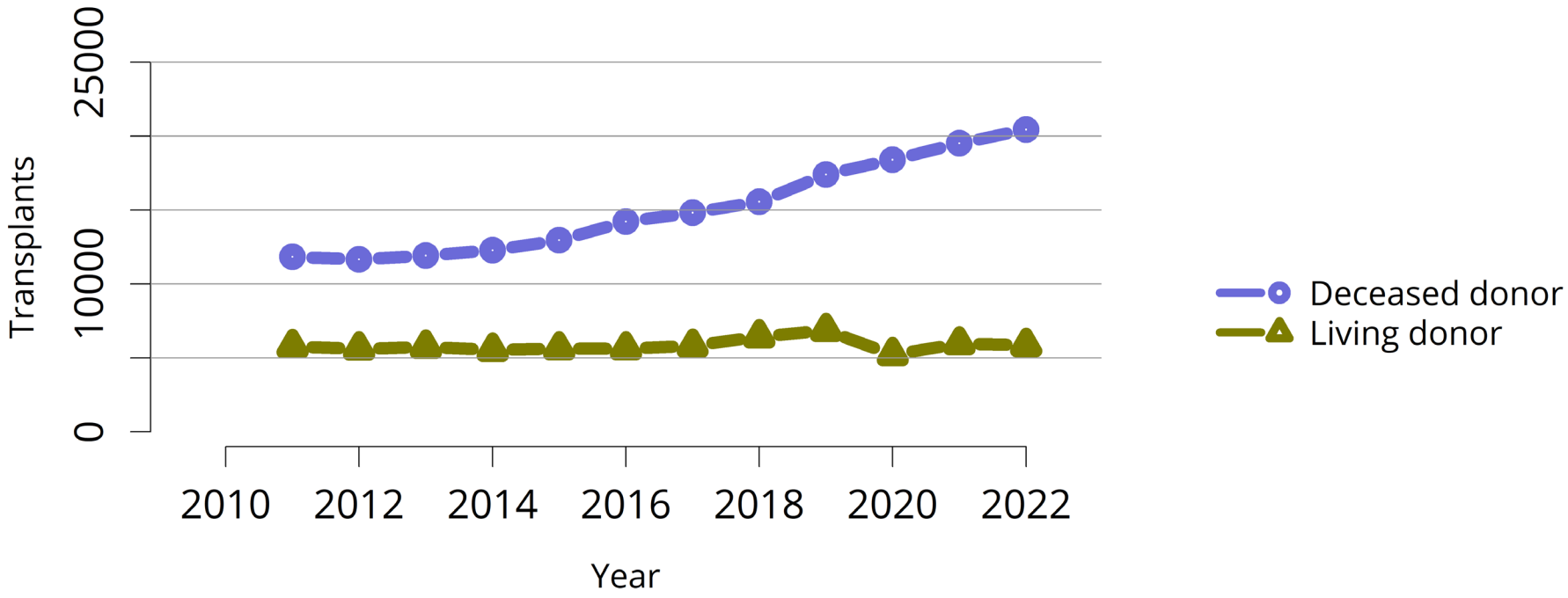


Figure KI 65: Total kidney transplants by donor type



OPTN/SRTR 2022 Annual Data Report

Wearable Artificial Kidney

Xenotransplantation

Xenotransplantation

- Genetically modified pig kidneys have been shown to function in non-human primates for 2-3 years
  - Anand et al, *Nature* 2023; 622:393-401
- Shorter term results have been seen with human recipients declared brain dead
  - Locke et al, *JAMA Surg* 2023; 158:1106-1108
  - Montgomery et al, NEJM 2022; 386: 1889-1898

Xenotransplantation

- Richard Slayman
  - 62 yo male from Weymouth, MA
  - ESRD/DM/HTN with previously failed renal transplant
  - Back on dialysis with poor tolerance of treatment
  - Limited dialysis access options
    - 2 procedures/month

Xenotransplantation

- Saturday March 16, 2024
  - Transplant performed at Mass General
  - Induction
    - Thymoglobulin
    - Rituximab
    - Steroids
    - Ravulizumab (experimental complement inhibitor)
- April 3, 2024
  - Discharged home
    - Tacrolimus
    - Mycophenolate
    - Prednisone
- May 11, 2024
  - Died “suddenly”
  - MGH press release
    - Death was “unrelated” to the transplant

Xenotransplantation

- April 12, 2024
  - Second pig kidney transplant performed at NYU Langone
  - 54 yo female with combined heart/kidney failure
  - Received LVAD first, then pig kidney 8 days later
    - Also got the pig thymus as well
- May 29, 2024
  - Kidney had to be removed
  - Concern for “lack of blood flow”
  - No concern for rejection
  - Patient returned to dialysis

Xenotransplantation

- Conclusions?
  - We are getting closer!
  - Kidneys can make urine “on the table”
  - Sicker patients don’t do well…
    - LVAD patients normally not eligible for transplant

Questions??

Thank You!