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

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ABSTRACT
Introduction While living donor (LD) kidney transplantation is the optimal treatment for patients with kidney failure, LDs assume a higher risk of future kidney failure themselves. LDs of African ancestry have an even greater risk of kidney failure post-donation than White LDs. Because evidence suggests that Apolipoprotein L1 (APOL1) risk variants contribute to this greater risk, transplant nephrologists are increasingly using APOL1 genetic testing to evaluate LD candidates of African ancestry. However, nephrologists do not consistently perform genetic counselling with LD candidates about APOL1 due to a lack of knowledge and skill in counselling. Without proper counselling, APOL1 testing will magnify LD candidates’ decisional conflict about donating, jeopardising their informed consent. Given cultural concerns about genetic testing among people of African ancestry, protecting LD candidates’ safety is essential to improve informed decisions about donating. Clinical ‘chatbots’, mobile apps that provide genetic information to patients, can improve informed treatment decisions. No chatbot on APOL1 is available and no nephrologist training programmes are available to provide culturally competent counselling to LDs about APOL1. Given the shortage of genetic counsellors, increasing nephrologists’ genetic literacy is critical to integrating genetic testing into practice.

Methods and analysis Using a non-randomised, pre–post trial design in two transplant centres (Chicago, IL, and Washington, DC), we will evaluate the effectiveness of culturally competent APOL1 testing, chatbot and counselling on LD candidates’ decisional conflict about donating, preparedness for decision-making, willingness to donate and satisfaction with informed consent and longitudinally evaluate the implementation of this intervention into clinical practice using the Reach, Effectiveness, Adoption, Implementation and Maintenance framework.

Ethics and dissemination This study will create a model for APOL1 testing of LDs of African ancestry, which can be implemented nationally via implementation science approaches. APOL1 will serve as a model for integrating culturally competent genetic testing into transplant and other practices to improve informed consent. This study involves human participants and was approved by Northwestern University IRB (STU00214038). Participants gave informed consent to participate in the study before taking part.


STRENGTHS AND LIMITATIONS OF THIS STUDY
⇒ The type II hybrid study design enables simultaneous evaluation of the intervention and the implementation of the intervention with a coequal focus.
⇒ Participating centres’ location in different geographic regions enhances generalisability.
⇒ Study sites agreed to the same overall workflows and study protocol.
⇒ The Apolipoprotein L1 implementation process will be standardised by disseminating protocols, scripts and materials to both sites to ensure fidelity to the intervention and its delivery.
⇒ A limitation is that the study does not use DNA testing to assess living donors’ ancestry; however, DNA testing is not consistent across labs and would be cost-prohibitive.

BACKGROUND
Living donor (LD) kidney transplantation is the optimal treatment for patients with
kidney failure,1 2 with greater patient and graft survival and quality of life than deceased donor transplantation3 4 or dialysis.5 6 Patients of African ancestry have disproportionately greater rates of chronic kidney disease (CKD) and kidney failure compared with White patients. They also comprise disproportionately greater representation on the transplant waitlist but receive fewer transplants than White patients.7 8 The estimated risk of kidney failure at 15 years post-donation is higher in LDs of African ancestry than in White LDs: 74.7 versus 22.7 per 10000 LDs.9 10 These findings have intensified the transplant field’s concerns with protecting LD safety, improving LD informed consent and reducing LD disparities in post-donation kidney disease.11-13 LD, clinician and health system factors contribute to this disparity for LDs,14 15 along with systemic racism and social determinants of health. In addition, the higher prevalence of CKD among patients of African ancestry compared with White patients has been attributed to Apolipoprotein L1 or ‘APOL1’ risk variants,16 which are found predominantly in individuals of African ancestry.16-18 Among patients of African ancestry without CKD, 13%–15% have two APOL1 risk variants, and 39% have one risk variant.10 19 Having two APOL1 risk variants is associated with a 10-fold greater odds of focal segmental glomerulosclerosis-attributed kidney failure.16 More than 3 million individuals of African ancestry in the USA are estimated to have two risk variants.20 Kidneys from deceased donors with two APOL1 risk variants had significantly greater risk of graft failure (two-fold HR) in recipients than kidneys from deceased donors with ≤1 variant.21 22 Young male LDs of African ancestry with two APOL1 risk variants were at highest risk of CKD post-donation compared with female and European American LDs.23

The research-to-practice gap

The 2017 KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors advises ‘… considering APOL1 genotyping in LD candidates with sub-Saharan African ancestors’,24 25 given that APOL1 risk variants evolved in this region. The American Society of Transplantation in 2015 reported that current data were insufficient to support testing all LD candidates of African ancestry due to the lack of long-term population-level data on APOL1 risk variants25 and the lack of APOL1’s specificity in predicting disease.26 27 APOL1 testing is controversial because of the lack of definitive evidence on the causal link between APOL1 risk variants and LDs’ health outcomes, and the consequent ethical dilemmas raised, as described below. Thus, some physicians are waiting for results from the NIH-funded APOLLO study before implementing APOL1 testing into their clinical practice.28 Others posit that LDs of African ancestry should be screened for APOL1 variants to risk stratify LDs; the presence of two risk variants should comprise a relative contraindication to donation requiring careful counseling and consent of LDs.12 26

APOL1 testing of LDs raises the ethical dilemma of whether to permit LDs of African ancestry with two APOL1 risk variants to donate.29 30 Donating could place such LDs at even greater harm, thereby challenging: (a) the ethical principle of non-maleficence as LDs gain no direct medical benefit from donation,31 32 and (b) the ethical justification for living donation: when ‘benefits to both the donor and the recipient outweigh the risks associated with the donation and transplantation’.33 Not allowing LDs of African ancestry with two risk variants to donate could protect their safety by reducing their risk of CKD, but not donating could exacerbate disparities in access to LD transplantation for candidates of African ancestry and reduce patient survival.26 34

Genetic counselling and shared decision making (SDM) about undergoing APOL1 genetic testing and living donation with APOL1 risk variants are especially warranted given that donating is a preference-sensitive decision and APOL1 poses elevated risks for LDs.35 Transplant physicians are increasingly adopting APOL1 testing,36 37 but they do not consistently inform LD candidates about APOL1 genetic testing, perform genetic counselling or practice SDM with LDs.36-39 This variation results partly from physicians’ lack of practical knowledge and skills in APOL1 counselling, and fear that APOL1 testing will deter LDs from donating, which would further exacerbate African American transplant candidates’ disparities in access to LD kidney transplantation.30 36

Genetic counselling is ‘the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease’.40 Counselling involves education about inheritance, testing and prevention to promote informed choices and includes SDM.40 Counselling is effective in reducing decisional conflict, increasing knowledge and improving accuracy of risk perception,41 which improve informed consent. Importantly, while LDs are usually eager to donate to improve family or friends’ health, many are uncertain about donating.42-46 Concerns about long-term health conditions after donation were a reason for LDs’ reluctance to donate among 34% of potential donors (n=53) participating in in-depth interviews in a study in the Netherlands42 and among 40% of LDs (n=174) in a retrospective US survey study.45 Although most (87%) LDs of African ancestry in an interview study (n=23) expressed willingness to undergo APOL1 testing, fewer (61%) would have donated if they had two risk variants.47 In addition, most interviewed LDs of African ancestry (81%) ‘strongly agreed’ or ‘agreed’ that APOL1 test results would have helped them decide whether to donate.47 Most LDs of African ancestry (82%) in a focus group study (n=17) also would have wanted to receive genetic counselling about APOL1 testing during LD evaluation.44 Thus, APOL1 risks may magnify LDs’ decisional conflict about donating,47 which, as a prospective survey study of potential donors (n=53) in Taiwan found, is significantly associated with LDs’ lower likelihood to actually donate.43 However, no studies have trained transplant
Barriers to the clinical integration of genomic testing include: providers’ lack of knowledge and preparedness to provide genetic services; healthcare systems do not enable electronic health records (EHRs) to make readily accessible genetic test results, and clinical practice guidelines advise APOL1 testing LDs of African ancestry but do not specify how to ascertain ancestry. ‘Race’-based care or ‘racialised medicine’ conflates the outmoded social construction of ‘race’ as biological differences between groups of people with the genetic concept of ancestry and reinforces racism to the detriment of the health of individuals of African ancestry.

