

Kidney Disease and Health Equity: What is important to know

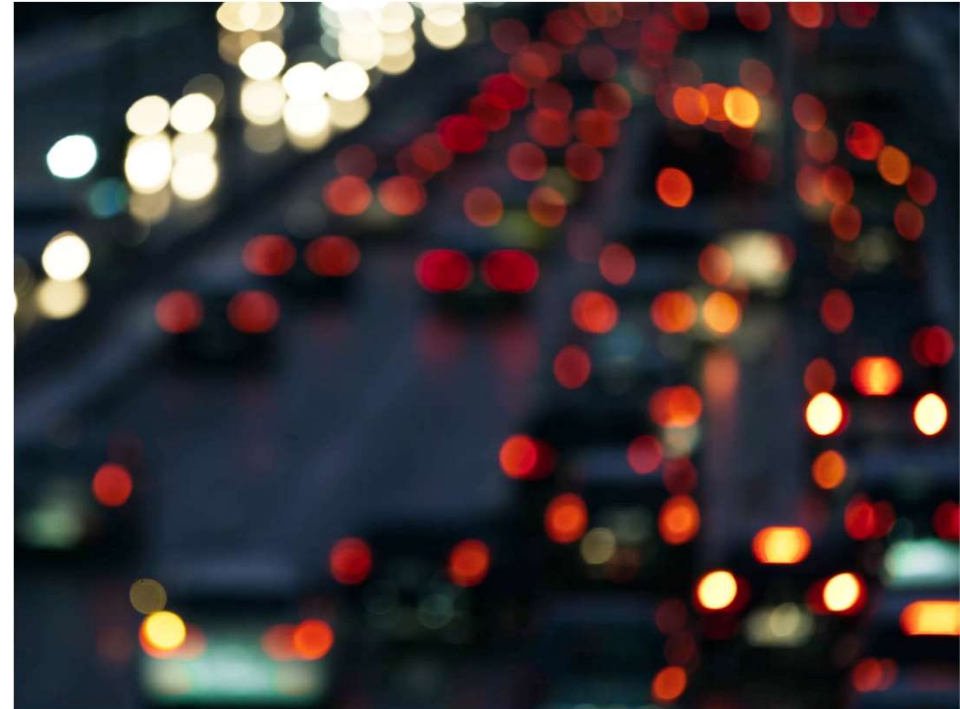
Bessie A. Young, MD, MPH,
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Medicine

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University of Washington



Statement Honoring the Land on which the University of Washington Stands

UW Medicine acknowledges the land we occupy today as the traditional home of the Tulalip, Muckleshoot, Duwamish and Suquamish or Coast Salish tribal nations. Without them we would not have access to this healing, working, teaching and learning environment. We humbly take the opportunity to thank the original caretakers of this land who are still here.

<https://www.realrentduwamish.org>



Case: Mrs. J

- 56 yo African American woman with a history of diabetes, hypertension and an elevated creatinine
- Past History: hypertension, diabetes for 10 yrs
- Family history: kidney failure requiring dialysis in 2 relatives
- PE: BP 170/90
 - Lungs: clear
 - CV: regular rate and rhythm
 - Abd: soft nontender
 - Ext: 2+ edema
- Laboratory Tests
 - Stage 3-4 kidney disease
 - HbA1c=8.5-diabetes not well controlled
- Renal Ultrasound shows 2 kidneys that are normal size and shape
- Question: what is the underlying cause of her kidney disease and how should we approach her work up?
- What can she do to help to decrease the progression of her kidney disease?

Objectives

- Discuss who is affected with Chronic Kidney Disease (CKD) in the US
- Review common and new risk factors for CKD
- Discuss CKD, APOL1 and Ethics of Genetic Testing
- What can I do to improve my kidney function?

Objectives

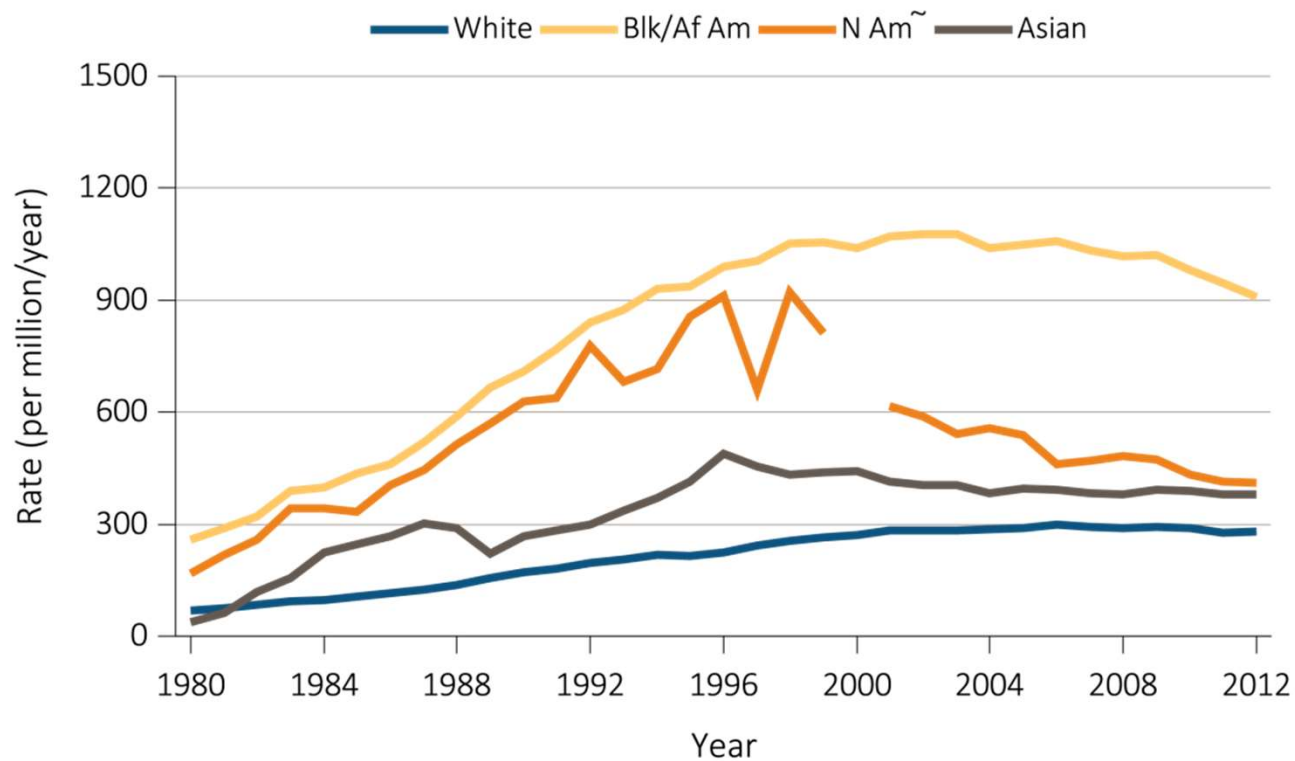
- Discuss who is affected with Chronic Kidney Disease (CKD) in the US
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Background

- Chronic Kidney Disease (CKD) affects 37 million Americans at a cost of \$124 Million.
- African American and Black people have a 3-4-fold greater incidence of kidney failure or endstage kidney disease (EKRD) than whites
- African American/Black people comprise 12% of the population but 34% of dialysis patients.



ESRD incidence rate, per million/year, by race, in the U.S. population, 1980-2012



Social Determinants of Health

- The spaces where we are born, live, work, play, learn, and age.
- They determine our outcomes from disease.
- They affect our quality of life.

Social Determinants of Health



Social Determinants of Health
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 Healthy People 2030

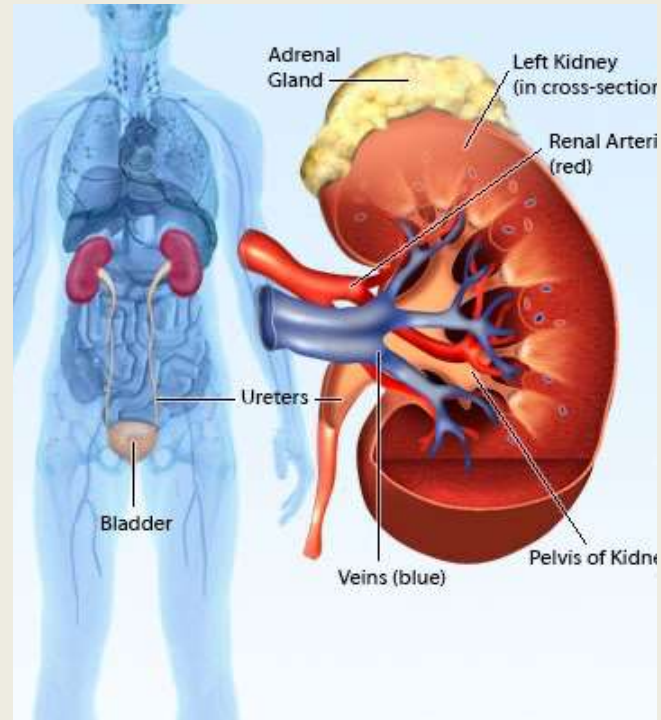
Healthy People 2030 Goals

- Attain healthy, thriving lives and well-being free of preventable disease, disability, injury, and premature death.
- Eliminate health disparities, achieve health equity, and attain health literacy to improve the health and well-being of all.
- Create social, physical, and economic environments that promote attaining the full potential for health and well-being for all.
- Promote healthy development, healthy behaviors, and well-being across all life stages.
- Engage leadership, key constituents, and the public across multiple sectors to take action and design policies that improve the health and well-being of all.



What do the Kidneys Do?

- Filter the blood for toxins
- Maintain stable fluid and volume status
- Help maintain stable blood pressure
- If kidneys don't work, consequences include:
 - Anemia
 - High blood pressure or hypertension
 - Swelling or edema
 - Tiredness or fatigue



What do the Kidneys Do?

