Chronic Kidney Disease and ADRD

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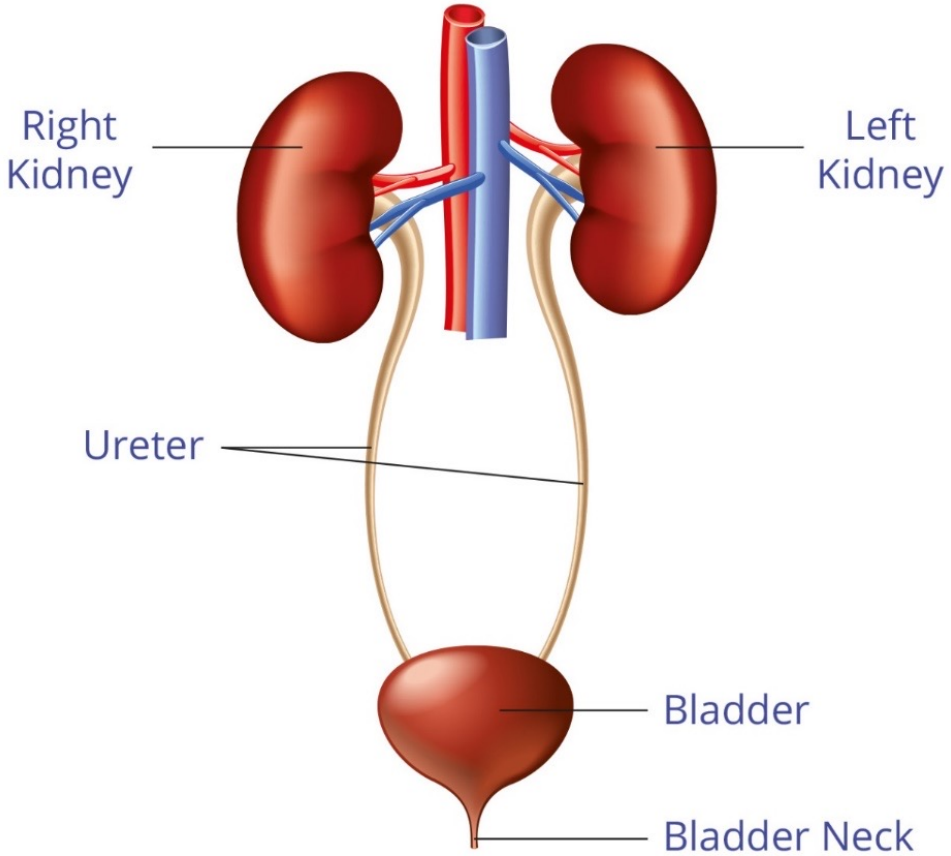
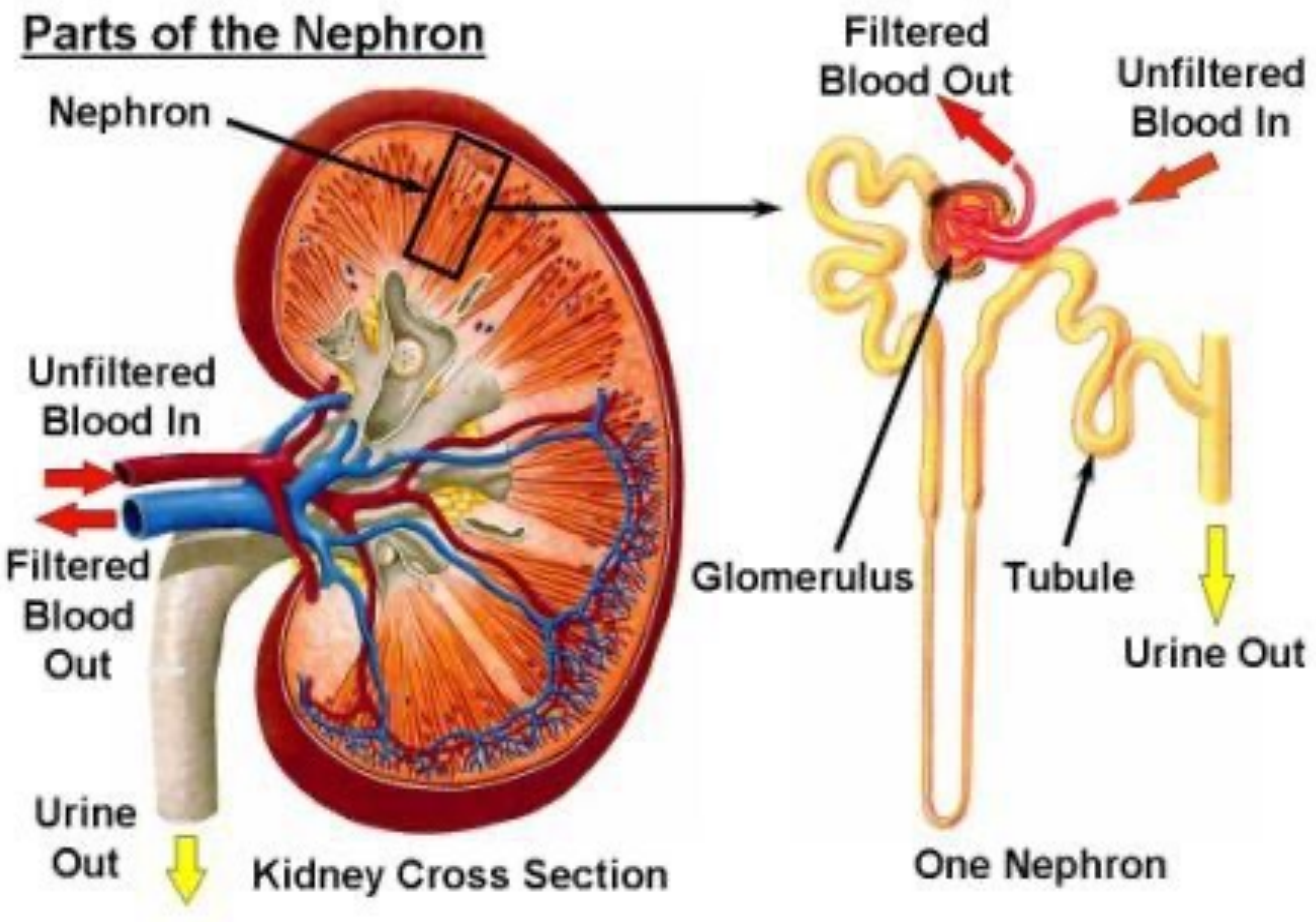
March 7, 2023