Systemic racism adversely affects health outcomes and contributes to health disparities across multiple levels of influence (eg, individual, interpersonal, community, societal) among multiple domains of influence (biological, behavioural, physical, sociocultural, healthcare system). In the organ transplant context, numerous forms of systemic barriers exist across all levels and domains of influence, including: limited access to insurance coverage for transplantation, providers’ poor-quality communication about and limited referral to transplantation, and transplant allocation policies. Such systemic barriers have contributed to disproportionately lower rates of organ transplantation among African American patients and other minoritised patients.

Genetic testing is one factor that can potentially contribute to systemic racism in transplantation and in other clinical contexts. Genetic testing can potentially exacerbate or mitigate systemic racism. On one hand, genetic testing can magnify systemic racism if it is not offered in an equitable way to all patients. At the individual level, many individuals of African ancestry hold cultural concerns about genetic testing (eg, beliefs and concerns about misuse of testing, mistrust in the medical system) and fear that APOL1 test results would lead to psychological distress, stigmatisation of the community of African ancestry and health insurance discrimination. On the other hand, preparing the transplant provider workforce to offer APOL1 genetic testing to all LDs of African ancestry and to provide genetic counselling in a culturally appropriate manner can help to reduce inequities by eliminating provider bias, acknowledging historical distrust of institutions and fostering trust. Culturally competent care can increase knowledge among people of African ancestry about donation and LD rates.

**Study aims**

**Aim 1. Adapt Gia and transplant counselling to APOL1 for use in routine clinical practice.** We will adapt a chatbot, Gia® (Genetic Information Assistant), and nephrologist counselling to ensure that they are culturally targeted and competent, by engaging communities of African ancestry and experts in genetics, transplantation and bioethics. The goal of the adaptation process is to ensure implementation of the genetic testing and counselling components on a broad scale with minimal disruption to provider workflow.

**Aim 2. Evaluate the effectiveness of this intervention on decisional conflict, preparedness and willingness to donate in a two-site, non-randomised, pre–post trial design.** We hypothesise the intervention will:

- H₁: decrease LDs’ decisional conflict about donation.
- H₂: increase LDs’ preparedness for decision-making about donation.
- H₃: not decrease LDs’ willingness to donate.

**Aim 3. Evaluate the implementation of this intervention into clinical practice by using the RE-AIM framework to longitudinally evaluate nephrologist counselling practices and LDs’ satisfaction with informed consent.**

We will use the Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework to longitudinally evaluate implementation outcomes (ie, acceptability, appropriateness, feasibility, reach, adoption and fidelity). We hypothesise implementation will:

- H₁: increase nephrologists’ knowledge and skill in delivering counselling for APOL1 testing and donation.
- H₂: increase LDs’ satisfaction with informed consent about donation.

**METHODS**

**Overview and rationale for the study design**

Because genetic testing and chatbots are effective interventions, scientific focus can be shifted towards the implementation of genetic testing and the chatbot for APOL1 and LDs of African ancestry. The non-randomised clinical trial, with a pre–post implementation evaluation, uses a type II effectiveness–implementation hybrid approach to simultaneously and rigorously test a prospective implementation strategy during an effectiveness trial to facilitate translation into clinical practice. Accordingly, control arm participants will be recruited during the pre-implementation period, and intervention arm participants will be recruited during the post-implementation period.

**Study sites**

The proposed study will be conducted at Northwestern University (Chicago, IL) and Georgetown University (Washington, DC). Both transplant programmes have a large number of Black/African American LDs and are in cities with large populations of Black/African American people (30%-Chicago, 47%-DC). Neither site systematically identifies the African ancestry of LDs or has a policy on LD selection for APOL1 testing. Neither site uses SDM to aid in donation decisions.

**APOL1 genetic testing and counselling programmes**

**APOL1 genetic testing**

1. Asking all LD candidates about their ancestry: asking all LDs about their ancestry will include LDs with...
African ancestry who might otherwise be missed. This approach coincides with a pan-ethnic genetic screening paradigm and avoids reinforcing the phenotype-based construct of ‘race’ for selecting LDs for \textit{APOL1} testing.

2. **Offering \textit{APOL1} genetic testing to all LD candidates with African ancestry that pass initial screening; half of LD candidates do not pass.** Testing LDs early avoids unnecessary expense of other tests for LDs who will be ruled out. \textit{APOL1} genotyping all LD candidates of African ancestry is cost-effective in preventing CKD.\textsuperscript{75}

**\textit{APOL1} genetic counselling**

1. **A clinical chatbot will provide pre-\textit{APOL1} genetic testing information based on LDs’ information needs.** Chatbots increase informed treatment decisions and reduce decisional conflict.\textsuperscript{76,77} This study will create the first chatbot on \textit{APOL1}.

2. **Nephrologists will provide post-\textit{APOL1} counselling about test results to normalise \textit{APOL1} in the routine LD evaluation process (table 1).** Nephrologists will engage in SDM with LDs who test positive for two risk variants about donating, as recommended.\textsuperscript{78}

3. **A culturally competent educational brochure on \textit{APOL1} that our team previously developed will be given by nephrologists to LD candidates of African ancestry during evaluation and be available in the transplant centre waiting room.**\textsuperscript{48}

**Implementation strategies**

We will use several implementation strategies to accomplish the study’s aims,\textsuperscript{79} multiple methods to document them and the Implementation Research Logic Model (IRLM)\textsuperscript{81,82} (figure 1) to specify the conceptual associations between determinants, strategies and the hypothesised/observed mechanisms and outcomes that result. The Implementation Research Logic Model (IRLM) provides a comprehensive set of strategies to be used. The following strategies are the primary focus of the study: establishing academic–community partnership, leveraging a Community Advisory Board (CAB), engaging patients, using a chatbot, educating and training transplant nephrologists, integration of genetic testing into the EHR and financing \textit{APOL1} testing. Additional details on each of the primary strategies are available in online supplemental file 1 and online supplemental file 2.

**Patient and public involvement**

We established a CAB comprised of transplant patients and community leaders who provided input on the study design, outcome measures, informed consent and recruitment and retention procedures. The CAB will review study results to provide insights into interpretation and foster dissemination.

**Assessment strategy, measures and data analysis**

**\textit{APOL1} intervention**

The \textit{APOL1} testing programme has been designed to fit within the routine LD evaluation process of the two sites, which limits LD clinic visits to 1 day. LDs will have four touchpoints of data collection (table 2). Between the labs (eg, blood, EKG, CT) and nephrology visit, research staff will screen all LDs by asking the 3 ancestry screening questions, obtain informed consent for study participation, conduct baseline surveys and provide the chatbot link to use for 5–7 min (T1). Tablets will be provided if LDs do not have a smartphone. The three ancestry questions include: ‘What ethnic/racial groups do you identify with?’ (eligible for study: Black, African American, Jamaican, Barbadian, Grenadian, Brazilian from Salvador, Trinidadian, Panamanian, Honduran, Haitian, Garifunan, Palenque, Guyanese, Dominican, Peruvian, Belizean

