

# APOL1 Screening: Opportunities, Lessons Learned and Evidence to Support Screening *and Enhance Equity*

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Elder Mimsie Robinson DPhil, Bethel Gospel Assembly



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# OVERVIEW

Screening with an equity lens; straddling race & ancestry

The who's and the how's of screening

Whose voice? Whose choice?



# THE INEQUITY

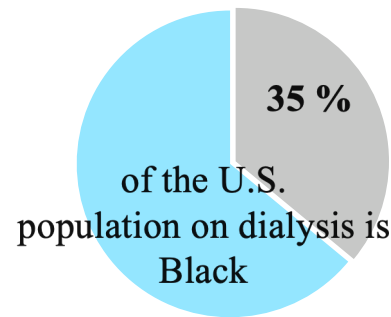
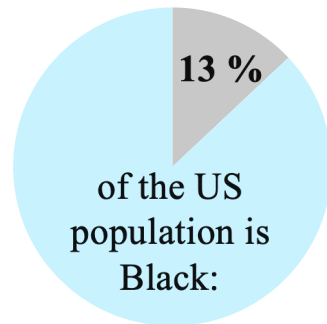
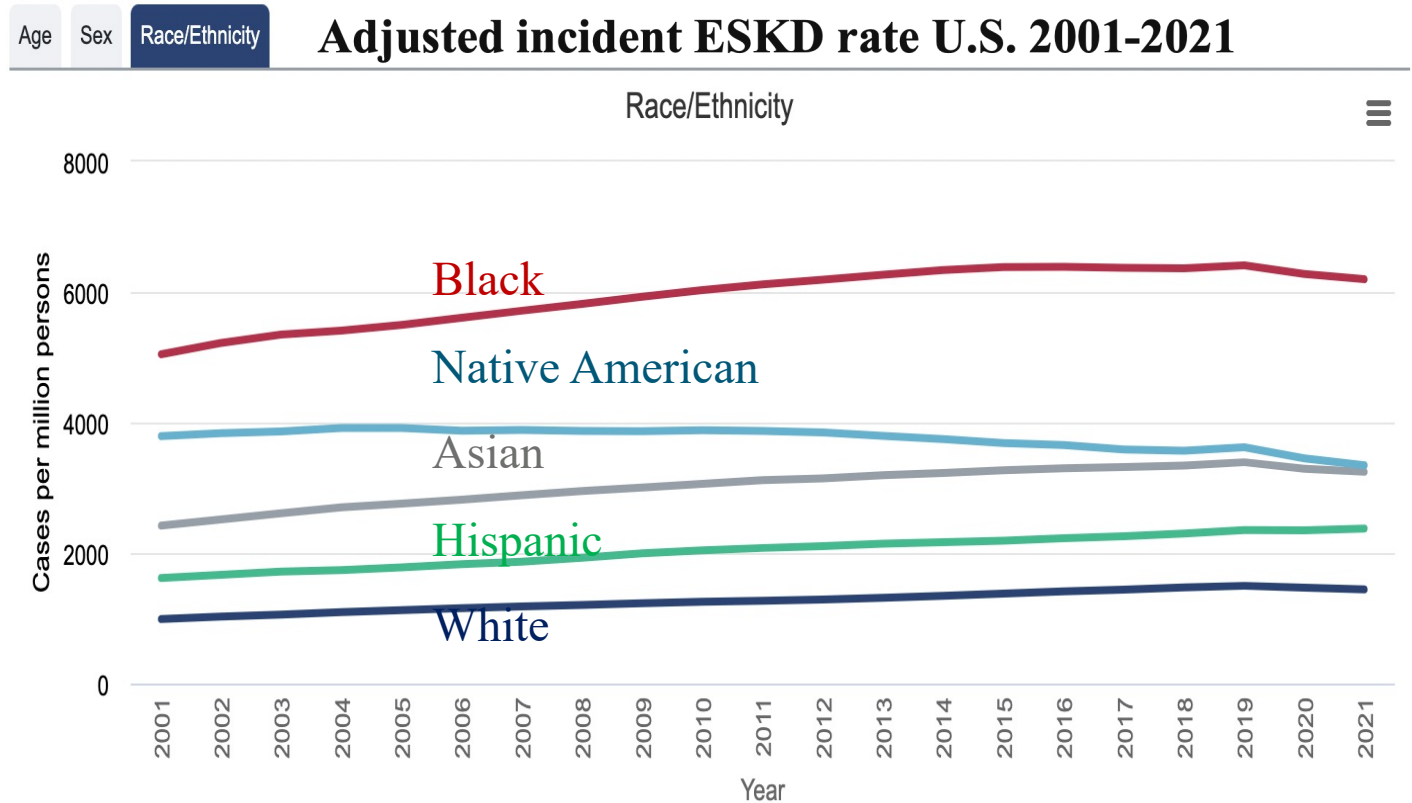


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# Will these figures look different at GMXXV?