Genitourinary system



Kidney: Nephron



GFR Equations

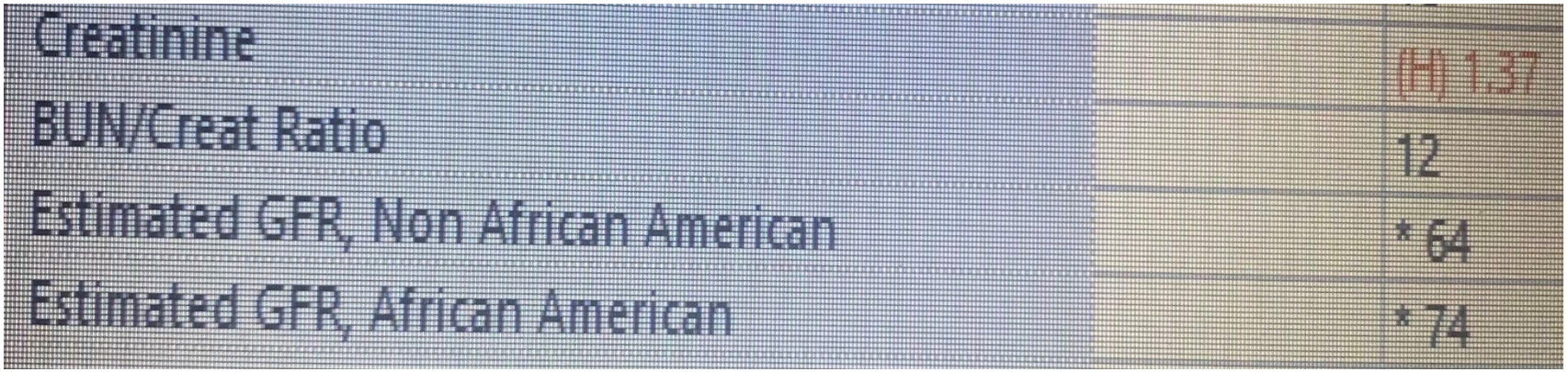
- **Serum creatinine**
- **Cockcroft-Gault Equation**
  - **CrCl (ml/min) = (140-age) x lean body wt (kg) / Cr x 72. then multiply by 0.85 if women**
- **MDRD Equation**
  - **CrCl (ml/min) = 175 x SCr (exp[-1.154]) x Age (exp[-0.203]) x (0.742 if female) x (1.21 if black)**
- **CKD-EPI Equation (elderly more precise)**
  - **$GFR = 141 \times \min(Scr/\kappa,1)^{\alpha} \times \max(Scr/\kappa,1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] X 1.159 [if black]**

Kidney function

- Estimated GFR (eGFR) reporting at Emory Healthcare uses the CKD-EPI equation and it reports out kidney function for African-Americans vs. Non African-Americans.

- CKD-EPI Equation:

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



CKD Definition (KDIGO - 2012)

- Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for 3 months, with implications for health and CKD is classified based on cause, GFR category, and albuminuria category.

KDIGO Work Group. KDIGO 2012 Clinical Practice Guidelines for Evaluation and Management of CKD. Kidney International Suppl 2013;3:1-150.

Stages of CKD

G category Stages

- **GFR**
  - **G1 >90 ml/min**
  - **G2 60-89 ml/min**
  - **G3a 45-59 ml/min**
  - **G3b 30-44 ml/min**
  - **G4 15-29 ml/min**
  - **G5 Kidney Failure, <15 ml/min**

A category

- **Albuminuria**
  - **A1 <30 mg/g**
  - **A2 30-300 mg/g**
  - **A3 >300 mg/g**

Prevalence of CKD

- **Prevalence of CKD in the United States: A Sensitivity Analysis Using the National Health and Nutrition Examination Survey (NHANES)**
  - 1999-2004
  - 13.07 % of adults
  - 26.3 million Americans
  - MDRD Study equation