- Your kidneys filter extra water and wastes out of your blood and make urine.
- Your kidneys also help control blood pressure so that your body can stay healthy.
- [If someone has Kidney disease, it means their kidneys are damaged and can't filter blood like they should.](#)
- [This damage can cause toxins to build up in the body. It can also cause other problems that can harm your health.](#)

Stage of CKD	eGFR result	What it means
Stage 1	90 or higher	<ul style="list-style-type: none"> - Mild kidney damage - Kidneys work as well as normal
Stage 2	60-89	<ul style="list-style-type: none"> - Mild kidney damage - Kidneys still work well
Stage 3a	45-59	<ul style="list-style-type: none"> - Mild to moderate kidney damage - Kidneys don't work as well as they should
Stage 3b	30-44	<ul style="list-style-type: none"> - Moderate to severe damage - Kidneys don't work as well as they should
Stage 4	15-29	<ul style="list-style-type: none"> - Severe kidney damage - Kidneys are close to not working at all
Stage 5	less than 15	<ul style="list-style-type: none"> - Most severe kidney damage - Kidneys are very close to not working or have stopped working (failed)

Dismantling Race-Based Medicine



Naomi Nkinsi

Pronounced [Now-me En-kinsee]

she/hers

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FAMED 525 Course

Thursday October 6, 2022

Thank you to content co-creators: Radhika Rajan, MD, Ry Garcia-Sampson MD/MPH, Michelle Munikywa, MD/PhD, and Angela Zhang, MD

eGFR and Kidney Function: History of Race Correction



12) Why are there different estimated levels of GFR for African Americans, males and females, and people of different ages?

- African American patients:
The CKD-EPI and MDRD Study equations include a term for the African American race to account for the fact that African Americans have a higher GFR than Caucasians (and other races included in the CKD-EPI datasets and MDRD Study) at the same level of serum creatinine.
This is due to higher average muscle mass and creatinine generation rate in African Americans.
Clinical laboratories may not collect data on race and therefore may report GFR estimates using the equation for Caucasians. For African

Image: https://www.kidney.org/sites/default/files/docs/12-10-4004_abe_faqs_aboutgfrrev1b_singleb.pdf

Racism and the eGFR Algorithm

- MDRD & CKD-Epi: Black participants (unclear how race was defined) were 10-12% of sample. **“Black ethnicity was an independent predictor of higher GFR. Previous studies have shown that on average, Black persons have greater muscle mass than white persons (41– 43).”**
 - Cohn et al: Study n= 26 black females and 21 Black males. Not clear how race determined. They cite Trotter et al, **“Densities of bones of white and negro skeletons”** which looked at 80 adult skeletons and determined that bones of Black bodies were denser than bones of white bodies.
 - Harsha et al: Study n= 99 Black children. Race was determined visually. Also cites Trotter et al. Black boys were older as a group, more adolescents. **Concluded that Black kids have denser bones and thinner skin folds compared to white kids.**
 - Worrall et al: Study n= 30 Black (defined as Afro-Caribbean: West Indian) and 30 white hospital workers across professions. Results said that creatinine kinase was independent of lean body mass. Felt that separate reference ranges should be established for black patients.

eGFR and Kidney Function: What this Means and Why it Matters

Black race variable leads to increase in eGFR value meaning that these patients **need to have greater decline in kidney function** in order to be classified as having

Using the CKD-Epi equation, you input values for two patients with history of hypertension coming in to see you in order to calculate their eGFR.

CKD-EPI for Adults (Conventional Units)

Serum creatinine (mg/dL)*
1.5

Age*
50

African American? Yes No

Gender Male Female

Calculate

GFR value (mL/min/1.73 m²**) **54 mL/min/1.73 m²**

*This equation should only be used for patients 18 and older.
**The NKDEP presently recommends reporting estimated GFR values greater than or equal to 60 mL/min/1.73 m² simply as "≥ 60 mL/min/1.73 m²," not an exact number.

CKD-EPI for Adults (Conventional Units)

Serum creatinine (mg/dL)*
1.5

Age*
50

African American? Yes No

Gender Male Female

Calculate

GFR value (mL/min/1.73 m²**) **Above 60 mL/min/1.73 m²**

*This equation should only be used for patients 18 and older.
**The NKDEP presently recommends reporting estimated GFR values greater than or equal to 60 mL/min/1.73 m² simply as "≥ 60 mL/min/1.73 m²," not an exact number.

Table 10. Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m ²)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

“Without the MDRD eGFR race adjustment, 3.3 million (10.4%) more Black Americans would reach a diagnostic threshold for Stage 3 Chronic Kidney Disease, 300,000 (0.7%) more would qualify for beneficial nephrologist referral, and 31,000 (0.1%) more would become eligible for transplant evaluation and waitlist inclusion.”

-Evaluating the Impact and Rational of Race-Specific Estimations of Kidney Function: Estimations from U.S. NHANES, 2015-2018

Racism in medicine impacts justice

How a Race-Based Medical Formula Is Keeping Some Black Men in Prison

The formula, which helps estimate kidney health, has been discarded by many hospitals. But some judges still use it to decide whether to release those potentially endangered by Covid-19.

Give this article



A Black man at a federal prison complex in West Virginia filed a lawsuit on Wednesday, demanding that the Bureau of Prisons stop adjusting the kidney function scores of Black inmates. Bryan Anselm for The New York Times



By Joseph Goldstein

Published April 22, 2022 Updated April 25, 2022

“In an appeal filed last year, Mr. Robinson’s lawyer pointed out the racial consequence of the old formula: **‘If Mr. Robinson were white his medical data would indicate that he was suffering from chronic kidney disease.’**”

Student advocacy leads to change

NKF and ASN Release New Way to Diagnose Kidney Diseases



Both Organizations Recommend Race-Free Approach to Estimate GFR

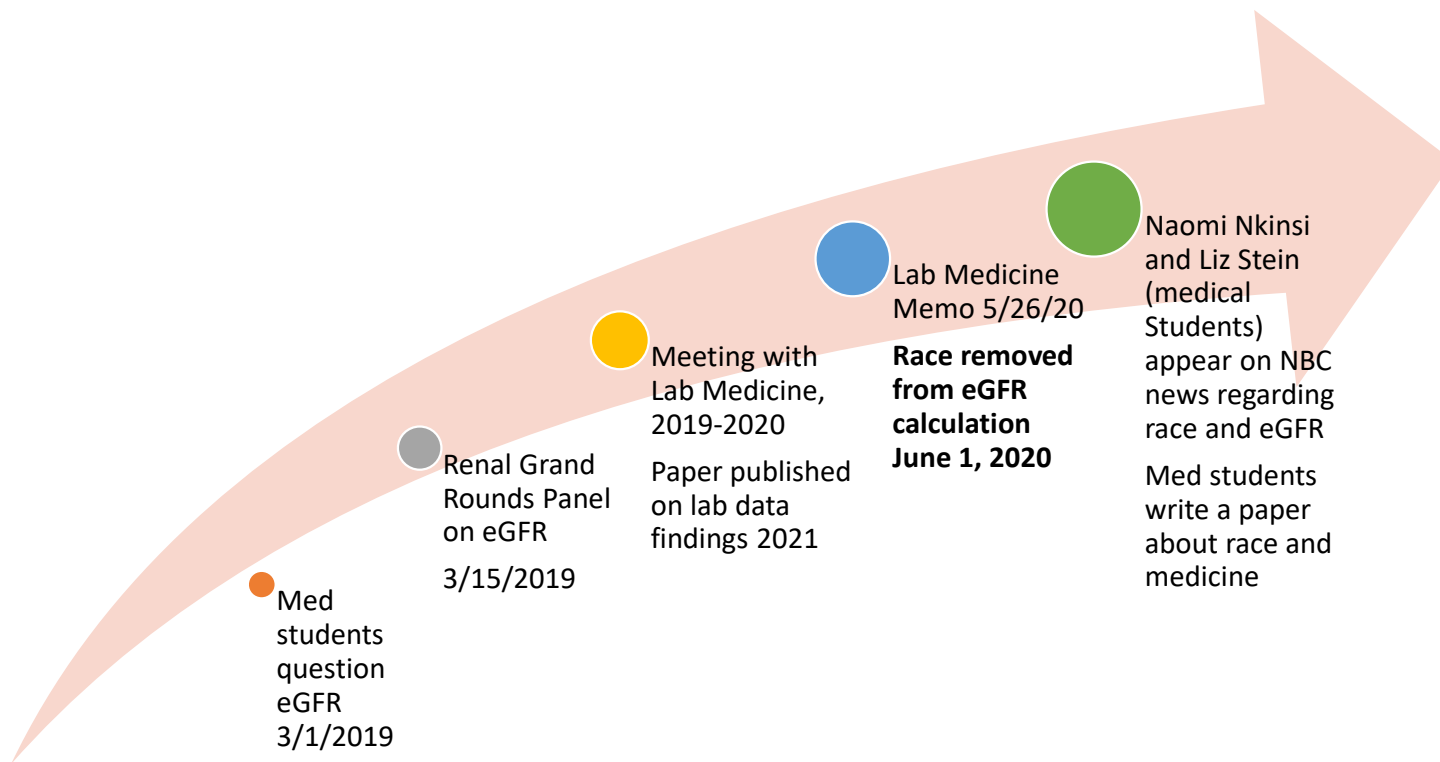
Sept. 23, 2021, New York, NY – Today, the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases has released its final report, which outlines a new race-free approach to diagnose kidney disease. In the report, the NKF-ASN Task Force recommends the adoption of the new **eGFR 2021 CKD EPI creatinine equation that estimates kidney function without a race variable. The task force also recommended increased use of cystatin C combined with serum (blood) creatinine, as a confirmatory assessment of GFR or kidney function.** The final report, published today online in the *American Journal of Kidney Diseases (AJKD)* and the *Journal of the American Society of Nephrology (JASN)*, was drafted with considerable input from hundreds of patients and family members, medical students and other trainees, clinicians, scientists, health professionals, and other stakeholders to achieve consensus for an unbiased and most reasonably accurate estimation of GFR so that laboratories, clinicians, patients and public health officials can make informed decisions to ensure equity and personalized care for patients with kidney diseases.

