PROMOTING EQUITY IN KIDNEY HEALTH:

LEVERAGING OPPORTUNITIES AND CELEBRATING WINS

NC-KTI PROGRAM

Keisha Gibson, MD MPH
Senior Vice Chair of Clinical Affairs
Chief, Pediatric Nephrology
UNC Kidney Center

MY PATHWAY TO MEDICINE

NIH
NIEHS

1892
WSSU
Biomedical Research
Infrastructure Center

UNC
SCHOOL OF
MEDICINE

THE KIDNEYS

- Found in the back on either side of the spine
- Help regulate blood pressure, remove waste and water, signal your body to make red blood cells, play key role in bone health and calcium balance, and help regulate growth in children
- Filter about 120 to 150 quarts of blood to produce about 1 to 2 quarts of urine, composed of wastes and extra fluid

Kidney disease stage and eGFR

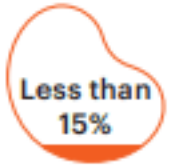
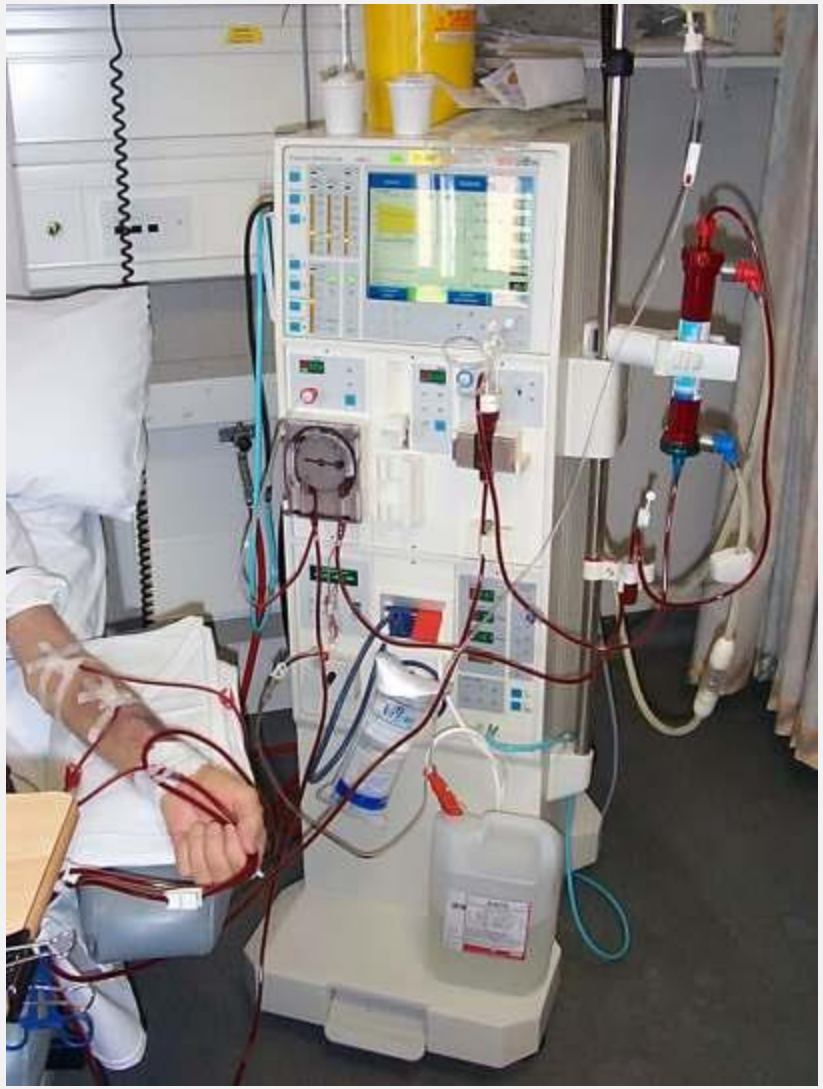
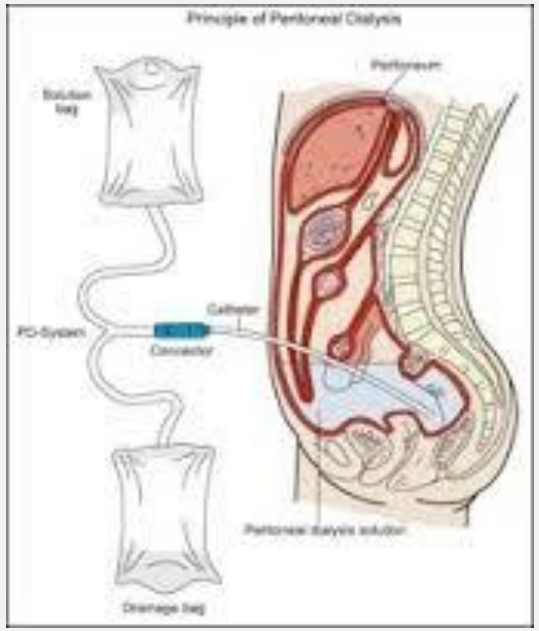
Stage	Description	eGFR	Kidney Function
1	Possible kidney damage (e.g., protein in the urine) with **normal** kidney function	90 or above	
2	Kidney damage with **mild loss** of kidney function	60 to 89	
3a	**Mild to moderate** loss of kidney function	45 to 59	
3b	**Moderate to severe** loss of kidney function	30 to 44	
4	**Severe loss** of kidney function	15 to 29	
5	Kidney **failure**	Less than 15	