Collins et al. Am J Kidney Dis 53:218-228. 2009

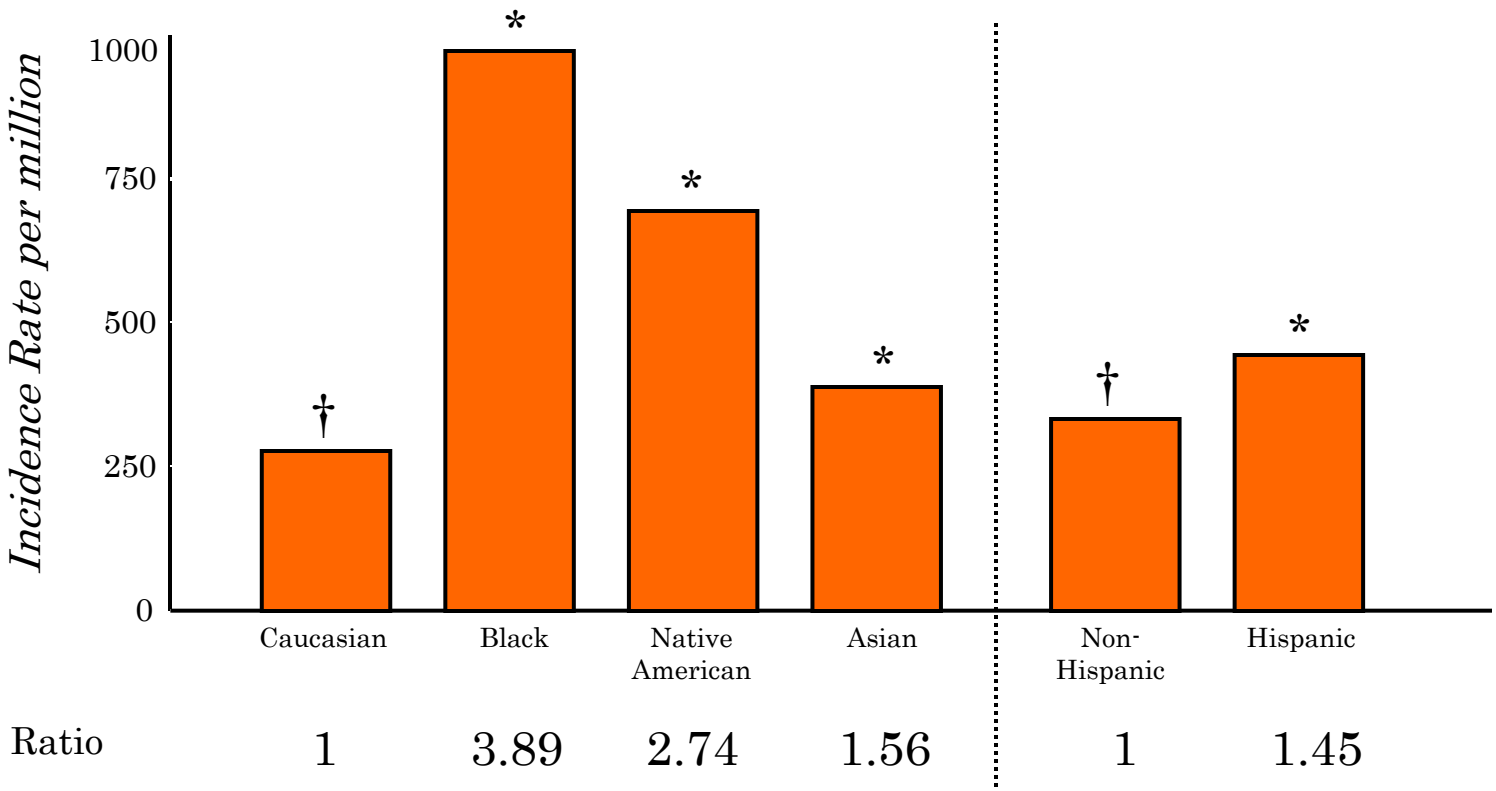
Prevalence of CKD

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

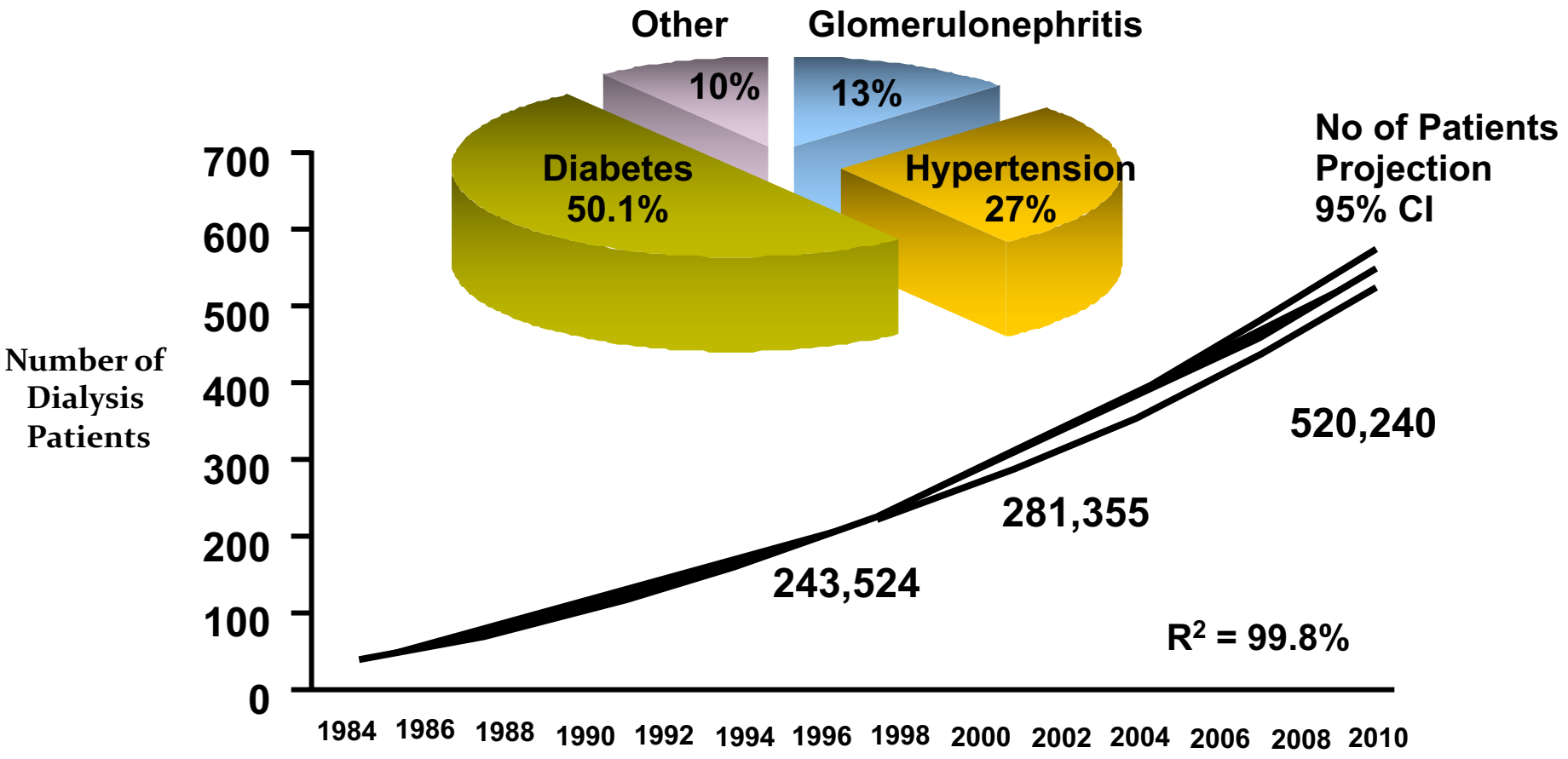
KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, 2013.

Stage 5 CKD Incidence Rates per Million Vary by Ethnicity



*P<0.0001, †Reference population.
Data adjusted for age and gender from 2001 in United States Renal Data System. 2003 Annual Data Report. Available at: www.usrds.org.

Primary Diagnosis For Patients Who Start Dialysis



United States Renal Data System. Annual data report

CKD Risk Factors

- Diabetes
- Hypertension
- Coronary artery disease
- Obesity
- Genetics/family history
- Older age
- Chronic illnesses (HIV, Lupus)
- Nephrotoxic medications (like NSAIDS, some chemotherapy)

Predictors for Progression

- **Level of GFR (kidney function at baseline)**
- **Albuminuria (protein in urine)**
- **Hypertension**
- **Race and male gender**
- **Advanced age**
- **Obesity and smoking**
- **Poor glycemic control (diabetes)**
- **Ongoing nephrotoxic medication use (NSAID pain meds, certain antibiotics or chemo)**
- **Hyperlipidemia and cardiovascular disease**

KDIGO Work Group. KDIGO 2012 Clinical Practice Guidelines for Evaluation and Management of CKD. Kidney International Suppl 2013;3:1-150

CKD Treatment Recommendations

- The 2012 KDIGO guidelines on the evaluation and management of BP in CKD recommended:
  - a goal BP ≤130/80 mm Hg for patients with CKD (with or without diabetes) and micro- or macroalbuminuria (protein in urine).
  - and a goal of ≤140/90 mm Hg for those without albuminuria.
- Some recommendations of <130/80 for everyone.
- The guideline also recommended using ACEi or ARB in diabetic patients and patients with protein in urine.
  - Examples: Lisinopril (ACEi) and losartan (ARB)
- SGLT2 inhibitors (Farxiga and Jardiance)