How the University of Washington Implemented a Change in eGFR Reporting

Naomi T. Nkinsi ¹ and Bessie A. Young ^{1,2,3,4}

KIDNEY360 3: 557–560, 2022. doi: <https://doi.org/10.34067/KID.0006522021>

UW Timeline



Slide 21

BAY1

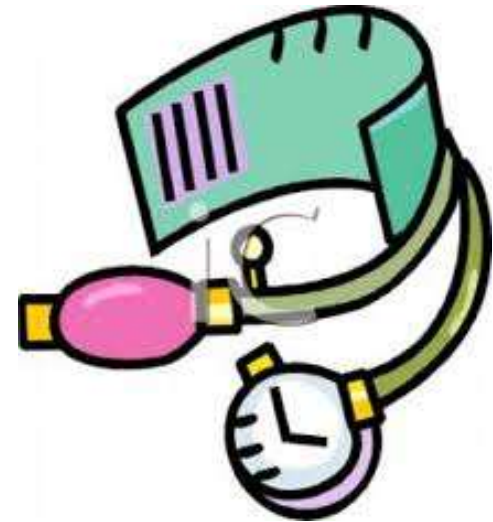
Bessie A Young, 9/8/2021

Objectives

- Discuss who is affected with Chronic Kidney Disease (CKD) in the US
- Review common and new risk factors for CKD
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Common Risk Factors for CKD

- Diabetes
- Hypertension
- Cardiovascular Disease (Heart Disease)
- Family History of kidney disease
- Genetic Diseases



Racial and Ethnic Differences in Diabetic Nephropathy

- Diabetes disproportionately affects minorities
- Diabetes accounts for 50% of new cases of ESRD
- Little was known about differences and risk factors for progression



Racial and Ethnic Differences in Diabetes

Racial and Ethnic Differences in Microalbuminuria

Pathophysiology/Complications

ORIGINAL ARTICLE

Racial Differences in Diabetic Nephropathy, Cardiovascular Disease, and Mortality in a National Population of Veterans

BESSIE A. YOUNG, MD, MPH^{1,2,3}
CHARLES MAYNARD, PHD^{1,4}
EDWARD J. BOYKO, MD, MPH^{1,2}

ease (ESRD) or dialysis dependence in the U.S. (6). Compared with Caucasians, racial minority populations are disproportionately affected by diabetes (7,8) and

We then asked the question...

What are some of the new risk factors for chronic kidney disease in African Americans?

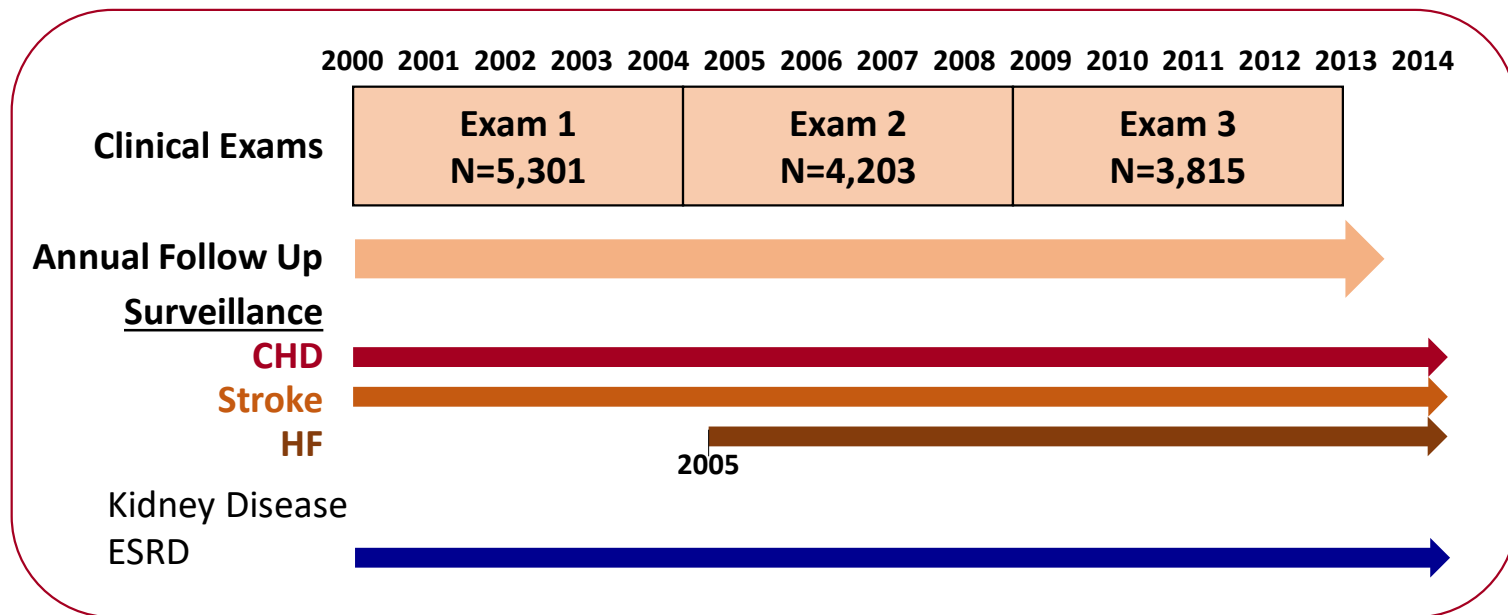


Jackson Heart Study



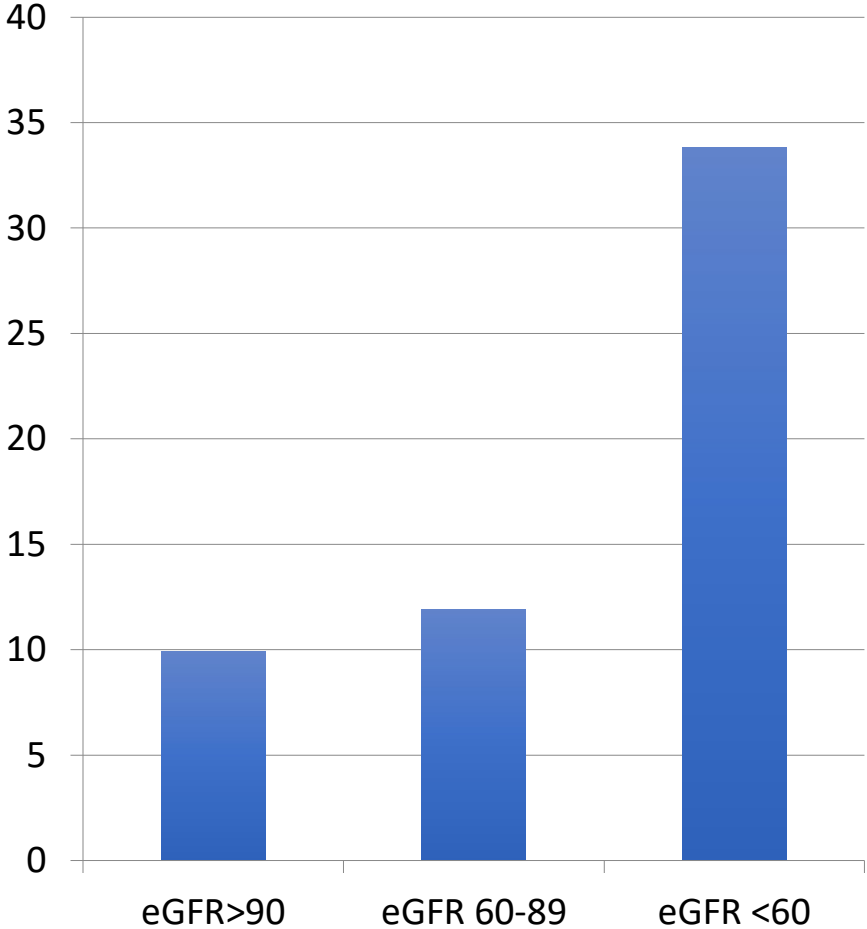
- Largest prospective NIH funded study of cardiovascular disease in African American individuals.
- Study involves 5,301 African American people from Jackson MS
- 3 Exams with data collected at each point
 - 2000-2004
 - 2005-2008
 - 2009-2012
- Kidney Disease National Institutes of Health (NIH) funded study

JHS Longitudinal Data Capture



Rapid Kidney Function Decline in JHS

- Young, AJKD, 2016



Risk Factors Associated with Rapid Kidney Function Decline >30% over 10 Years

Variable	All JHS Participants Adjusted Odds Ratios (95% CI)	JHS with Albuminuria Adjusted Odds Ratios (95% CI)
Age (per 10yr increase)	1.88 (1.57-2.27)	1.88 (1.56, 2.28)
Income		
Low	2.34 (1.19-4.60)	1.84 (0.90, 3.76)
Lower-middle	1.83 (1.07-3.13)	1.61 (0.92, 2.81)
Upper –middle	1.49 (0.93-2.39)	1.42 (0.88, 2.29)
Affluent	1.00 (Ref)	1.00 (Ref)
Education (ref College)		
<High School	1.94 (1.08-3.50)	2.09 (1.14, 3.83)
Systolic Blood Pressure	1.39 (1.17-1.64)	1.29 (1.09-1.53)
Diabetes	1.75 (1.18-2.60)	1.57 (1.09-2.27)
Current Smoker	1.92 (1.08-3.41)	1.65 (0.96-2.84)

Conclusions

Chronic Kidney Disease is prevalent in African Americans.

Risk factors for rapid kidney function decline include age, diabetes, HTN, and albuminuria.

