# Controversies Conference on APOL1 Kidney Disease

# Moving towards routine *APOL1* genetic testing: ethical implications in kidney transplantation

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- Relationships with commercial interests:
  - Grants/Research Support: NIH, CIHR, Ministry of Education
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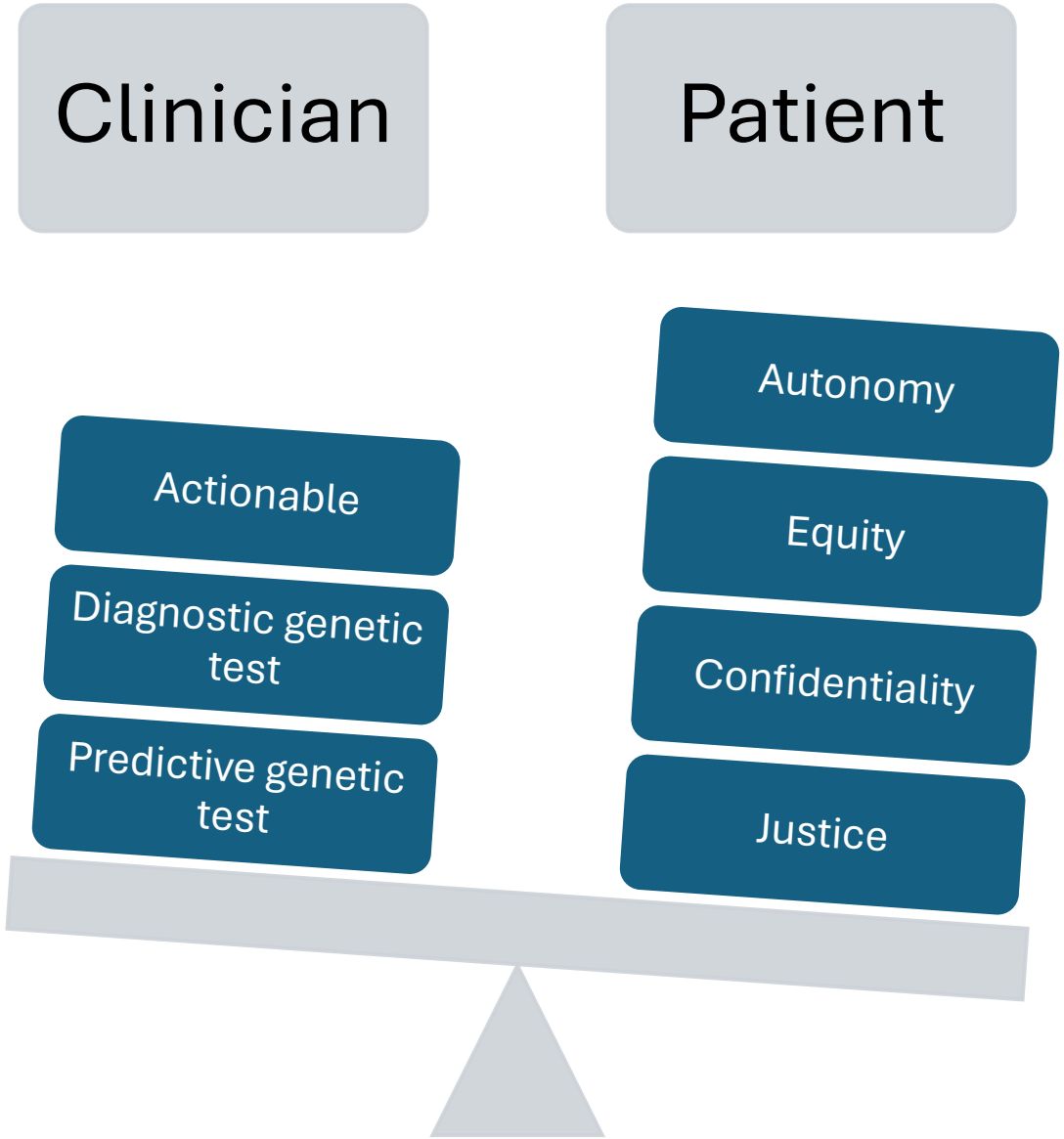
  - Consulting Fees: Vertex

# Case

- Medical student wanted to donate to her mother who has been on dialysis for 2 years
  - She finds out she is a carrier for high-risk *APOL1* haplotype
  - She is prevented from donating to her mother
  - But no one can tell her own long-term risk and what she needs to do to prevent chronic kidney disease
  - And if she donates, no one can tell her long-term risk of progression to CKD with a single kidney
  - She now feels like a “ticking time bomb”
  - No one has considered that she may lose her mother given the high mortality rate on dialysis and long waits for deceased donor transplant

# Case

- Medical student wanted to donate to her mother who has been on dialysis for 2 years
  - She finds out she is a carrier for high-risk *APOL1* haplotype
  - She is prevented from donating to her mother clinical utility when research is pending
  - But no one can tell her own long-term risk and what she needs to do to prevent chronic kidney disease Understanding risk when prevalence and penetrance varies and other gene or environmental factors are important
  - And if she donates, no one can tell her long-term risk of progression to CKD with a single kidney medical uncertainty
  - She now feels like a “ticking time bomb” psychological impact of testing
  - No one has considered that she may lose her mother given the high mortality rate on dialysis and long waits for deceased donor transplant what is actionable?
  - She questioned whether she should have had testing




# Considerations for genetic testing

# *APOL1* testing in US transplantation

## 2024

- Delphi Consensus of 27 patients, donors, surgeons, nephrologists and genetic counsellors (majority self-identified as Black/African American)
- Development of a chatbot to provide results

## 2023

- Focus groups of 10 transplant nephrologists

## 2022

- Survey of 331 potential living donors, recipients, waitlisted persons and also non transplant patients in 3 transplant programs

## 2020

- 585 participants self identified as African American from the general population using simulated questions on risk

## 2019

- 17 African American donors from a single center through 4 focus groups to assess impact on treatment, sociocultural factors and health benefits

## 2018

- 23 African American donors from a single center focus groups/survey

## 2017

- Transplant Expert Panel

# Consistent findings among all studies

- Autonomy in testing is critical
- Return of results and decision making based on those results are shared with patient and clinician
- Education is vital for patients, families, and all clinicians
- Engagement with patients, families and communities is vital for any study
  - Ensures culturally appropriate education and type of methods
  - Addresses concerns of study design, approach and returning of results
- Differences by region are rarely addressed
- How education, perceptions and beliefs may alter shared decision making  globally is unknown

# Evaluating ApoL1 Genetic Testing Policy Options for Transplant Centers

## A Delphi Consensus Panel Project with Stakeholders

*Tristan McIntosh,[1] Heidi Walsh,[1] Kari Baldwin,[1] Ana Iltis,[2] Sumit Mohan, Melody Goodman,[5] and James M. DuBois[1]*

- Community Advisory Council
- https://www.apollocommunity.net/

Clin J Am Soc Nephrol. 2024 Apr 1;19(4):415-417. doi: 10.2215/CJN.000

# The Road to APOL1 Genetic Testing in Transplantation

Rulan S Parekh [1]

# Evaluating ApoL1 Genetic Testing Policy Options for Transplant Centers: A Delphi Consensus Panel

CJASN
Clinical Journal of the American Society of Nephrology

Delphi consensus panel focused on ApoL1 clinical policy questions

27 panelists

2 rounds of educational webinars

3 rounds of surveys

**Panelists**

Kidney transplant donors/recipients

Deceased donor family members

Nephrologists

Genetic counselors

Transplant surgeons

70% of panelists identified as Black or African American

Panel reached consensus on one or more acceptable policy options

**Key elements of consensus**

- Ask potential donors about African ancestry rather than race
- Make testing decisions only after discussion with donors
- Encourage but do not require disclosure of results to blood relatives and organ recipients
- Use test results to inform shared decision making—never unilateral decisions by transplant programs

**Conclusions:** The panel supported policy options involving discussion and shared decision making among patients, donors, and family stakeholders. There was opposition to unilateral decision making by transplant programs and prohibiting donation altogether.

Tristan McIntosh, Heidi Walsh, Kari Baldwin, et al. ***Evaluating ApoL1 Genetic Testing Policy Options for Transplant Centers: A Delphi Consensus Panel Project with Stakeholders***. CJASN doi: 10.2215/CJN.0000000000000397. **Visual Abstract by Nayan Arora, MD**

Clin J Am Soc Nephrol. 2024 Apr 1;19(4):415-417. doi: 10.2215/CJN.0000000000000445.