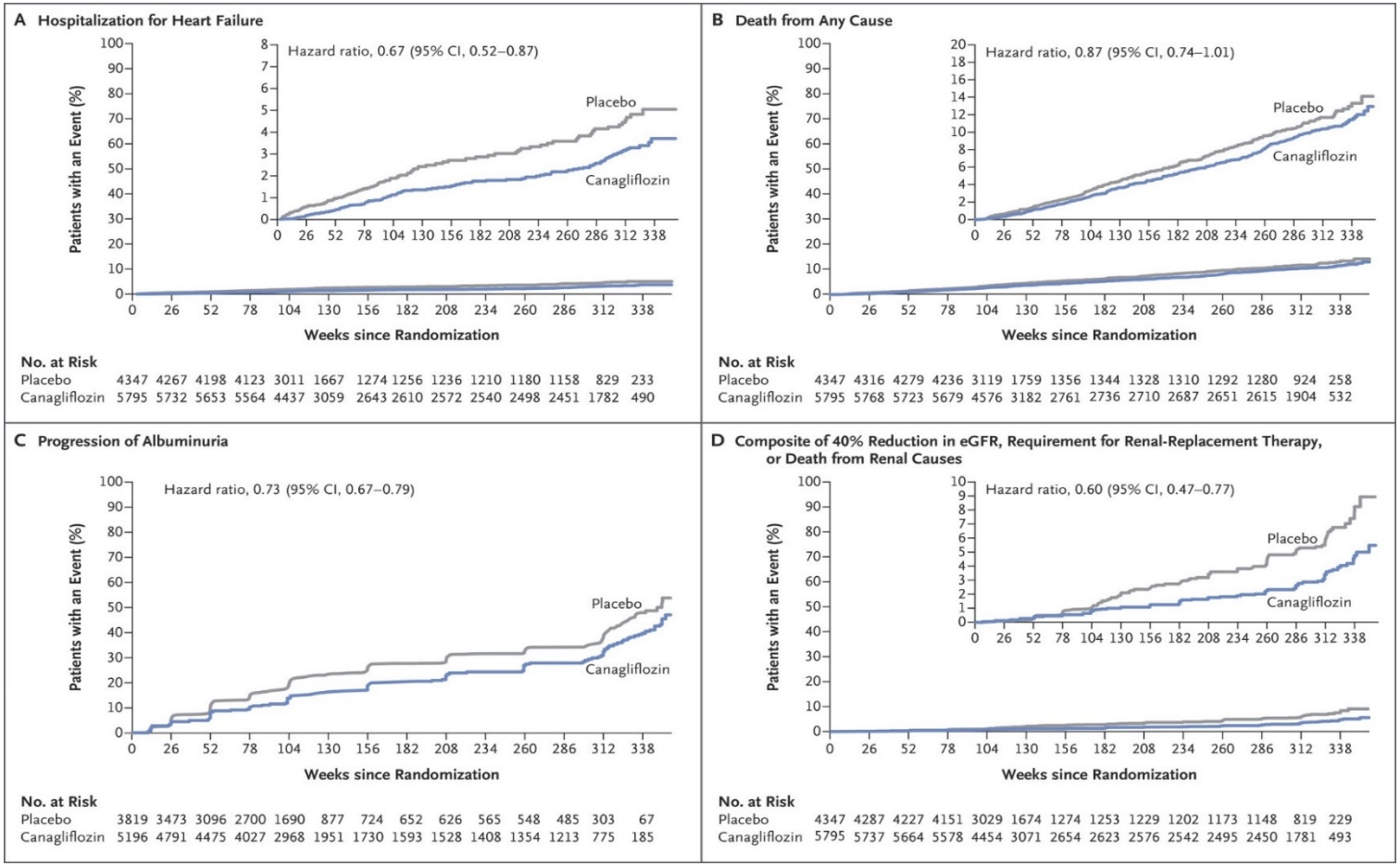
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

Bruce Neal, M.B., Ch.B., Ph.D., Vlado Perkovic, M.B., B.S., Ph.D., Kenneth W. Mahaffey, M.D., Dick de Zeeuw, M.D., Ph.D., Greg Fulcher, M.D., Ngozi Erondu, M.D., Ph.D., Wayne Shaw, D.S.L., Gordon Law, Ph.D., Mehul Desai, M.D., and David R. Matthews, D.Phil., B.M., B.Ch., for the CANVAS Program Collaborative Group*

- In this report of two randomized trials, patients with type 2 diabetes at risk for cardiovascular disease received the sodium–glucose cotransporter 2 inhibitor canagliflozin or placebo and were followed for 188 weeks.
- Hypothesis: Canagliflozin reduced the risk of cardiovascular events.



The NEW ENGLAND JOURNAL of MEDICINE

Prevalence of CKD complications by GFR category

	>90%	60-89%	45-59%	30-44%	<30%
Anemia	4%	4.7%	12.3%	22.7%	51.5%
Hypertension	18.3	41	71.8	78.3	82.1
Vitamin D Deficiency	14.1	9.1	10.7	10.7	27.2
Acidosis	11.2	8.4	9.4	18.1	31.5
High phos	7.2	7.4	9.2	9.3	23
High PTH	5.5	9.4	23	44	72.5

KDIGO Work Group. KDIGO 2012 Clinical Practice Guidelines for Evaluation and Management of CKD. Kidney International Suppl 2013;3:1-150.