Behavioral factors include smoking

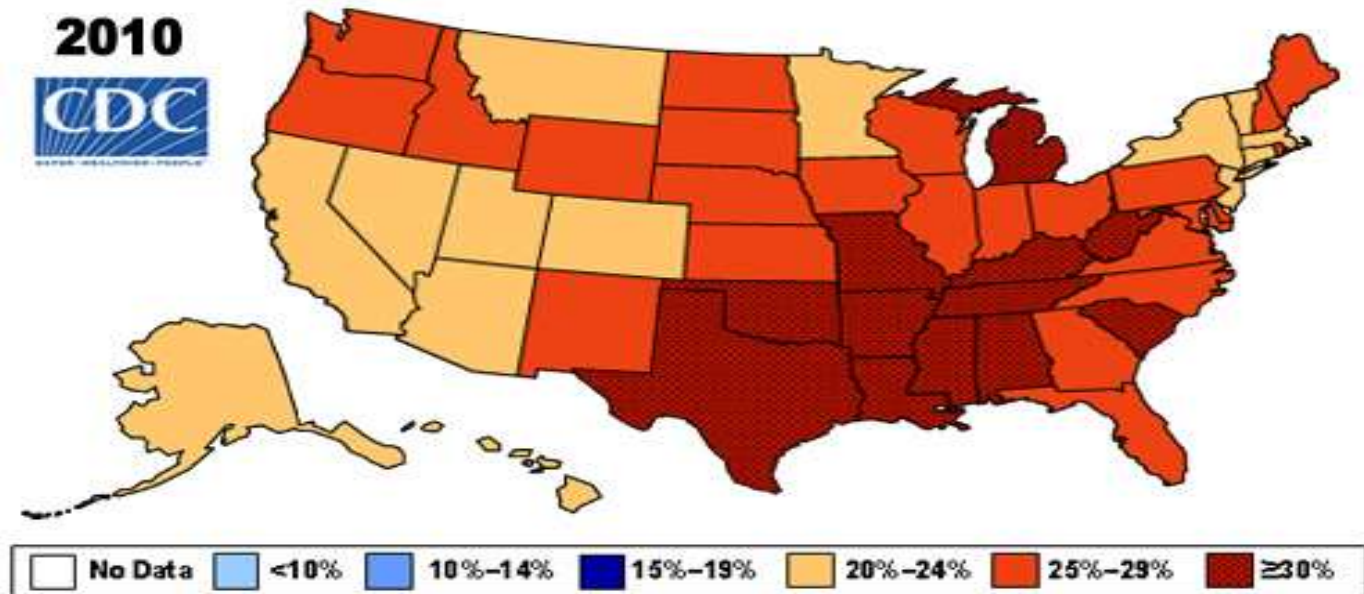
There is a need to evaluate other potential risk factors.

Novel Risk Factors for Chronic Kidney Disease Incidence and Progression

- Periodontal Disease is associated with increased inflammation
- Severe Periodontal Disease associated with 4-fold greater incidence of CKD
- Incidence Rate Ratio = 4.18
95% CI =1.68 – 10.39), p=0.002
after adjustment for age, gender, diabetes, and smoking status



Obesity in the United States

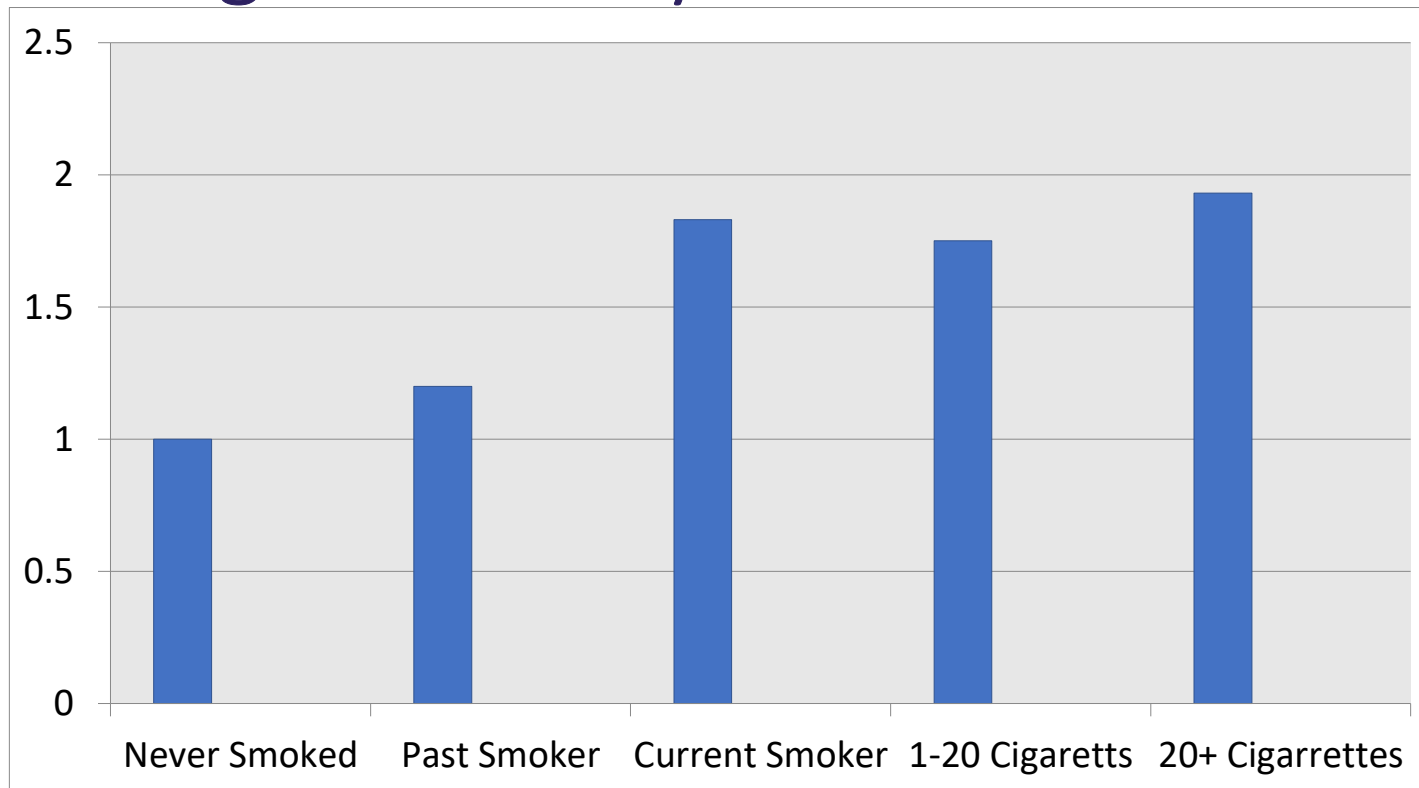


Smoking and Health

- Smoking is associated with lung cancer and increased risk of heart disease.
- Smoking cessation is routinely recommended as a preventive measure
- No consistent association with kidney disease development has been shown.



Risk of Rapid Kidney Function Decline based on Smoking and Kidney Disease



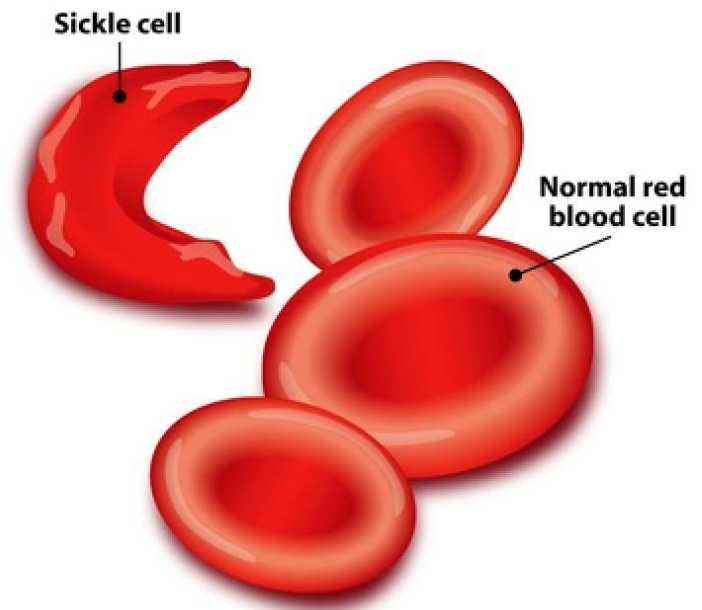
Hall, JAHA, 2016



Medicine

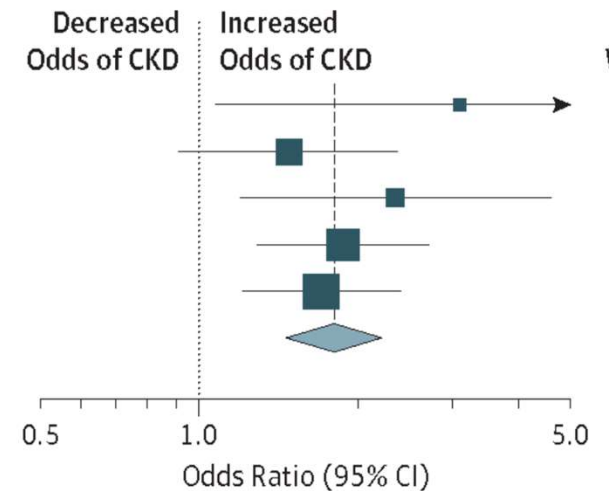
Sickle Cell Trait (SCT) and Chronic Kidney Disease

- Inheritance of a single copy of the hemoglobin S gene
- Affects 1 in 12 African Americans
- Estimated 300 million people affected worldwide
- Sickle Cell Disease (SCD) associated with kidney abnormalities
 - Decreased urinary concentrating ability, CKD, and ESRD
- Less is known about SCT and association with CKD



Association of Sickle Cell Trait with Incident Chronic Kidney Disease in African Americans

Study	No. of Participants		No. (%) With Incident CKD		Odds Ratio (95% CI)
	Noncarriers	SCT Carriers	Noncarriers	SCT Carriers	
CARDIA	775	72	20 (2.6)	5 (6.9)	3.09 (1.07-8.93)
MESA	1283	124	203 (15.8)	26 (21.0)	1.47 (0.91-2.36)
JHS	1388	114	91 (6.6)	14 (12.3)	2.33 (1.19-4.59)
WHI	1917	154	410 (21.4)	49 (31.8)	1.86 (1.28-2.70)
ARIC	3118	211	434 (13.9)	46 (21.8)	1.69 (1.20-2.39)
Overall ($I^2 = 0.0\%$, $P = .66$)					1.79 (1.45-2.20)



JAMA. 2014;312(20):2115-2125. doi:10.1001/jama.2014.15063

Figure Legend:

Meta-analysis of Odds Ratios for Incident CKD Using Creatinine Values Comparing Sickle Cell Trait Carriers With Noncarriers. CKD indicates chronic kidney disease; eGFR, estimated glomerular filtration rate; SCT, sickle cell trait. Incident CKD was defined as development of an eGFR level lower than 60 mL/min/1.73 m² during follow-up. All models adjusted for age, sex, clinic or region, African genetic ancestry, hypertension, and diabetes. The size of data markers indicate the weight of study.

