

# You Are Just Now Telling Us About This? African American Perspectives of Testing for Genetic Susceptibility to Kidney Disease

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Variants of the *APOL1* gene, which encodes apo L1, confer increased risk for CKD, ESKD, and reduced cadaveric kidney transplant survival, and likely contribute to kidney disease disparities among African American individuals in the United States. To date, few studies have gathered African Americans' perspectives on *APOL1* testing practices. In this *Perspective*, we describe the results of a study designed to gather informed input about the potential benefits and risks of *APOL1* testing in routine patient care and in kidney transplant settings. Despite mixed views among study participants, they generally expressed support for testing, especially in kidney transplant programs, and many urged broad-based efforts to educate African Americans about the discovery of *APOL1* gene variants and their implications for kidney disease.

This article's title, "You are just now telling us about this?," reflects a sentiment voiced in a community deliberation, one of three held with African Americans to discuss testing for variants of the *APOL1* gene. "Why are we not knowing about this?" a deliberant asked. "I know you have to do research before you come out with anything but it's been a while and still no one has heard about it." Although mistrust of research and medical establishments punctuated all deliberations, most deliberants strongly endorsed offering *APOL1*

testing to African Americans in some settings.

*APOL1* risk variants are associated with a two-fold greater risk of CKD, a seven- to ten-fold greater risk of nondiabetic ESKD, and an increased risk of kidney transplant failure, and they likely contribute to significant disparities in CKD and ESKD among African Americans.<sup>1–3</sup> An estimated 13% of African Americans have two of the *APOL1* high-risk alleles.<sup>4</sup> *APOL1* testing nonetheless remains controversial because only about 20% of African Americans with an *APOL1* risk genotype develop ESKD, the mechanism of injury and potentially modifying roles of environmental exposures or comorbid conditions are unknown, and no clinical interventions for *APOL1*-associated risk currently exist.<sup>5</sup> Recent studies of strict BP control show mixed results.<sup>6,7</sup>

## COMMUNITY DELIBERATIONS

To gather informed input about the potential benefits and risks of *APOL1* testing in routine patient care and kidney transplant settings, between September 2017 and January 2018, pursuant to institutional review board approval at each site, we conducted community deliberations with 39 members of the African American communities in Jackson, Mississippi; Nashville, Tennessee; and Seattle, Washington.

Community advisory boards at each site provided guidance on recruitment, community-based venues, and educational materials. Deliberations by design typically have small sample sizes, particularly when conducted face to face with intentional diversity in composition of deliberants.<sup>8</sup> For this study, recruitment sought to ensure that each deliberation comprised members of the black community with diversity in age, sex, educational level, and experience with or exposure to kidney disease. Each participant received \$250 for completing 2 days of deliberations.

Drawing on tenets of public deliberation,<sup>8–10</sup> we convened these participants to learn and deliberate about *APOL1* testing in clinical nephrology and kidney transplant settings. Public deliberation complements other forms of public engagement, such as surveys and town halls, by yielding opinions that are well informed and well considered rather than top of mind.<sup>11</sup> Grounded in theories of deliberative democracy, public

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deliberation engages ordinary people with diverse backgrounds and characteristics in reasoned, respectful, and value-rich discussion about an important issue that affects them. We designed these community deliberations to promote such discussions, and aimed at providing recommendations to those who will make decisions about best practices in *APOL1* testing in routine patient care and kidney transplant programs.

To achieve these ends, participants received educational material—a two-page document (Supplemental Material) describing CKD and its progression, risk factors for CKD including *APOL1*-related risk variant, and racial disparities in kidney disease—before meeting for deliberations and revisited this document during deliberations. In addition, an expert (B.A.Y.) with experience in conveying information about kidney disease to lay audiences gave an interactive lecture about what is known and unknown about *APOL1* and kidney disease during the deliberations, and remained in the room to address scientific questions. The educational materials and lecture were fact-based and nonpartisan, putting the *APOL1* genetic risk in a broader epidemiologic context of social factors implicated in racial disparities in kidney disease.

Deliberants met for 10 hours over 2 days to provide time for learning, discussion, and overnight reflection (Figure 1). The deliberations were audio-recorded, augmented by minutes that included individuals' views, reasons for their views,

recommendations by the whole group, and disagreements and reasons for disagreement. Participants completed a pre-deliberation survey with questions testing basic knowledge of kidney disease, including risk factors and management. This presurvey also included questions on participants' views regarding the importance of input from their community about health and health care, and about methods they considered helpful for providing such input about health care policies and practices. Participants completed a post-survey with questions similar to those in the presurvey and additional questions about the quality of the deliberations.