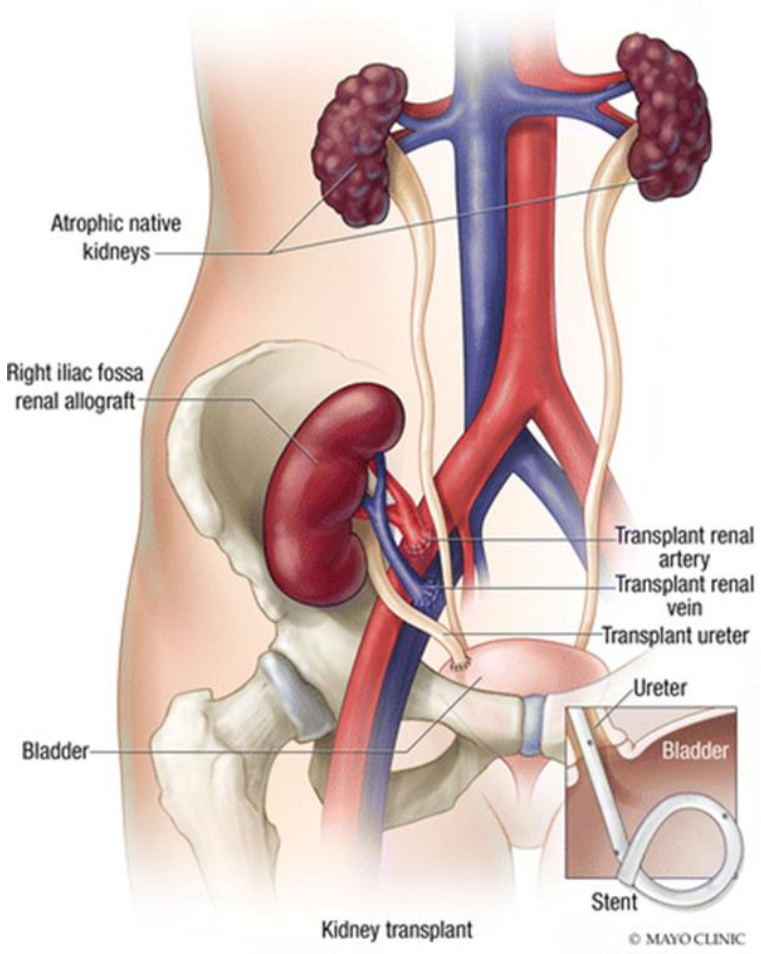
Image from National Kidney Foundation



Hemodialysis

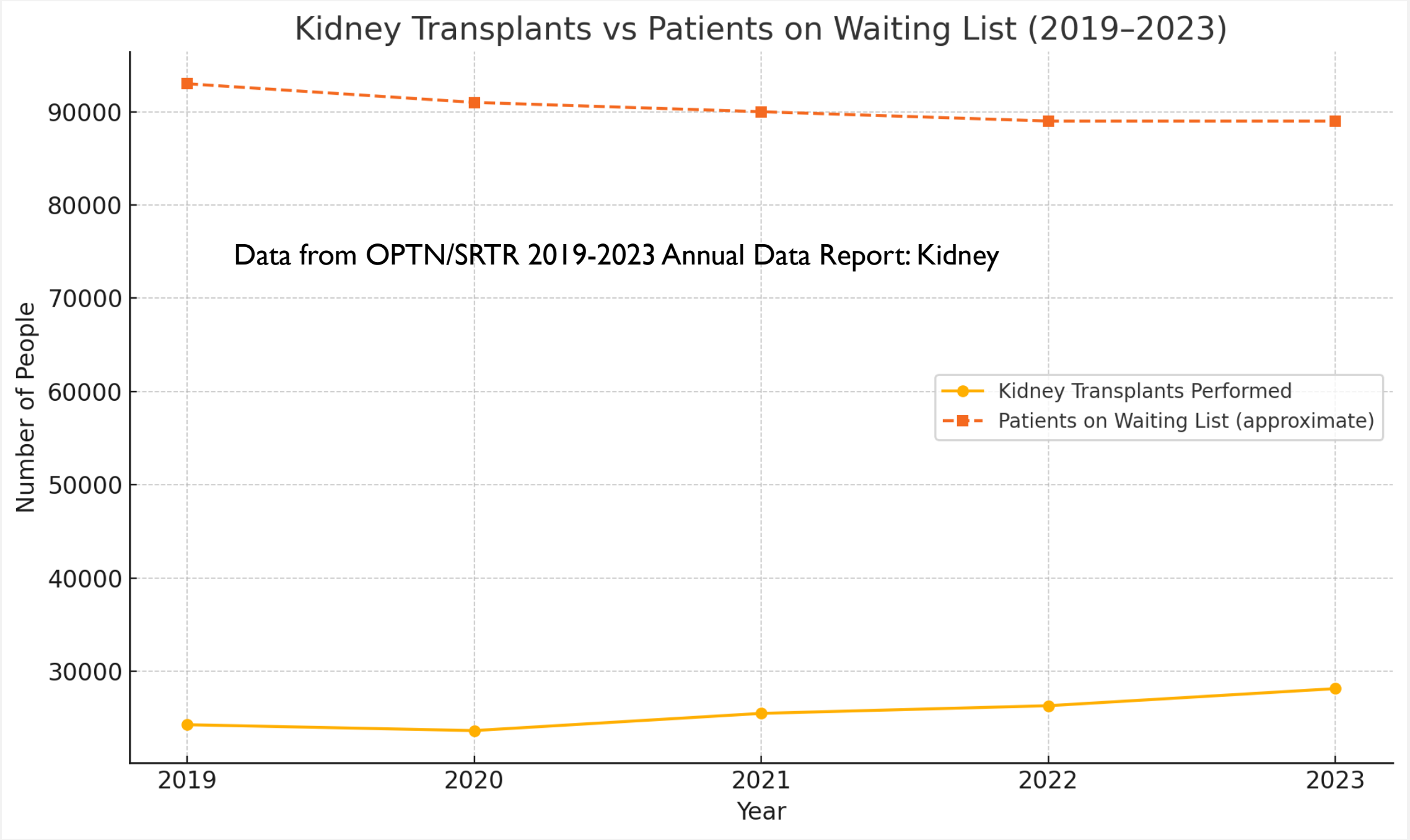
Peritoneal Dialysis





Pros	Cons
Improved Quality of Life	Surgical Risks
Decreased Morbidity & Mortality	Long-Term Medication & Side Effects
Dietary Freedom	Cost
Return to Normal Activities	Organ Availability

KIDNEY TRANSPLANTATION


Kidney Transplants vs Patients on Waiting List (2019–2023)
Data from OPTN/SRTR 2019-2023 Annual Data Report: Kidney
Number of People
90000
80000
70000
60000
50000
40000
30000
2019
2020
2021
2022
2023
Year
Kidney Transplants Performed
Patients on Waiting List (approximate)

OBJECTIVES

- Review the landscape of disparities in kidney health; in particular for minoritized communities
- Consider the importance of integrating epidemiological, clinical, and translational research
- Identify policies that have impacted kidney health
- Summarize strategies and interventions that have successfully promoted equity in kidney health

37 MILLION AMERICANS HAVE KIDNEY DISEASE

8th
Leading cause of death in the United States

9 in 10
Adults don't know they have kidney diseases

33%
of the people on dialysis in the United States are Black, even though Black people comprise **13%** of the nation's population

Managing kidney diseases costs the US Medicare Program alone **$130 billion** including **$50 billion** for kidney failure alone

1%
Medicare population has kidney failure, but **7%** Medicare budget dedicated to their care

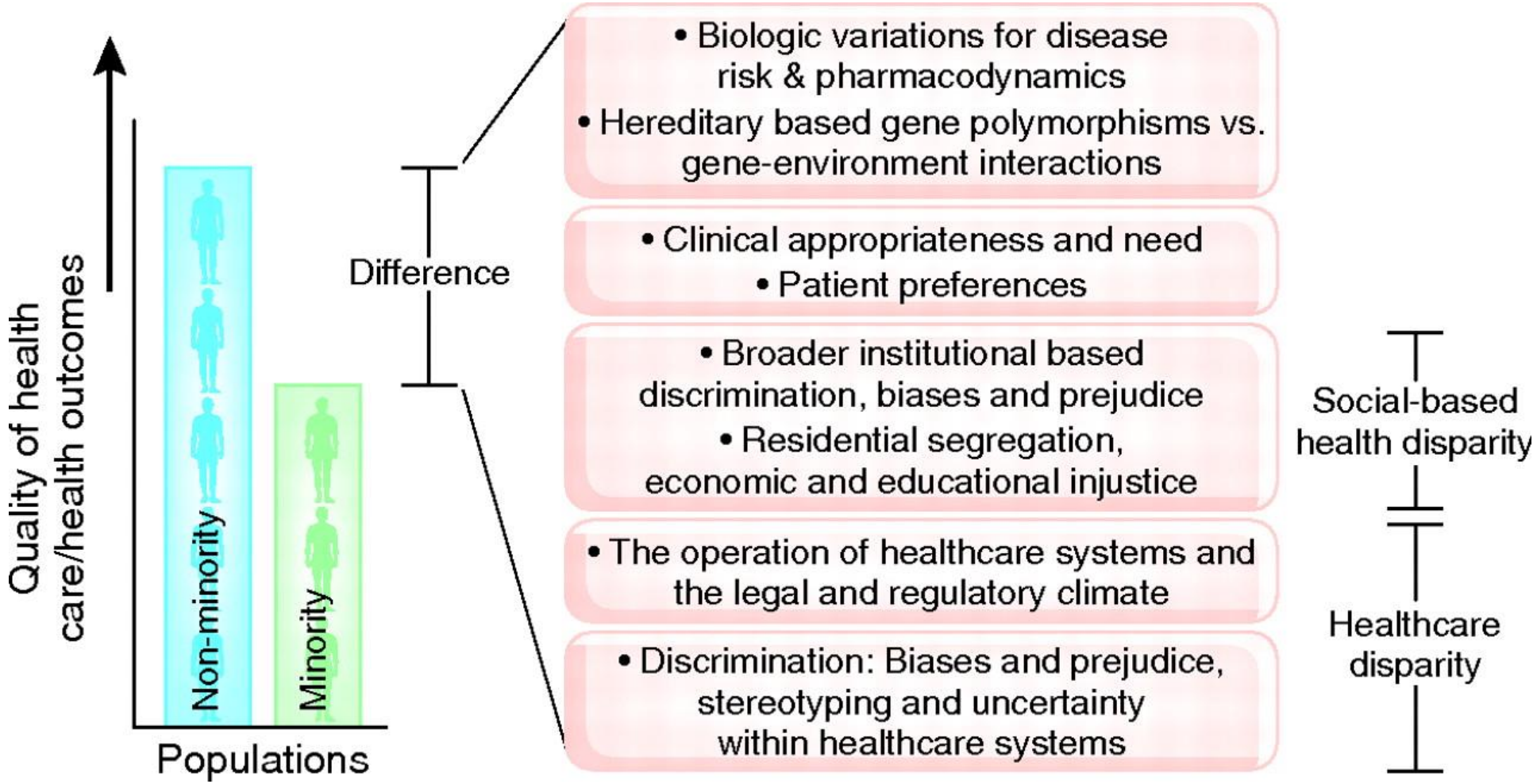
Kidney failure prevalence is **3.5 times** greater in Black people and **2.7** times greater in Native Hawaiians and Pacific Islanders compared to White people

100,000 People
Start dialysis every year: More than **50%** will die within **5** Years