Sickle Cell Trait and CKD Conclusions



Sickle cell trait is associated with prevalent CKD, new onset CKD, kidney function decline, and albumin in the urine in a large group of 15,975 African American individuals.



Sickle cell trait may explain a portion of the racial differences in CKD but not all the increased risk.



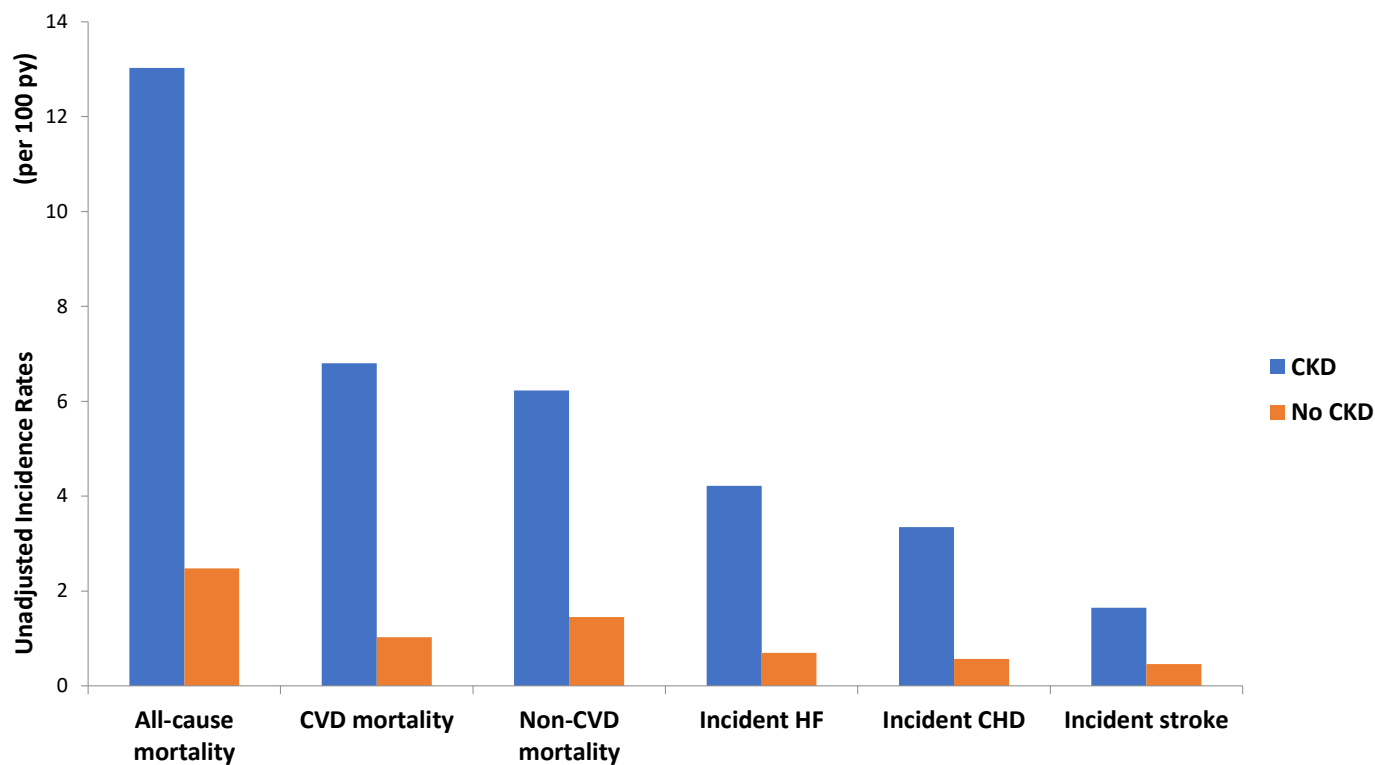
Further research is needed to determine if targeted interventions of other known CKD risk factors may decrease incidence and progression of CKD.

Heart Failure (HF), Cardiovascular Disease (CVD), and Stroke in JHS

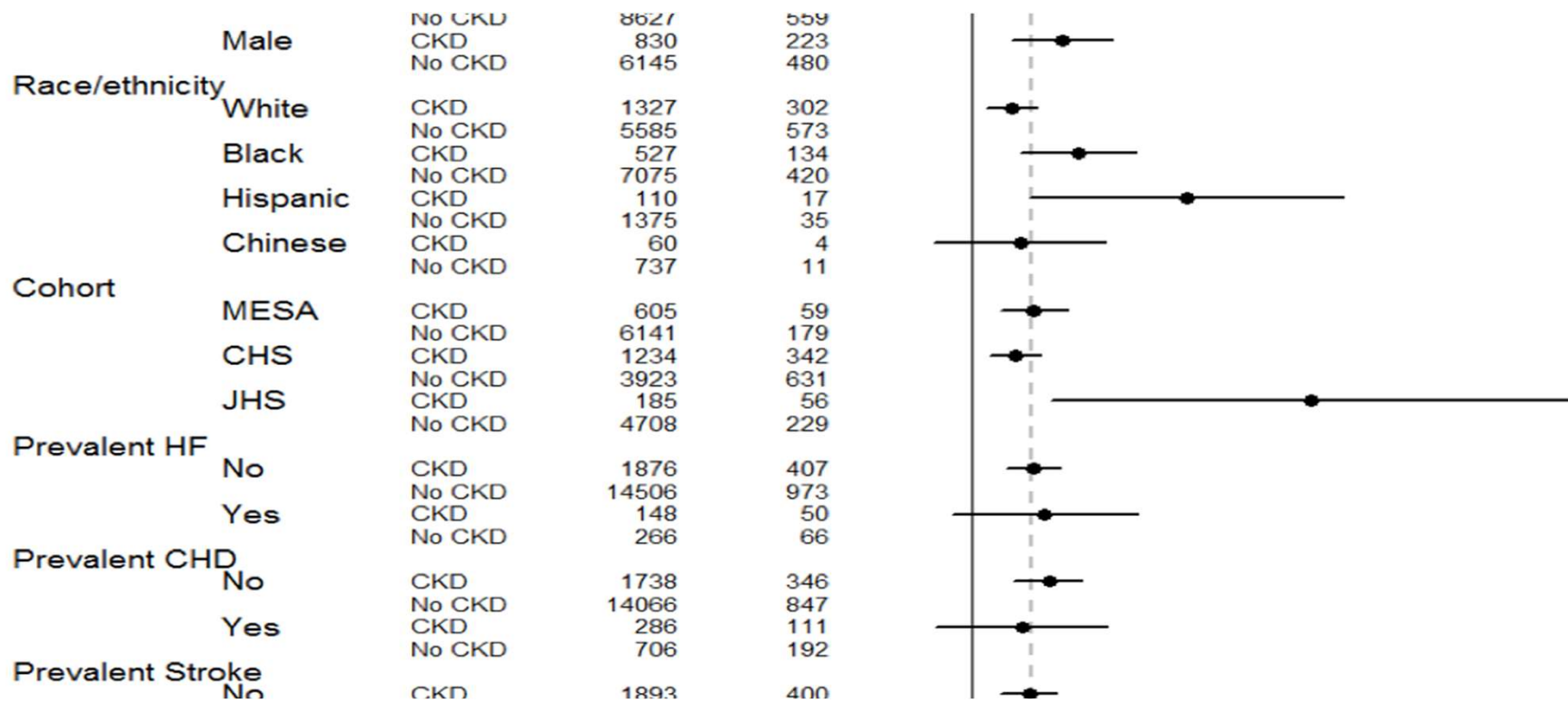
- Heart Failure is highly prevalent in African American people compared to white people
- Hypertension and stroke incidence and prevalence are high in African American people
- There is a bidirectional affect of kidney disease on heart disease
- Less is known regarding how heart failure, CVD, and stroke differ in people with CKD compared to normal kidney function



Unadjusted incidence rates of Heart Disease events in subjects with vs. without CKD in JHS



JHS Participants had more episodes of Heart Failure than other Cohort Studies



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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} Carl D. Langefeld,^{8,9} Taras K. Oleksyk,¹⁰ Andrea L. Uscinski Knob,⁴ Andrea J. Bernhardt,¹ Pamela J. Hicks,^{7,8} George W. Nelson,¹¹ Benoit Vanhollebeke,⁵ Cheryl A. Winkler,¹² Jeffrey B. Kopp,¹¹ Etienne Pays,^{5†} Martin R. Pollak^{1,13†}

Science 329, 841 (2010)