Active facilitation at each site (by E.B. and E.M.U.) sought to ensure that all participants had an opportunity to be heard, that minority viewpoints were not marginalized or silenced, and that underlying reasons for viewpoints were elicited. The deliberations addressed *APOL1* testing in the context of routine patient care (day 1) and kidney transplant (day 2). Each day's discussion began with an introductory discussion, followed by a brief session that outlined the ground rules for the deliberations. Plenary and small group discussions were used to create different types of group dynamics and learning, with the small group's sessions (which were not audio-recorded) promoting space and encouragement for more reticent participants.

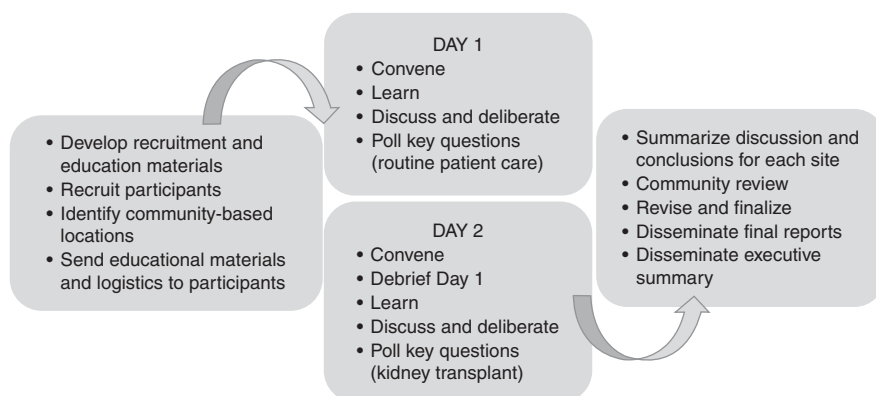
Deliberations culminated with participants voting on key questions about best practices in *APOL1* testing in routine patient care and kidney transplant

programs. These polling questions (Supplemental Material) were developed in consultation with the project's scientific advisory board regarding which issues were salient and timely for the nephrology community. We also used these polling questions to structure the deliberations over the 2 days, and used two rounds of polling to enable deeper consideration and exchange among participants. We captured participants' justifications for their responses to polling questions *via* notes, flip charts, and audio-recordings. The lead facilitator (E.B.) drafted the results of each deliberation, which were reviewed by the cofacilitator (E.M.U.) and expert (B.A.Y.) and revised as needed, and then reviewed by the research team and community deliberants before finalizing.

## PERSPECTIVES ON *APOL1* TESTING

Participants were 49% men, aged 20–82 years, with high school to graduate-level education. The annual household income for one third of participants ranged from \$20,000 to \$40,000; the rest had annual incomes ranging from <\$20,000 to >\$60,000. Some had kidney disease or family members with kidney disease, including patients on dialysis and kidney transplant recipients.

Participants expressed strongest support for *APOL1* testing in kidney transplant settings, with unanimous support for testing cadaveric kidneys (100%), near-unanimous support for offering testing to living donors (95%), and considerable but strongly contested support for mandatory testing of living donors (73%). Support for testing turned largely on grounds that donor kidney *APOL1* status has known clinical implications, allowing living donors and recipients to factor into their respective decision-making process the *APOL1* risks of potential donor CKD and decreased post-transplant graft longevity. Some participants argued that potential recipients needed, and perhaps had a right to, this information to make truly



**Figure 1.** Deliberation method schematic.

informed decisions about whether to accept the kidney. However, opposition to required (versus optional) testing of living donors was vigorous and stable across two rounds of polling at all sites, on grounds that mandatory testing would violate people’s autonomy and rights and possibly lead to negative outcomes, such as deterring potential donors and shrinking the pool of available kidneys. Table 1 provides illustrative quotes of participant perspectives on key questions and background issues that surfaced. Participants’ support for

voluntary *APOL1* testing in the kidney transplant context aligns with Ross and Thistlethwaite’s proposal for voluntary *APOL1* testing during the transplant work-up for prospective living donors of African ancestry, after provision of education and counseling to these potential donors.<sup>12</sup>

We also polled participants on whether living donors with *APOL1* risk should be prohibited from donating a kidney. Most participants (90%) opposed such a policy, arguing it could decrease kidney supply, violate respect for autonomy, and pose

psychologic burdens. The few participants who supported such a policy did so on grounds that it could yield a healthier donor kidney pool and protect donors from their own altruistic inclinations.