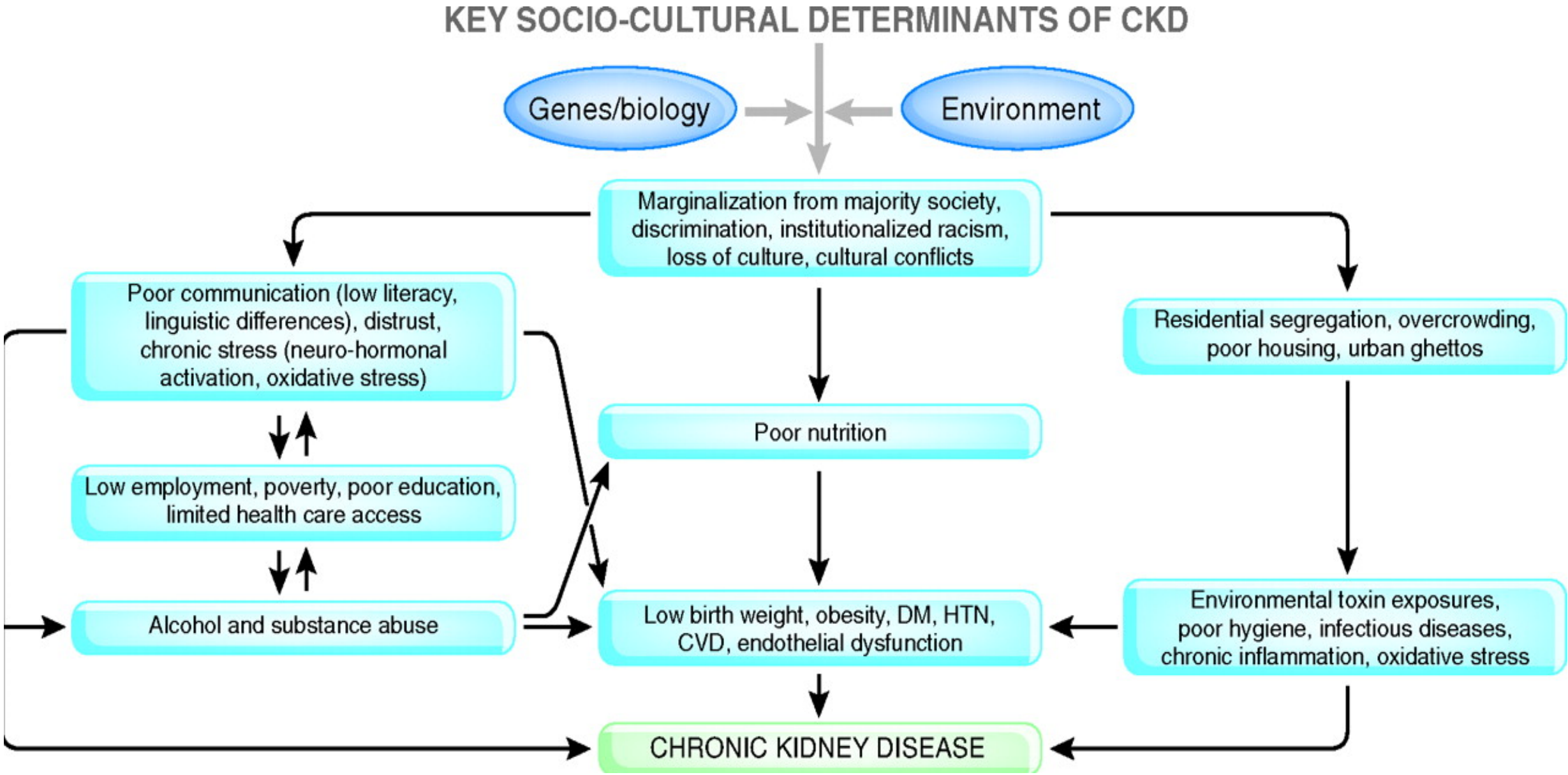
33%
Patients initiating dialysis live in ZIP codes with **≥20%** population below poverty line

Home dialysis
40% to 50% lower among Black and Latinx people compared to White people

American Society of Nephrology



Norris, JASN 2008



Norris, JASN 2008

THERE IS NO GENETIC BASIS FOR RACE

99.99% of genes are shared by all humans

Variation exists in only **0.01%** of the human genome

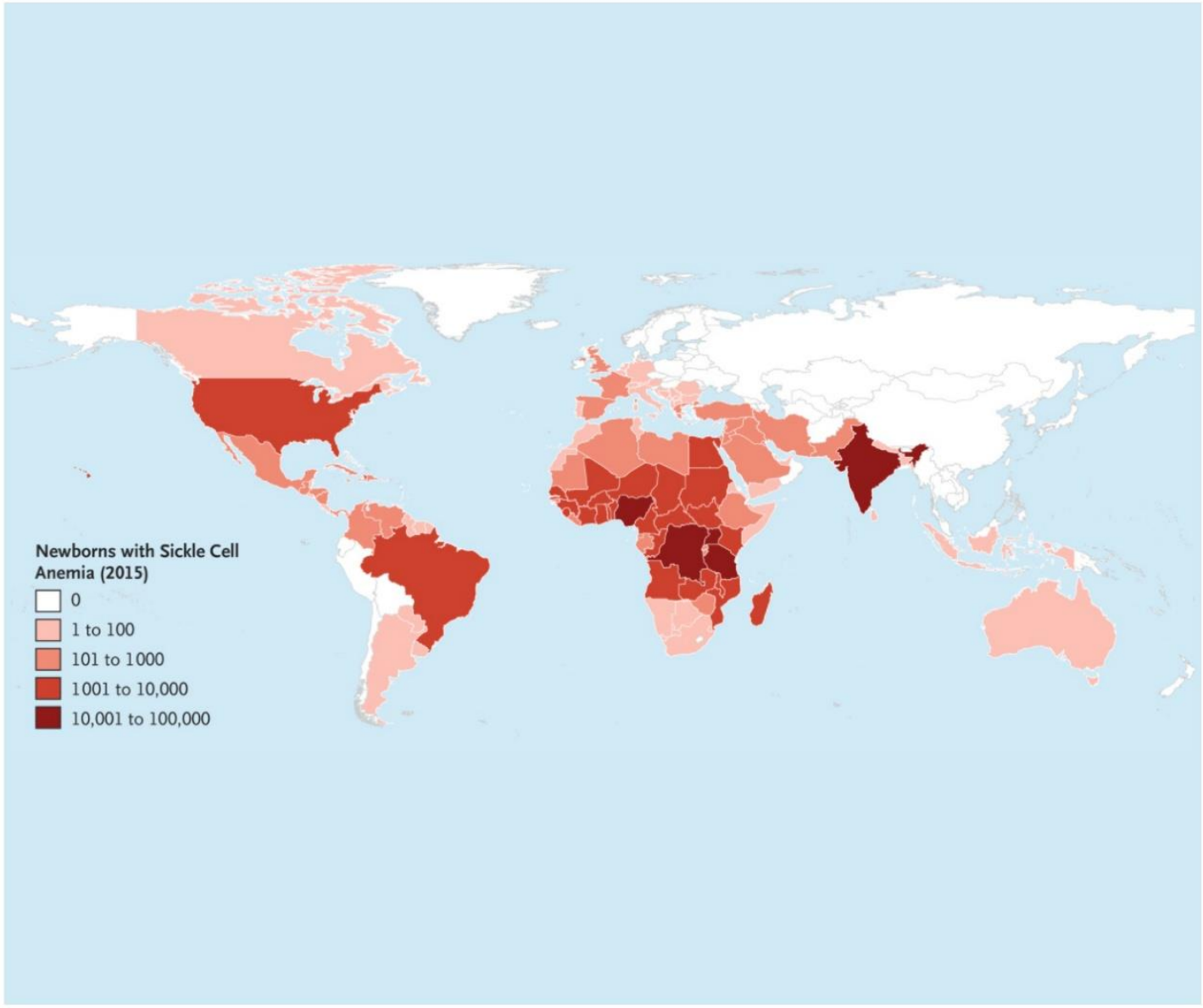
GENETIC ANCESTRY

Involves sharing a genetic line of descent

Some population groups are more likely to carry certain alleles because of shared ancestry

This may or may not be mapped onto regions of the world

*The 3 countries with the highest rates of newborns with Sickle Cell Disease in the world are Nigeria, Congo, and India



APOL1 VARIANTS ARE FOUND IN 2010 IN THE SEARCH FOR GENETIC UNDERPINNING FOR HIGH RATES OF CKD IN BLACK PATIENTS

Hum Genet (2010) 128:345–350
DOI 10.1007/s00439-010-0861-0

SHORT REPORT

Missense mutations in the *APOL1* gene are highly associated with end stage kidney disease risk previously attributed to the *MYH9* gene