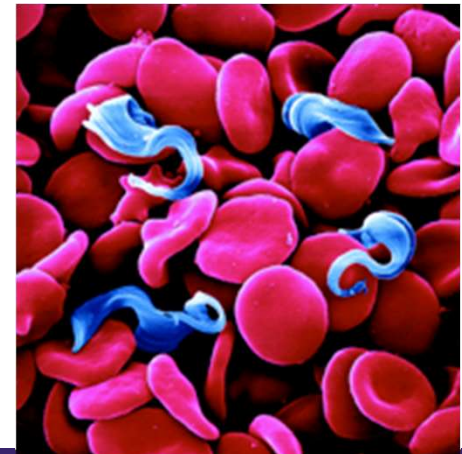
APOL1 Genetic Variants

- Apolipoprotein L1 genetic variants are associated with protection from trypanosomes-parasite
- Variants arose 3000-6000 years ago in Africa and are associated with resistance to the lethal form of African Sleeping Sickness acquired from the bite of the Tsetse Fly
- Variants are only present in people of African descent
 - Someone is called “high risk” if they have 2 of the risk variants

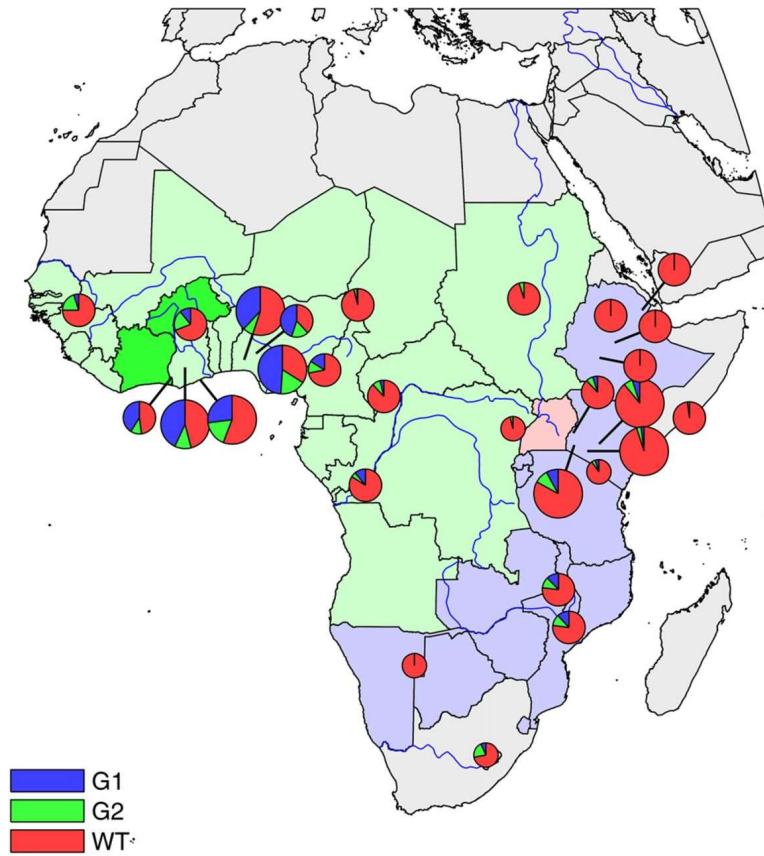
Tsetse Fly



Trypanosomes



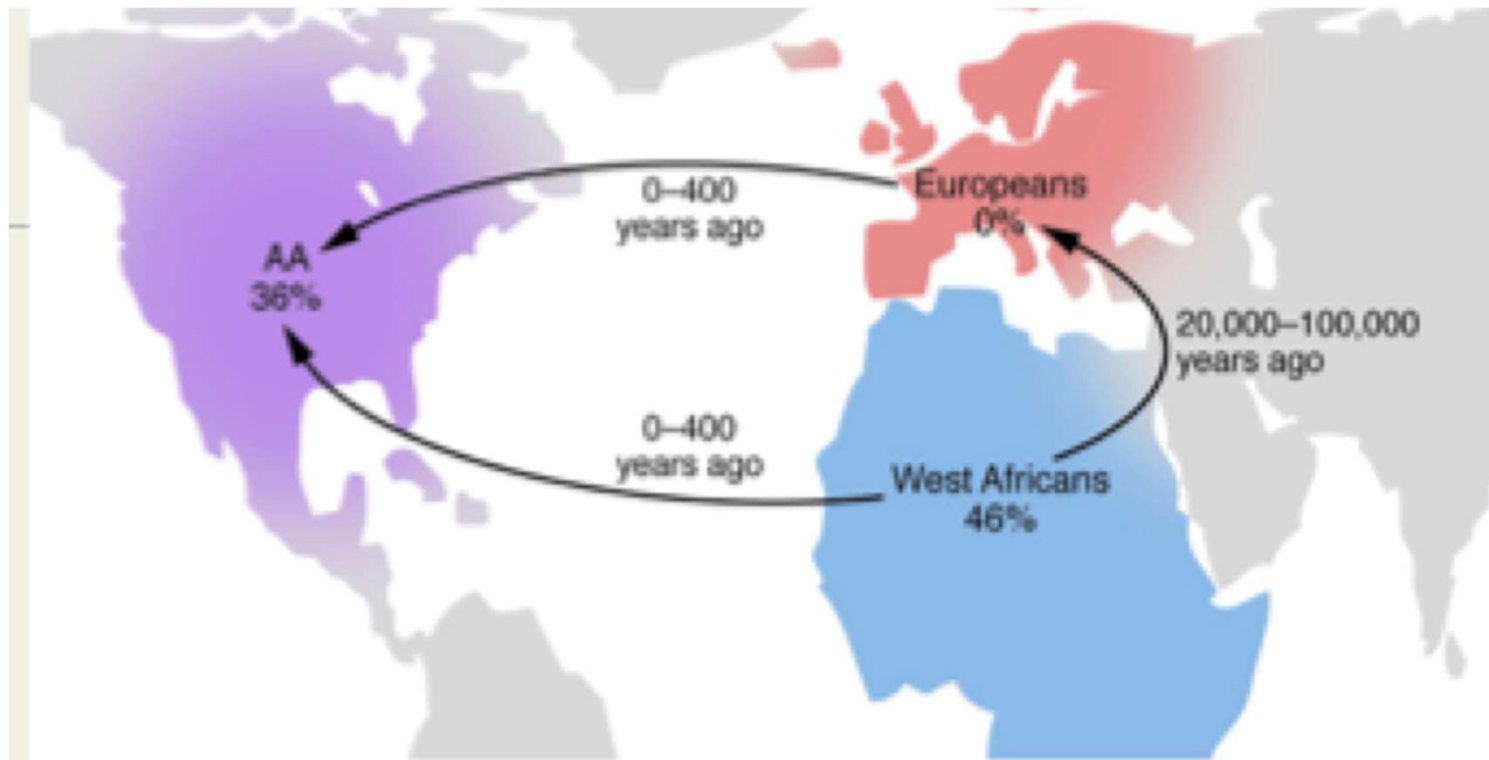
Distribution of the G1 and G2 APOL1 variants across Africa.



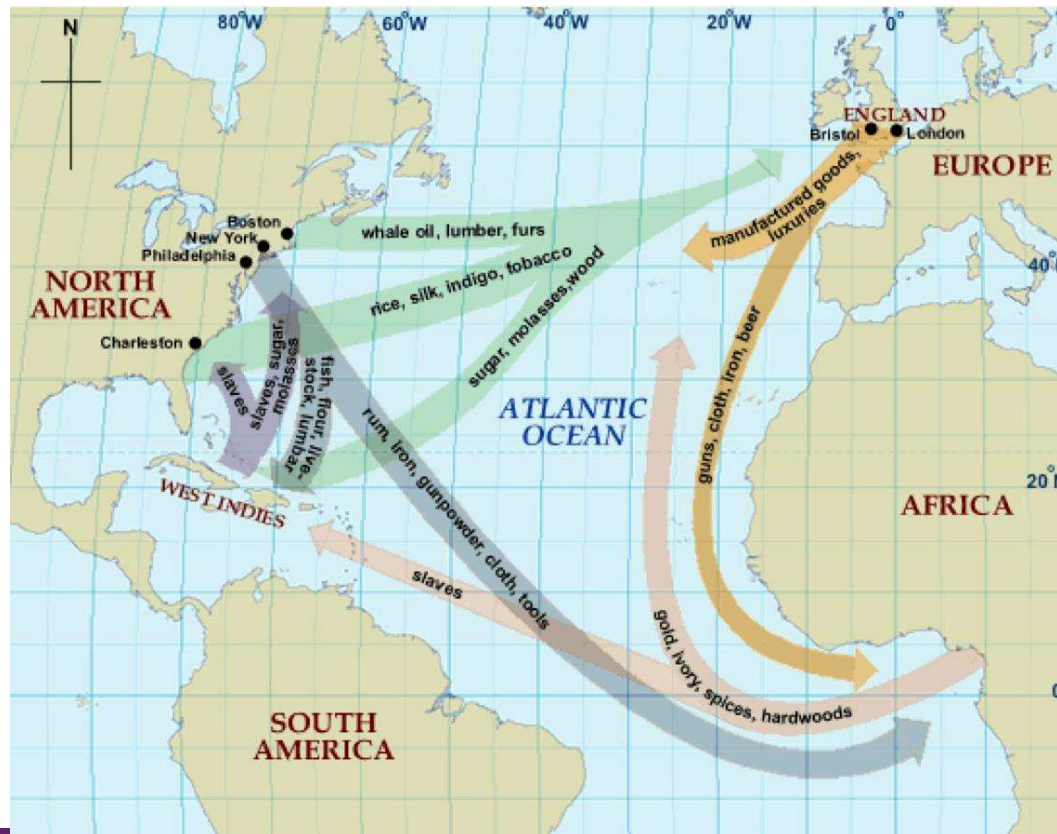
Etty Kruzel-Davila et al. *Nephrol. Dial. Transplant.*
2016;31:349-358