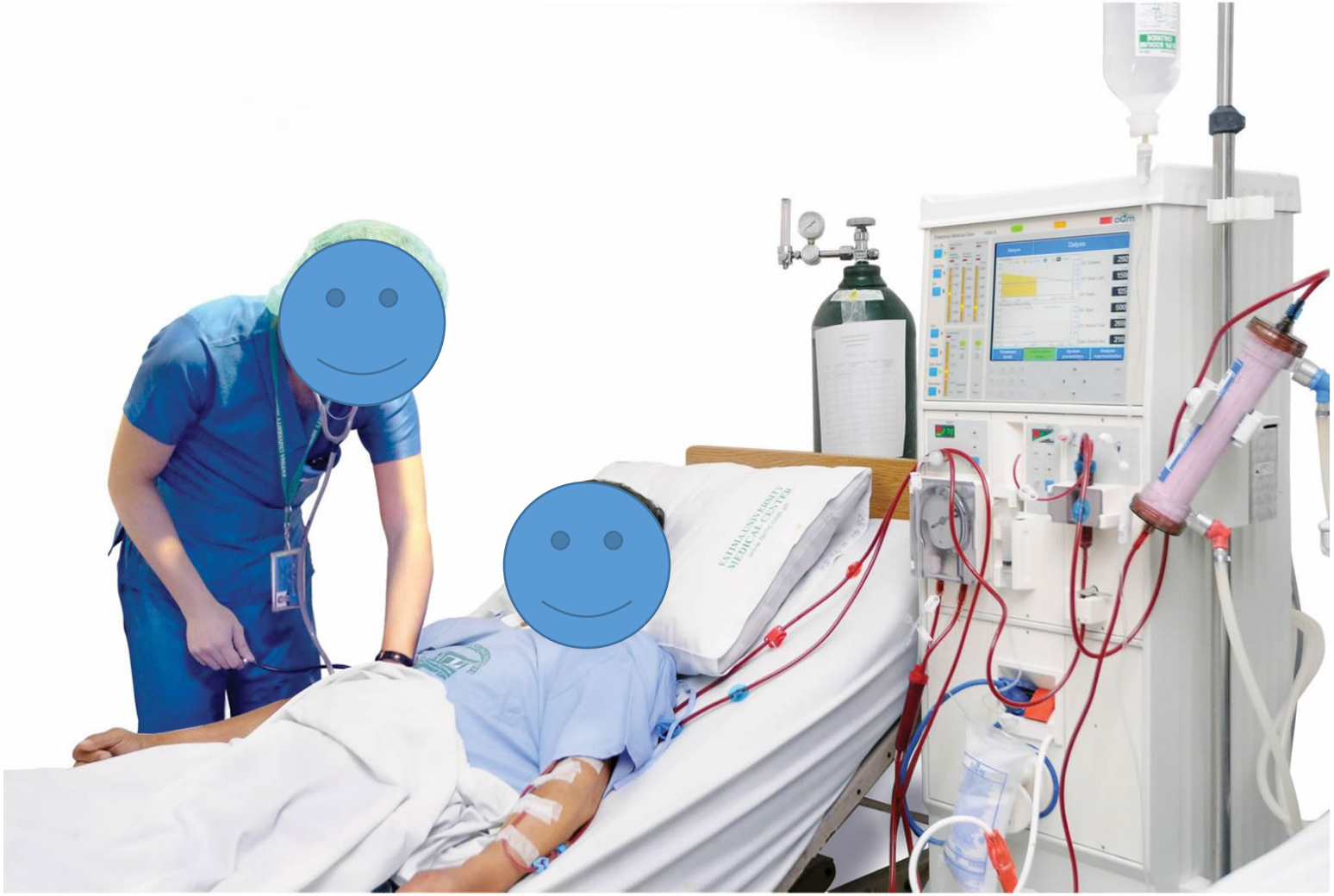
Cardiovascular Disease

- Dyslipidemia
  - Screen all patients with Chronic Kidney Disease (CKD)
- Rationale:
  - High prevalence of cardiovascular disease
  - Possible contribution to progression of CKD
- LDL goal < 100 mg/dL
  - Treatment of TG important if >500mg/dL
  - *Controversial KDIGO Guidelines 2013 on Lipid Management – released 2014*
    - *Not to follow LDL but put all with CKD on statins and lifestyle modification for TG levels*

Initiation of Dialysis
End-stage Kidney Disease
Kidney Failure

- Indications:
  - GFR approximately 10 mL/min/1.73m^2
    - **A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis. BA Cooper et al.** N Engl J Med 2010; 363:609-619
  - **Malnutrition (low albumin, weight loss)**
  - **AEIOU**
    - **Acidosis, Electrolyte problems, Intoxication, Overload (fluid), and Uremia (BUN)**
- Preparation:
  - KDIGO – nephrologist – eGFR <30 for all, before if >300 mg/day proteinuria, uncontrolled bp, significant hematuria, AKI, and fast progression (>5 ml/min/year).
  - Dialysis preparation if initiation within 1 year.
  - Choice of modality and dialysis access placement

Hemodialysis



Risk Factors

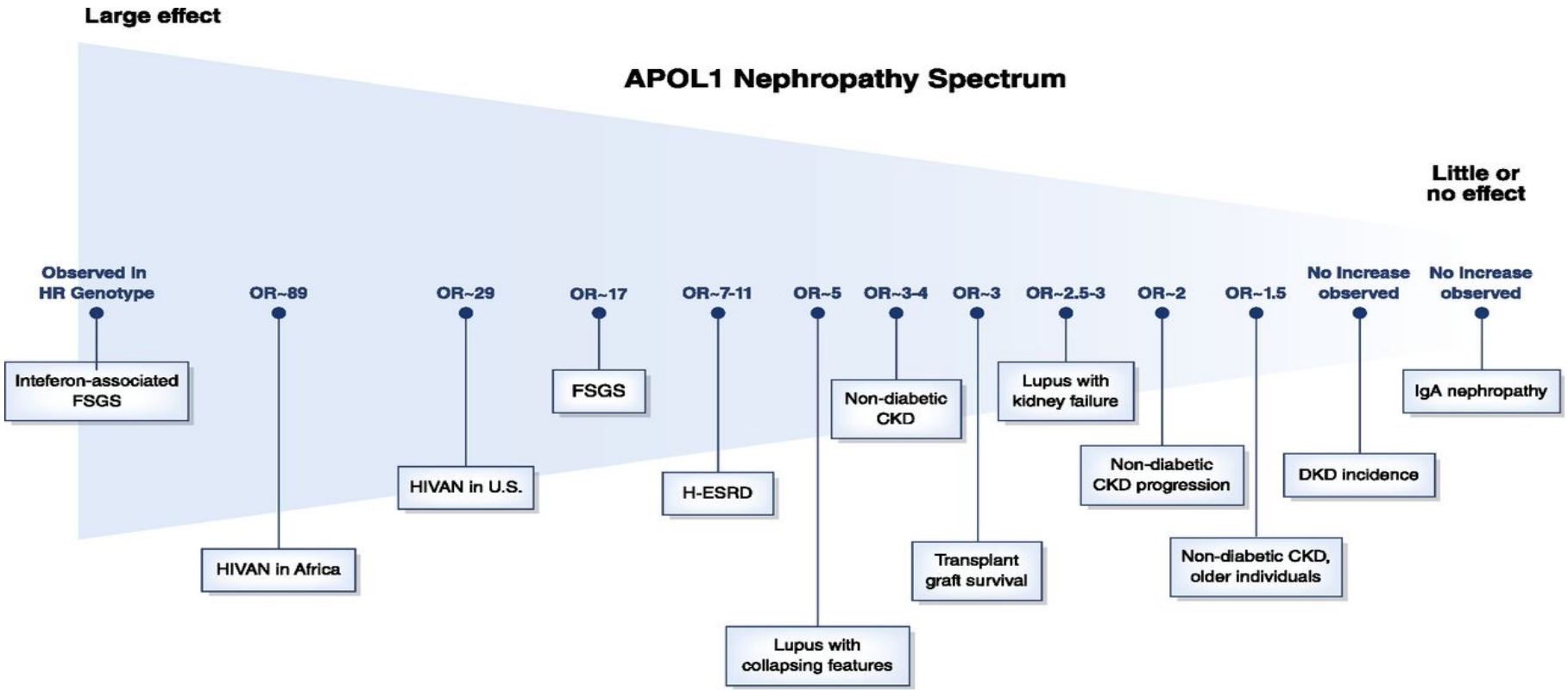
Dementia

- Genetics
  - Family history
- Hypertension
- Diabetes
- Smoking
- High cholesterol
- Older age
- Coronary artery disease
- Stroke (cerebrovascular disease)
- Obesity
- Physical inactivity
- Chronic illnesses (HIV/Lupus)
- CKD
- Medications