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<tr>
<th>Table 1</th>
<th>\textit{APOL1} counselling training programme content domains</th>
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<tr>
<td><strong>Module</strong></td>
<td><strong>Description: after completing the training, nephrologists will be able to...</strong></td>
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<tr>
<td>Introduction</td>
<td>Articulate the programme’s purpose and who it is designed to help</td>
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<tr>
<td>\textit{APOL1} and kidney disease</td>
<td>Define \textit{APOL1} and its relationship to kidney disease</td>
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<td>\textit{APOL1}: risks, benefits and limitations of living kidney donation and genetic testing to living donors, their family and their recipients</td>
<td>Describe the risks of having two risk variants on LDs’ post-donation health, their reproduction and on other family members; communicate about genetic risks as modifiable vs non-modifiable</td>
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<tr>
<td>Genetic variation and ‘Race’: knowledge and practice</td>
<td>Communicate about \textit{APOL1} and address the values and beliefs among people of African ancestry about genetic testing in a culturally and socially sound manner</td>
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<tr>
<td>Access, insurance, privacy, and confidentiality of testing and test results</td>
<td>Explain how LDs’ privacy and confidentiality of test results will be protected; the limits of the Genetic Information Nondiscrimination Act of 2008; what will happen to test results, and who has access to them</td>
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<tr>
<td>Ethics</td>
<td>Compare ethical implications of donating and not donating</td>
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<tr>
<td>Shared decision-making</td>
<td>Engage in SDM with LD candidates with two risk variants about donating; explain the relative benefit to recipients of LDKT vs staying on dialysis</td>
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<tr>
<td>Case study discussion</td>
<td>Apply concepts learnt in modules to an actual case.</td>
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\textit{APOL1}: Apolipoprotein L1; LD, living donor; LDKT, Living Donor Kidney Transplantation; SDM, shared decision-making.
Native American); ‘Are you aware of any biologically-related family with African ancestry?’ and ‘What is your ancestry?’83 84 After LDs meet with the nephrologist, staff will ask for informed consent for APOL1 testing, collect a saliva sample and mail it to the laboratory. Research staff call LDs a week later to qualitatively assess LDs’ perceptions of the chatbot, and its impact on outcome measures (T2). Clinical decision support in the EHR will alert the nephrologists when APOL1 test results return and will prompt the nephrologists to call LDs to discuss the APOL1 test results and engage in SDM about donation. Research staff will call LDs 1–2 business days thereafter to qualitatively assess LDs’ perceptions of the counselling and its impact on outcome measures (T3). During year 1, which serves as the preimplementation control phase, both sites will only assess T1 and T4 LD outcomes.

Statistical analyses
Descriptive summaries will be generated for all data (eg, means and SD, medians, IQR and ranges for continuous data; counts and frequencies for categorical data). Graphical summaries (ie, histograms, boxplots) will be used to assess distribution shapes and evaluate transformations to improve normality. To evaluate potential differences in LD demographic and clinical characteristics before and after implementing the APOL1 intervention, summary statistics will be compared for LDs in the control and intervention enrolment periods within each centre.

Analyses for H1 will employ a linear mixed effect model with fixed effects for arm (pre or postimplementation) and study period. The included random centre effect will allow for separation of within-centre and between-centre variance estimates. Analyses for H2 and H5 will employ similar methods for preparedness for decision-making and satisfaction with informed consent, respectively. Analyses for H3 will be conducted under a non-inferiority framework. Specifically, we will estimate a CI for the difference in medians to compare the willingness to donate between the preimplementation and implementation periods. If the lower limit of a two-sided 95% CI is within the margin of non-inferiority, we will have evidence that the APOL1 counselling intervention does not meaningfully reduce the willingness to donate. We will assume a non-inferiority margin of 1.5 units, which reflects a negligible difference in scores. Young (age 35–44 years), male, LDs of African ancestry with APOL1 risk variants have the highest risk of developing CKD, although most LDs are women.23 85

Figure 1 Implementation research logic model. APOL1, Apolipoprotein L1; LD, living donor; NU, Northwestern University; GU, Georgetown University; CSAT, Clinical Sustainability Assessment Tool; RACE, Racial Attributes in Clinical Evaluation. Determinants are rated using Damschroder et al’s (2013) coding system of the relative strength on a scale from –2 (strong negative impact), –1 (weak negative impact), 0 (neutral or mixed influence), 1 (weak positive impact), 2 (strong positive impact).

Superscripted letters indicate conceptual relationships between elements of the model ending with the implementation outcome. Note that not all determinants have an associated implementation strategy and not all strategies have a hypothesized mechanism; emphasis was placed on the causal paths associated with the study aims and hypotheses.
Thus, planned subgroup analyses will consider assessment of LD outcomes by sex and age groups. These analyses will be deemed exploratory given power considerations.

### Implementation of the APOL1 testing programme into clinical practice

Assessment of determinants is focused on the inner and outer context variables of the Consolidated Framework for Implementation Research (CFIR).86 Implementation evaluation follows the RE-AIM evaluation framework (table 3).87–90 We will also test changes in knowledge and self-efficacy for genetic counselling among nephrologists as a hypothesised mechanism affecting their decision to adopt the APOL1 counselling component of the intervention.

### Determinants

We will conduct in-depth interviews91 92 with nephrologists about their perceived facilitators, barriers, organisational capacity and adaptations to the APOL1 testing programme using the CFIR interview guide (www.cfir-guide.org). Nephrologists will be interviewed before implementation, after implementation and before the implementation period ends. Interviews will be conducted in person or by phone by an experienced interviewer, last 30–45 min, and be audio-recorded.

### Acceptability, appropriateness, and feasibility

We will conduct brief phone surveys to assess LDs’ and nephrologists’ perceptions of the APOL1 testing and counselling programme using validated surveys93 and standard methods94 with LDs at T3 and T4. Nephrologists are surveyed after completing training but before enrolling LDs, after administering the APOL1 intervention for 2 months and after 1 year.

### Reach and adoption

We will calculate Reach using study enrolment data using continuous 3-month sampling periods to closely approximate LDs counselled at any given point. We will use non-linear growth modelling approaches to examine rate of change in reach over time. Reach is also the proportion of LDs who consent and give saliva samples out of LDs offered APOL1 testing. We expect to achieve an 80%
reach rate at the centre level. We will determine the representativeness of participants by comparing demographic characteristics between participants and non-participants. Adoption is the number and proportion of nephrologists who deliver genetic counselling to ≥1 enrolled participant. We will assess whether nephrologists vary in offering counselling based on LD and nephrologist factors using analysis of covariance (ANCOVA) and multiple regression. Reach and adoption rates will be compared across centres using analysis of variance (ANOVA) and within-nephrologist using multilevel modelling techniques.

Fidelity
The extent to which the APOL1 testing programme is delivered as intended will be assessed by: (1) nephrologist adherence to prescribed counselling behaviours and (2) adherence to the chatbot strategy. Because counselling occurs by telephone, research staff will be present to audio-record discussions, and thereafter listen to a random sample (50%) of sessions (in the control and intervention arms) using a standardised observer checklist to document and evaluate the observed delivery and quality of prescribed counselling behaviours to generate a fidelity score. We will compare fidelity across nephrologists (ANCOVA), across centres (ANOVA) and across time to test for drift (non-linear mixed model with time by nephrologist interaction). We will evaluate improvement in nephrologists' counselling skills by comparing the fidelity between nephrologists counselling LDs in the control versus intervention arms, and by nephrologist sex/gender, using correlations and regressions. Few studies examine adaptations to interventions, which can affect fidelity. We will track types of and reasons for adaptations using Stirman’s FRAME (Framework for Reporting Adaptations and Modifications-Enhanced) via interviews with nephrologists as our team has done previously. Chatbot fidelity metrics will include: number of LDs who launched the chatbot ≥1 time, number of questions asked or information requests submitted and duration (minutes) of chatbot use. We will assess whether the effects of the intervention (ie, LDs' reduced decisional conflict, increased preparation) vary as a function of fidelity to the intervention (ie, nephrologist and chatbot metrics) using ANCOVA. We will treat EHR integration

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<th>Table 3</th>
<th>Measurement strategy for implementation outcomes</th>
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<td>Variable/construct</td>
<td>Measure(s)/metrics</td>
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<td>RE-AIM Implementation Evaluation Framework</td>
<td>Reach</td>
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<td>Effectiveness (of the APOL1 intervention)</td>
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<td>a. Acceptability</td>
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<td>b. Appropriateness</td>
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<td>c. Feasibility</td>
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<td>d. Fidelity</td>
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<td>Sustainment</td>
<td>Clinical Sustainability Assessment Tool seven domains (three items each) (Engaged Leadership and Staff; Engaged Stakeholders; Planning and Implementation; Workflow Integration; Monitoring and Evaluation; Organisational Context and Capacity; Outcomes and Effectiveness). It is reliable, usable and valid in a pilot study (n=126) with internal consistencies ranging from (α=0.82–.89).</td>
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APOL1, Apolipoprotein L1; EHR, electronic health record; LD, living donor.
as an independent variable that may affect the implementation process. Because EHR integration is designed to most proximally support nephrologist behaviours of engaging in post-test counselling and performing SDM, we will examine site-level differences in EHR integration to understand quantitative differences in nephrologist fidelity metrics.