NDT
Nephrology Dialysis Transplantation

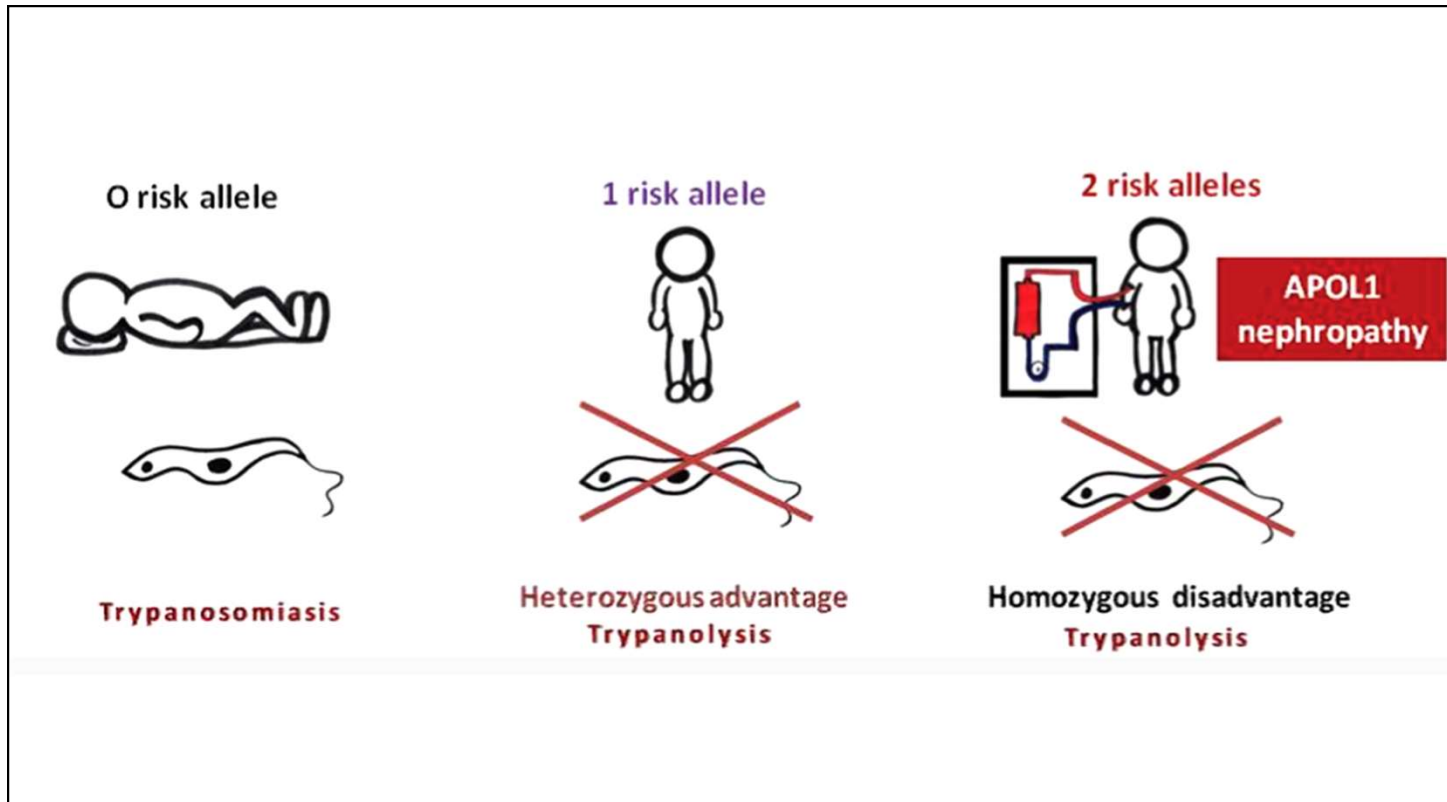
Why don't White people have APOL1 Risk?



Trade Routes for Enslaved People from Africa to North America



APOL1 Risk AND Kidney Failure



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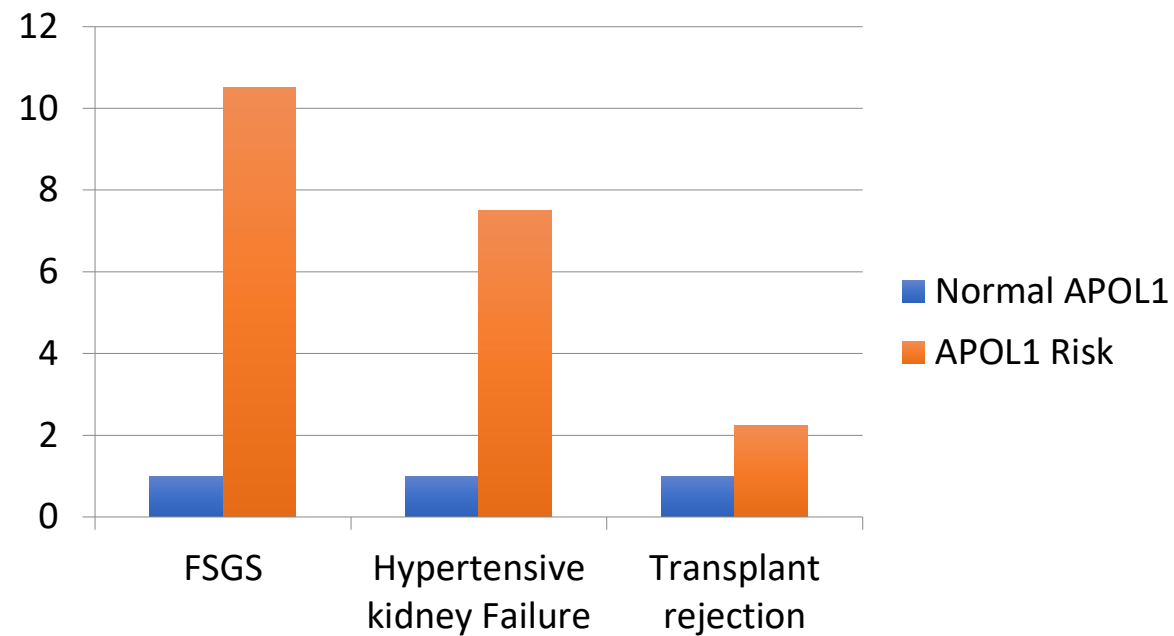
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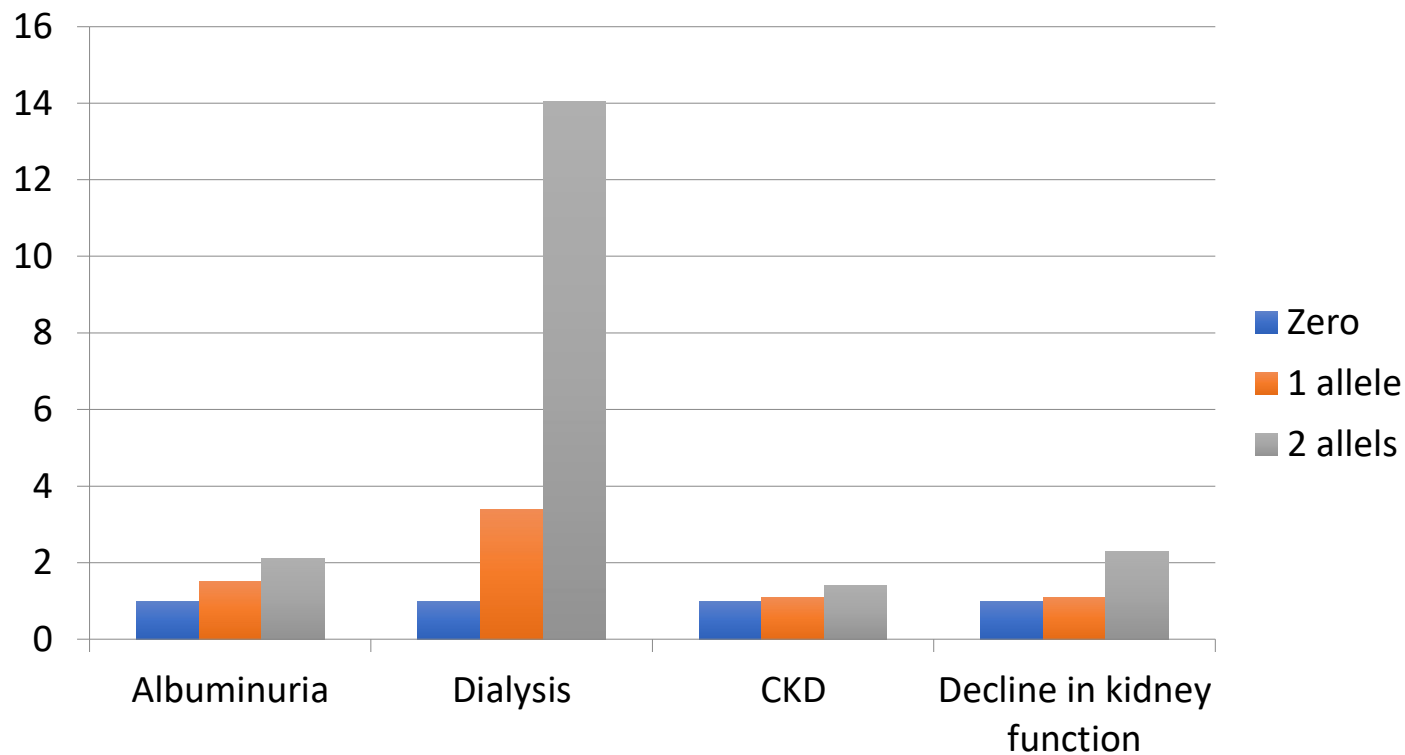
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UW Medicine

Risk of Kidney Failure or Transplant Rejection in African Americans with APOL1 Risk



APOL1 Variants and Kidney Disease from the Jackson Heart Study



Ethics of Genetic Testing

- Legacy of mistrust in the African-American Community
 - Tuskegee Study
 - Covid
- Sickle Cell Testing
 - Programs in the 1970's associated with mistrust in Black Community
- Polycystic Kidney Disease
 - Policy of "Don't ask, don't tell" in Nephrology
 - Diagnosis led to concerns regarding health insurance and preexisting disease.