# The Road to APOL1 Genetic Testing in Transplantation

Rulan S Parekh [1]

**Should genetic testing to only those that self-report African ancestry**

- Africa is not monolithic and variability in prevalence of *APOL1* differs between countries and within ethnic groups
- Admixture in the Carribean and Brazil and Hispanic persons suggest that screening is important in this group as well
- Admixture is increasing globally

**Did not address the psychological stress as a result of uncertainty of risk**

**Raises the issue of ongoing education given evolving epidemiology of *APOL1***

# 2024

> BMJ Open. 2023 May 15;13(5):e067657. doi: 10.1136/bmjopen-2022-067657.

## Implementation of a culturally competent *APOL1* genetic testing programme into living donor evaluation: A two-site, non-randomised, pre-post trial design

Justin D Smith [1 2], Akansha Agrawal [3], Catherine Wicklund [4], Debra Duquette [3], John Friedewald [3], Luke V Rasmussen [5], Jessica Gacki-Smith [6], S Darius Tandon [7], Lutfiyya N Muhammad [8], Clyde W Yancy [9], Siyuan Dong [10], Matthew Cooper [11], Alexander Gilbert [12], Aneesha Shetty [13], Elisa J Gordon [14]

Affiliations + expand

PMID: 37188469 PMCID: PMC10186444 DOI: 10.1136/bmjopen-2022-067657

> J Community Genet. 2024 Apr;15(2):205-216. doi: 10.1007/s12687-024-00698-8. Epub 2024 Feb 13.

## Development of a culturally targeted chatbot to inform living kidney donor candidates of African ancestry about APOL1 genetic testing: a mixed methods study

Elisa J Gordon [1], Jessica Gacki-Smith [2], Matthew J Gooden [2], Preeya Waite [2], Rochell Yacat [3], Zenab R Abubakari [3], Debra Duquette [4], Akansha Agrawal [5], John Friedewald [5], Sarah K Savage [6], Matthew Cooper [7 8 9 10], Alexander Gilbert [3], Lutfiyya N Muhammad [11], Catherine Wicklund [12]

Affiliations + expand

PMID: 38349598 PMCID: PMC11031529 DOI: 10.1007/s12687-024-00698-8

- **Community Advisory Board**
- **Scientific Advisory Board**

# 2019

> Prog Transplant. 2019 Mar;29(1):26-35. doi: 10.1177/1526924818817048. Epub 2018 Dec 13.

## A National Survey of Transplant Surgeons and Nephrologists on Implementing *Apolipoprotein L1* (*APOL1*) Genetic Testing Into Clinical Practice

Elisa J Gordon [1], Catherine Wicklund [2], Jungwha Lee [3], Richard R Sharp [4], John Friedewald [5]

Affiliations + expand

PMID: 30541404 PMCID: PMC9527710 DOI: 10.1177/1526924818817048

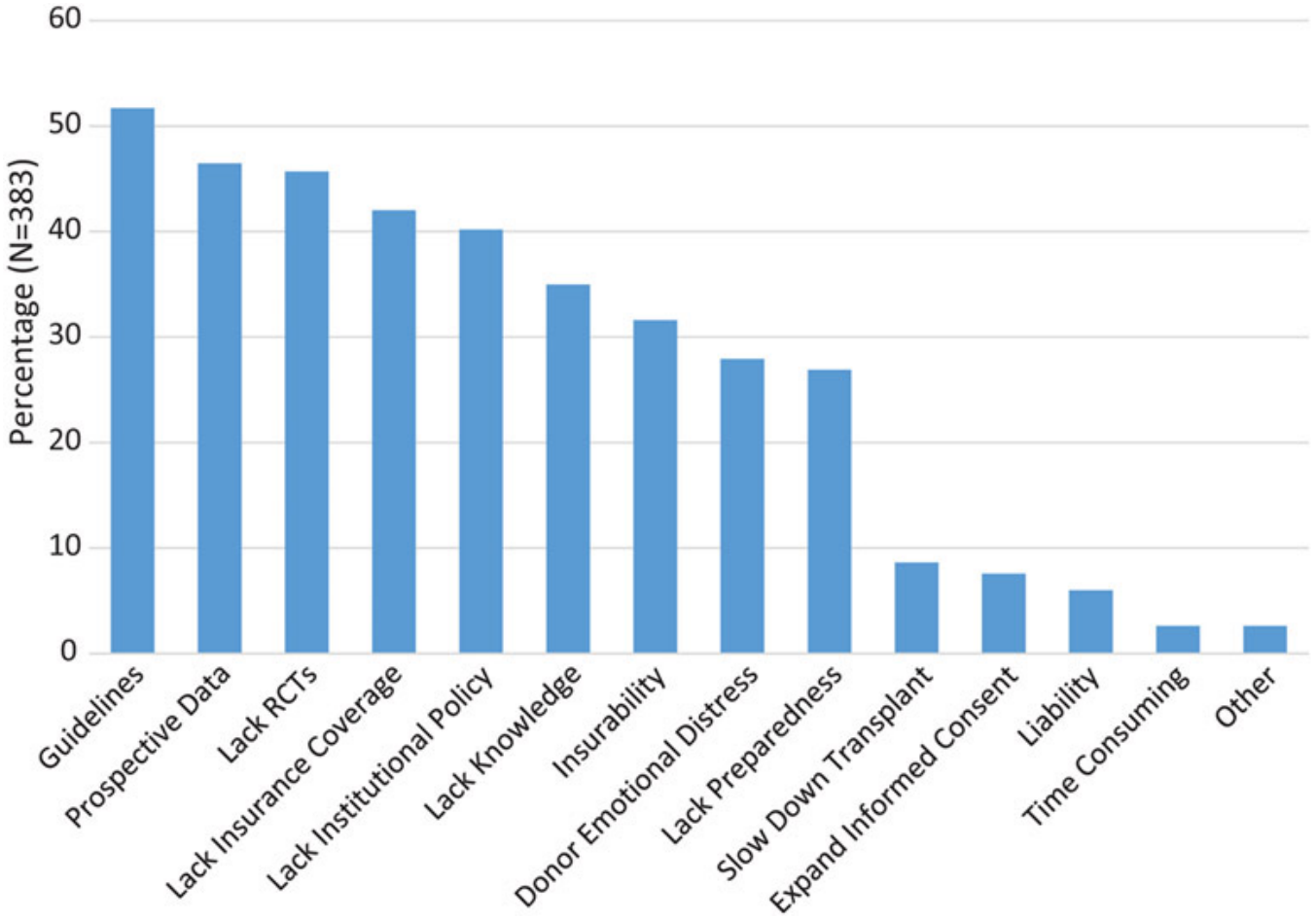
> Prog Transplant. 2019 Sep;29(3):239-247. doi: 10.1177/1526924819854485. Epub 2019 May 30.

## A Focus Group Study on African American Living Donors' Treatment Preferences, Sociocultural Factors, and Health Beliefs About Apolipoprotein L1 Genetic Testing

Elisa J Gordon [1], Daniela Amórtegui [2], Isaac Blancas [2], Catherine Wicklund [3], John Friedewald [4], Richard R Sharp [5]

Affiliations + expand

PMID: 31146624 DOI: 10.1177/1526924819854485



# CKD

> Kidney Med. 2022 Sep 29;4(12):100549. doi: 10.1016/j.xkme.2022.100549. eCollection 2022 Dec.

## *APOL1* Genetic Testing in Patients With Recent African Ancestry and Hypertension: A Pilot Study of Attitudes and Perceptions

Krista L Lentine [1], Anthony N Muiru [2], Kathryn K Lindsay [1], Yasar Caliskan [1], John C Edwards [1], Aliza Anwar Memon [1], Amy K Mosman [1], Kana N Miyata [1], Than-Mai Vo [1], Barry I Freedman [3], Amber Carriker [4], Chi-Yuan Hsu [2], Marie D Philipneri [1]

> Glob Health Epidemiol Genom. 2017 Sep 4:2:e13. doi: 10.1017/gheg.2017.9. eCollection 2017.

## Developing the science and methods of community engagement for genomic research and biobanking in Africa

P Tindana [1], M Campbell [2], P Marshall [3], K Littler [4], R Vincent [5], J Seeley [6], J de Vries [7], D Kamuya [8]; H3Africa Community Engagement Working Group


Randomized Controlled Trial > Contemp Clin Trials. 2016 Mar:47:101-8. doi: 10.1016/j.cct.2015.12.020. Epub 2015 Dec 30.

## Determining the effects and challenges of incorporating genetic testing into primary care management of hypertensive patients with African ancestry

C R Horowitz [1], N S Abul-Husn [2], S Ellis [3], M A Ramos [4], R Negron [5], M Suprun [6], R E Zinberg [7], T Sabin [8], D Hauser [9], N Calman [10], E Bagiella [11], E P Bottinger [12]

Randomized Controlled Trial > JAMA Netw Open. 2022 Mar 1;5(3):e221048. doi: 10.1001/jamanetworkopen.2022.1048.