Participants were more circumspect about *APOL1* testing in routine patient care. Specifically, 64% endorsed offering the test to all black patients, 21% favored offering the test only to black patients with CKD risk factors, and 10% supported offering testing only to black patients with signs of CKD. Support relied heavily on perceptions of personal and

**Table 1.** Participant perspectives

	Potential Benefits of Testing
Perceived utility in routine care	“We gotta know. First thing I would do is live a healthier life, change my lifestyle, and maybe they will find a cure at some point or a way to help us better.” <i>Seattle</i> “Not a lot I can do, but at least I know.” <i>Seattle</i>
Perceived utility in kidney transplant	“If [the donor has] <i>APOL1</i> risk and they hand off their kidney, then the other kidney might fail.... So the donor needs to know, and the recipient needs to know.... Everyone should be tested and just have the knowledge.” <i>Seattle</i>
Research (both settings)	“If they test everybody for it and they see enough people have it, it may prompt them to study it more and figure out if they can make a medicine or cure for it. But enough people have to have it first.... The numbers would have to probably go up, because like we said, there is a lot of racism. So stuff that affects black people does not really get researched...” <i>Nashville</i>
Potential risks of testing	
Perceived lack of utility in routine care	“What difference does it make? If I take the test, it’s just going to be part of my record that I have this genetic disorder. But nothing can be done about it, there is no preventive medicine....” <i>Nashville</i> “I just don’t buy this incentivization [idea]. I don’t. We have the information. We all know that black people get hypertension. Adding one more thing, it is not as if this is the reason I am going to start running.” <i>Seattle</i>
Reduced kidney supply	“If you do the test ... and you discover they have <i>APOL1</i> , at some point they are going to establish that you cannot get a kidney from somebody who has that. That is going to put a lot of black folk at the bottom of the list again.” <i>Nashville</i>
Discrimination and stigmatization	“The first thing that I thought ... is, ‘oh another category where we can’t trust the doctors because they are not going to give us the information anyway, and that’s a form of discrimination. We are usually the last people to get information about anything, and then we have to fight for it.” <i>Seattle</i>
Psychologic burdens	“I have this knowledge and now I am going to be sitting at home petrified.” <i>Nashville</i> “This test will bring about paranoia.” <i>Nashville</i>
Misunderstanding/confusion	“If you tell someone ‘you have the risk, they say, “oh God I am going to die.” this [information] is good, if you understand it. This is perfect, if you understand it.” <i>Nashville</i>
Mistrust of health care and research and importance of community engagement	“It’s been 7 years since they have known about this and they have not come up with a solution?” <i>Jackson</i> “Any time you study us you are looking for a reason to exclude us. ... You are finding it, but you cannot do anything for me except raise my insurance rates, so why are you finding it?” <i>Nashville</i> “I feel like [community education and programs are] really important. In the African American community, when we see the government doing something to help us or bring awareness to something, we may be more likely to do it. I always think about how we get the short end of the stick or get left out. Black people were strung out with crack for years and nobody cared. White people are strung out on heroin and now it is an epidemic and the government doing all these things to help them and all these studies .... I feel like if they did that with this the African American community could see that they do care about us.” <i>Nashville</i>

clinical utility. Many believed that knowing one's *APOL1* risk status would increase awareness and knowledge about kidney disease, motivate better lifestyle habits, and that risk status would be important information to share with children and other family. Participants also envisioned clinicians being able to use the information to improve or intensify care, a perception that persisted for some even when reminded that interventions to inform clinical care on the basis of *APOL1* status do not currently exist. Participants also expressed hope that testing might enable more research, yield treatments, and ultimately eliminate racial disparities in CKD and ESKD. Horowitz *et al.*<sup>13</sup> identified some of these same views in the context of a clinical research study that interviewed patients of African ancestry before, immediately after, and 30 days after they underwent *APOL1* risk testing. These patients felt knowing one's *APOL1* status would be useful to families and motivate positive health behaviors and close clinical management and monitoring.<sup>13</sup>