**Sustainability**
At the end of the implementation period, all nephrologists will complete the Clinical Sustainability Assessment Tool to assess preferences and perceptions of factors influencing intervention sustainability. The seven domains (three items each) have good internal consistency ($\alpha$ range=0.84–0.92) and confirmatory factor analysis results demonstrated very good fit of the seven domain structure of the tool. The seven domains demonstrate very good fit of the seven domain structure of the tool. Increasing nephrologists’ knowledge and skills in APOL1 counselling

Increasing knowledge and self-efficacy in counselling skills is hypothesised to affect whether they adopt counselling, which will ultimately impact LDs’ outcomes. We will assess practical knowledge and self-efficacy before and after the APOL1 counselling training programme via a 13-item survey, widely used in other provider counselling training programmes; and surveys of beliefs about race (nine items) ($\alpha=0.61–0.69$), attributes of race (eight items) ($\alpha=0.86$) and genetic variation knowledge (eight items). $H_0$ will be analysed by evaluating increases in practical knowledge and self-efficacy via a Wilcoxon signed-rank test to compare the survey scores on the pretest to the survey scores on the post-test. Due to sample size limitations, we will examine the relationship between changes in knowledge and skill with adoption in a separate analysis, rather than a formal test of mediation, to obtain parameter estimates to power a future study of this mechanistic path.

**Qualitative data analysis**
All audio-recorded focus groups (aim 1) and interviews (aim 2 and aim 3) will be transcribed and analysed for themes emergent from the data using constant comparison and inductive and deductive coding methods. Initial codebooks will be developed by establishing deductive codes derived from moderator and interview guide questions. Through an iterative, constant comparative process, research staff will derive inductive codes emergent from the data to stay grounded in the respondent’s point of view by independently reviewing, comparing and openly coding the first set of five transcripts at each site. A series of retreats will be held, whereby staff will compare codes and resolve coding discrepancies in order to refine the codebook until reaching thematic saturation. All transcripts will be independently coded using NVivo (QSR International) until reaching inter-rater reliability (Kappa >0.80). Thereafter, all transcripts will be independently coded by at least two research staff and any discrepancies in coding will be resolved through discussion. A summary of each theme will be written by reviewing and comparing all segments of text for a given code across participants/focus groups. Multiple coders and intercoder agreement checks will increase rigour and reliability of the codebook. Qualitative data analysis software will aid in coding. We will increase the rigour and reproducibility of qualitative findings via: intermittent member checks with focus group (FG) participants, CAB members and nephrologists to obtain their feedback and verify accuracy of findings, thereby increasing credibility. Using thick description and an audit trail will increase dependability and transferability. Self-reflexivity and triangulation will increase confirmability. Results from aim 2 and aim 3 interviews will be used to understand implementation processes and help contextualise aim 3 quantitative results.

**CURRENT STATUS AND PROTOCOL MODIFICATIONS**
To date, we completed adaptation of the Gia chatbot, which involved conducting n=10 focus groups. We also completed adaptation of the APOL1 counselling training programme and obtained approvals to provide Continuing Medical Education and Maintenance of Certification (MOC) credits to nephrologists partaking in the programme, which is anticipated to begin in July 2022. We began recruitment in September 2021 for the LD trial, and as of 13 May, we have obtained informed consent and enrolled n=60 LDs of African ancestry in the control arm. Despite a year of concerted meetings and efforts to identify ways to automate the integration of APOL1 genetic test results directly into Epic, Epic policies pertaining to research and resource limitations at the laboratory prohibited this from occurring, requiring the uploading of faxed results by clinical staff. This change did not impact the research plan as transplant nephrologists still had a mechanism to review results in Epic. We made several protocol modifications since study inception. With regard to the chatbot, we designed Gia in English but not in Spanish given additional costs involved. Also, per focus group feedback to ensure ample time to complete it prior to the nephrologist visit, Gia would be delivered over 7–12 min rather than 5–7 min, as originally anticipated. We also adapted the educational brochure on APOL1 for nephrologists to hand out to LDs based on updated empirical research and CAB feedback, which is available by request to the corresponding author. The APOL1 counselling training programme did not undergo focus group evaluation because needs assessment interviews and team consultation sufficed to finalise programme content and format, as proposed. However, focus groups were conducted among nephrologists to assess their clinical decision support needs for optimal EHR integration. Regarding recruitment modifications, recruitment shifted to virtual then hybrid (virtual and in-person) at one site (Georgetown). Additionally, recruitment was slower than anticipated due to COVID-19, hiring delays, adapting the recruitment and implementation strategies...
to virtual recruitment, and IRB and contractual delays. Thus, the timeframe for launching the control arm was delayed by 2 months (Northwestern) and 5 months (Georgetown), and the intervention arm was delayed by 2 months (both sites).

Regarding data collection modifications, both nephrologist pretest and post-test counselling discussions with LDs are recorded for LD participants in the control and intervention arms to enable a direct comparison between them due to using an identical assessment strategy. Research staff provided nephrologists a digital recorder to record nephrologist counselling discussions with LDs, rather than observing discussions in person. We adapted the observer checklist to be tailored to the study aims for fidelity monitoring purposes. Additional survey measures are being collected at all time points (eg, Generalised Anxiety Disorder 7-Item), and current measures are being collected at additional time points for additional situations for both arms. For example, we added Preparedness to Donate at all time points, the Preparation for Decision Making Scale is no longer asked at T1, but asked at T2, T3 and T4, and The Shared Decision-Making Questionnaire is being asked at T2 and T4 in addition to T3.

DISCUSSION

The results of this study will serve as a model for implementing genetic testing and counselling that improves the informed consent of living kidney donor candidates of African ancestry who are at risk of having two APOL1 risk variants. Because APOL1 risk variants increase LD candidates’ risks of kidney failure post-donation, clinical practice guidelines recommend engaging in counselling, and many ethicists have argued that it is unethical to not inform donor candidates about their risks. Thus, it is essential that LD candidates of African ancestry receive culturally and ethically sound counselling to ensure that they make informed treatment decisions about donating. Ensuring that transplant counselling practices are culturally and ethically sound is especially important because transplant programmes currently vary on their use of counselling and SDM for LD candidates who underwent APOL1 genetic testing.

The model of integration of genetic testing and counselling in this study will be available for dissemination to other transplant programmes in the USA to improve informed decision-making for LD candidates and, thus, foster greater safety in the donation process. Specifically, this will demonstrate an effective strategy for how to scale up genetic counselling services through the use of chatbots to deliver foundational information and training nephrologists to deliver components of genetic counselling and SDM. Furthermore, this model will be important for demonstrating how to integrate genetic test results into the EHR to enhance streamlined clinical decision support for physicians.

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Supplemental File 1

Description and Supporting Evidence for the Primary Implementation Strategies

**Academic-community partnerships.** Community engagement refers to “the process of working collaboratively with groups of people who are affiliated by geographic proximity, special interests, or similar situations with respect to issues affecting their well-being”(1). Community engagement will help integrate APOL1 testing in a socially sound manner(2). Guided by best practices in community-engaged research, including building trust, equity, respect, and capacity-building(1, 3), study investigators will enlist the expertise of community members via our Community Advisory Board (CAB) across all study aims to improve outcomes(4).