## Effects of Testing and Disclosing Ancestry–Specific Genetic Risk for Kidney Failure on Patients and Health Care Professionals: A Randomized Clinical Trial

Girish N Nadkarni [1 2], Kezhen Fei [3 4], Michelle A Ramos [3 4], Diane Hauser [5], Emilia Bagiella [3], Stephen B Ellis [2], Saskia Sanderson [2], Stuart A Scott [2 6 7], Tatiana Sabin [3 4], Ebony Madden [8], Richard Cooper [9], Martin Pollak [10], Neil Calman [4 5], Erwin P Bottinger [1 2 11], Carol R Horowitz [2 3 4]

JAMA Network Open

# RCT: Effects of Testing and Disclosing Ancestry-Specific Genetic Risk for Kidney Failure on Patients and Health Care Professionals

## POPULATION

**690 Men, 1360 Women**

Adults with African ancestry with hypertension and without existing chronic kidney disease

**Mean age, 53 y (range, 18-70 y)**

## SETTINGS / LOCATIONS

**15 Academic, community, and safety-net practices in 2 US health care systems**

## INTERVENTION

**2050** Randomized

**1795 Intervention group**
Patients received *APOL1* genetic testing results from trained staff who used clinical decision support

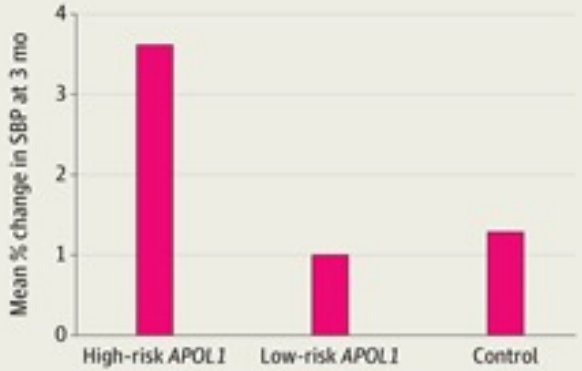
**255 Control group**
Control patients received *APOL1* genetic testing results after a 12-mo follow-up visit

## PRIMARY OUTCOME

Coprimary outcomes were change in systolic blood pressure (SBP) at 3-mo and 12-mo urine kidney disease screening between Patients with high-risk *APOL1* genotypes and patients with low-risk *APOL1* genotypes

## 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 GN, Fei K, Ramos MA, et al. Effects of testing and disclosing ancestry-specific genetic risk for kidney failure on patients and health care professionals: a randomized clinical trial. *JAMA Netw Open*. 2022;5(3):e221048. doi:10.1001/jamanetworkopen.2022.1048

# Need more research……

- Consider clinical context
  - CKD, FSGS or transplant donor/ recipient
  - Actionable vs not actionable
  - Diagnostic vs predictive
  - Overall disease prevalence which may alter test characteristics
  - Consider who gets tested
  - Economic impacts of testing
  - Gaps in knowledge lead to more uncertainty
- Address regional differences in ethical, social and legal implications

# Multiple frameworks to approach data to move genetic testing into clinical use

# Frameworks to move genetic tesing into clinical care

**TABLE S-1** Comparison of Frameworks

| Method | Purpose | Approach | Strengths | Weaknesses |
|---|---|---|---|---|
| USPSTF | Preventive interventions in primary care | Formal analytic framework; evidence assessment related to key questions to establish a "chain of evidence" | Formal grading system incorporating evaluation of benefits and harms and rating of evidence | Focus on preventive services results in a focus on clinical-utility outcomes that are not relevant to all clinical applications |
| Fryback–Thornbury | General medical-test assessment | Hierarchic representation of levels of efficacy for medical tests | Allows an evaluator to determine what evidence types need to be assessed for a given test purpose or desired outcome | Lacks a formal evidence-based assessment procedure |
| ACCE | Analytic process for evaluating evidence on genetic tests | Standard set of 44 questions that are organized according to different evidence types (analytic validity, clinical validity, clinical utility, ELSI) | Provides a highly granular approach to assessing different evidence types | Does not provide details on evaluating the strength of evidence; developed for single-gene tests and may be difficult to extend to multigene panels or genome-scale sequencing tests |

| Method | Purpose | Approach | Strengths | Weaknesses |
|---|---|---|---|---|
| EGAPP | Systematic approach to evidence-based assessment of genetic tests | Hybrid approach using analytic framework similar to USPSTF and evaluation of evidence types articulated by ACCE | Flexibility to evaluate different "topics" in genetic testing, including a wide array of potential outcomes of interest, and integration of formal evidence-based reviews | Focus on single-gene tests may be difficult to extend to broader genomic technologies |
| GETT | Structure for systematic identification and organization of published evidence on genetic testing | List of 72 defined items grouped into categories | Helps stakeholders to determine whether knowledge base is sufficient for genetic-technology assessment | Does not provide details on evaluating the strength of evidence; developed for single-gene tests and may be difficult to extend to multigene panels or genome-scale sequencing tests |
| McMaster University | Evaluation model to guide public coverage for new predictive genetic tests in Ontario, Canada | Combines technology assessment with coverage decision making from payer's perspective | Defines criteria for determining coverage, anticipates the need for payers to identify evidentiary thresholds, and considers conditional coverage scenarios | Developed for the Canadian health system; lacks a formal evidence-based assessment procedure |
| Frueh and Quinn | Framework to facilitate communication between test developers and health-technology evaluators | Relevant to both regulatory and payer decisions | Articulates several axes of testing that provide more nuanced or diverse evaluation outcomes than traditional clinical validity and clinical utility | Lacks a formal evidence-based assessment procedure; examples of applications of six questions directed mainly toward companion diagnostics |

NOTE: ACCE = analytic validity, clinical validity, clinical utility, and associated ethical legal and social implications; EGAPP = Evaluation of Genomic Application in Practice and Prevention; ELSI = ethical, legal, and social implications; GETT = Genetic testing Evidence Tracking Tool; USPSTF = US Preventive Services Task Force.

# Genetic/genomic testing: defining parameters for ethical, legal and social implications (ELSI)

1. Universal Declaration on the Human Genome and Human Rights, UNESCO 1997
2. Oviedo Convention, Council of Europe 1997
3. Review of Ethical Issues in Medical Genetics, WHO 2003
4. International Declaration on Human Genetic Data, UNESCO 2003
5. Declaration of Reykjavik, WMA 2019
6. Medical genetic services in Developing Countries. The Ethical, Legal, and Social Implications of Genetic Testing and Screening, WHO 2006
7. Guidelines for Quality Assurance in Molecular Genetic Testing, OECD 2007
8. Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes, Council of Europe 2008
9. Report of the International Bioethics Committee on Updating Its Reflection on the Human Genome and Human Rights, UNESCO 2015

| | Criteria | Sub-criteria |
|---|---|---|
| Ethical | Patient rights | Right to health |
| | | Free and informed consent |
| | | Knowing or not knowing results and implications |
| | | Respect for privacy and confidentiality |
| | | Respect for human dignity |
| | Non-discrimination | Avoid genetic reductionism |
| | | Genetic exceptionalism |
| | | Avoid stigmatization |
| Legal | Protection of the Information | Actions to ensure the protection of biological samples, and all physical and electronic information |
| | Testing | Circumstances of application |
| | | Advantages, disadvantages and limitations |
| | Health regulation | Qualified health personnel |
| | | Surveillance |
| | | Medical-patient-company responsibility |
| | | Countries responsibility |
| | | Analytical validity |
| | | Validity and clinical utility |
| | | Laboratory accreditation |
| | Commercialization | Direct-to-consumer testing |
| | | Medical tourism |
| | | Advertising |
| | | Cross-border business |
| Social | Counseling | Pre-clinical and post-results |
| | | In clinic |
| | Training | Education and dissemination |
| | Reporting of Results | Concept of health and disease |
| | | Communication of the risks |
| | | Unexpected findings |
| | Accessibility | Access to services under the principle of justice |

Ascencio-Carbajal et al. BMC Medical Ethics (2021) 22:156

# Ethical questions to consider for APOL1 genetic testing among those with CKD, FSGS or transplant donor/recipient

| | Criteria | Sub-criteria |
|---|---|---|
| Ethical | Patient rights | Right to health |
| | | Free and informed consent |
| | | Knowing or not knowing results and implications |
| | | Respect for privacy and confidentiality |
| | | Respect for human dignity |
| | Non-discrimination | Avoid genetic reductionism |
| | | Genetic exceptionalism |
| | | Avoid stigmatization |

# Legal questions to consider for APOL1 genetic testing among those with CKD, FSGS or transplant donor/recipient

| | Criteria | Sub-criteria |
|---|---|---|
| Legal | Protection of the Information | Actions to ensure the protection of biological samples, and all physical and electronic information |
| | Testing | Circumstances of application |
| | | Advantages, disadvantages and limitations |
| | Health regulation | Qualified health personnel |
| | | Surveillance |
| | | Medical-patient-company responsibility |
| | | Countries responsibility |
| | | Analytical validity |
| | | Validity and clinical utility |
| | | Laboratory accreditation |
| | Commercialization | Direct-to-consumer testing |
| | | Medical tourism |
| | | Advertising |
| | | Cross-border business |

# 23andMe Offers a New Report on APOL1-Related Chronic Kidney Disease

August 5, 2020 By 23andMe under Health and Traits

Today, 23andMe added a new Genetic Health Risk report on APOL1-related chronic kidney disease that has particular relevance for customers with African ancestry.