Black individuals- 2-3x risk of End Stage Kidney Disease vs. White individuals



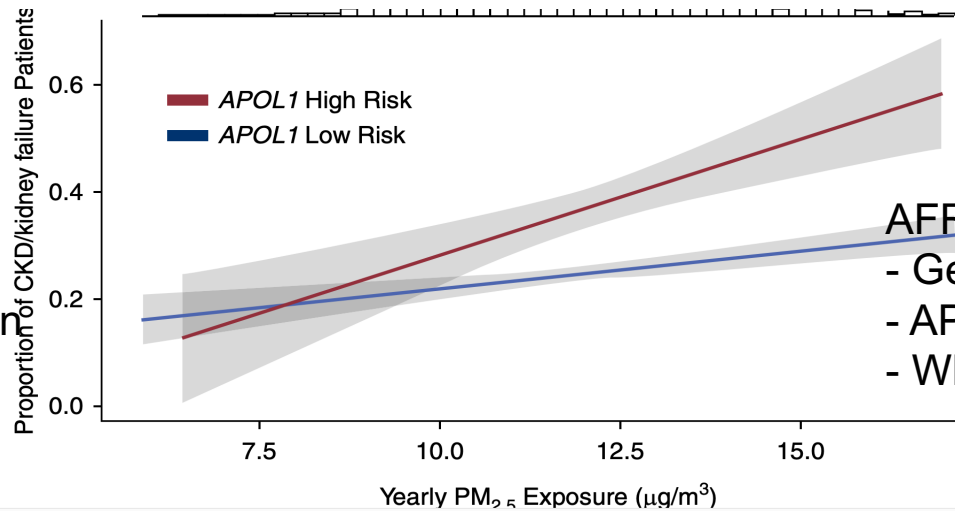
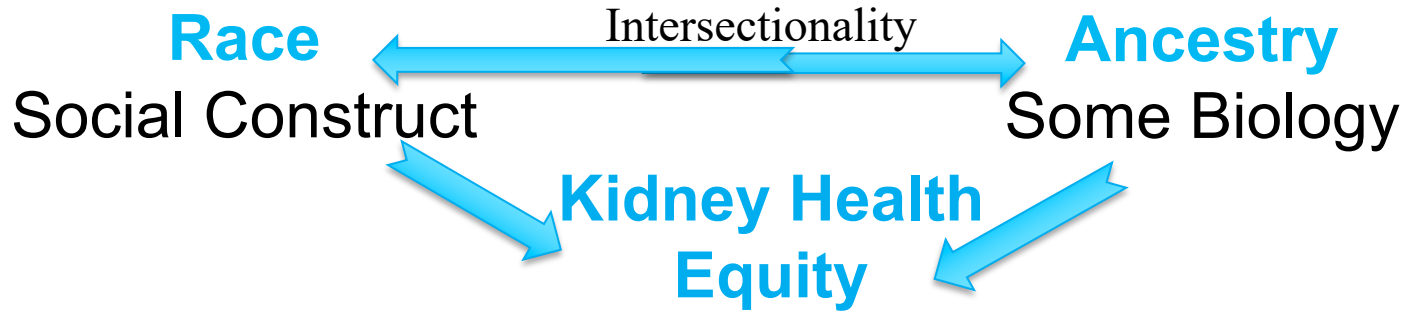
# REASONS FOR THE INEQUITY



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# Multiple Determinants of Inequity