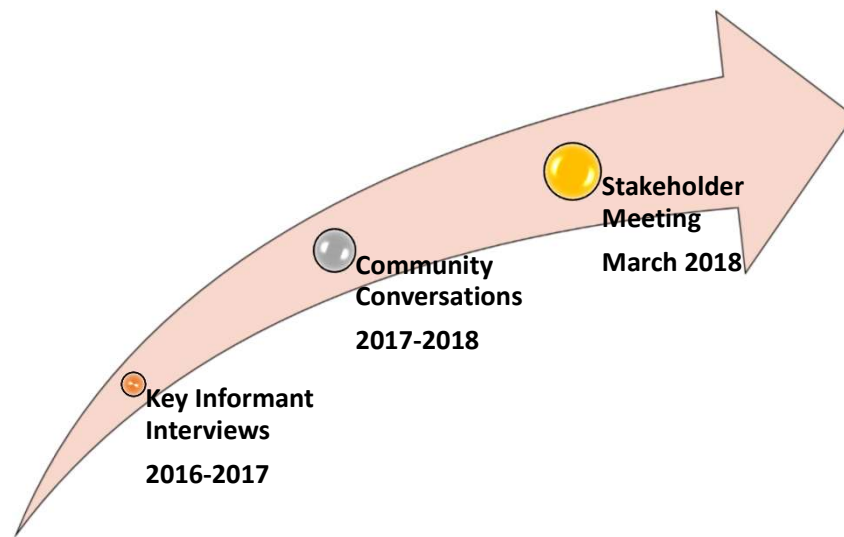


Genetic Testing for APOL1 and Risk of Kidney Disease

- How should genetic testing be done?
 - Should everyone be screened?
 - Who has access to the information?
 - How long is the information kept
 - What if we find out disease is associated with genetic abnormalities thought to be benign?
 - Sickle Cell Trait?
 - Do people have a right to know if they were screened for a disease as a child and now it has been found to be associated with an actionable disease?



Community-Based Evaluation of APOL1 Genetic Testing in African Americans



Develop APOL1 Policies, Guidelines, Educational Information on Genetic Testing



DRAFT CONCLUSIONS FROM APOL1 STAKEHOLDER MEETING

1. African Americans should be informed about APOL1 risk
2. APOL1 testing should be integrated into renal transplant programs
3. APOL1 testing is NOT recommended for routine clinical use or screening, because there are no specific actions or treatments to improve outcomes for people with APOL1 risk
4. Research is needed to ensure better understanding of APOL1 risk
5. Involvement of members of the African-American community in development of policies and educational material about APOL1 risk and APOL1 testing will help to ensure that testing policies address community needs and preferences

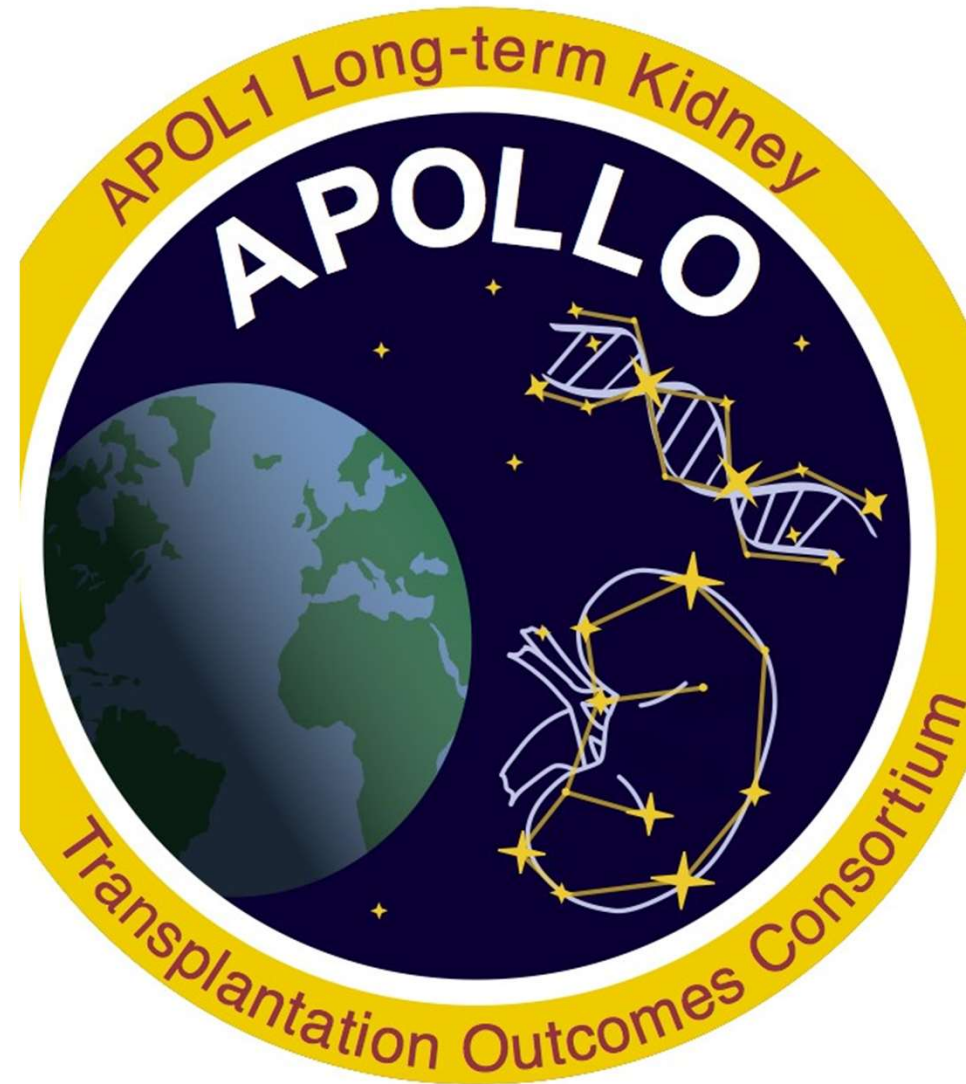


APOL1 Long Term Kidney Transplantation Outcomes: APOLLO

Multicenter, prospective longitudinal cohort study

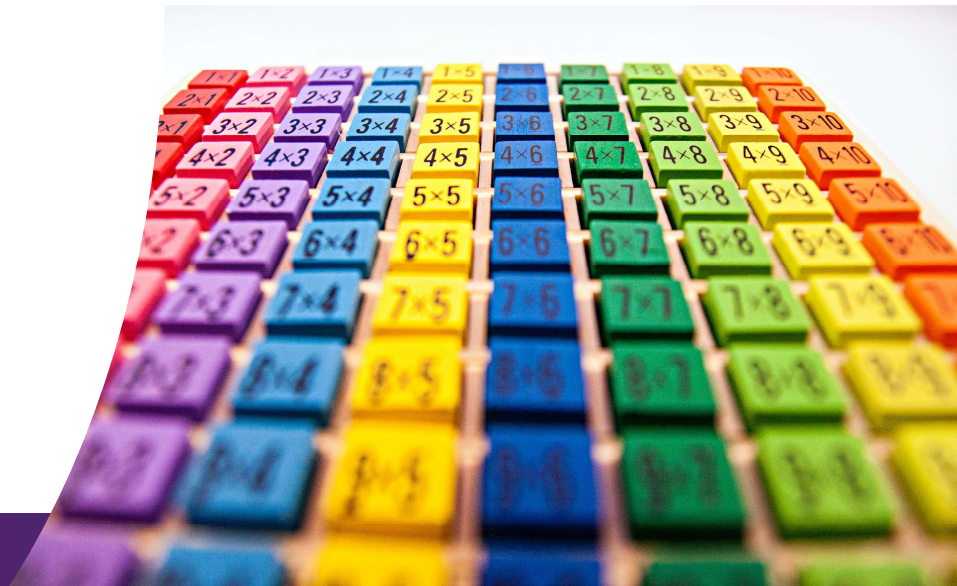
Aims:

- Confirm prior findings of decreased graft survival from APOL1 donors and Progression of CKD in APOL1 Living Donors
- Evaluate for other causes
- Follow for long-term outcomes, especially in living donors
- Provide safety data for potential living donors



What can I do to improve my kidney function?

- KNOW YOUR NUMBERS!
- Blood pressure-normal is 120/80
- Diabetes-glucose and hemoglobin A1c 7-7.5%
- Weight and BMI less than 26



- Know what medications you are on!
A Healthy lifestyle helps!

- SGLT2 inhibitors improve kidney function and protect the heart by increasing excretion of glucose.

- Farxiga
- Jardiance
- Glyxambi
- Synjardy
- Steglatro
- Xigduo XR



Case: Mrs. J

- ID/CC: 56 yo African American woman with kidney disease, hypertension, diabetes
- Kidney Biopsy showed diabetic nephropathy and Focal Segmental Glomerular Sclerosis
- She rapidly progressed to needing dialysis
- She underwent gastric bypass and lost a significant amount of weight.
- She received a kidney transplant from her daughter is doing well
- She now has normal kidney function



Conclusions

- CKD in African American and Black people is prevalent in the community
 - Some people progress rapidly while others do not
- Differences include traditional risk factors and some novel factors
- Newer genetic factors for CKD/ESRD include *APOL1* polymorphisms and Sickle Cell Trait
- Genetic Testing for *APOL1*/SCT being done, but ethics of testing need to be determined.
- New paradigms for genetic testing and delivering results are needed that involved community views.
- Know your numbers to protect your kidneys!

Thank-you!

- Questions?
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Questions



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