$90 OFF

## Health + Ancestry Service

Get personalized genetic insights and tools that can help make it easier for you to take action on your health.

- 150+ personalized reports
- Includes Ancestry + Traits Service

Add to cart ~~$249~~ $159

Limit 3 kits. Offer ends Oct 31.



Let's talk about

# APOL1-Related Chronic Kidney Disease

## Relevant ethnicities

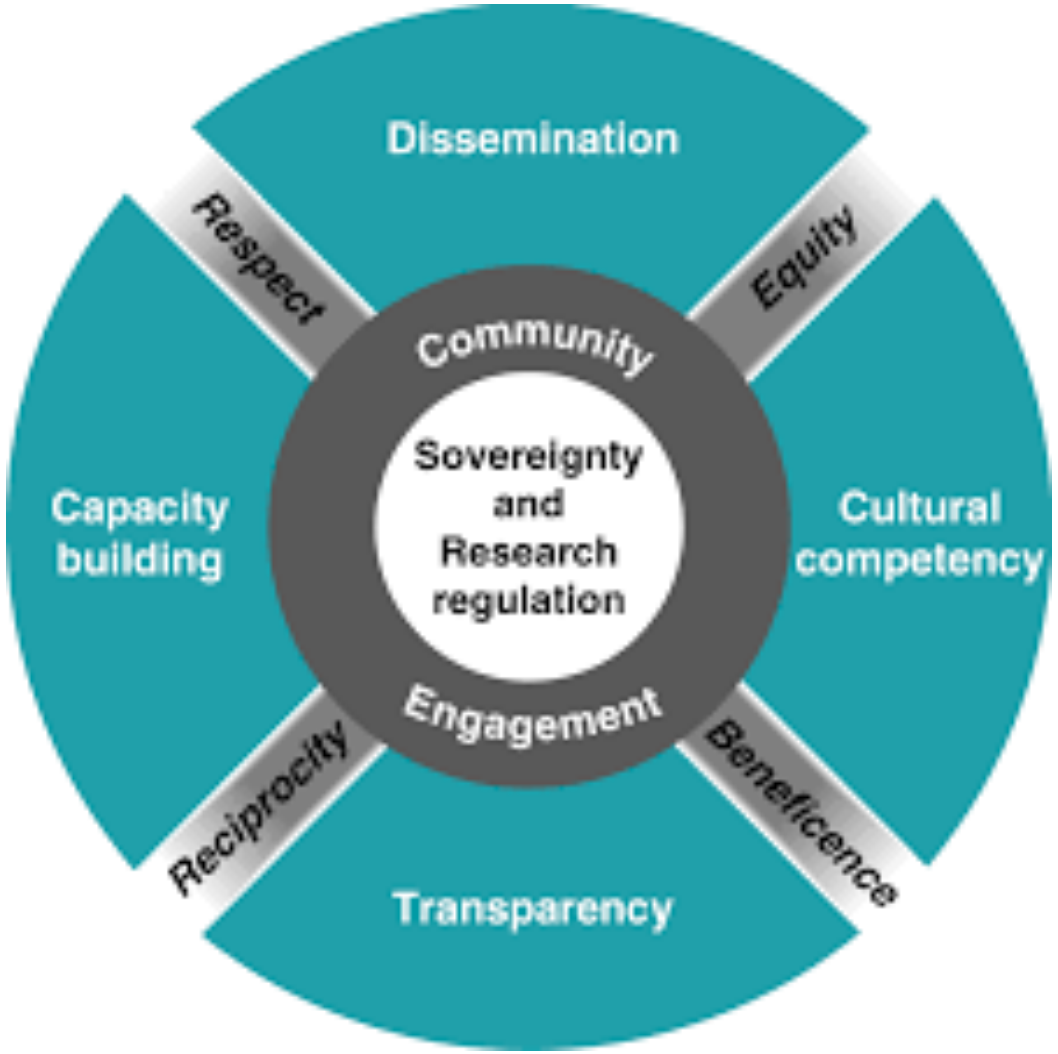
- The variants included in this test are most common and best studied in people of **African** descent.
- These variants are also found in people with African ancestry, including people of **Hispanic** or **Latino** descent.

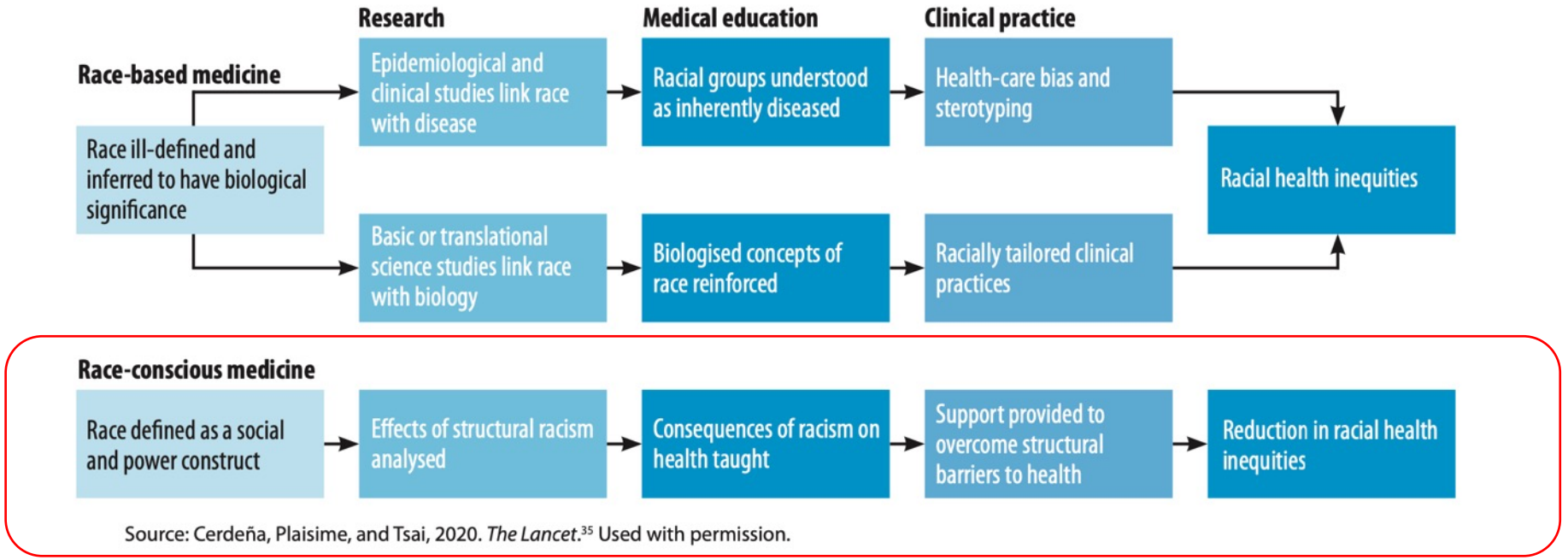
# Social questions to consider for APOL1 genetic testing among those with CKD, FSGS or transplant donor/recipient

| | Criteria | Sub-criteria |
|---|---|---|
| Social | Counseling | Pre-clinical and post-results |
| | | In clinic |
| | Training | Education and dissemination |
| | Reporting of Results | Concept of health and disease |
| | | Communication of the risks |
| | | Unexpected findings |
| | Accessibility | Access to services under the principle of justice |

# Need more research

# Indigenous framework for genetic testing






Source: Cerdeña, Plaisime, and Tsai, 2020. *The Lancet*.[35] Used with permission.