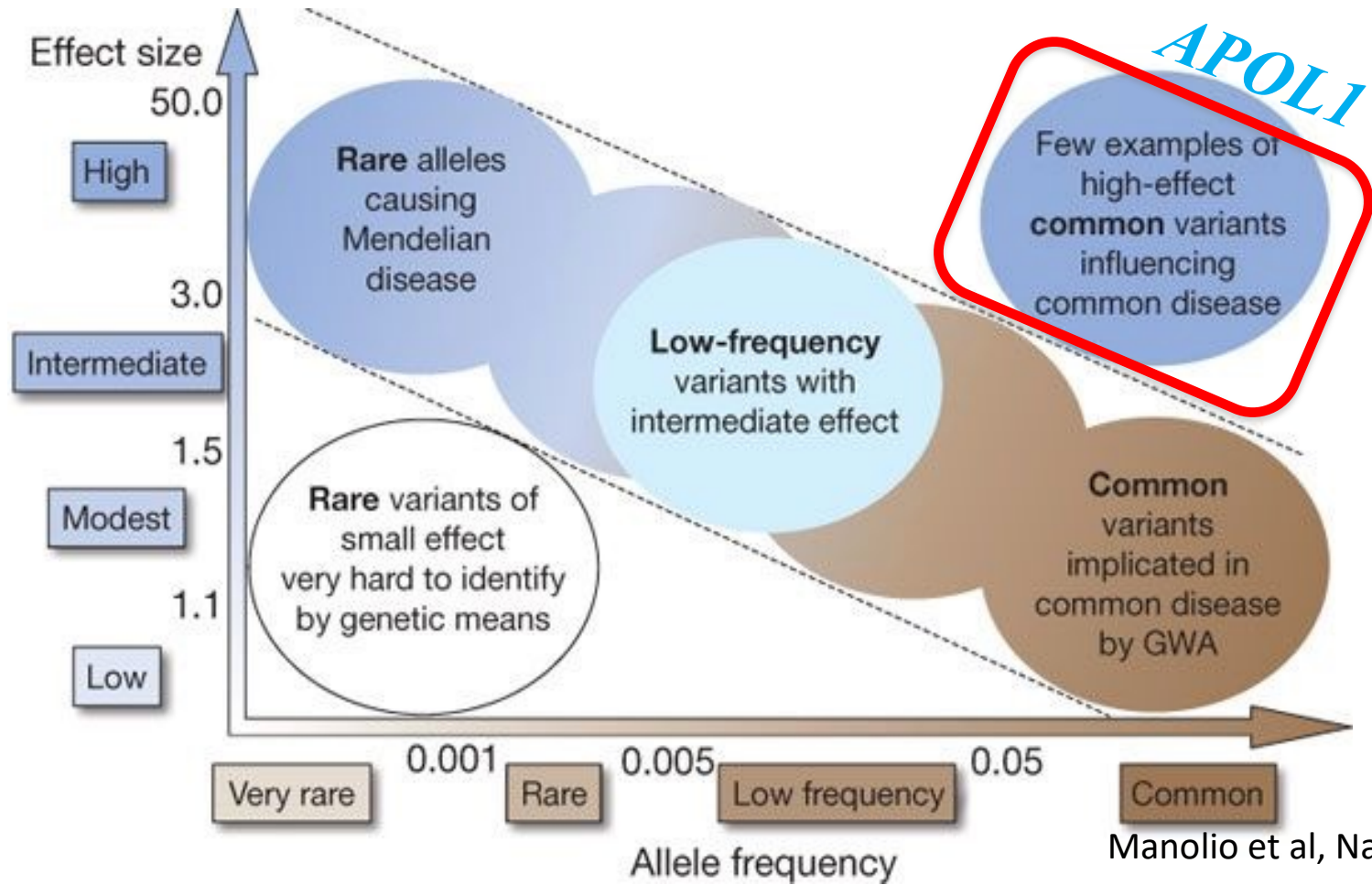
**BLACK RACE**

- Residential Segregation
- > exposed to air pollution
- Which is nephrotoxic.

**AFRICAN ANCESTRY**

- Geographic Threat
- APOL1 protectant
- Which is kidney harming.

# APOL1 & CKD: Common, Powerful, Related to Afr. Ancestry



Manolio et al, Nature 2010

**APOL1 [2] Risk Copies: ~10% Lifetime Risk of ESKD (5-10x increase)  
Found in ~1/7 people who self report Black race or have Afr. ancestry**