CKD

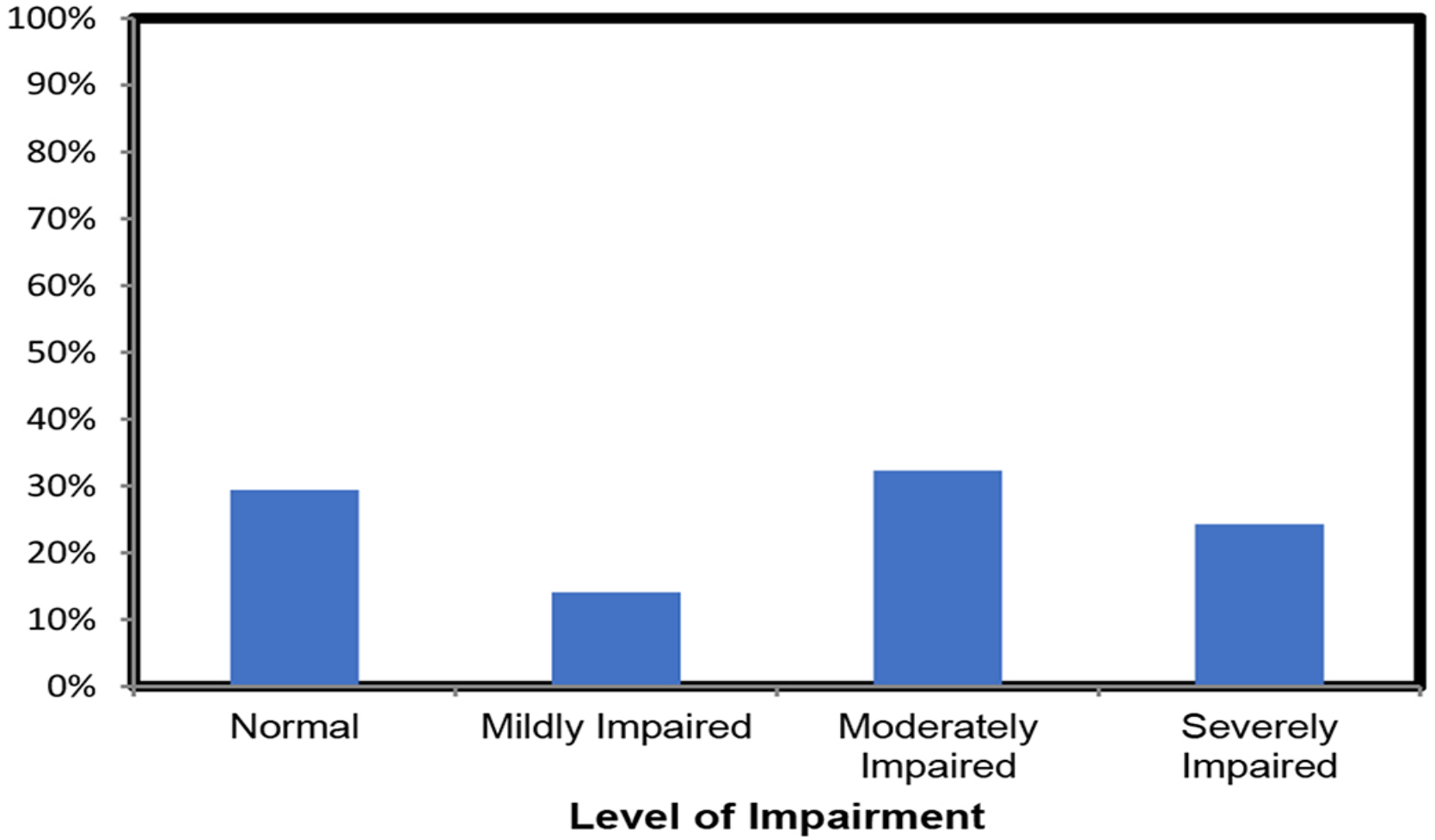
- Diabetes
- Hypertension
- Coronary artery disease
- Obesity
- Genetics/family history
- Older age
- Chronic illnesses (HIV, Lupus)
- Nephrotoxic medications

APOL1 risk variants increase the risk of many different types of kidney disease in blacks