- American Medical Association and Association of American Medical Colleges
- Advancing Health Equity: Guide on Language, Narrative and Concepts..
- ama-assn.org/equity-guide

# Advancing health equity
# Language, narrative and concepts

# Informed use of race, ethnicity and ancestry

| | | Equity focused alternative | Commonly used | Comment |
|---|---|---|---|---|
| Race | Self-ascribed | Black | black | System of categorizing people that arises to differentiate groups of people in hierarchies to advantage some and disadvantage others.<br><br>Associated Press recommends not capitalizing white, recognizing that "white people generally do not share the same history and culture, or the experience of being discriminated against because of skin color." |
| | Self-ascribed | white | Caucasian | |
| Ethnicity | Self-ascribed | African Americans<br><br>West Africans<br><br>Country | | Social construct and category based on shared geography, language, ancestry, traditions or history. Boundaries of authenticity (that is, who or what "counts" in recognizing members of an ethnic group) are often changeable and dependent on generational, social, political and historical situations. |
| Ancestry | Gene variants/ genome | | | Genetic ancestry is the genetic origin of one's population. Genetic admixture, or genetic exchange among people from different ancestries, is an important characteristic of many populations and may correlate with individuals' risk for certain genetic diseases |

American Medical Association and Association of American Medical Colleges
Advancing Health Equity: Guide on Language, Narrative and Concepts..
ama-assn.org/equity-guide

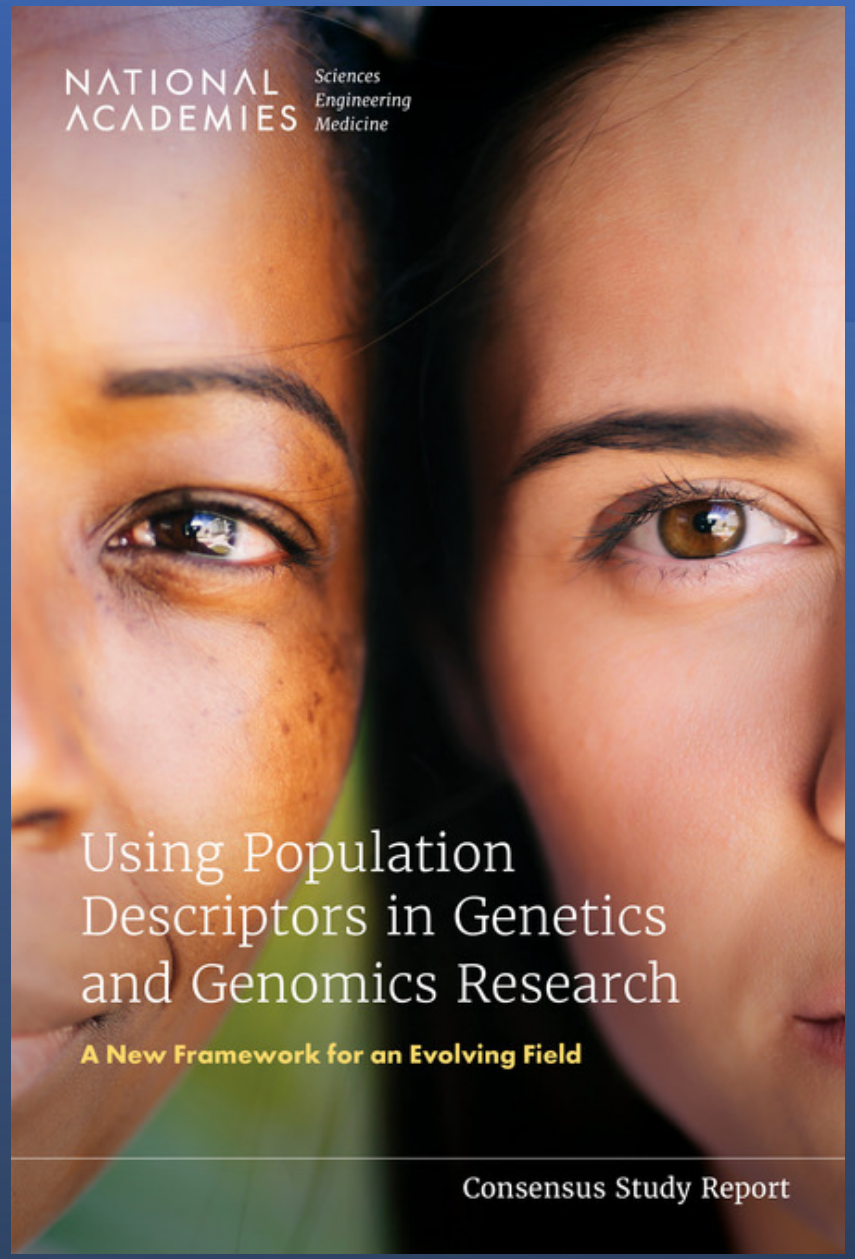
N Engl J Med 2021; 384:474-480 doi:10.1056/NEJMms2029562
*JAMA.* 2021;326(7):621-627. doi:10.1001/jama.2021.13304

# Conflation of genetic ancestry and race

- “Genetic data have led clinical investigators to focus on *APOL1* polymorphisms as a key, rather than a contributory, explanatory variable in racial disparities in kidney disease…..This approach, however, is based upon a misapplication of population genetics and exacerbated by conflation of genetic ancestry and race”

Vanessa Grubbs

APOL1, Black Race, and Kidney Disease: Turning Attention to Structural Racism 2021 Jun;77(6):857-860


NATIONAL ACADEMIES
Sciences
Engineering
Medicine
Using Population Descriptors in Genetics and Genomics Research
A New Framework for an Evolving Field
Consensus Study Report

1

**Population descriptor ≠ group label.**
A population descriptor is a way to classify individuals according to perceived differences among groups; a group label is a specific name used to describe a population.

**Researchers often use population descriptors inconsistently and/or inappropriately.**
Race, for example, should not be used for analysis in most genomics studies. It may be used for some health disparities studies.

2

4

**Genetic ancestry** refers to the lines or paths through an individual's family tree by which they inherited DNA from specific ancestors. It can be useful when studying human evolutionary history.

**Genetic similarity**, a measure of genetic resemblance among individuals, is preferred in many other contexts because it moves away from race and the misconception that humans can be grouped into discrete categories.

Sometimes funders require collection of Office of Management and Budget (OMB) Standards categories to report demographic information of research participants, but **use of OMB categories is not required for scientific analysis.**

3

Editorial

August 17, 2021

# Updated Guidance on the Reporting of Race and Ethnicity in Medical and Science Journals

Annette Flanagin, RN, MA[1]; Tracy Frey, BA[2]; Stacy L. Christiansen, MA[3]; et al

» Author Affiliations | Article Information

*JAMA*. 2021;326(7):621-627. doi:10.1001/jama.2021.13304

Editorial

# *CMAJ*'s new guidance on the reporting of race and ethnicity in research articles

Matthew B. Stanbrook and Bukola Salami

CMAJ February 13, 2023 195 (6) E236-E238; DOI: https://doi.org/10.1503/cmaj.230144

Comment > JAMA. 2024 Apr 16;331(15):1276-1278. doi: 10.1001/jama.2024.3737.

# Guidance on Use of Race, Ethnicity, and Geographic Origin as Proxies for Genetic Ancestry Groups in Biomedical Publications

W Gregory Feero [1 2], Robert D Steiner [3 4], Anne Slavotinek [5 6], Tiago Faial [7], Michael J Bamshad [8 9], Jehannine Austin [10 11], Bruce R Korf [12 13], Annette Flanagin [14], Kirsten Bibbins-Domingo [14]

Affiliations + expand

PMID: 38470200 DOI: 10.1001/jama.2024.3737

# Case

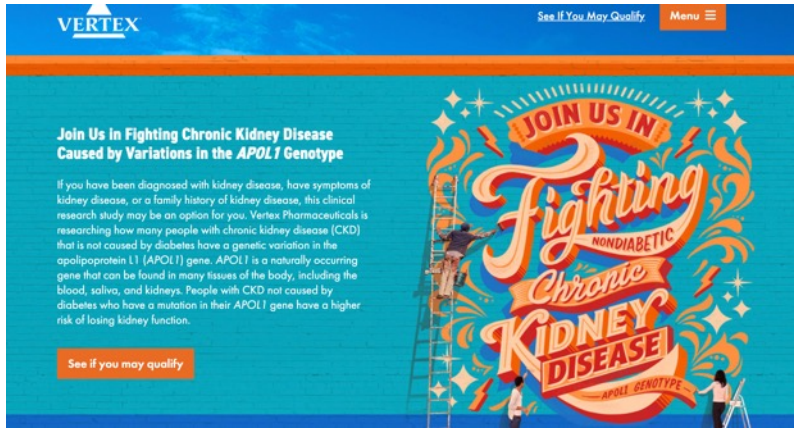
- Medical student wanted to donate to her mother who has been on dialysis for 2 years
  - She finds out she is a carrier for high-risk *APOL1* haplotype
  - She is prevented from donating to her mother clinical utility when research is pending
  - But no one can tell her own long-term risk and what she needs to do to prevent chronic kidney disease understanding risk when prevalence and penetrance varies and other gene or environmental factors are important
  - And if she donates, no one can tell her long-term risk of progression to CKD with a single kidney medical uncertainty
  - She now feels like a “ticking time bomb” psychological impact of testing
  - No one has considered that she may lose her mother given the high mortality rate on dialysis and long waits for deceased donor transplant what is actionable?
  - She questioned whether she should have had testing