# Acknowledging Perspectives on Genetic & CKD Disparities

**Genetic ethicist:** Don't touch this- you will set the disparities movement back 30 years.

**Harlem pastor:** Now maybe White doctors won't judge Black people on dialysis as not caring enough or not being compliant. They'll recognize that there's more to kidney disease than bad behavior.





# THE SCREENING

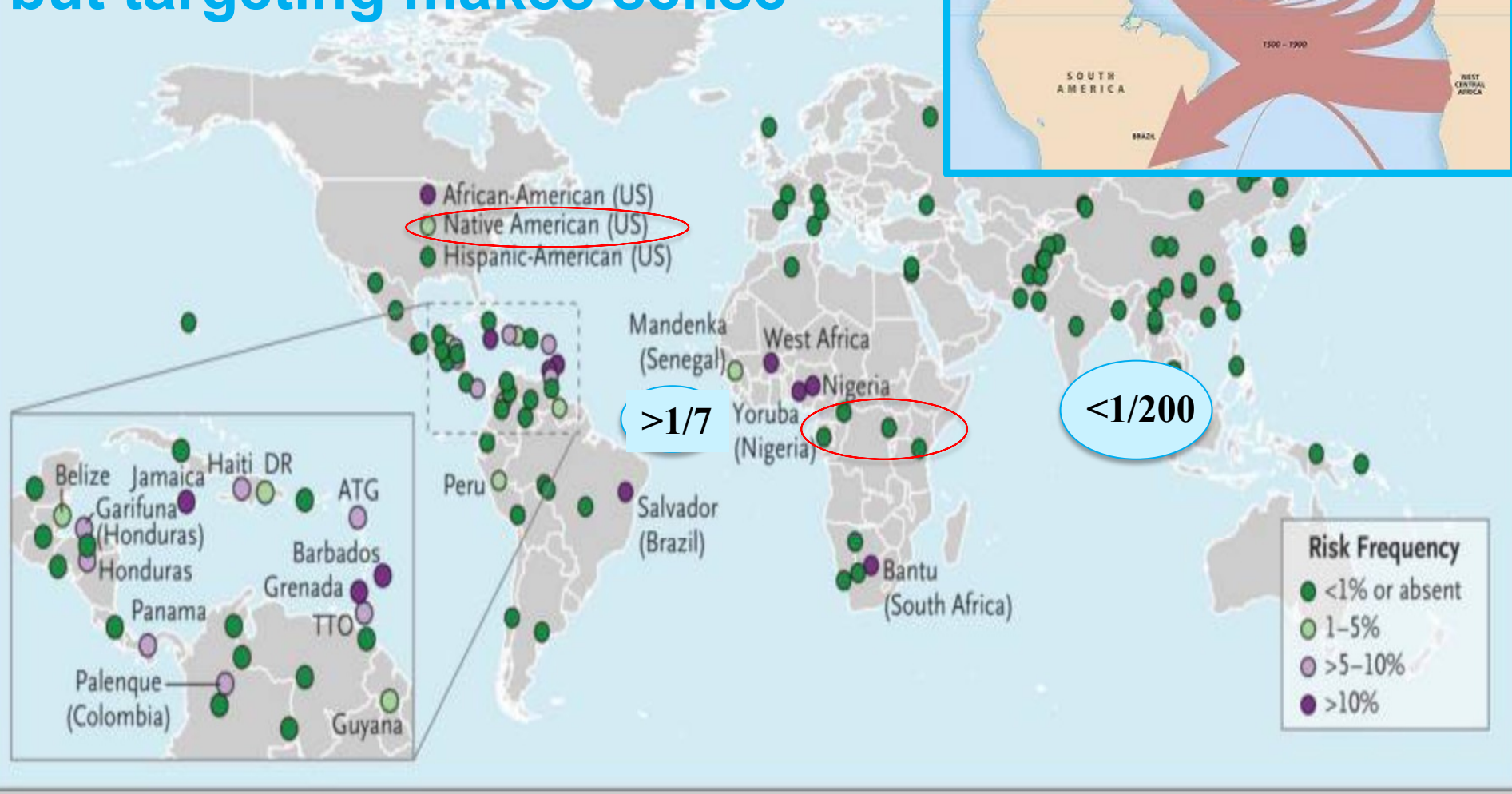
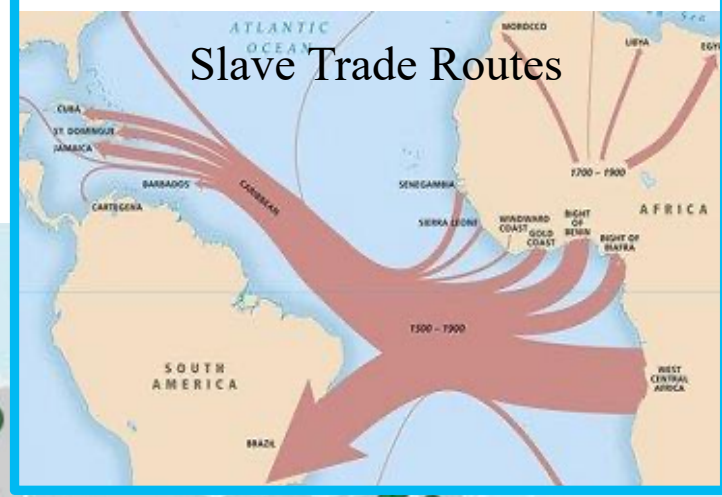
- Who?