David J. Friedman, and Martin R. Pollak
CJASN doi:10.2215/CJN.15161219

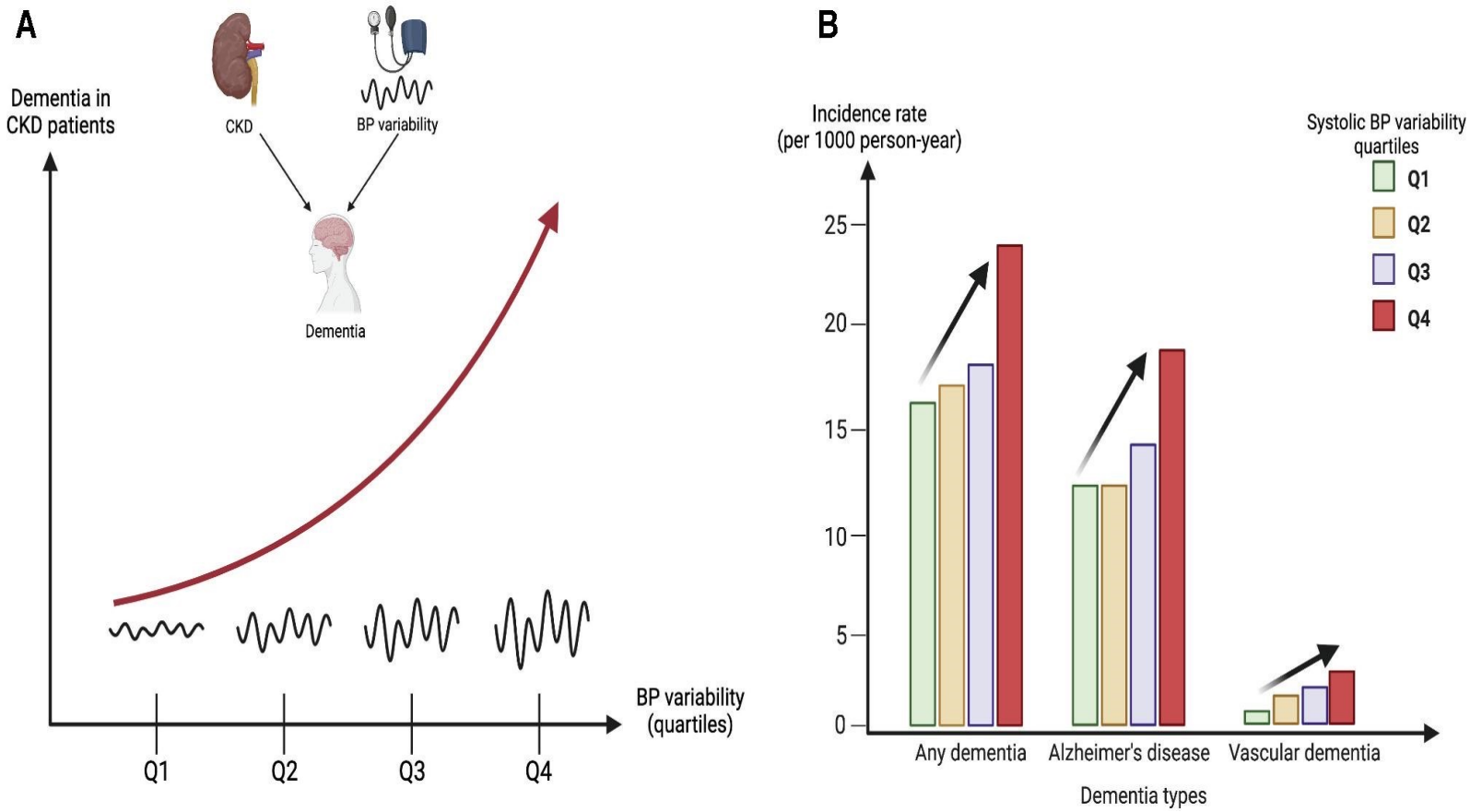
CJASN



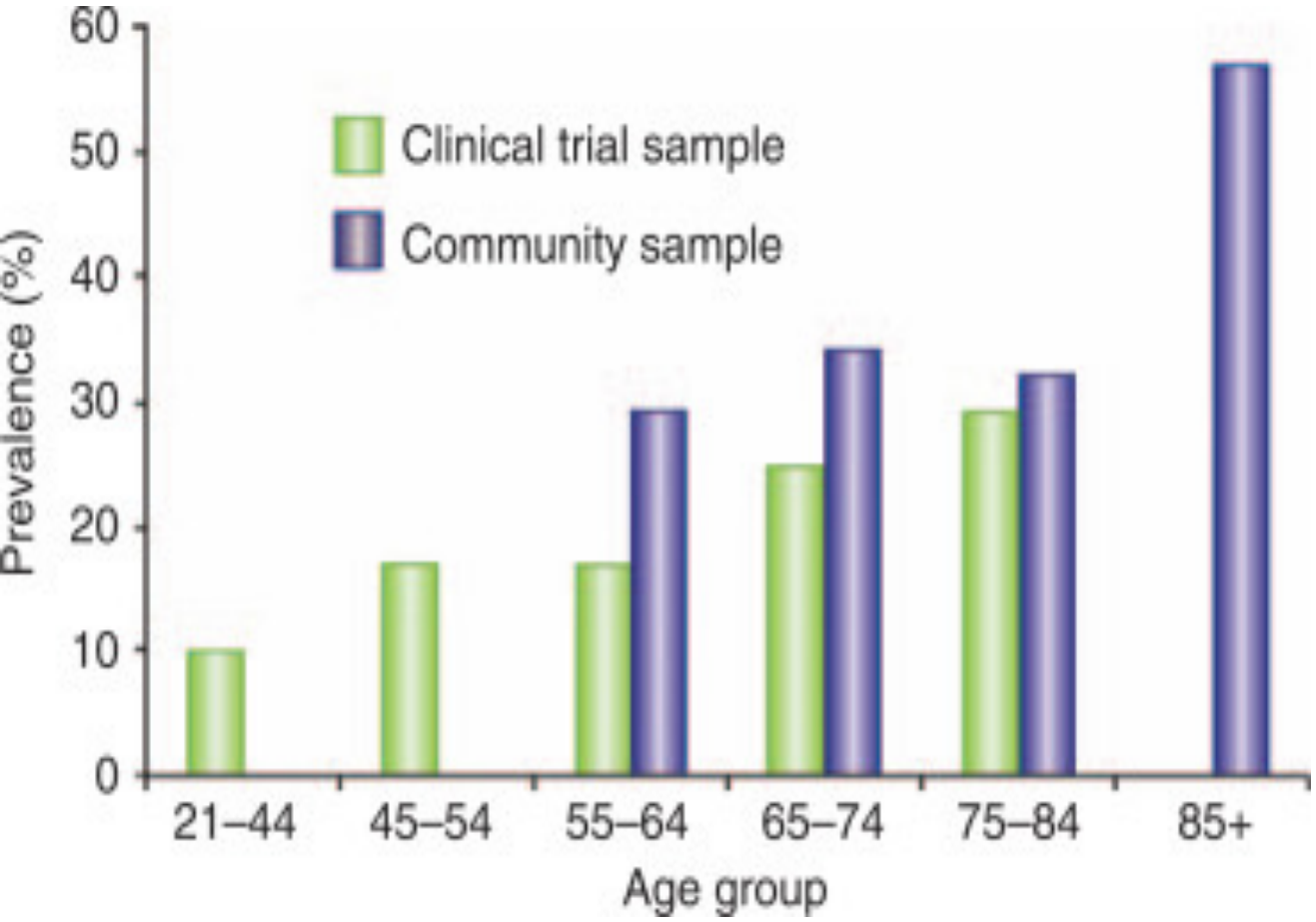
Cognitive impairment in dialysis patients. A comprehensive battery of neurocognitive tests was administered in the first hour of hemodialysis to 314 patients

Drew D et al. Am J Kidney Dis. 74(6): 782-790.