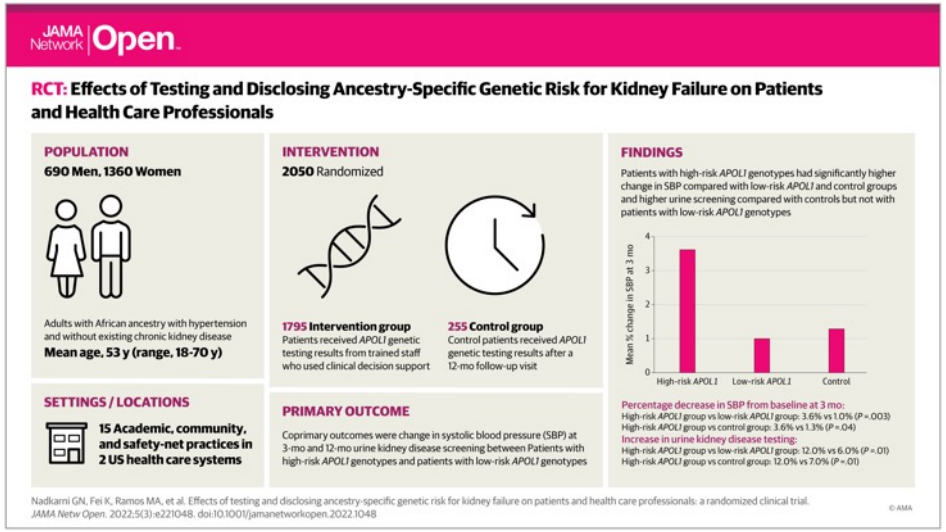
# Need more research

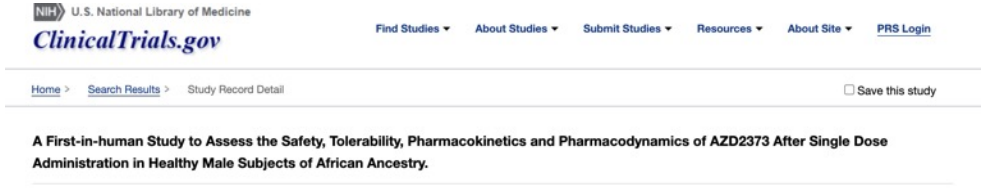
- Recommendations
  - All studies should include patient and community engagement to inform approach from research questions to knowledge translation
  - Address specific ELSI criteria to generate evidence for ongoing testing
    - Actionable vs not actionable
    - Diagnostic vs predictive
    - Specific clinical scenarios ie transplant vs CKD vs FSGS
  - Consider changing populations locally and globally
  - Genetic information is only one contributor to account for underlying disparities in health
  - Reporting using new guidance will improve our reporting