- What conditions?



# WHO? "Pretest Probability"

## *APO11* not a race gene, but targeting makes sense



# WHAT Conditions for *APOL1* screening

## Existing Recommendations:

FSGS, HIVAN, Lupus Nephritis- Prognosis, Adherence

Preeclampsia- identify risk, monitor

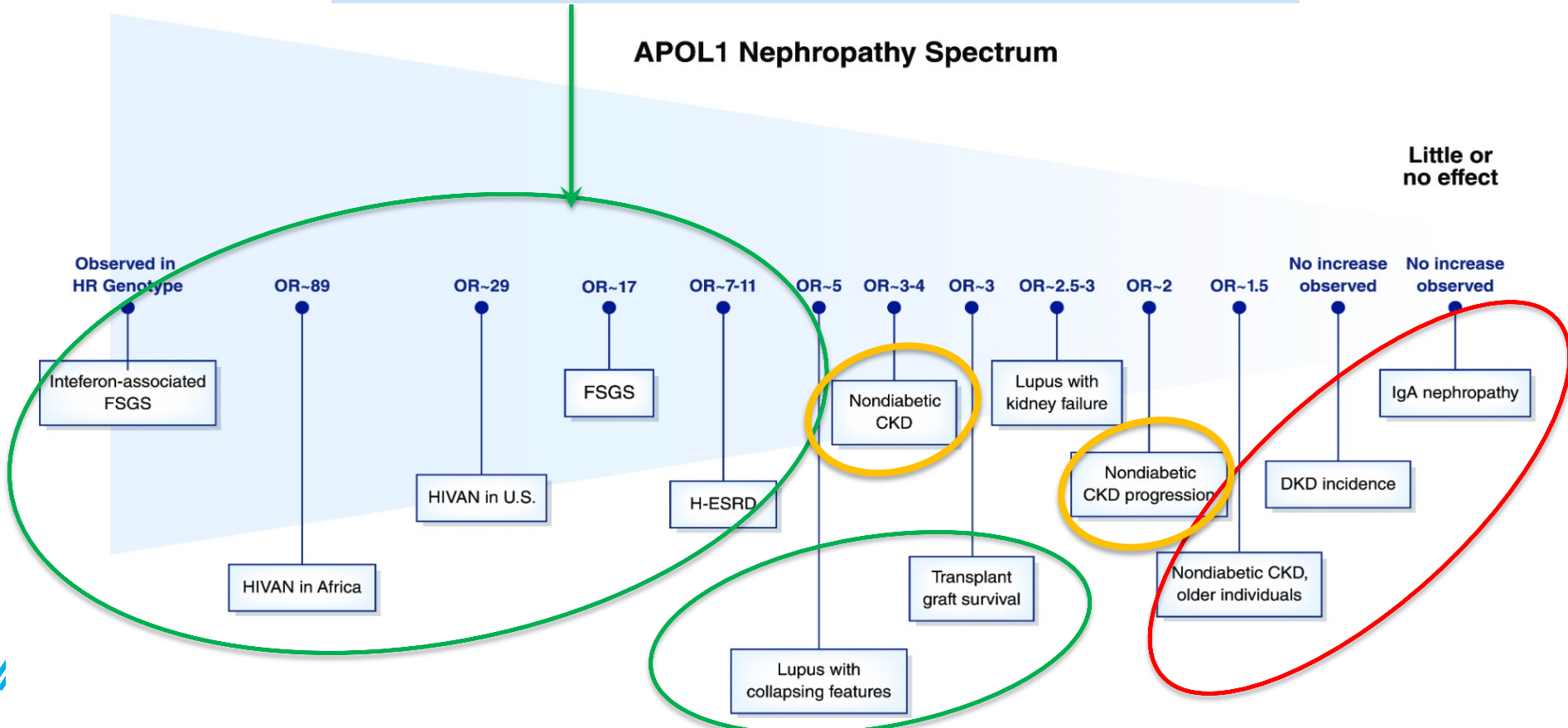
Kidney Transplant

Kopp et al.  
CJSAN. 2020  
Friedman et al  
CJSAN 2021

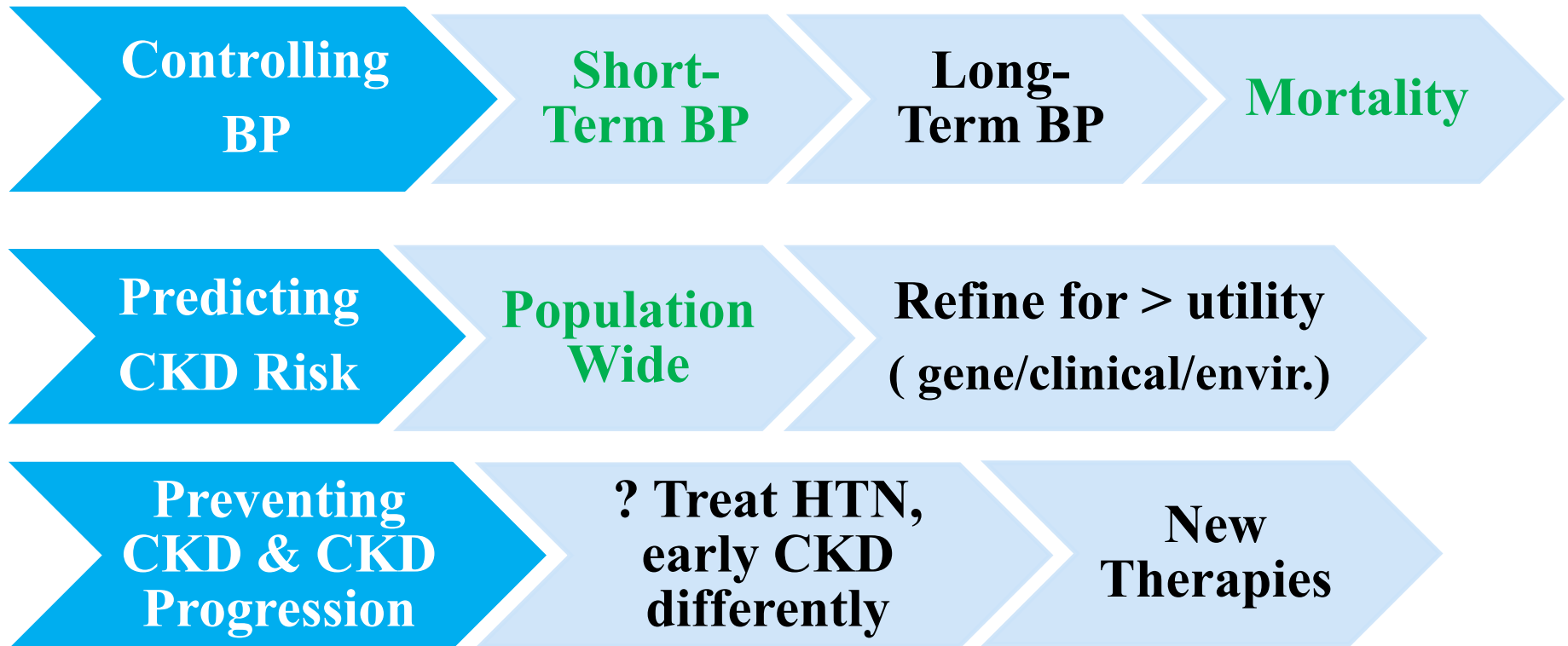
Large effect

### APOL1 Nephropathy Spectrum

Little or no effect



# Where more screening utility research is needed: HTN & Early CKD



# Short-term BP control w/risk disclosure

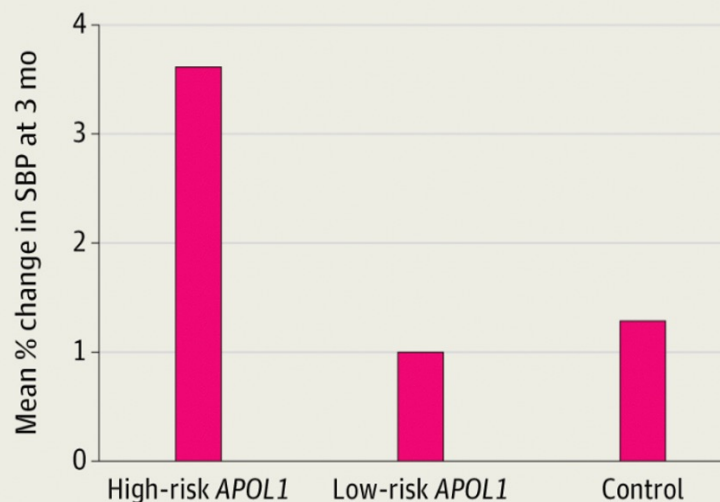
## Primary Care Pragmatic Trial Randomized re disclosure

- ▶ Full community engagement
- ▶ >2000 pts, 15 sites NYC
- ▶ GCs trained staff; staff returned results
- ▶ Providers got BPAs in EHRs

## BP Decreased in APOL1+ & more CKD screening

### FINDINGS

Patients with high-risk *APOL1* genotypes had significantly higher change in SBP compared with low-risk *APOL1* and control groups and higher urine screening compared with controls but not with patients with low-risk *APOL1* genotypes