Association between Blood Pressure variability and incidence of dementia in CKD patients



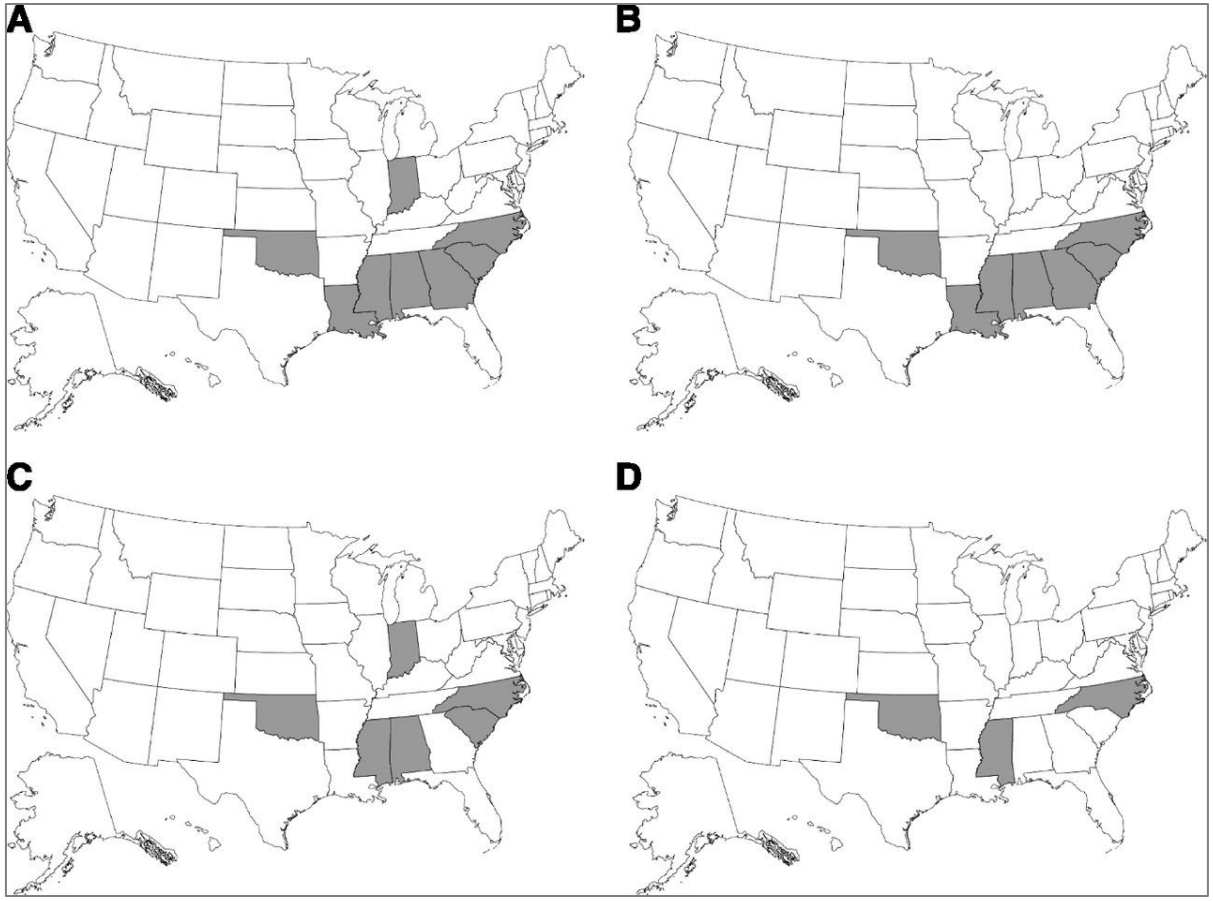
Clin Kidney J, Volume 15, Issue 8, August 2022, Pages 1447–1449, https://doi.org/10.1093/ckj/sfac028



M. Kurella Tamura, B. Larive, M. Unruh, *et al.*
Prevalence and correlates of cognitive impairment in the frequent hemodialysis network (FHN) trials
Clin J Am Soc Nephrol, 8 (2010), pp. 1429-1438 -Modified Mini-Mental State Exam score <80

Stroke and dialysis in the stroke belt

Stroke and the "Stroke Belt" in Dialysis: Contribution of Patient Characteristics to Ischemic Stroke Rate and Its Geographic Variation



Wetmore, James B.; Ellerbeck, Edward F.; Mahnken, Jonathan D.; Phadnis, Milind A.; Rigler, Sally K.; Spertus, John A.; Zhou, Xinhua; Mukhopadhyay, Purna; Shireman, Theresa I.

Journal of the American Society of Nephrology24(12):2053-2061, December 2013.

doi: 10.1681/ASN.2012111077

Strokes are generally more common in the southern United States. States with O/E adjusted odds ratios significantly >1 for new ischemic stroke, after successive adjustments. (A) Adjusted for age. (B) Adjusted for age and sex. (C) Adjusted for age, sex, and race. (D) Full multivariable adjustment.

Association between cholinesterase inhibitors and kidney function decline in patients with Alzheimer's dementia.

kidney INTERNATIONAL

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Population

11, 898 patients with an incident Alzheimer's dementia diagnosis

Jan 2007 – Dec 2018

Observational study in health system's data: SCREAM and Swedish dementia Registry.

Exposure

Start treatment with cholinesterase inhibitors within three months from diagnosis (n=6,803) vs non-start (n= 5,095)

Median 3.0 years follow-up

Findings

	Adjusted Hazard ratio (95% CI) of use vs non-use
CKD progression Composite of >30% decline or kidney replacement therapy or kidney related death	**0.82** (0.71-0.96)
Kidney replacement therapy or kidney related death	**0.68** (0.51-0.89)
All-cause mortality	**0.79** (0.72-0.86)

Xu H et al, 2022

CONCLUSION:

In patients with Alzheimer's dementia undergoing routine care, use of cholinesterase inhibitors (vs no-use) was associated with lower risk of CKD progression, lending indirect support to the role of cholinergic anti-inflammatory pathway activation on preservation of kidney function.

Summary

- Risk factors of CKD
  - Diabetes, Hypertension, Coronary artery disease, Obesity, Genetics/family history, Older age, Chronic illnesses (HIV, Lupus), and nephrotoxic medications (like NSAIDS, some chemotherapy)
- Common causes
  - Diabetes #1, Hypertension #2, Glomerulonephritis #3
- Treatment of CKD
  - Treat underlying causes (i.e diabetes/hypertension)
  - ACEi (i.e lisinopril or enalapril) and ARBs (i.e losartan or valsartan)
  - SGLT2i (i.e Jardiance and Farxiga)
- CKD and ADRD
  - Similar risk factors
  - CKD risk factor for ADRD
  - High prevalence of cognitive impairment and dementia/ADRD in CKD/ESRD (dialysis)
  - Causes of ADRD in CKD/ESRD – blood pressure, uremia (toxins), stroke

Thank you!

KIDNEY HEALTH FOR ALL

PREPARING FOR THE UNEXPECTED, SUPPORTING THE VULNERABLE!

9 MARCH 2023

World Kidney Day™

#worldkidneyday #kidneyhealthforall
www.worldkidneyday.org

World Kidney Day is a joint ISN IFKF-WKA initiative