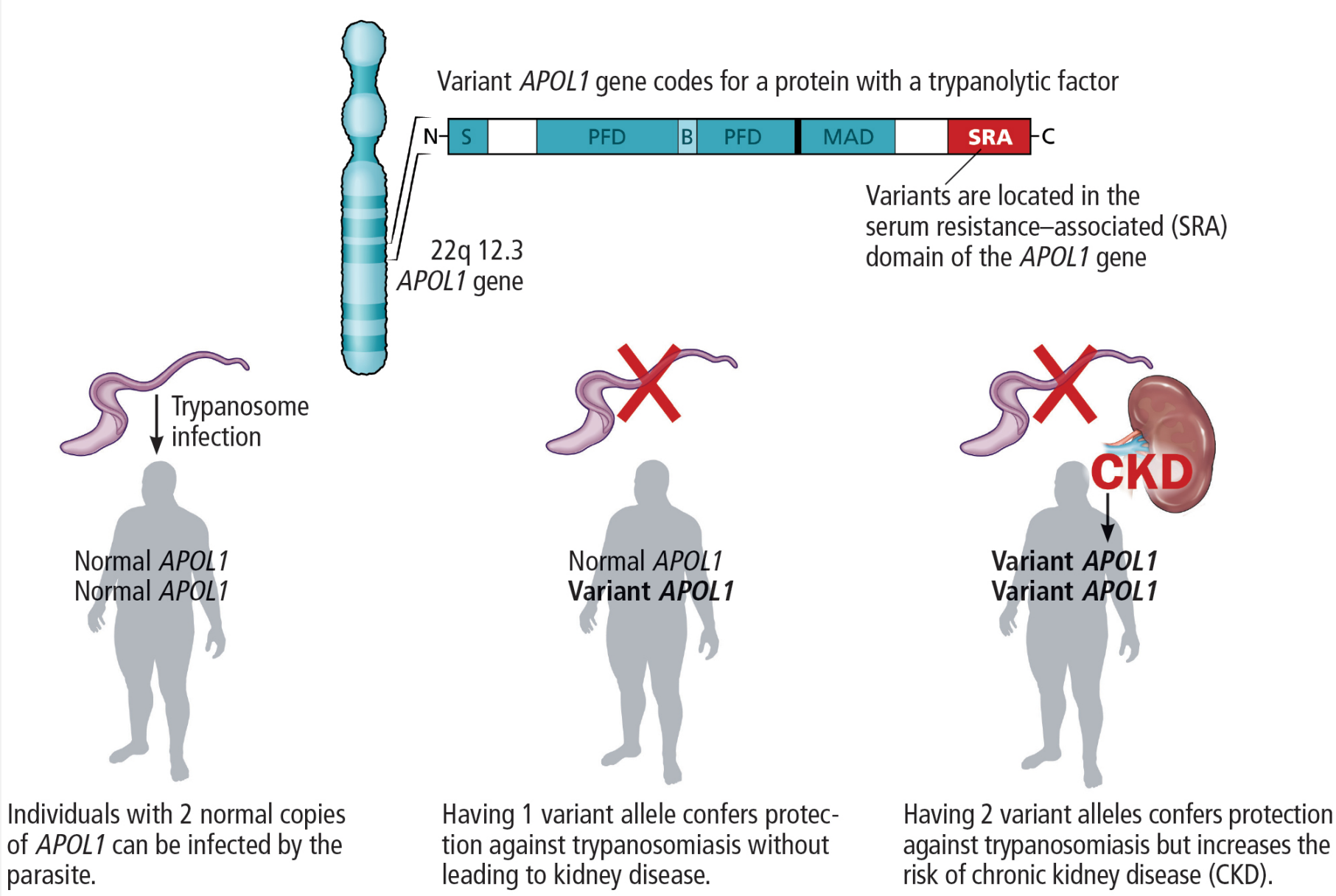
Shay Tzur · Saharon Rosset · Revital Shemer · Guennady Yudkovsky · Sara Selig · Ayele Tarekegn · Endashaw Bekele · Neil Bradman · Walter G. Wasser · Doron M. Behar · Karl Skorecki

Published in final edited form as:
Science. 2010 August 13; 329(5993): 841–845. doi:10.1126/science.1193032.

Association of Trypanolytic ApoL1 Variants with Kidney Disease in African-Americans

Giulio Genovese[1,2,*], David J. Friedman[1,3,*], Michael D. Ross[4], Laurence Lecordier[5], Pierrick Uzureau[5], Barry I. Freedman[6], Donald W. Bowden[7,8,9,10,11,12], Carl D. Langefeld[9,10,11,12], Taras K. Oleksyk[13], Andrea Uscinski Knob[4], Andrea J. Bernhardy[1], Pamela J. Hicks[7,8,9,10,11,12], George W. Nelson[15], Benoit Vanhollebeke[5], Cheryl A. Winkler[14], Jeffrey B. Kopp[15], Etienne Pays[5,17], and Martin R. Pollak[1,16,17]

APOL1 and kidney disease



Individuals with 2 normal copies of *APOL1* can be infected by the parasite.

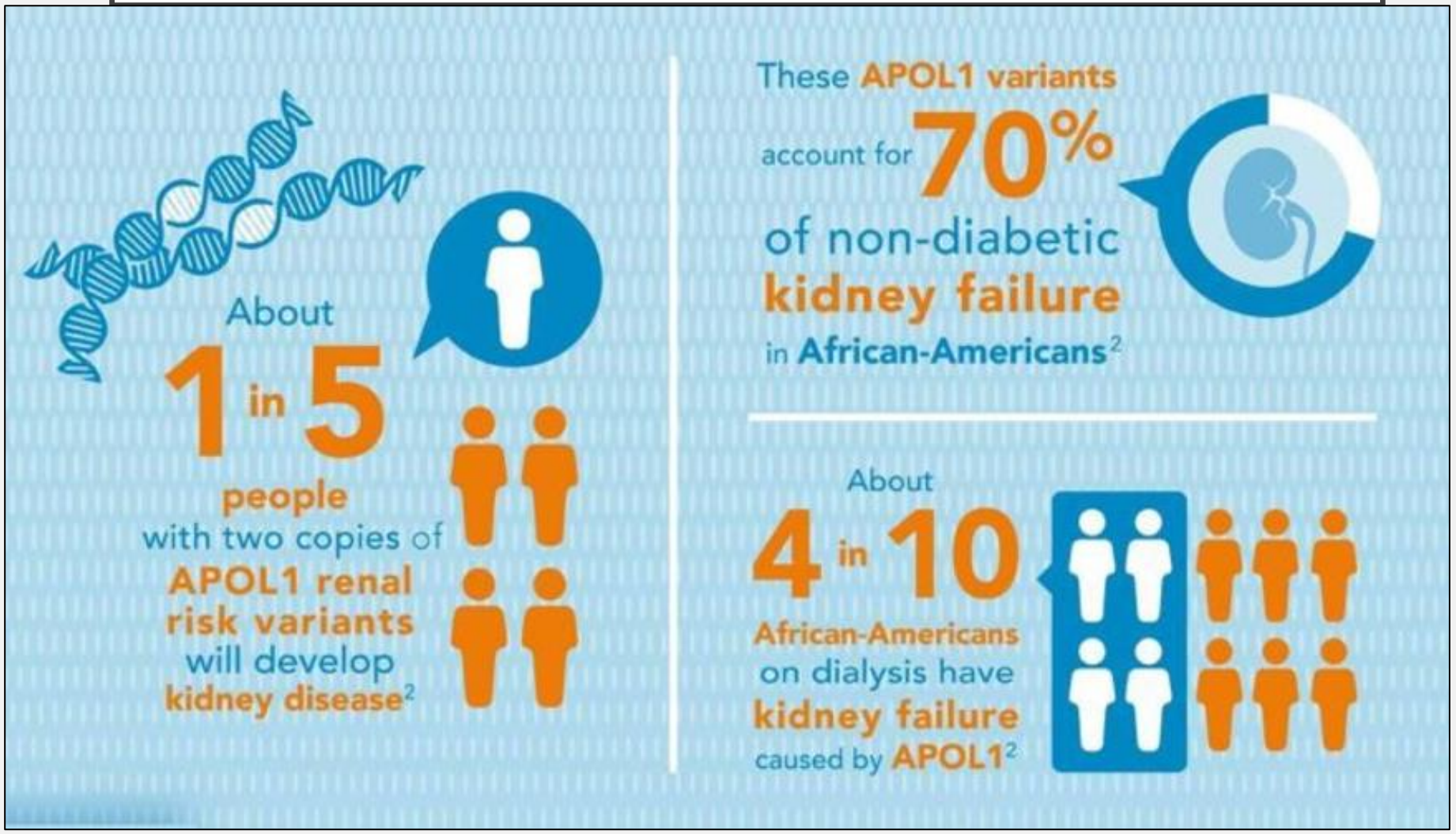
Having 1 variant allele confers protection against trypanosomiasis without leading to kidney disease.

Having 2 variant alleles confers protection against trypanosomiasis but increases the risk of chronic kidney disease (CKD).