In contrast, only two (5%) of our study's participants saw no personal or clinical benefit and did not support offering the test to anyone; they expressed doubt that knowledge of *APOL1* status would motivate better health practices and took at face value the current lack of clinical utility. Indeed, some saw greater potential for harms, such as psychologic burdens—such as fear, anger, and distress—that could afflict individuals as well as black communities, given the ancestry-specific nature of *APOL1* variants. Regardless of whether participants supported or opposed testing, two potential risks resonated across all three sites: breaches of privacy and discrimination in health care, life insurance, and employment. Even avid supporters of testing underscored these concerns and advocated for policies protecting privacy and confidentiality. Participants also raised concerns that offering the test only to African Americans might exacerbate racism and stereotyping. In contrast, Horowitz *et al.*<sup>13</sup> reported that the patients in their study thought having a genetic risk and genetic testing for kidney disease in black people could

counter stigmatization and negative stereotyping of them as nonadherent or having social or behavioral reasons for being sicker than white individuals.

Finally, as we noted above, some participants were struck by the lapse of some 8 years between reporting of the discovery of *APOL1* genetic variants in the scientific literature and their learning of these variants' existence and potential relevance to their health. Sentiment ranged from surprise to anger that an important risk factor for a serious, sometimes fatal disease that takes an outsized toll on African Americans had not been widely shared with black communities, and discussions about mistrust of medical and research establishments ensued. This facet of the deliberations merits noting because of its poignancy in this era of patient and participant engagement and open science, which relies on the trust of empowered citizens.<sup>14</sup> Although deliberative engagement is not the only approach to building a more informed, empowered, and trusting United States population, we believe it can contribute to this cause, and may have particular value as an approach to engaging the minority and marginalized communities who shoulder a disproportionate burden of disease. Our study's pre- and postdeliberation surveys provide some support for this view, with most participants (79%) indicating they value this form of engagement in the pre-deliberation survey, increasing to 95% after participating in the process.

Using a deliberative approach to gather informed input from African Americans, we found strong support for *APOL1* testing of some African American subgroups in kidney transplant and patient care and for broad communication about *APOL1*-related risk to African American communities. As genomic research increasingly yields genetic associations with significant informational complexity, communicating with participants and patients in effective, equitable, and responsible ways about what those results mean for them and their families poses a serious challenge to 21st century research and medicine. The stakes are raised when risk variants affect populations who are burdened by excess disease

and also harbor mistrust of the medical system. As science continues to evolve to inform best practices about *APOL1* risk testing, studies such as ours suggest that charting a responsible way forward requires meaningful and continued involvement of the communities whose health is at stake.

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## DISCLOSURES

None.

## SUPPLEMENTAL MATERIAL

This article contains the following supplemental material online at <http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2018111091/-/DCSupplemental>.

Supplemental Appendix. XXX.

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## Expanding the Patient's Voice in Nephrology with Patient-Reported Outcomes

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As patient-oriented care has expanded in health care, the use of patient-reported outcomes (PROs) to evaluate patients' health has increased as well. A PRO is defined by the US Food and Drug Administration as “any report coming from patients about a health condition and its treatment, without interpretation of the patient's response by a clinician or anyone else.”<sup>1,2</sup> PROs can complement more traditional, biologically based, clinical measures of patients' health, such as BP or albuminuria, by adding information about the patient's perceptions of their own health. For example, PROs measuring health-related quality of life (HRQOL) look into how the patient feels (wellbeing) and what they can do (functionality). HRQOL includes physical, mental, and social health, and provides a comprehensive view of how a

patient is affected by an illness like ESKD. Applications for PROs in ESKD include monitoring of individuals or groups of patients in clinic, evaluating the effectiveness of new treatments, and performance and quality monitoring of kidney clinics.

Implementation of PROs has begun to yield benefits in many fields, such as oncology and orthopedics. For example, in a landmark publication in *JAMA* of patients with metastatic cancer who were receiving routine chemotherapy, Basch *et al.*<sup>2</sup> found that electronic monitoring of symptoms using PROs, and sending alerts to clinicians when distressing symptoms were indicated, was associated with improved patient survival compared with a control group (hazard ratio for death, 0.83; 95% confidence interval, 0.70 to 0.99;  $P=0.04$ ).

Because the PRO-based electronic symptom monitoring system used in this study allowed for brief, easy-to-complete symptom assessments, these findings also point to efficiency gains in patient management possible with PROs. In orthopedics, because of their salience in characterizing postsurgical health and recovery,<sup>3</sup> PROs capturing physical functioning have been embraced by the American Orthopedic

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