**Community Advisory Board (CAB).** A CAB was established in March 2020 to prepare for and collaborate on the study. We will convene the CAB monthly in Year 1 to provide feedback on: study design, enrollment, consent, and data collection procedures; genetic counseling content domains; and SDM approach. The CAB will also ensure that the content, expression, tone, and delivery of the chatbot information and nephrologist counseling address both ‘surface’ (i.e., images of cultural expression, photos, colors) and ‘deep’ (i.e., values, beliefs, language shared by group members) cultural structures to increase receptivity to APOL1 counseling by LDs of African ancestry(5). The CAB will convene quarterly in Years 2-5 to provide input on study recruitment and retention, interpret early data, and troubleshoot data collection challenges.

**Engage patients.** Focus groups will be conducted in 3 iterative phases of user-centered design to iteratively gather end-user preferences(6) on nephrologist counseling and chatbot wireframes, content, design, and functionality, and on whether the counseling is informative and culturally sensitive (Year 1)(7). They will assess ways to minimize the possibility of “racializing medicine” in how nephrologists counsel APOL1 test results in a socially conscious manner. Ten focus groups will be conducted, each with ~8 African ancestry community members for 120 minutes. Focus groups will be led by experienced moderators using a moderator’s guide (see Supplemental File 2), as research staff take field notes(8). They will be audio-recorded. A demographic survey will be administered at the end of focus groups.

**Chatbot.** Chatbots, a conversational agent, is a form of artificial intelligence (AI)-driven service delivery that uses text- or voice-based recognition “software designed to simulate human conversation”(9) (Figure S1). Through AI technology, natural language processing, chatbots can assess the user’s language to predict requested information and provide basic genetic information. The use of chatbots is feasible and effective in increasing knowledge of and satisfaction with decisions about genetic testing(10, 11), informed decision-making(10), and other topics(12-18). Chatbots perform information-giving responsibilities of the few genetic counselors in the US(19). Thus, chatbots can relieve constraints on clinicians’ time so they can focus on interpreting genetic test results for patients and guiding decision-making(9, 20). Patients report a 4.6 out of 5 in satisfaction rating, and 80%-85% comprehension rating for

![Figure S1. Screenshot of the Gia "chatbot"](image-url)
chatbots related to genetic results(21). A limitation of prior studies is that chatbots were
designed for the end user rather than with the end user(22). The proposed study will overcome
this shortcoming by adapting a chatbot for end users via engagement with the community of
people of African ancestry.

Invitae, a medical genetics company, offers a widely used HIPAA compliant, SOC-2
certified clinical chatbot called “Gia” (Genetic Information Assistant), that can be adapted to any
condition. Our prior work(23) identified the information needed on **APOL1** by LDs’ of African
ancestry and will inform tailoring Gia to APOL1(24). Gia will provide pre-test information about:
what **APOL1** is, why **APOL1** genetic testing is being offered, and its relevance to living donation
outcomes. The research team will refine Gia via community and scientific team engagement.
Invitae will refine content and delivery mode via cognitive interviewing and usability testing, and
survey administration. Several studies examined chatbot use in men and women of African
ancestry, demonstrating acceptability and efficacy(10, 12, 14, 16, 25, 26).

**Educate and train transplant nephrologists.** In a national survey of n=383 transplant
physicians (R03 AI126090-01): most believed that **APOL1** testing can help LDs of African
ancestry make more informed donation decisions (87%), and using **APOL1** testing offers better
clinical information about their eligibility for donation than existing evaluation approaches
(74%)(27). However, most (59%) did not know the right clinical scenario to order **APOL1** testing,
few (44%) knew how to interpret **APOL1** test results, and fewer (38%) felt prepared to counsel
LD candidates about the risks and benefits of **APOL1** genetic testing. Most (97%) would use
educational materials to counsel LDs of African ancestry about **APOL1** testing. These findings
suggest that nephrologists value **APOL1** testing, and need guidance on how to counsel LDs in
clinical practice. We will adapt NHGRI’s Inter-Society Coordinating Committee’s framework for
developing physician competencies in genomic medicine (i.e., “use genomic testing to guide
patient management” and “use genomic information to make treatment decisions”) to expedite
integrating genetic counseling into transplant practice(28), and adapt genetic counseling
provider education programs(29) to the **APOL1** context.

**APOL1 Counseling Training Program:**
1. An assessment using brief open- and closed-ended interviews by phone will be conducted
   of nephrologists’ information needs about **APOL1** and preferred format and content of the
   training program (e.g., webinar, in-person, etc.). Standardizing the **APOL1** counseling
   training program will support its scalability to other transplant centers(21).
2. Nephrologists will be trained in **APOL1** counseling by genetic counselors, nephrologists,
   an ethicist, and a cardiovascular health expert. Training will cover practical knowledge
   (“know how”) and counseling skills outlined in Table 1, including SDM as physicians lack
   training in SDM(30, 31). Content will derive partly from our prior work identifying
   nephrologists’ knowledge and counseling skill deficits on **APOL1**(27) and on the
   information needs of LDs of African ancestry and the members of their community(23, 32,
   33).
3. The **APOL1** Counseling Training Program content and format will be vetted by the
   scientific advisory board and other members of the study team.
4. The **APOL1** Counseling Training Program will be delivered in the preferred format, through
   a series of voice-over PowerPoint presentations and a case study video discussion.
5. Each presentation will be led by a member of the study team with expertise in the given
   topics (i.e., transplant nephrologist, racial equity, ethics, genetic counseling). Each
   presentation will briefly present current empirical data on **APOL1** and its relationship to
   chronic kidney disease, living donation, and health disparities. Additionally, each
   presentation will deliberately incorporate considerations of how **APOL1** raises concerns
   about health inequities, and provide ways to model culturally appropriate ways to
   communicate with potential living donors of African ancestry about **APOL1** testing and

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donation. Weaving in a health equity lens throughout each presentation will reinforce learning about ways to deliver culturally competent care in the context of evaluating potential living donors of African ancestry.

6. The case study will discuss a clinical scenario and model shared decision-making strategies and phrases that transplant nephrologists can use with a potential living donor about APOL1 testing and donation.

7. The Counseling Training Program will be CME and MOC accredited as an incentive to complete the training. It is important to note that this change in protocol early in the study comprises an additional implementation strategy to increase the likelihood of participation.

References Cited


Supplemental File 2

Study 1: Community Member Focus Group Moderator's Guide

**Introduction/Background [10-15 minutes]**

*Show Welcome Slide* Introduction

My name is [state name] and I am a [state title] working at Northwestern University. Today, I'll be guiding the discussion with you, and it will last about 90 minutes. I am also accompanied by my research colleagues, Dr. Elisa Gordon and Jessica Gacki-Smith.

*Show About the Study Slide* Focus of Discussion:

Before we get started, I'm going to share some important information for our discussion today. As you know, living kidney donation is a generous act. New studies show that living kidney donors have a higher chance of getting kidney failure than healthy people who did not donate. And, African American living donors have an even higher chance of getting kidney failure than White living donors. Some scientists think there is a genetic basis to this finding.

That's because there is a genetic basis to getting some kidney diseases. All people have a gene called APOL1. People are more likely to get kidney disease if they have 2 changes to the APOL1 gene, called 'gene variants'. African Americans are much more likely to have 2 APOL1 gene variants than are Whites. That's why African Americans are 4 times more likely to have kidney disease than are Whites.

Preliminary studies show that living donors with 2 APOL1 gene variants are more likely to get kidney failure after donating. This means that living donors with 2 APOL1 gene variants may have a higher risk of getting kidney failure.

Any questions?

Just because people have the 2 APOL1 gene variants does not mean that they will get kidney disease. So, scientists believe that the act of removing a kidney could be an environmental trigger that sets off kidney disease.

