Improving Kidney Disease Research in the Black Community: The Essential Role of Black Voices in the APOLLO Study


The National Institutes of Health (NIH)–funded APOL1 Long-Term Kidney Transplantation Outcomes (APOLLO) study involves genetic testing of biospecimens from up to 700 Black living kidney donors and 1,300 Black deceased kidney donors and will also test and track outcomes among racially diverse recipients of those kidneys.1 Given the racially targeted nature of APOLLO, the history of racism in the United States, and the current social background, this study cannot succeed without appropriately hearing and responding to the Black community’s study-related concerns and hopes.

The Community Advisory Council (CAC) has been integral to APOLLO, providing direction and oversight.2 The CAC was involved in developing the protocol, consent forms, manual of procedures, informational materials, and many other documents. The CAC’s voice was instrumental during the startup phase and continues to shape study policy and decisions. We describe the study, the CAC, and the CAC’s overarching points of guidance thus far, as this may be instructive to other research projects that target specific communities in the United States. In this discussion, “Black” refers to people with African ancestry including those who identify as African American.

The APOLLO Study

People with 2 copies of the risk variants in the apolipoprotein L1 gene (APOL1), termed G1 and G2, are more likely to develop kidney disease than those with 0 or 1 copy, yet most do not develop kidney disease.3,4 These variants are found almost exclusively in people with African, particularly West African and sub-Saharan, ancestry, in whom they may protect against a potentially fatal parasitic infection.5 Approximately 13% of the US Black population has 2 risk variants, though rates vary by ancestral region.5,6 Relying on socially constructed racial categories raises numerous problems. In the absence of an alternative for rapidly assessing donors’ likely continental ancestry, APOLLO relies on donor race as an imperfect proxy to identify individuals more likely to have risk variants.

APOLLO’s primary aim is to assess the effects of deceased kidney donors’ APOL1 genotype on recipient outcomes. Secondarily, it aims to determine the effects of living donors’ APOL1 genotype on their own health outcomes after kidney donation as well as recipient outcomes. As an observational cohort study, APOLLO poses minimal physical risks to participants, only involving collection of blood and sometimes urine from donors and their recipients.1

The APOLLO Community Advisory Council

The history of abuse and racism in research and ongoing racial health inequities create distrust among many Black people toward research and researchers.7-9 The CAC aims to protect and advance the interests of Black people involved in APOLLO and to maximize the likelihood that research results will benefit Black people. The CAC comprises individuals who have received a kidney transplant, have chronic kidney disease (CKD), have donated a kidney, or have relatives with CKD and who identify as Black or African American. Two research team members participate in and help to coordinate CAC activities (ASI and JMD).

The CAC participates fully in the biannual meetings of investigators and study coordinators, and holds monthly conference calls. Investigators proposing ancillary studies consult the CAC. Members of the CAC have access to the internal study website, which includes all study documents but not participant-level data. The CAC has a representative (NMJ) on the steering committee, which consists of the principal investigators from the 13 APOLLO clinical centers and

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coordinating center as well as representatives from the NIH, the United Network for Organ Sharing, and the Association of Organ Procurement Organizations, and also has representatives on several study subcommittees.

The importance of transparency to build and maintain trust permeates CAC discussions and informs its recommendations. The CAC impresses upon investigators that many people distrust research when their lives and health care experiences have been affected by racism: mistrust does not just arise from historical events such as the US Public Health Service Syphilis Study at Tuskegee. Investigators must earn and maintain trust. Even though APOLLO poses fairly minimal risks and does not involve experimentation on participants, transparency is paramount. We describe 2 areas where the CAC’s understanding of transparency shaped APOLLO.

**Transparency and Trust: Informing Participants**

Laws, regulations, and institutional review boards (IRBs) sometimes allow practices that the CAC believes lack transparency. The CAC called on investigators to provide additional information and developed publicly available infographics to support education and transparency. Based on CAC recommendations, all participants and the legally authorized representatives of deceased donors may request their APOL1 research genetic test results. All genetic testing is done in a CLIA-certified laboratory to facilitate this.

The CAC’s concerns about transparency also had implications for living donor recruitment. During preliminary discussions, a small number of investigators suggested sharing information about APOLLO and recruiting living donors shortly after kidney donation. The APOLLO steering committee and the CAC felt this was unacceptable. The CAC was concerned that for some living donors the APOLLO recruitment might be their first opportunity to learn about APOL1 variants. Not all transplant programs routinely discuss APOL1 with potential living donors. Two investigators suggested that all potential living donors should have information about APOL1 far enough in advance of donation to learn more about APOL1 risk factors and make decisions—a view many African Americans share.