Freedman, *Nat Rev Nephrol* 2016; Palmer, *JASN* 2013; Genovese, *Science* 2010

This risk allele is present in 14% of African Americans and can explain ~42% of the excess risk of CKD in Black patients

GENETICS OF KIDNEY DISEASE

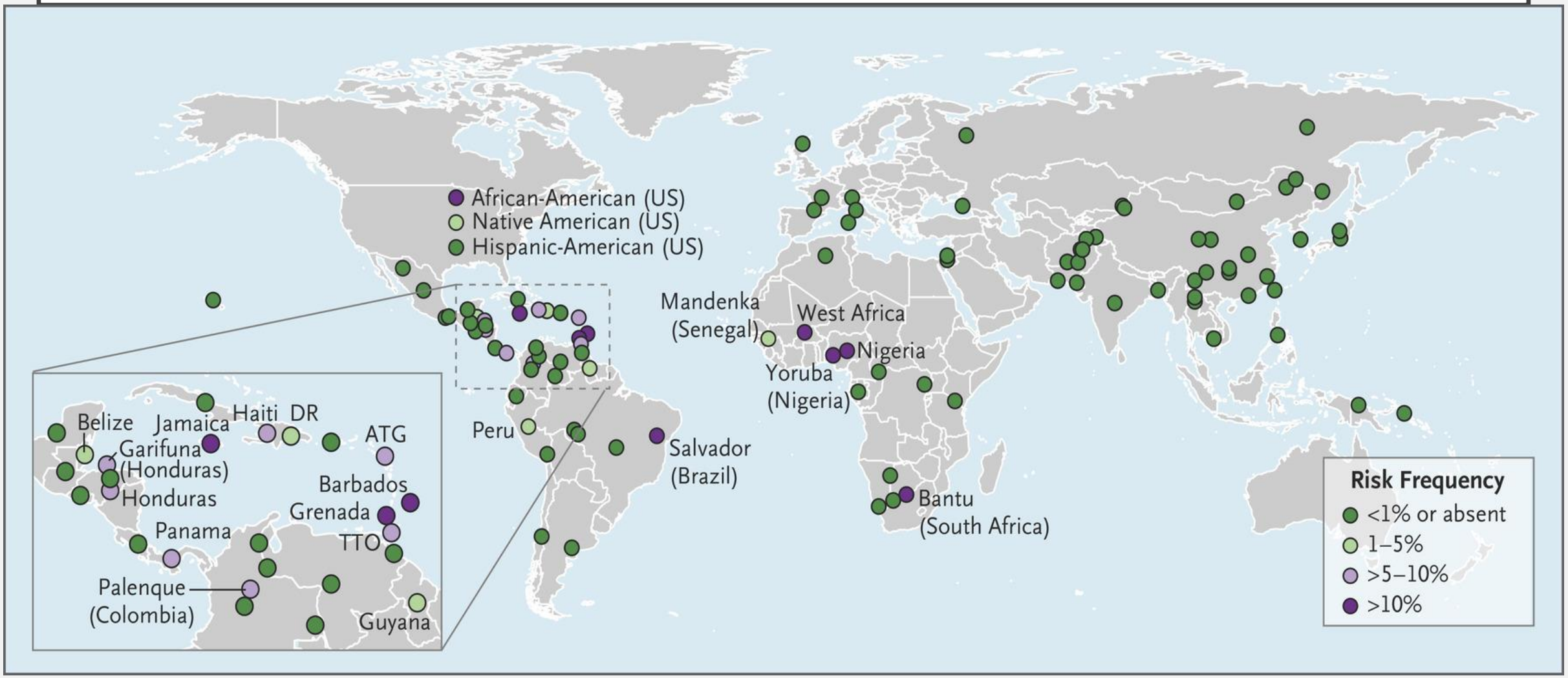


[2]Freedman BI, Cohen AH. Hypertension-attributed nephropathy: what's in a name?. *Nat Rev Nephrol*. 2016;12(1):27-36. doi:10.1038/nrneph.2015.172. http://www.ncbi.nlm.nih.gov/pubmed/26553514

[2]Palmer ND, Freedman BI. APOL1 and progression of nondiabetic nephropathy. *J Am Soc Nephrol*. 2013;24(9):1344-1346. doi:10.1681/ASN.2013060589. http://www.ncbi.nlm.nih.gov/pubmed/23813212

[2]Genovese G, Friedman DJ, Ross MD, et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. *Science*. 2010;329(5993):841-845. doi:10.1126/science.1193032. http://www.ncbi.nlm.nih.gov/pubmed/20647424

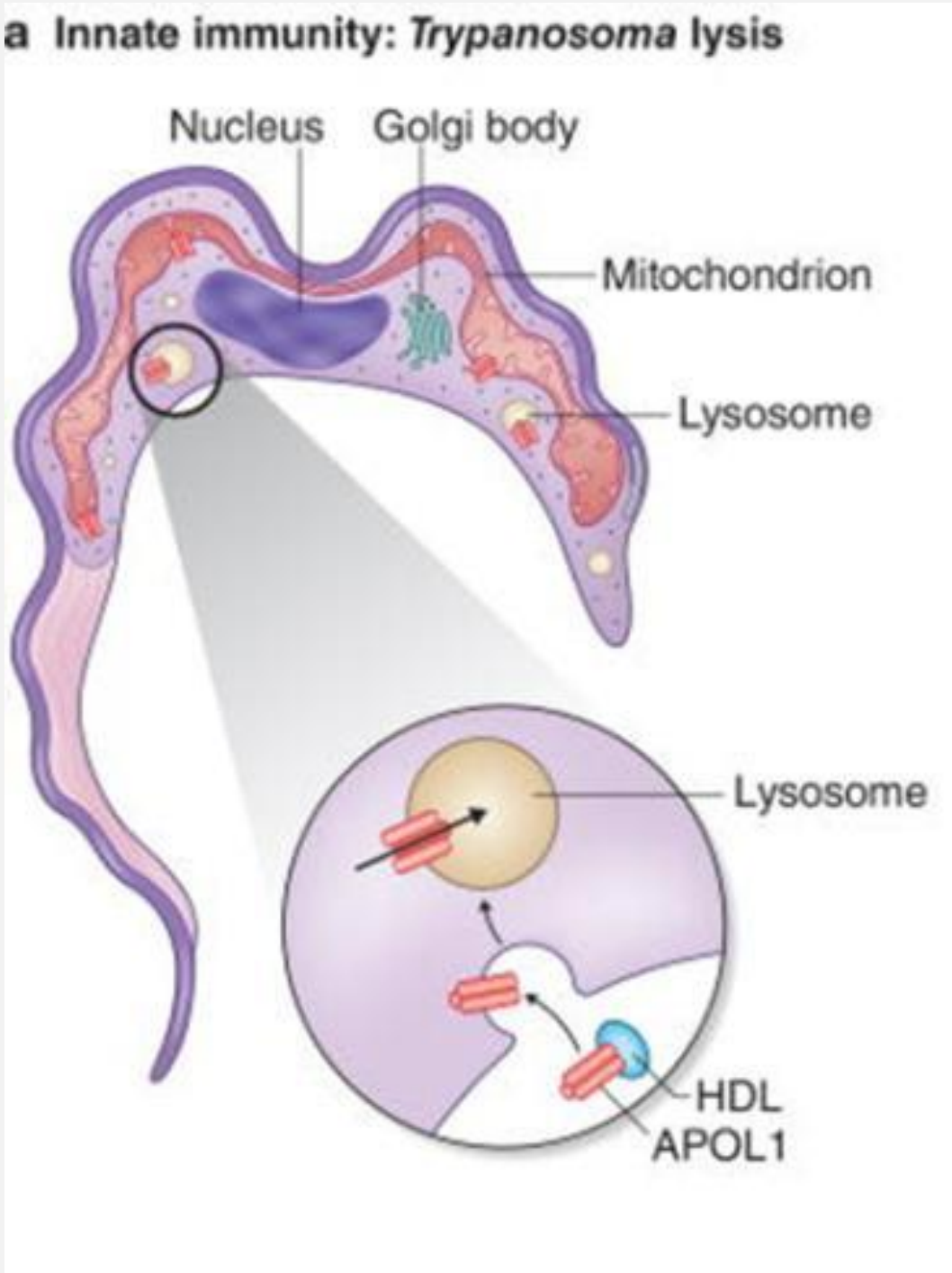
PREVALENCE OF *APOL1* VARIANTS GLOBALLY



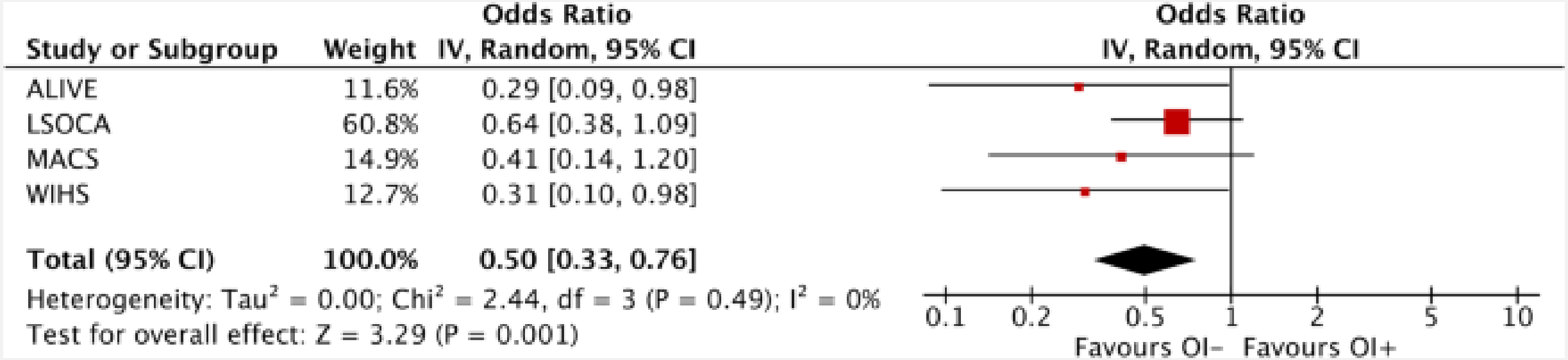
Nadkarni et. Al NEJM 2018

BIOLOGICAL FUNCTIONS OF *APOL1*

- Component of HDL made in the liver, also expressed in kidney, brain and vasculature
  - Arterioscler Thromb Vasc Biol. 2009; 29:870–876
- Circulating APOL1 has a known role in innate immunity against trypanosoma infection (sub-Saharan Africa)
- Positive selection explains the high prevalence of variants



Forest plot showing the odds ratios (OR) of opportunistic infection (OI) for the carriage of 2 versus 1 or 0 *APOL1* variant alleles in the meta-analysis of four HIV/AIDS cohorts.