Transplant doctors are now being extra cautious and offering a genetic test to African American living donor candidates to find out if they have 2 APOL1 gene variants. Doctors want to be sure that African American donors make an informed decision about donating, by having more personalized information about their risks and benefits of donating.

Any questions?

*Go through the next sections quickly* Purpose of the Focus Group:

Now, that brings me to our study. Our study goal is to give APOL1 testing to all African American living donor candidates to help them make informed decisions about donating. Any time you get a genetic test, then someone needs to give you information about it and counsel you about the results.

We developed a [first draft/second draft/beta draft] of 2 new educational materials that give information and counsel living donor candidates about APOL1 to help donors make informed decisions about donating.
Today, we would like your input on improving these materials:

1) First, is a chatbot. It is a form of artificial intelligence that uses text-based recognition software to simulate human conversation. A chatbot is delivered using a smartphone app. We are using a chatbot called “Gia” in this study to give information to live donor candidates about APOL1 genetic testing.

2) Second, we prepared information that a transplant doctor can use to counsel a live donor candidate about their APOL1 genetic test results.
Before we get started, let's go over some ground rules:
I ask of you that:
- First, we are interested in your opinions.
- Next, we are here to learn from you. You are the expert on these topics.
- Only one person speak at a time
- When you start to talk, please state your name
- Everyone participate with no one dominating
- Give details and examples.
- Say why you agree or disagree with another person’s responses
- If you do not understand any question, please let me know and I will rephrase it.
- We are audio-recording the discussion so that we can remember what you said. Only the research staff will listen to the recordings.
- After the discussion ends, I'll ask you to fill out a brief survey about your views of the discussion. This will be an online survey that you can access with the link I will send to you via email. When you're done with that, we will compensate you for your time.

Participant Introductions:
Let’s now go around the room and introduce ourselves. Please tell us your name and share something about yourself. [Call each person by name and ask them to introduce themselves]

Now let’s start
We’re going to start by sharing the link to the Gia chat so that everyone can try it out right now. The link to the chat is pasted in the Zoom chat. Please click the link and take about 5 or so minutes to run through it now. After everyone is done, we’ll have a discussion about it.

What do you see on the screen when you click the link?
[Wait 7 minutes while everyone reviews Gia chat]

Okay, we’re going to start up our discussion now. I want to find out from everyone, how far did you get in the Gia chat? What is the last thing you saw?

What did you think?
What worked well/what didn’t work well?
What do you think of the way Gia looks? How can we improve the way it looks?
- color, images, text font, what “Gia” looks like

What did you like/what did you not like about your experience with the chat?

What did you think of the onboarding instructions at the beginning?
Was it obvious where the menu was located?
- Should it say “Menu”, or should we specify in the chat that it is at the top left corner?
How can we make these instructions clearer?
Now, we want to get your feedback on specific language and sections of the chat. I am going to share my screen and we will go through the Gia chat together. As we go through the chat, reflect on the time when you were being evaluated as a living donor. Keep in mind, we will be showing this chat to potential living donors before they visit the Nephrologist.

**GO THROUGH CHATBOT ON SCREEN (30 minutes)**

**Questions to Ask During the Chat Review:**

13 out of every 100 (13%) people who identify as Black or African American have 2 APO\(L\)\(1\) risk variants.

Donor candidates with African ancestry are asked to do the APO\(L\)\(1\) genetic test because of their increased chances of having APO\(L\)\(1\) risk variants and getting kidney disease.

Do people who do not identify as Black or African American have these APO\(L\)\(1\) risk variants?

What do you think of having 3 response options here?

Our transplant team asks donor candidates what their ancestry is to personalize the evaluation process and the care that the team provides to each donor candidate.

For example, when evaluating kidney donor candidates, the transplant team sometimes runs tests based on the donor’s family history of kidney disease.

To find out about a donor’s family history, the team has traditionally asked the donor. But now, the team can get additional, personalized information by doing genetic testing.

The transplant team can find out if donors have APO\(L\)\(1\) risk variants through the

Should we keep this section?
What do you think of the phrasing?

**Donors who identify as Black or African American have higher chances of getting kidney disease after donating than donors who identify as White.**

- **Sure!**

- **Nearly 75 out of 10,000 Black African American living donors are estimated to get kidney disease 15 years after donating.**

- **By comparison, 23 out of 10,000 White living donors are estimated to get kidney disease 15 years after donating.**

- **Black African American living donors have a 3 times greater chance of getting kidney disease after donating than White living donors.**

- **However, it's important to remember that the chance of getting kidney disease is still quite small.**

- **Even 75 out of 10,000 is 0.75% (less than 1%).**

**What do you think of the way this is phrased?**

**Your test results will be shared with you, your transplant team, the genetic testing lab, and with authorized research personnel only.**

- **All genetic test results, like your other test results, are kept private in your medical records.**

- **There is a law called GINA (Genetic Information Nondiscrimination Act) that protects patients against discrimination based on genetic information.**

- **GINA helps protect against discrimination by health insurance providers and employers.**

**What do you think of this clarification of who the research personnel refers to: One solution is to do a tool tip over 'research personnel' that states something like: “This is the person who asked for your informed consent for this study, the Principal investigator of the study, and other staff working to collect and analyze study data.”**

**The section above mentions “authorized research personnel”.**

- **Who comes to mind when you hear that?**

- **How does that statement make you feel?**

**To clarify who 'research personnel' refers to, a box pops up when you hover over the phrase with the following description:**

- **“This is the person who asked for your informed consent for this study, as well as the Principal investigator of the study, and other staff working to collect and analyze study data.”**

- **What do you think of this language? Does it help to allay any concerns/answer questions?**

- **How do you feel about the sharing of your test results with these people?**
Would this phrasing encourage donors to complete the APOL1 testing NOW, as opposed to LATER?

- Is knowing who pays for this genetic test necessary?
- Should we add that the test is free and does not go through the donor’s insurance?
- Is this the correct location for this information?

What do you think of this sentence about HIPAA?

- Is the hover-over definition adequate?
- Alternatively, we can replace it with, “the law says we cannot share personal information” – would this be better?
  - Should we put this phrase in place of the term HIPAA?

How do you feel about Gia making this comparison between Black/AA and Latinx or White?
• Should we include statistics for Asian people here also? Is that needed?

Thank you very much for considering donating the gift of life.
The transplant team's goal is to make sure that living kidney donation is safe for each donor.

Is the first sentence in the right place of the chat?

All people have 2 copies of the APOL1 gene. One is passed down from each biological parent.

People can have different versions of the APOL1 gene. We call these variants.

Variants can result in things like different eye colors. Variants are part of what makes each person unique. Sometimes a variant of a gene can be associated with health issues, but many variants have no impact on health.

People with two of these risk variants have a higher chance of getting kidney disease than people without these risk variants.

Is this definition of ‘variant’ clear?

APOL1 risk variants are most commonly found in people with African ancestry, like Blacks/African Americans, Caribbeans, and Central/South Americans.

Is Afro-Caribbean the correct term to use here?

Sure!

Nearly 75 out of 10,000 Black/African American living donors are estimated to get kidney disease 15 years after donating.

By comparison, 23 out of 10,000 White living donors are estimated to get kidney disease 15 years after donating.

It’s important to remember that there is still a chance of getting kidney disease.
Is the last sentence worth keeping? Should we convey that the risk is low?

The APOL1 genetic test is easy to complete.

APOL1 genetic test is done by taking a saliva sample. This means spitting into a tube that gets sent to a laboratory.

If you choose to get the APOL1 test, the saliva sample will be collected after your kidney doctor visit. A research staff member will assist you.

Is this the correct location for this information?

One of these tests looks at a gene called Apolipoprotein L1 or ‘APOL1’, which is known to be related to kidney health.

APOL1 genetic testing is a new way for the transplant team to evaluate a donor’s future chances of getting kidney disease.

You will be having a lot of discussions during your donor evaluation about the risks related to donating.