#### Percentage decrease in SBP from baseline at 3 mo:

High-risk *APOL1* group vs low-risk *APOL1* group: 3.6% vs 1.0% ( $P = .003$ )

High-risk *APOL1* group vs control group: 3.6% vs 1.3% ( $P = .04$ )

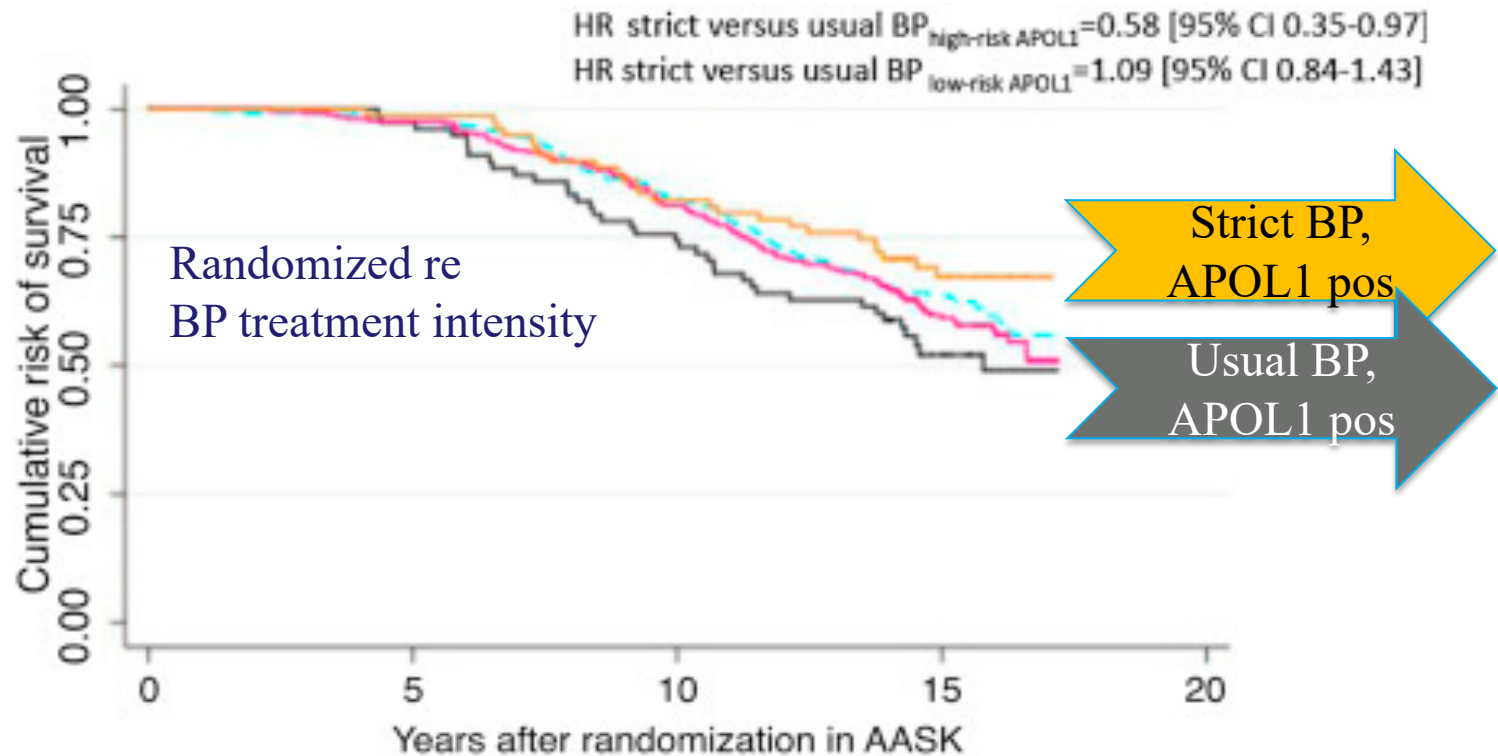
#### Increase in urine kidney disease testing:

High-risk *APOL1* group vs low-risk *APOL1* group: 12.0% vs 6.0% ( $P = .01$ )

High-risk *APOL1* group vs control group: 12.0% vs 7.0% ( $P = .01$ )

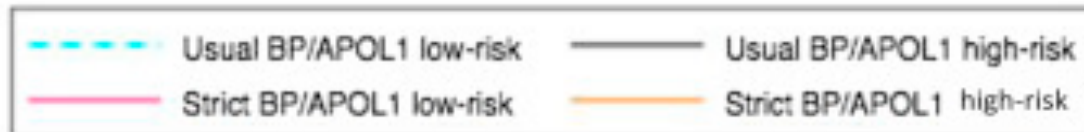
Nadkarni et al JAMA ON 2022

# Intensive BP control in people with *APOL1* high- risk genotypes- survival benefit



## Number at risk

Usual BP/APOL1 low-risk	264	261	235	192	59
Usual BP/APOL1 high-risk	78	78	65	50	12
Strict BP/APOL1 low-risk	261	256	235	186	57
Strict BP/APOL1 high-risk	79	79	71	62	20