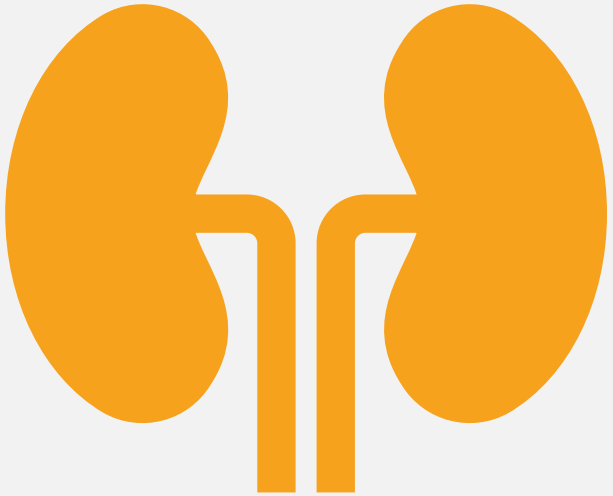


An, Comm Bio 2021

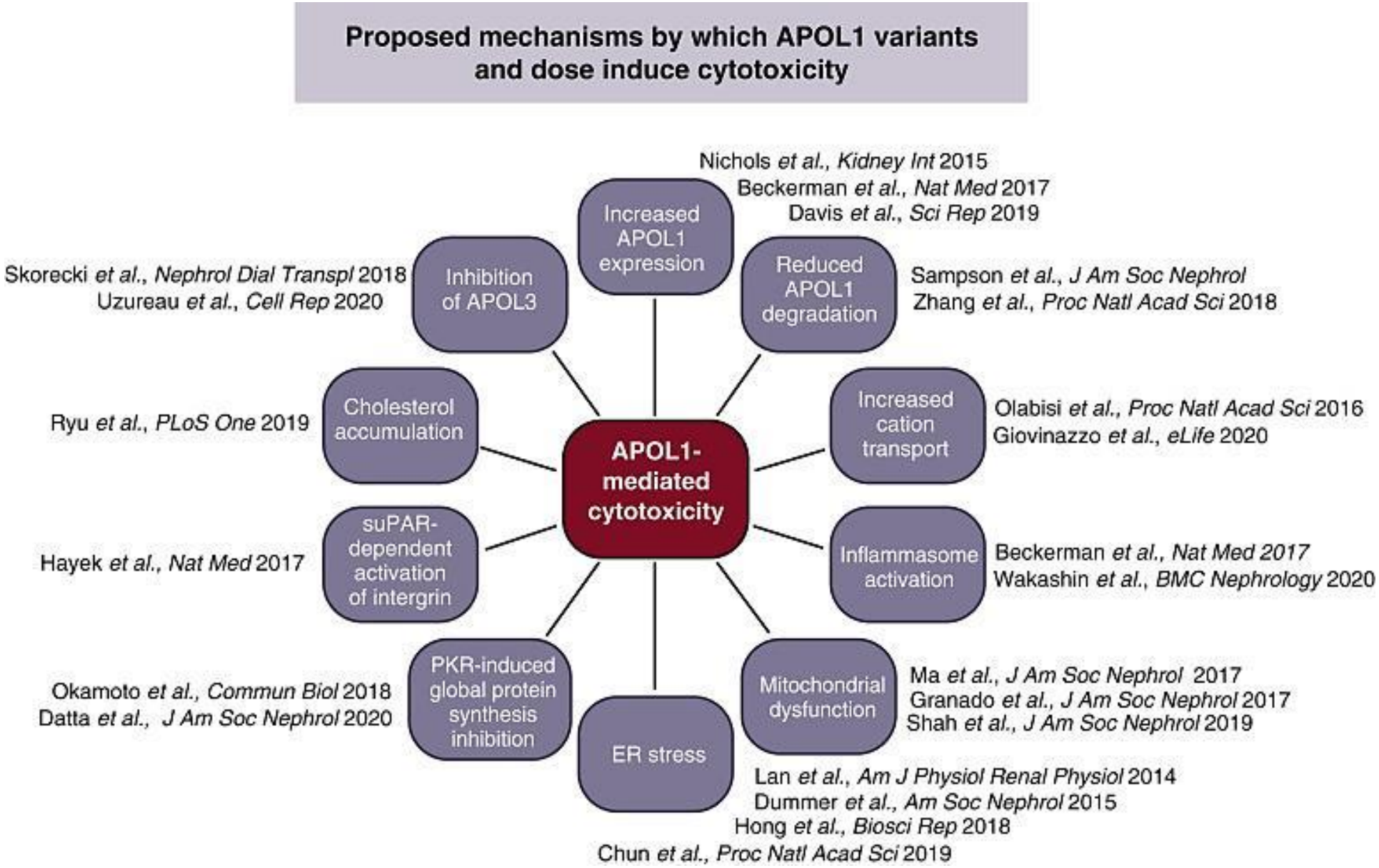
APOL1 RISK VARIANTS AND DISEASE

APOL1 RISK VARIANTS AND DISEASE

- Risk of Kidney disease
- CKD progression in HTN, Diabetes
- Heart disease
- Pre-eclampsia
- Sickle cell
- Transplantation
- Virus-induced nephropathy (including COVID)
- Glomerular diseases



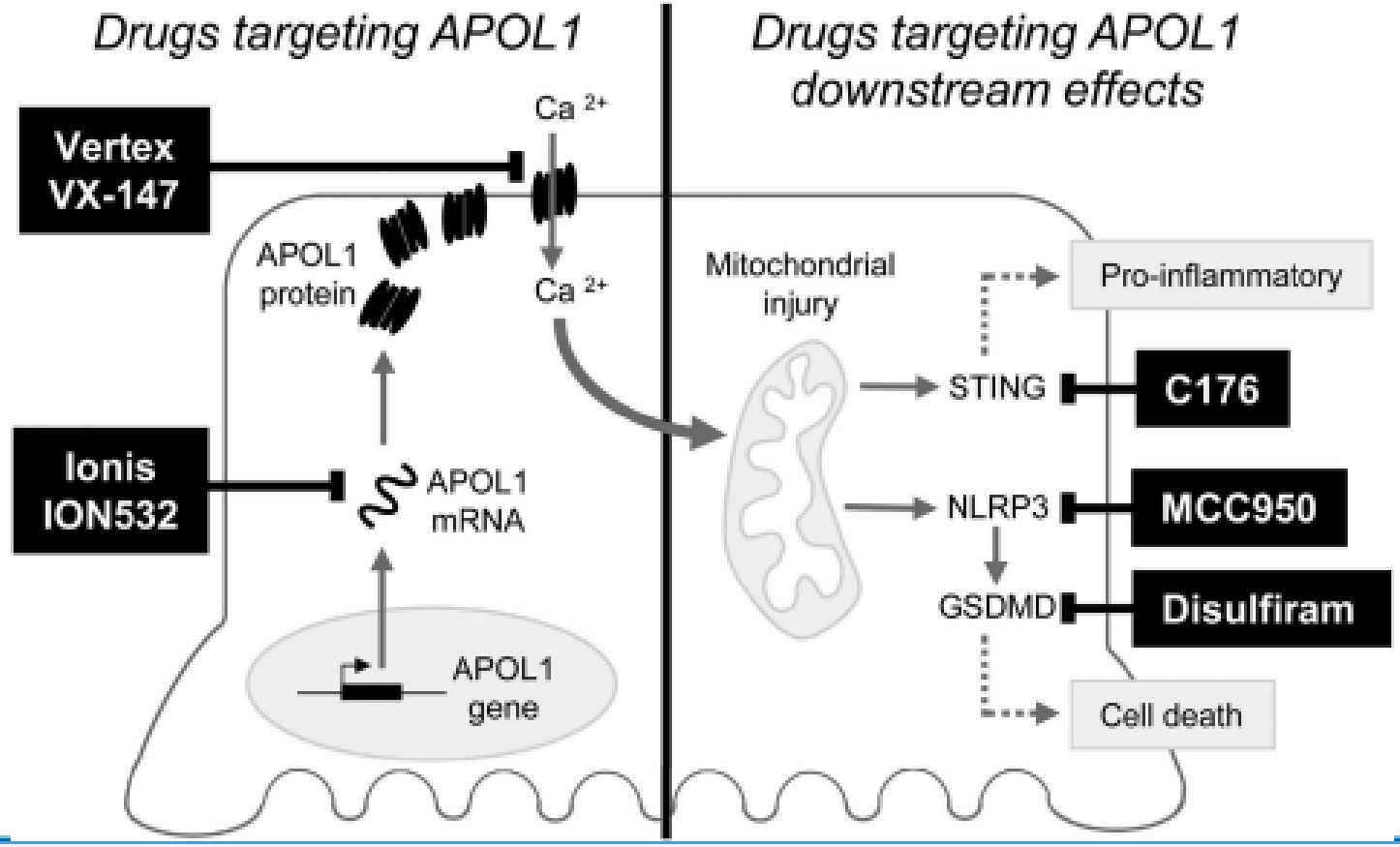
PROPOSED MECHANISMS OF APOL1 VARIANTS AND DISEASE