In this chat, we're mostly focused on APOL1.

That makes sense Can you remind me how genes work?

- How do you feel about the word “risks” compared to pros and cons?

Why do APOL1 risk variants occur mostly in people with African ancestry?

The APOL1 risk variants evolved about four thousand years ago in Sub-Saharan Africa to protect against sleeping sickness.

Thanks, I got it

- Does the response “The APOL1 risk variants evolved and so on...” answer the question about why APOL1 risk variants occur mostly in people with African ancestry?
- Does the hover-over description about sleeping sickness help answer the question?
  - Hover-over: “Sleeping sickness is an infectious disease typically found in Sub-Saharan Africa that is transmitted by the tsetse fly. Infected individuals experience fever, headaches, extreme fatigue, neurological symptoms, and other problems.”

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Do this hover-over sentence provide enough information?
  - Is this a feature you noticed as you went through the chat on your own?
  - How can we make this hover-over feature more noticeable?
- What else can we do to do a better job answering this question?

Sure!

Nearly 75 out of 10,000 Black/African American living donors are estimated to get kidney disease 15 years after donating.

By comparison, 23 out of 10,000 White living donors are estimated to get kidney disease 15 years after donating.

Thanks, I got it

- Do you like the first word, “Sure!”?
- How do you feel about the use of the exclamation mark in this context?
- What suggestions do you have for other responses that could be used in place of “Sure!”?
- Do you prefer the phrase “Sure, I'm happy to” more?

I know we went through a lot of information together.

If you would like a copy of this conversation, just enter your email address below.

name@domain.com

Submit Skip

- [Do round robin] Would you want to email yourself the chat script?
- Do you think we should include a message at the beginning of the chat to let people know that this email function is available?
- Should we add this sentence: “Would you like me to include some resources in the email along with the transcript?”
The chance that someone in the general population with 2 \textit{APOL}1 risk variants will get kidney disease in their lifetime is up to 20\% (or up to 20 people out of 100 people).

However, most people who have 2 \textit{APOL}1 risk variants DO NOT develop kidney disease.

- For this statistic, would it help to provide a comparison like: “By comparison, people have a 1 out of xxx chance of dying from \textit{xyz}”

Sometimes a certain version of a gene can be associated with health issues.

For example, if a person has a version of a gene that is associated with kidney health, then their chance of having kidney disease may increase.

This brings us back to our discussion of \textit{APOL}1.

- Some previous focus group participants were concerned that the current response option may not fit the tone of Gia, given the serious nature of the information presented. Looking at the text in this section, what do you think of this response option?
  - Does the response option fit the tone of the information Gia presents?
  - Should we change it to “Alright, let’s move on” or “Alright, let’s continue”?  

People with two of these risk variants have a higher chance of getting kidney disease than people without these risk variants.

- How does this statement make you feel?
IRB #: STU00214038-MOD0010 Approved by NU IRB for use on or after 8/4/2021

- What do you think of the highlighted sentence?
- Do you like this instruction? Is it helpful?
- Did you notice this as you began the chat?
- Should we keep this?

- How can we make the questions and answers clearer?
- What other questions should we add to this list?
- Are there any we should cut?
- Would you prefer being able to select one question at a time, or would you prefer to select multiple questions at once and seeing all of the answers together?
- Here is another question: “If I have 2 APOL1 risk variants, what is the likelihood that my child will also have 2 risk variants?” Do you think we should add this?
- Another question is, “Who is responsible for my post-transplant care?” Should we add this question?
- Should we add this question, “Will my results disqualify me from donating?”
- Should we add a brief statement saying that users can go through all the questions and not just one?
- “Does APOL1 testing happen before the other evaluation testing?” Is this something you would want to know?
Before we finish, I'll give you some links to helpful information you might want to check out after your appointment.

Here is a link to read more about GINA: [https://www.eopc.gov/genetic-information-discrimination](https://www.eopc.gov/genetic-information-discrimination)

And here are some links to learn more about kidney disease, living donation, and maintaining health as a living kidney donor:

- [https://www.kidney.org/](https://www.kidney.org/)

If you would like a copy of this conversation, just enter your email address below.

![Email Address Form]

- Based on feedback from earlier focus groups, we added website links so that users could get access to additional information. What other topics would you want us to provide links to? That is, what topics from the chat would you like to know more about?
  - What additional resources would you like to see here?
  - Would you want a link to see video testimonies of other living donors?
    - Would you prefer to see testimonies of African American living donors?
QUESTION GUIDE: CHATBOT [30 minutes]

Appearance [3 minutes]
First, let’s talk about the way Gia looks.

- What do you think of the way Gia looks?
  - color, images, text font, what “Gia” looks like
- How can we improve the way it looks?

[Show GIA Avatars – Slide]
- We are working to make Gia look more like the people who will be using the chat. We have four different options in the way that the face of Gia can look. Which one do each of you prefer?
  - What improvements would you make?

Design & Functionality [5 minutes]
Now, let’s talk about Gia’s design and how it functions.

- What do you think of the way you interact with Gia?
  - How can we improve the way you interact with it to make it easier?
  - What was confusing in the way the chat works?
- What do you think about the phrases or words used on the buttons at the bottom of the screen during the chat?
  - Are the responses ‘Okay’ and ‘Got it’ fine?
  - Are there other words that would work better?
  - Would words like ‘Next’ or ‘Continue’ be better?
- What do you think of the default font size?
- As you can tell, the information is presented kind of like a branching tree. There’s the main pathway and sometimes 2 response options are provided: one to continue on the main pathway, and one if you want more information on a subject. After you finish reading about the additional information, you’re put back on the main pathway. What do you think about that design?
- Should we use “kidney doctor (nephrologist)” throughout? Or just one of those terms? Which term?

[Show Slide] Looking back at this section describing GINA, should we add information about the penalties for violating GINA?
  - For example, we could add a sentence like, “If someone violates GINA, they could be forced to pay a fine ranging from $2,500 to $500,000 per incident.”
  - In this sentence, is “protects” the right word to underline for the tooltip, or is there another word that would be better?
    - There is a law called GINA (Genetic Information Nondiscrimination Act) that protects patients against discrimination by health insurance providers and employers based on genetic information. Fines for violating GINA range from $2,500–$500,000.

[Show Slide] Here are 3 statistics:
  1. “In 2021, 465 Black/African American people donated a kidney, representing
7.8% of all living kidney donors nationally.
2. “In 2021, 777 Black/African American patients received a living donor kidney transplant, representing 2.8% of all Black/African American patients on the waiting list.
3. “28,251 Black/African Americans are waiting for a kidney transplant, as of January 16, 2022.”

- Which of these statistics are important to know? Which is the most important? Which is the least important?
- Where do they belong in Gia? Either:• In the Q&A section at the bottom of the chat?
• Or in the resources section, e.g., “Statistics about AA kidney patients and living donors”
• Or, as a hover over in the body of the chat?
- In the question/answer section at the end of the chat, we are planning to develop additional questions and include these statistics as the answers.
  - Should we keep these statistics in the question/answer section of Gia?
  - Do you find this information helpful to know?

- Should we put the Gia avatar in the body of the chat? If so, where? (the icon would remain on the top of the chat as well)
  - How many times would you like to see the avatar in the chat?

- [Show Slide] Do you think potential donors should be given this information? Would this information scare them from donating?
  - Will I get chronic kidney disease if I donate with 2 APOL1 gene variants?
    - You can have 2 APOL1 gene variants, but still not get chronic kidney disease.
    - Environmental factors, along with having the 2 gene variants, may trigger chronic kidney disease.
    - Living kidney donors have a higher chance of getting chronic kidney disease than healthy non-donors.
    - Black/African American living donors have an even higher chance of getting chronic kidney disease than White living donors. APOL1 gene variants may contribute to Black/African Americans’ higher chance.
    - Early research on APOL1 gene variants in living donors suggests that having 2 APOL1 gene variants increases living donors’ chances of getting chronic kidney disease after donating.
    - Black/African American living donors with 2 APOL1 gene variants had worse kidney function than those with 1 or 0 gene variant on average 12 years after donating.