# HOW BEST TO SCREEN

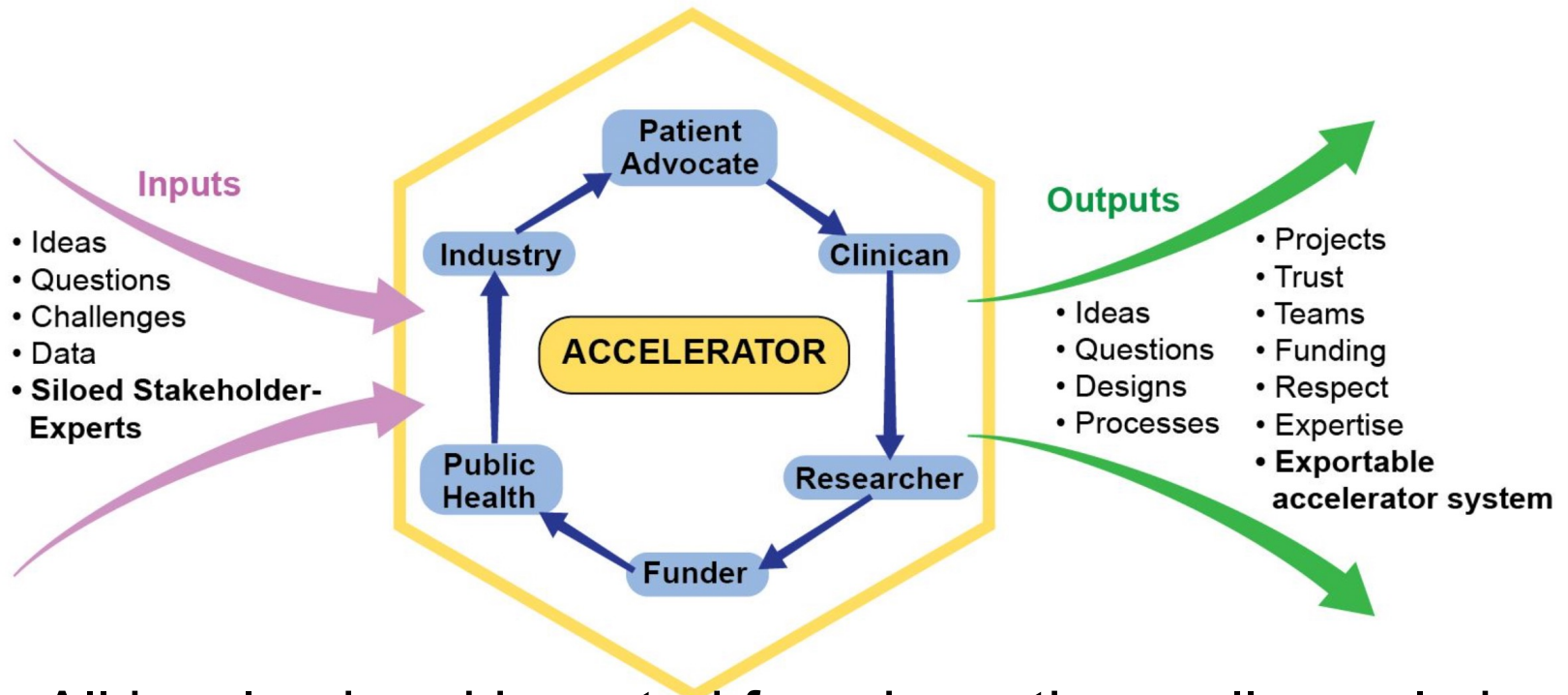


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# TRANSLATION IS A TEAM VENTURE



- All involved and invested from inception, call people in
- Answer for each group
  - *Why is this important for me, what do I do with results?*
- Pilot every step & build from everyone's angles
- Asset- based, take the long view





# Steps: Possible Research Questions

## Test

- Select Appropriate Patients
- Consent- appropriate or genetic exceptionalism?

## Result

- To Clinicians (refining Best Practice Alerts,...)
- To Patients- like other labs? Role of GCs\*

## Action

- Further Testing, Treatments (current, emerging)
- Cascade Screening
- Monitor for benefit and harm

\* Role of GC's: Front-line or vs. guide/specialist

- 100% offered free GC → 0% met with GC in NYC, prelim <1% nationally
- 96% would recommend
- >97% satisfied with process, content, messenger



# New Therapies

Does Inaxaplin Reduce Proteinuria in Persons with Two *APOL1* Variants?



## With an eye toward equitable development

Perspective

When Actions Speak Louder Than Words — Racism and Sickle Cell Disease

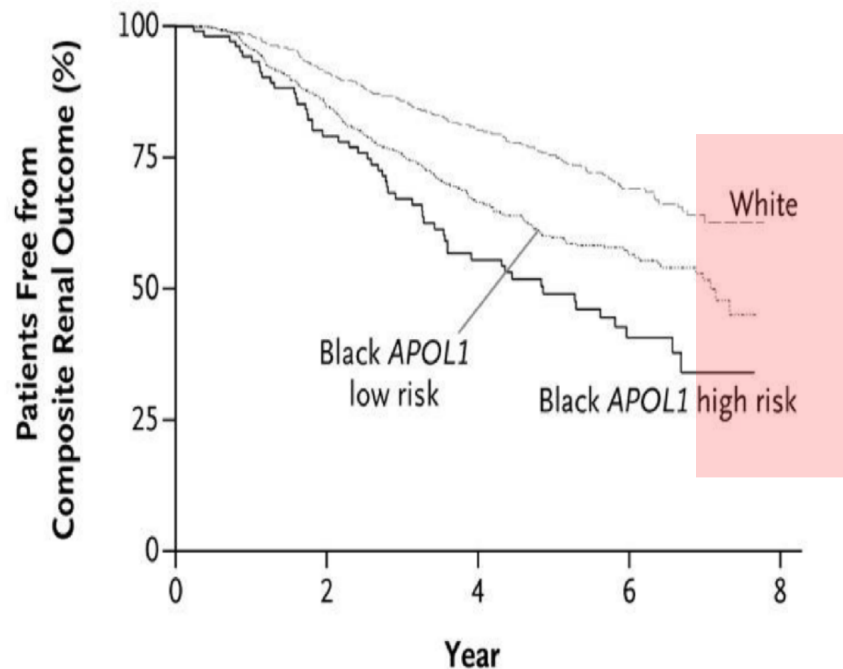
Alexandra Power-Hays, M.D., and Patrick T. McGann, M.D.