Even though living donors make donation decisions independent of APOLLO and APOLLO would not alter their care, the CAC recommended that all living donors receive information about APOLLO or APOL1 testing at least 1 month before donor nephrectomy. The CAC and steering committee agreed to a 2-week minimum to align with clinical realities (the CAC was consulted regarding additional adjustments during the COVID-19 pandemic). The CAC had 3 primary reasons for requiring advance notice:

1. Learning about APOL1 too close to the time of or after donation could cause psychosocial harms. Living donors might be upset they were not given this information earlier and might worry about their own or their recipient’s health.

2. Learning about APOL1 after donation might undermine donor trust if they felt they should have received information earlier. This could make them less likely to participate in APOLLO, undermining the study, and could harm their relationship with their transplant physicians.

3. Investigators should not be complicit with, or appear to support, withholding information potential living donors deserve.

The CAC requested verifiable documentation of the advance disclosure of APOL1 information, given that biomedical research in the United States is situated in a history of racist policies and practices. Critically, APOLLO investigators never proposed withholding information about APOL1 from potential living donors; rather, the CAC’s transparency concern involved clinical practices that were not under APOLLO investigators’ control. Although research and clinical practice may be distinct for regulatory purposes, patients and potential participants might experience them as connected in ways that have significant implications for the ethical conduct of research.

**Transparency and Trust: Who Stands to Benefit?**

APOLLO’s mission is “to improve the lives of those who donate or receive a kidney by learning more about genetic variations . . . found among some people of African descent.” It is vital to communicate this message—and especially the potential benefits—to the Black community, to potential participants, and to families making organ donation decisions.

The CAC found investigators would often speak about APOLLO’s benefits in terms of gaining scientific knowledge. As an observational study, APOLLO offers participants no direct potential clinical benefits. Further, IRBs often prohibit investigators from making statements that sound like promises of benefit. In contrast, the CAC felt that the investigators needed to clearly articulate how this study was designed and intended to benefit Black patients in the future.

Black people face significantly higher rates of kidney disease, are less likely to receive kidney transplants, and are more likely to experience graft failure than European Americans. The Kidney Donor Risk Index (KDRI) is a quality indicator used in allocating deceased donor kidneys to recipients. It includes self-reported donor race and treats Black donor race as indicative of poorer organ quality because, on average, kidney transplants from Black donors fail earlier than transplants from non-Black donors. The KDRI contributes to many kidneys from Black donors being discarded rather than transplanted. If APOLLO reveals that APOL1 genotype accounts for a significant portion of these earlier allograft failures, genotype could replace race in the KDRI, potentially reducing the number of kidneys that are discarded and eliminating the problematic reliance on race in kidney discard policies.

Black living kidney donors experience worse health outcomes after donation than European Americans. If
APOLLO’s findings contribute to our understanding of who is actually at heightened risk from donating a kidney, more people might be willing to donate. This could help reduce the existing disparity in access to living donor kidney transplants.\(^\text{21,22}\) Above all, understanding the relationship between APOL1 risk variants and kidney health may empower people to make wise health choices and informed decisions.

Conclusions

The CAC’s guidance to APOLLO researchers has been motivated by challenging common research assumptions (Table 1). The APOLLO research team has been open to hearing these and has relied on CAC guidance to navigate these assumptions. The CAC has promoted respect for participants, minimized the risk of harm, and helped foster trust.\(^\text{2}\) Relying on the CAC’s guidance also may improve research recruitment and ultimately the ability to obtain valuable, generalizable knowledge from the APOLLO study.

The APOLLO CAC has engaged Black people as partners in all aspects of research to acknowledge past abuses, prevent harm to the Black community and Black individuals, promote better research, foster confidence, and advance health equity, providing a model for engaging other communities in future health research activities.

| Table 1. CAC Revisions to Common Research Assumptions |
|---------------------------------|-----------------|
| **Common Research Assumptions** | **CAC Revisions** |
| It is sufficient to comply with research regulations and IRB requirements. | Given past and current experiences of racism, earning the trust of participants may require more information than research regulations and IRBs require. |
| In a clinical observational study, it is crucial to separate the research component from the clinical care component. | Participants may not view the clinical and research components as separate. Researchers may need to share additional information and avoid any connection with clinical practices that lack or appear to lack transparency. |
| An observational study will not offer direct benefits. It is unethical to promise downstream benefits to participants or say too much about possible future benefits. | It is essential to articulate how a study that does not offer participants direct benefit is meant to benefit the community as a whole, especially disadvantaged communities. For APOLLO, the benefit to the Black community must be clearly described. |

Abbreviations: APOLLO: APOL1 Long-Term Kidney Transplantation Outcomes; CAC, Community Advisory Council; IRB, institutional review board.

References


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