THERAPEUTIC PIPELINE FOR APOL1 KIDNEY DISEASE

AJKD

Bruggeman et al



Bruggeman LA, Azhibekov T, O'Toole JF. Moving Toward a Common Pathogenic Mechanism and Therapeutic Targets for APOL1 Nephropathies. Am J Kidney Dis. 2022 Jun;79(6).

nature communications

Article

https://doi.org/10.1038/s41467-023-43020-9

Strong protective effect of the *APOL1* p.N264K variant against G2-associated focal segmental glomerulosclerosis and kidney disease

Received: 25 August 2023

A list of authors and their affiliations appears at the end of the paper

Accepted: 30 October 2023

Targeting the Uneven Burden of Kidney Disease on Black Americans

New treatments aim for a gene variant causing the illness in people of sub-Saharan African descent. Some experts worry that focus will neglect other factors.

NYT May 2022

"All populations have genetic variants, but the action of those variants is determined by the environment in which those people live…..People want to find simple explanations for complex phenomena. Find a genetic variant and make the story simple, but that's not how it works. Environmental effects are really important." --Dr. Joseph Graves (Professor, NC A&T)

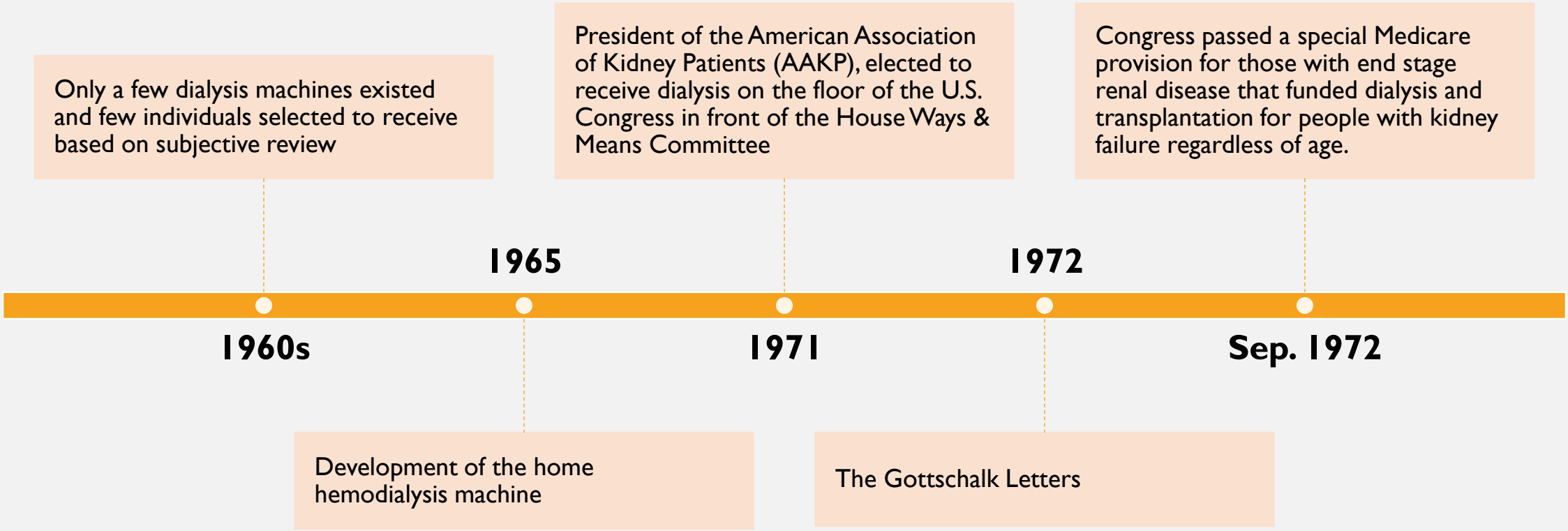
"---a laser focus on variants may let policymakers ignore the social and economic disparities underlying the disease. [But] --we don't want to pretend that the biology doesn't exist. That would not be doing the community any good." ---Dr. Opeyemi Olabisi (Professor, Duke Nephrology)

THEY DECIDE WHO LIVES, WHO DIES: MEDICAL MIRACLE PUTS MORAL BURDEN ON SMALL COMMITTEE

The Seattle Artificial Kidney Center Admissions and Policy Committee, in a photograph taken by Lawrence Schiller for *Life* magazine

Life. 1962; **53**: 102-125

HISTORY OF ESKD CARE IN THE US



2019 : ADVANCING AMERICAN KIDNEY HEALTH INITIATIVE

Executive Order Championed by HHS

1

Reducing the number of Americans developing end-stage renal disease by 25 percent by 2030

2

Having 80 percent of new ESRD patients in 2025 either receiving dialysis at home or receiving a transplant

3

Doubling the number of kidneys available for transplant by 2030

The NEW ENGLAND JOURNAL of MEDICINE

MEDICINE AND SOCIETY

Debra Malina, Ph.D., *Editor*

Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms

Darshali A. Vyas, M.D., Leo G. Eisenstein, M.D., and David S. Jones, M.D., Ph.D.

Dropping Race-Based eGFR Adjustment Gains Traction in US

Mitchel L. Zoler, PhD

July 06, 2020

TALE OF TWO PATIENTS

65 yo White male with CKD (Cr-2.4)

eGFR 27

Not approved to get MRI scan with contrast

65 yo Black male with CKD (Cr-2.4)

eGFR 32

Approved to get MRI scan with contrast

Table 2 Reclassification of African-American CKD Patients into Less Severe CKD Stages After Removal of Race Multiplier Term from CKD-EPI Equation. Gray Shading and Bold Text Indicates Patients Who Are Reclassified. *CKD*, chronic kidney disease; *eGFR*, estimated glomerular filtration rate

	eGFR categories *without* race multiplier term (ml/min/1.73m2), n (%)			
eGFR categories using existing eGFR equation(*with* race multiplier term) (ml/min/1.73m^2), n	CKD 3A eGFR 45-59 (n=618)	CKD 3B eGFR 30-44 (n=1069)	CKD 4 eGFR 15-29 (n=435)	CKD 5 eGFR < 15 (n=103)
CKD 3A eGFR 45-59 (n=1167)	618 (53)	**549 (47)**		
CKD 3B eGFR 30-44 (n=687)		520 (75.7)	**167 (24.3)**	
CKD 4 eGFR 15-29 (n=295)			268 (90.8)	**27 (9.2)**
CKD 5 eGFR <15 (n=76)				76 (100)
Total (n=2225)				

Ahmed, J Gen Intern Med 2020

JASN®
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Up Front Matters | Special Article

A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease

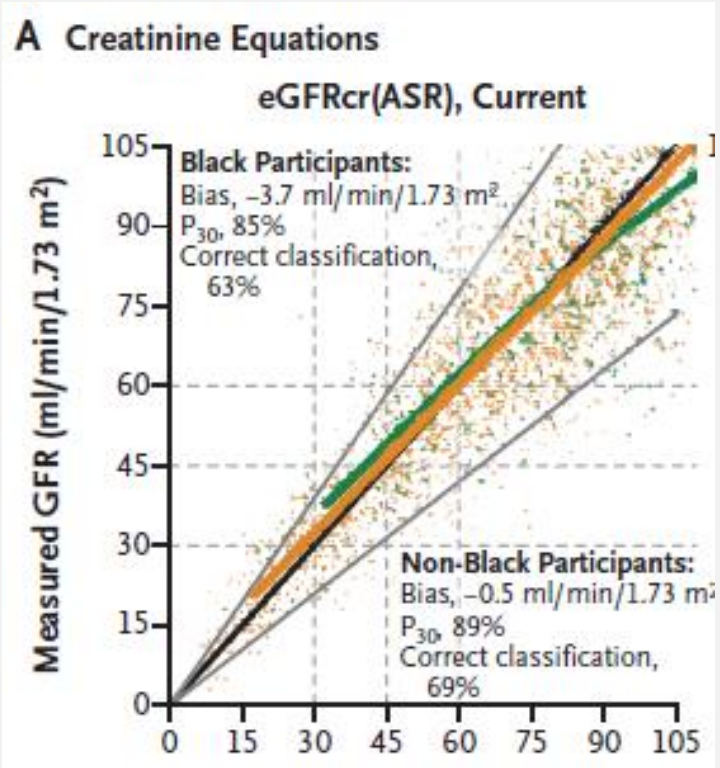
Cynthia Delgado, Mukta Baweja, Deidra C. Crews, Nwamaka D. Eneanya, Crystal A. Gadegbeku, Lesley A. Inker, Mallika L. Mendu, W. Greg Miller, Marva M. Moxey-Mims, Glenda V. Roberts, Wendy L. St. Peter, Curtis Warfield and Neil R. Powe