# Thank you

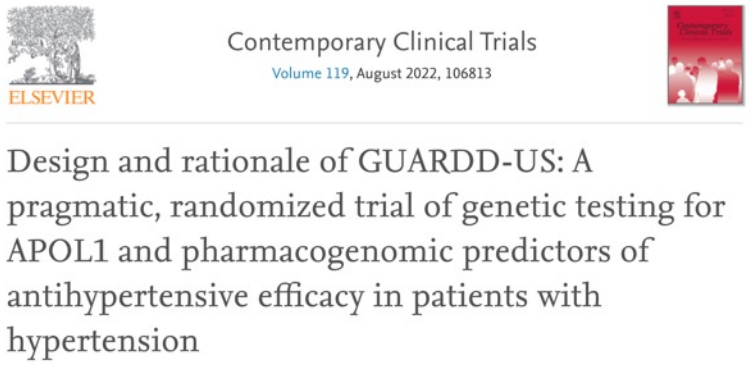
# Trials for *APOL1*



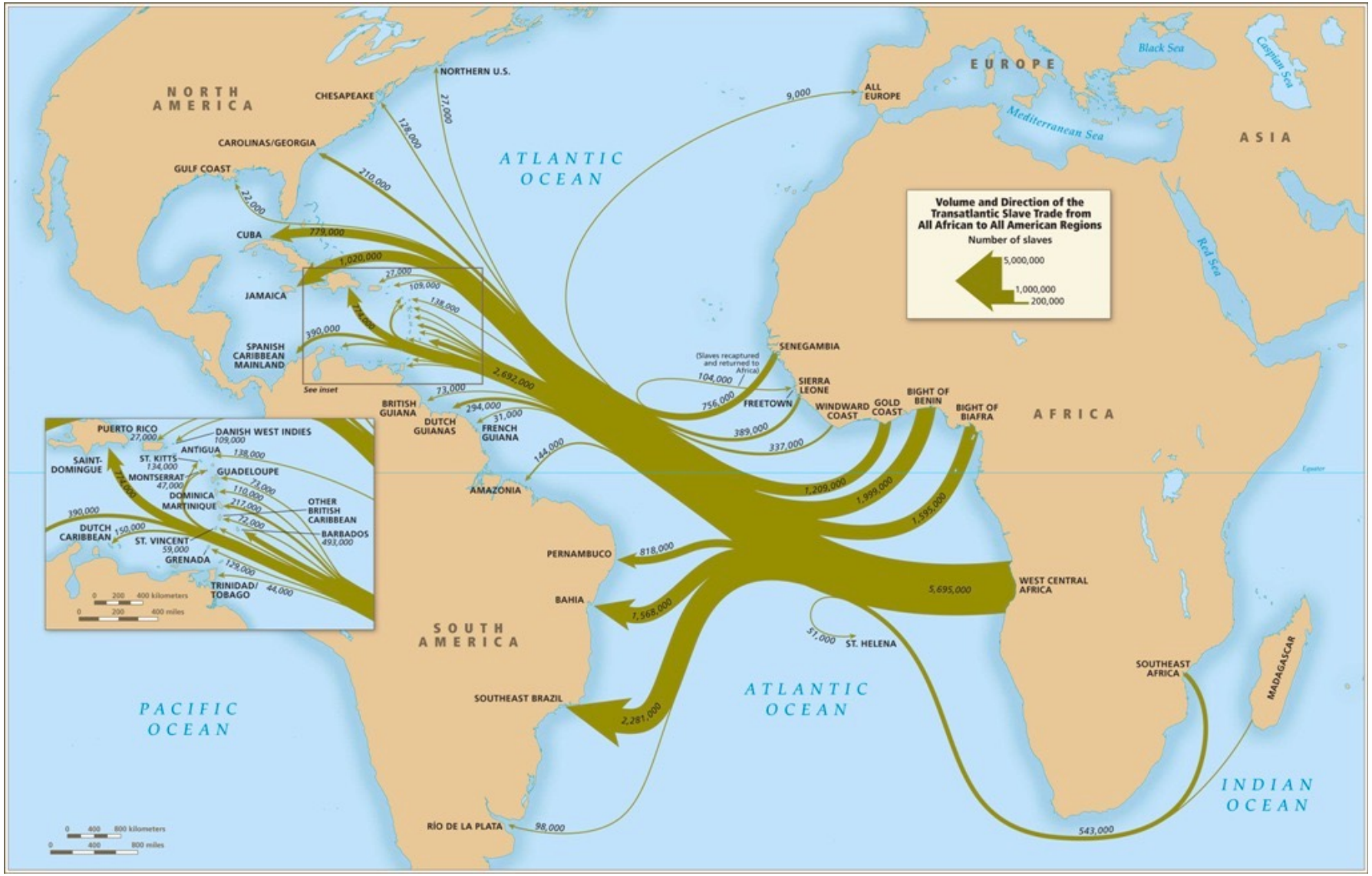







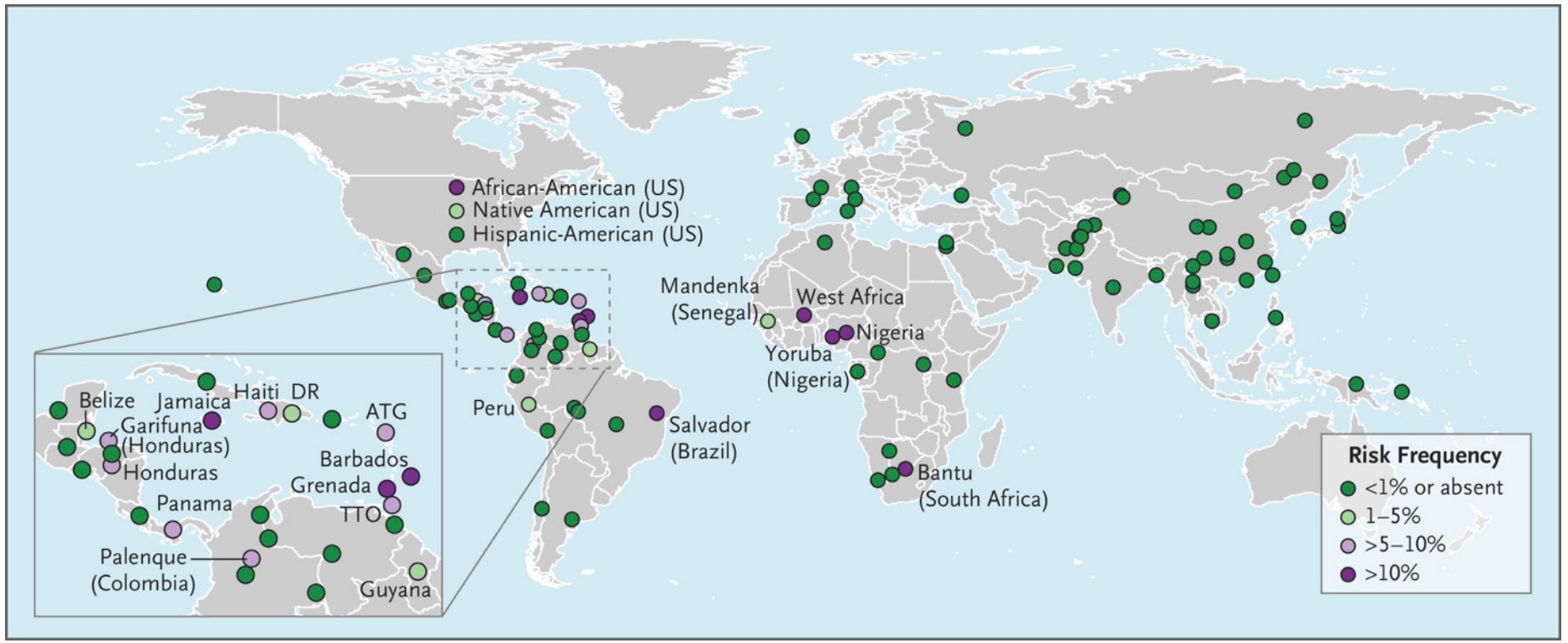
# Who are carriers of *APOL1* risk variants?

# Volume and direction of the trans-Atlantic slave trade- 12,521,337 Africans were enslaved



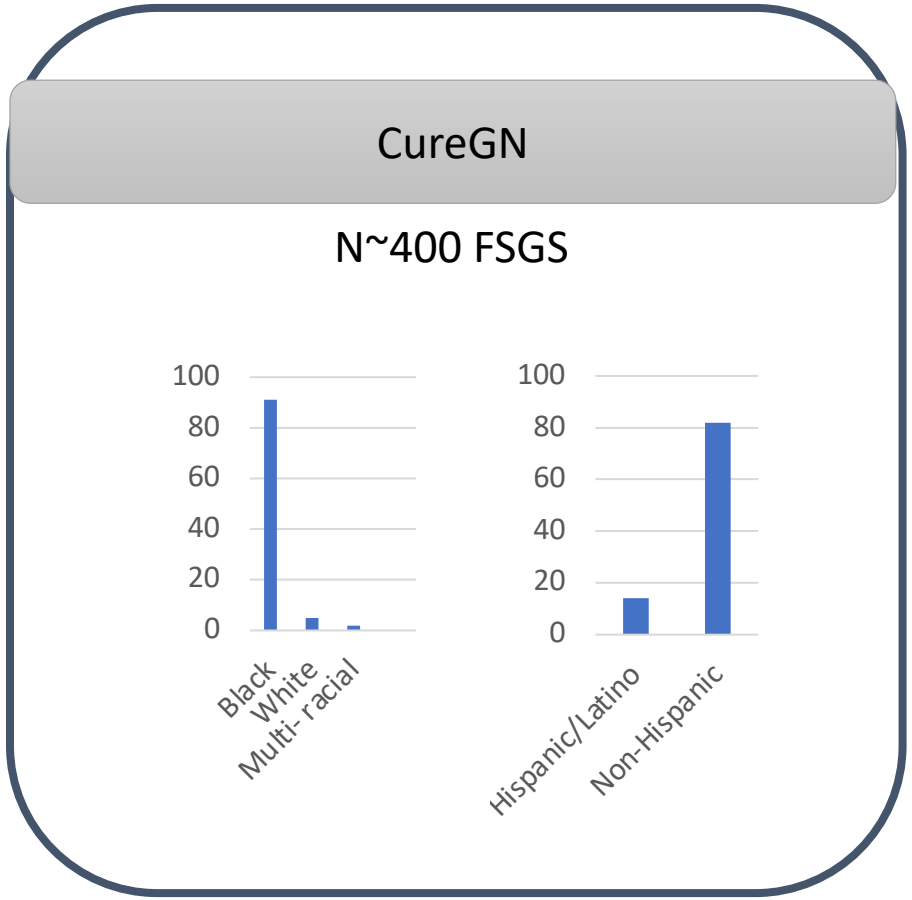
# Frequency of *APOL1* risk variants vary worldwide

Higher prevalence in regions reminiscent of slave trade patterns




Hum Mol Genet. 2011 Jun 15;20(12):2450-6.
N Engl J Med. 2018 Dec 27;379(26):2571-2572.