Cystic Fibrosis affects 1/3 fewer Americans (primarily White) than Sickle Cell but receives 7-11 x the research funding/patient

# BUMPS AND CAUTIONS



# It's not all all genetic



APOL1 risk alleles **fail** to account for all racial disparities in rates of ESKD and CKD progression

Parsa et al NEJOM 2013

Racial disparities in CKD outcomes are not all explained by *APOL1*

Interventions to improve outcomes in Black people with and without the *APOL1* high-risk genotype are desperately needed.

Grams et al JASN 2016



# Perils of Paternalism: They won't act. They will be harmed. They don't believe us

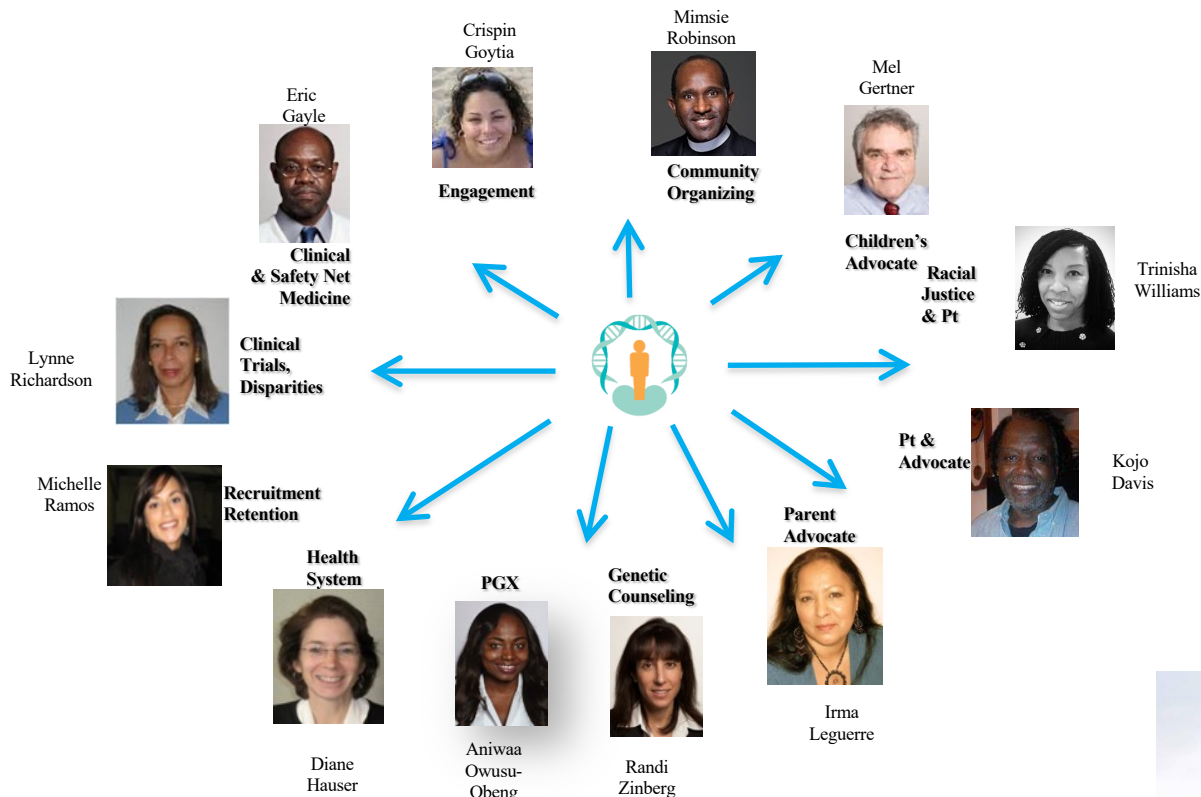
	What Patients Said (all statistically significant)		What their Clinicians said
	APOL1 low risk n=1471	APOL1 high risk n=219	n=486 89% response
Made lifestyle change*	47%	71%	34%
Took BP meds more often*	58%	87%	
Concern about insurance	7%	8%	53%
Results lead to worry/upset	1%	8%	59%
Regret getting test	1%	2%	n/a

\*Even those negative changed behavior- most did not know BP harms kidneys before

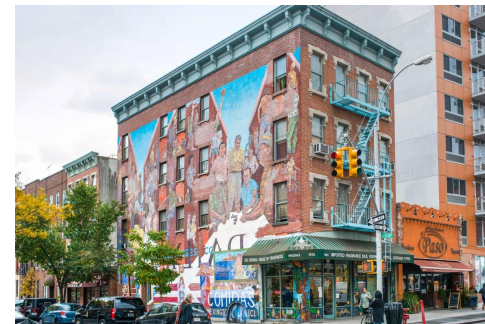
## Listen to & learn from patients (& PCPs)

## Who (mis)trusts who?

# Thanks to: Community, Clinical, Academic Partners NHGRI and thank you!



## On Behalf of Our Genomics Board



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