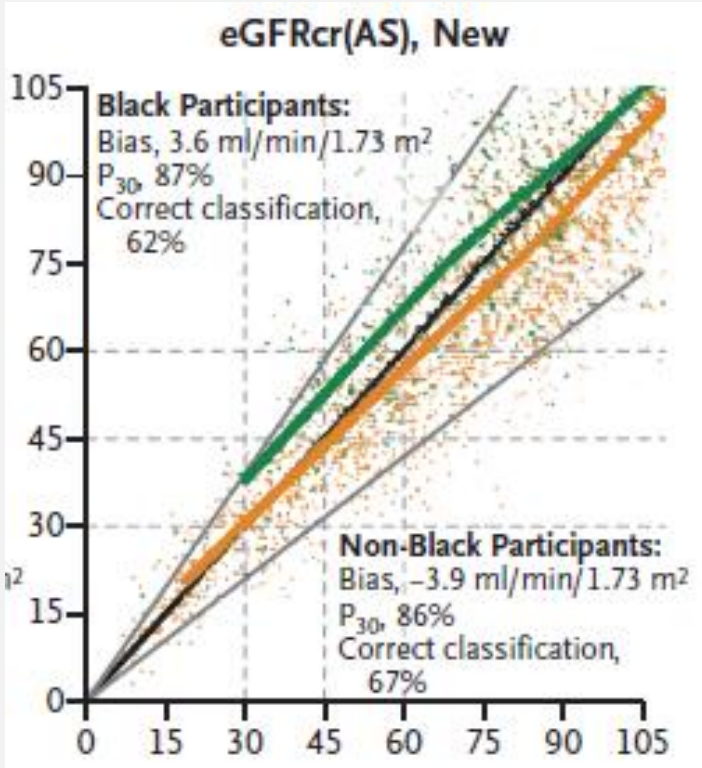
JASN December 2021, 32 (12) 2994-3015; DOI: https://doi.org/10.1681/ASN.2021070988

CKD-EPI 2021 $EGFR_{CR}$

eGFR = 142 x min(SCr/κ, 1)α x max(SCr/κ, 1) -1.200 x 0.9938Age x 1.012 [if female], where SCr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is -0.241 for females and -0.302 for males

Similar performance characteristics to previous equations without potential consequences that disproportionately affect any one group of individuals





Inker et al. 2021

NKF-ASN TASKFORCE RECOMMENDATIONS

UNC SCHOOL OF MEDICINE

A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease

Recommend immediate implementation of the *CKD-EPI creatinine equation refit without the race variable* in all laboratories in the U.S.

The equation refit excludes race in the calculation and reporting, includes diversity in its development, is immediately available to all labs in the U.S. and has acceptable performance characteristics and potential consequences that do not disproportionately affect any one group of individuals.

Recommend national efforts to facilitate increased, routine, and timely use of cystatin C, especially to confirm eGFR in clinical decision-making

Encourage and fund research on GFR estimation with new endogenous filtration markers and on interventions to eliminate racial and ethnic disparities

The Task Force gathered input from diverse stakeholders and carefully reviewed the evidence to create these recommendations

Cynthia Delgado, Mukta Baweja, Deidra C. Crews, et al. *A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease.* *AJKD DOI:* 10.1053/j.ajkd.2021.08.003, *JASN DOI: 10.1681/ASN.2021070988*

Visual Graphic by Edgar Lerma, MD, FASN

JASN AJKD

If a transplant hospital:

•**Registered a candidate** to the waiting list **without a qualifying eGFR value**, and at a later date used a race-inclusive eGFR calculation to qualify the candidate to begin accruing waiting time

Then the transplant hospital may:

•**Recalculate the candidate's eGFR** using a race-neutral calculation and **update** the candidate's qualifying eGFR date in Waitlist℠

UNC BREAKING DOWN BARRIERS IN KIDNEY TRANSPLANT

Multidisciplinary team

51.9% (501 out of 965) of patients on the waitlist were affected

311 patients received extra waiting time

Average number of days added was 1,073 -- one patient received 21 additional years waiting time!

18 patients who received extra waiting time were transplanted within a few months!

FORWARD STRATEGIES

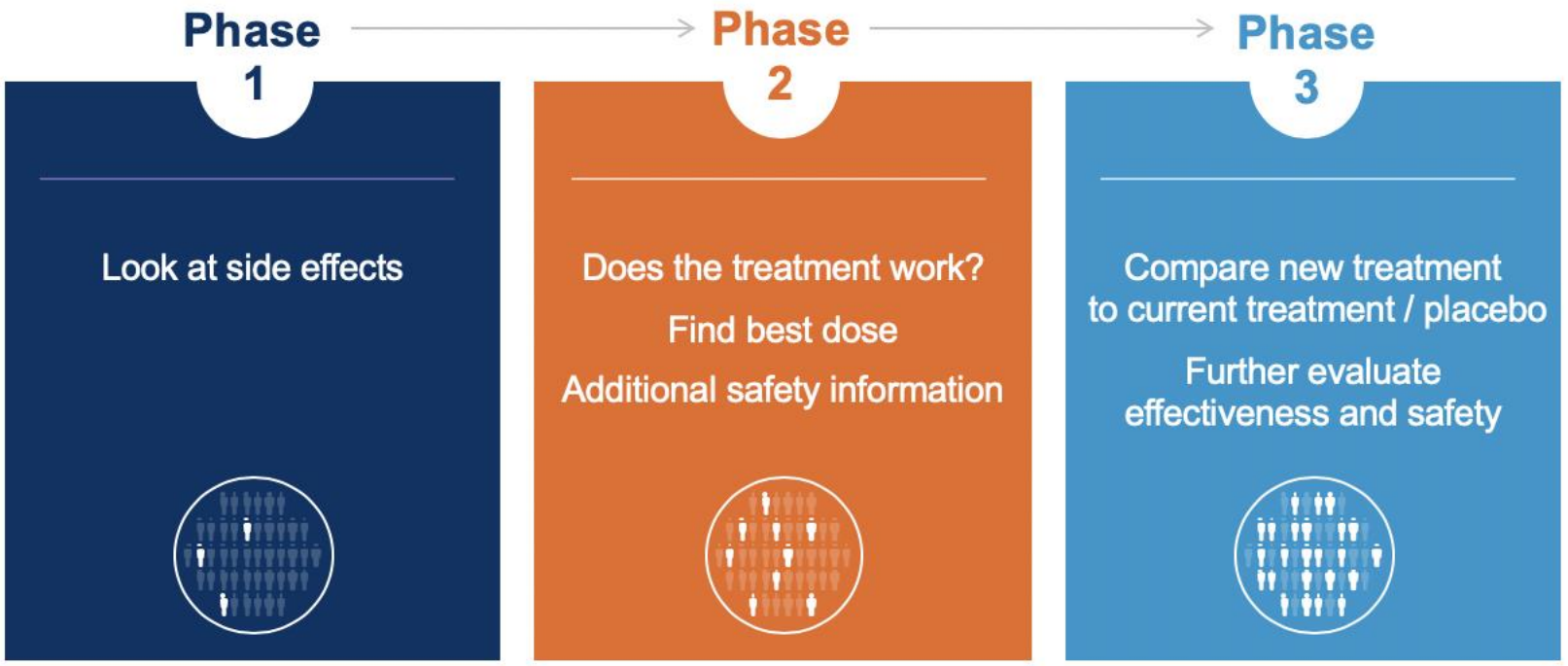
Not advocating to ignore race: Doing so blinds us to the impacts of race as a social construct

Using tools with race as a predictor risks interpreting racial disparities as fixed facts vs. injustices that require intervention

People self-define their race in different ways, and many people are of mixed race, making any single category flawed

CLINICAL TRIALS OVERVIEW

- Clinical studies are research studies involving people
- Their goals are to find out if a new treatment is safe and effective
- There are 3 main phases of clinical studies before a drug can be approved:



EXCITING TIME FOR CLINICAL TRIALS IN RARE KIDNEY DISEASES

CARE and JUSTICE
FOR APOL1-MEDIATED KIDNEY DISEASE

AMPLITUDE

APOL1 Long-term Kidney Transplantation Outcomes Consortium
APOLLO

R3R01-ASFSGS-201

LIPOSORBER® LA-15
LDL ADSORPTION COLUMNS
Instructions for use in adult and pediatric Focal Segmental Glomerulosclerosis (FSGS)
FSGS

ACTION3
FSGS CLINICAL STUDY

eppik

NEW HEADWINDS IN RESEARCH

TAKE HOME POINTS

Kidney disease is a growing public health emergency and awareness as well as an expanded workforce is necessary

While individual level interventions are important, to address health inequities, continued progress in research along with policy driven change can have a larger influence in narrowing these gaps.

As healthcare providers and community leaders we all have power that should be leveraged to promote health equity