- [Show Slide] We have two options in the way that we can set up Gia. The first is having a set of questions that most people are likely to ask along with their answers. This is how the chat is currently set up. The second option is to allow people to type in their own questions. There are pros and cons to each option:
  - With the pre-selected questions, that makes it easier for users to know what to
ask but your own question might not be there,
  o With the option of typing in your question, you get to ask your own question, but Gia might not recognize your question, and that might make the user frustrated.
  o Which option would you prefer?

**Educational Materials: Content [5 minutes]**

*OK, now, let’s talk about the information included in Gia.*

- Would it help if the chat included links to the article references, evidence-based resources, and other trusted sources at the end of the chat?
  - This way, the user can know where the information in the chat came from and also know where to get more info if they want it?
- Did the information come across as scary or worrisome?
- For future focus groups, do you think people should use a smartphone to test Gia during the focus group? Or was it fine going through the chat together on the screen?
- Do you think the order of information presented in the chat is correct? What suggestions do you have to make the flow more logical?
- What information could we cut from Gia to make it shorter?

**Cultural Competency [10 minutes]**

*Now, let’s talk about how to make Gia more culturally competent by addressing African American’s values, beliefs.*

- How could we make Gia more culturally sensitive to African American perspectives?
- We are trying to move away from the concept of “race”, which is a social construct. Instead, we want to emphasize the genetic basis of the presence of APOL1 variants in the population.
  - Does the Gia content emphasize “race, when it should focus on genetics?
- How can Gia talk about APOL1 in a way that does not stigmatize the African American community?
- Many African Americans have reported concerns about undergoing genetic testing, such as a breach of confidentiality, and the information will be used to discriminate against them. What can we do to change Gia to allay such concerns?
- Many African Americans distrust doctors and the healthcare system because of a history of injustices in the way that they are treated in the health care arena. What can we change about Gia to increase African Americans’ trust in the healthcare system?
- What do you think of the green color of Gia’s responses? How can we make the color scheme more culturally sensitive?
- Would it be helpful to include statistics on the number of African American living kidney donors?
- How can we revise Gia to help African Americans’ feel more comfortable about...
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participating in medical research?

- Does Gia currently make stereotypes about African Americans? If yes, which stereotypes?
- Should Gia talk about any myths or stereotypes about African Americans and genetic testing? If yes, which myths or stereotypes should be addressed?
- Are there any symbols or phrases that should be added to Gia to make Gia more meaningful to African Americans?

**Using Gia**
*Let’s talk a bit about using a chatbot.*

- What do you think about living donors using Gia to get some basic information before talking to their transplant doctor?
- What barriers are there to using Gia in a healthcare setting?
- How would African Americans feel about using a chatbot like this?
  - The use of chatbots have been studied in other populations, but have not been tested among the African American community.
- After going through the entire chat, how did Gia make you feel about getting or not getting an APOL1 genetic test?
Gia-Specific questions [5 minutes]

1. [Show Slide #] [For Living Donor FGs]: Are the opening and closing phrases worded strongly enough to convey the appreciation to the potential donor?
   Opening: Thank you very much for considering donating the gift of life.
   Closing: And, thank you again for considering the heroic act of donating the gift of life.

If time permits:

2. [Show Slide] Which phrase do you like better:
   Gia: Keep in mind: like all tests, APOL1 genetic testing is voluntary
   Gia: Keep in mind: like all tests, APOL1 genetic testing is completely up to you.

3. Some people have suggested that we include a statement about the chance of getting kidney disease by having 1 APOL1 risk variant (in general, not after donating). The problem is that very little research on APOL1 has examined the risks of kidney disease by having 1 APOL1 risk variant. There isn't enough research to make any conclusion about it.
   - So, what should we do – leave out of the Gia chat this topic altogether? Or, should we include a brief discussion about how little is known about the risks of getting kidney disease by having 1 variant?
QUESTION GUIDE: TRANSPLANT DOCTOR COUNSELING CONTENT [10 minutes]

As a reminder, Gia will be given to potential donors before they meet with the Nephrologist. Part of our study involves training doctors on how to counsel donors in a culturally sensitive manner. Now, we would like your feedback on some of this Training Program content and how to make it better.

- Now that you’ve been through Gia, what do you think the conversation with the doctor might be like? Can you think of any questions you might have when meeting with the doctor?
  - Would it be helpful if Gia included a list of questions in the chat that you could ask your doctor?
- What phrases could a transplant doctor say to address the mistrust in the healthcare system that potential donors may have?
- Some African American living donors reported concerns that APOL1 genetic testing would be used to discriminate against or rule out African American donors – what phrases could a doctor use to address these concerns?
  - [Show Phrases Slide] We have developed some potential phrases for kidney doctors to use when counseling donors. Take a moment to read these.
    - Which phrases do you think are the best?
    - What are your favorites (for each slide)?
    - Which do you like/dislike?

What questions might people have about this study? – ask LDs this at the next FG

Conclusion [5 minutes]

We’ve got to wrap up our discussion in the next 5 minutes. [Do Round Robin for this section, calling on everyone]

I’d like to use this time to ask each of you two general questions:

1. Can you give me a final statement summarizing your thoughts and recommendations for the educational materials?

2. What do you think are the key takeaways for us to know from the discussion today?

This has been a great conversation. Thank you all so much for participating. [Staff] will now discuss the next steps with you.

[Staff]

As a reminder, please fill out the post-focus group survey online and then we will send you your e-gift card via email.

Before we hang up, we sent you the URL link to the post-focus group survey. Please confirm that you have received it before logging off. If you received it our discussion is complete. Have a great day!

If you have not yet received the URL link, please stay on the line while we help you to get it. Thank you!
Supplemental File 3

Power for Effectiveness Outcomes

All adult (age \( \geq 18 \) years), English-speaking (directed or non-directed) LD candidates with African ancestry who attend clinic evaluation will be recruited for study participation. In 2019, the number of AA LDs who attended the clinic visit was \(~40\) at NU and \(~60\) at GU. While the estimated participation rate based on prior research is \(86\%\)\(^{(1)}\), we anticipate being able to enroll at a slightly higher rate (\(\sim 90\%\)) given community engagement and culturally competent recruitment approaches\(^{(2-5)}\). Power estimations were based on assuming enrollment of 56 participants in the 10-month pre-implementation period and 240 in the post-implementation period for a total of 296. Our proposed sample size will provide 80-90\% power, with a two-sided type I error rate of 0.05, to detect differences in the mean decisional conflict scale (DCS) between arms ranging from 5.0 to 7.7, assuming standard deviations ranging from 12 to 14 (Table S1)\(^{(6)}\). Thus, our proposed sample size will provide adequate power to detect small to medium Cohen's D effect sizes\(^{(7)}\). As similar studies have observed even larger effects\(^{(8-10)}\), we anticipate seeing differences of at least this magnitude in our study. Power considerations were based on a simplified two-sample t-test; however, sample sizes were inflated upward by a factor of \((1/(1-R^2))\) for planned multivariable models, resulting in a necessary sample size of 370. We have assumed an \(R^2\) of 0.2, as an estimate of the square of the multiple correlation coefficient of the predictor of interest regressed on all other variables likely to be included in the model. Finally, we inflated our sample size to account for 5\% attrition\(^{(11-13)}\); thus, we plan to enroll a total of 74 participants in the control period and 316 in the intervention period. Of note, for \(H_3\) the proposed sample size will allow for construction of a confidence interval around the difference in the mean willingness to donate score with adequate precision to claim non-inferiority if the lower limit of the confidence interval does not intersect with the NI margin. We have assumed a confidence interval centered between 0 and -0.2, 90\% power, a one-sided type 1 error rate of 0.025, standard deviations of 2.6\(^{(14)}\) in both groups, and an NI margin of 1.5 units.

References Cited