# Self-reported identity of high-risk *APOL1* carriers

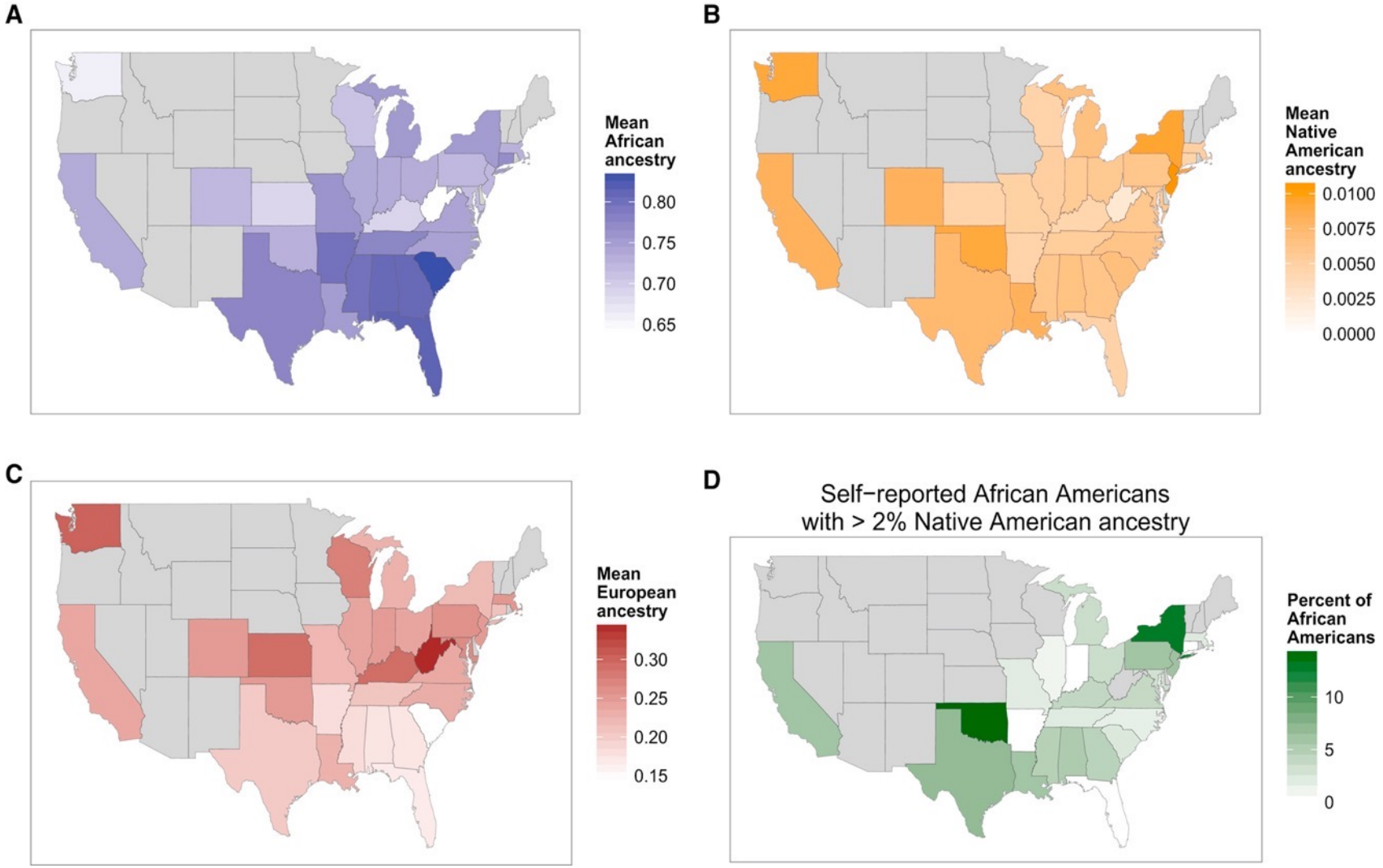



- Cross-sectional studies among Hispanic/Latino communities
  - NYC
    - Diabetic ESRD 6%
    - Non-Diabetic ESRD 20%
  - Hispanic Community Health Study/Study of Latinos
    - Caribbean/mainland 0.004%

*Nephrology Dialysis Transplantation*, Volume 27, Issue 4, April 2012, Pages 1498–1505,

J Am Soc Nephrol. 2017 Mar; 28(3): 915–922.

# Genetic Ancestry of African Americans, Latinos, and European Americans across the United States



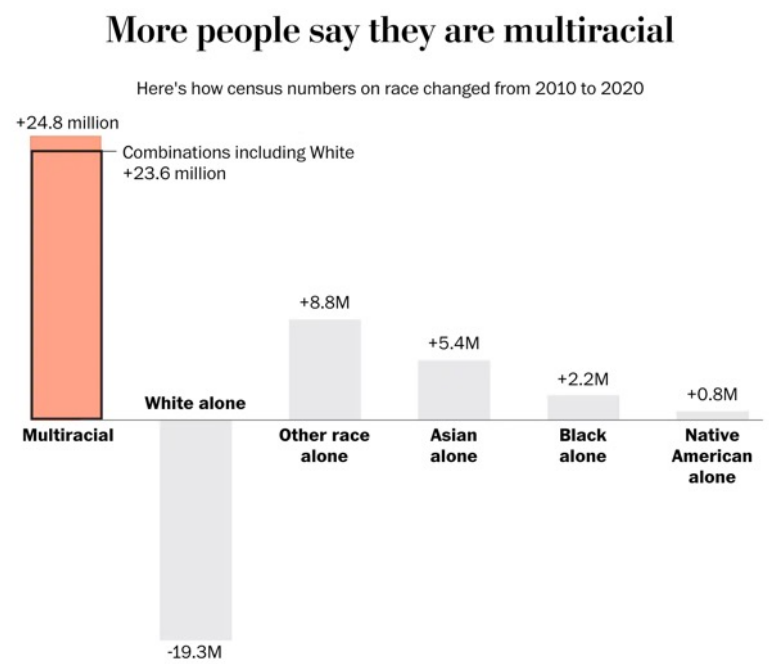

*The American Journal of Human Genetics* Volume 96 Issue 1 Pages 37-53 (January 2015)

# ‘We’re talking about a big, powerful phenomenon’: Multiracial Americans drive change

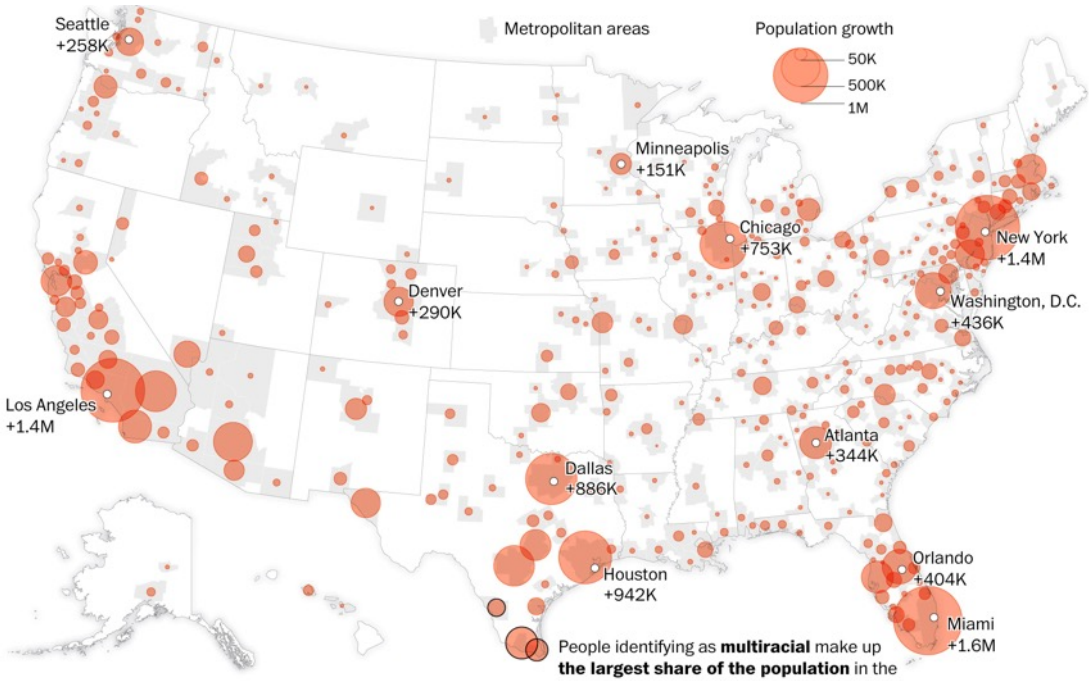
While still a relatively small part of the population, more Americans than ever identify as multiracial, according to the census

By Silvia Foster-Frau, Ted Mellnik and Adrian Blanco

October 8, 2021 at 8:00 a.m. EDT




Multiracial population growth in metropolitan areas



2023

Brief Communication

Kidney360

## Transplant Nephrologists' Preferences for Clinical Decision Support for *APOL1* Genetic Testing of Living Kidney Donors: A Focus Group Study

*Luke V. Rasmussen*[1], *Akansha H. Agrawal*,[2] *and Elisa J. Gordon*[3]

J Surg Res. 2022 Sep:277:116-124. doi: 10.1016/j.jss.2022.04.011. Epub 2022 Apr 27.

2022

## Apolipoprotein L1 Opinions of African American Living Kidney Donors, Kidney Transplant Patients, and Nonpatients

Dwight D Harris [1], Aaron Fleishman [1], Martha Pavlakis [2], Martin R Pollak [2], Prabhakar K Baliga [3], Vinayak Rohan [3], Liise K Kayler [4], James R Rodrigue [5]

Received: 28 April 2020 | Revised: 23 June 2020 | Accepted: 7 July 2020
DOI: 10.1111/ajt.16206

ORIGINAL ARTICLE

AJT

2021

## Opinions of African American adults about the use of apolipoprotein L1 (ApoL1) genetic testing in living kidney donation and transplantation

Margaret Berrigan[1,2] | Jasmine Austrie[1] | Aaron Fleishman[1,2] | Kenneth P. Tercyak[3] | Martin R. Pollak[2,4] | Martha Pavlakis[2,4] | Vinayak Rohan[5] | Prabhakar K. Baliga[5] | Liise K. Kayler[6] | Thomas H. Feeley[7] | James R. Rodrigue[1,2]

2018

> Am J Kidney Dis. 2018 Dec;72(6):819-833. doi: 10.1053/j.ajkd.2018.07.017. Epub 2018 Oct 22.

# African American Living Donors' Attitudes About APOL1 Genetic Testing: A Mixed Methods Study

Elisa J Gordon [1], Daniela Amórtegui [2], Isaac Blancas [2], Catherine Wicklund [3], John Friedewald [4], Richard R Sharp [5]

2017

*American Journal of Transplantation 2017; 17: 901–911*
*Wiley Periodicals Inc.*



doi: 10.1111/ajt.14173

Special Article

# Integrating *APOL1* Gene Variants Into Renal Transplantation: Considerations Arising From the American Society of Transplantation Expert Conference