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Beyond Consent: Building Trusting Relationships with Diverse Populations in Precision Medicine Research

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Abstract

With the growth of precision medicine research on health data and biospecimens, research institutions will need to build and maintain long-term, trusting relationships with patient-participants. While trust is important for all research relationships, the longitudinal nature of precision medicine research raises particular challenges for facilitating trust when the specifics of future studies are unknown. Based on focus groups with racially and ethnically diverse patients, we describe several factors that influence patient trust and potential institutional approaches to building trustworthiness. Drawing on these findings, we suggest several considerations for research institutions seeking to cultivate long-term, trusting relationships with patients: (1) address the role of history and experience on trust, (2) engage concerns about potential group harm, (3) address cultural values and communication barriers, and (4) integrate patient values and expectations into oversight and governance structures.

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Keywords

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Introduction: New challenges for precision medicine research

Precision medicine research represents a shift from local, disease-specific studies to large-scale, population-based research that links networked resources including biospecimens, electronic health record data, and self-reported consumer-based digital data. For example, the eMERGE network, initiated in 2007, links biospecimens and health data across a growing national consortium of medical research centers to support translational genomic research (eMERGE 2014). Building upon the success of programs and networks like eMERGE, the *All of Us* Research Program of the Precision Medicine Initiative was recently announced as a national effort to enroll a longitudinal cohort of patients representing a diverse cross-section of the U.S. population, whose information researchers will use to develop prevention and treatment strategies that take individual variability into account (Collins 2015; National Institutes of Health 2016).

Despite the potential of precision medicine research to improve disease prevention and treatment, and the widespread public support for the *All of Us* initiative (Kaufman et al. 2016), patients' perspectives on many of the key components of the precision medicine research enterprise—the translation of new discoveries from the "bench" into practice to improve health outcomes for individuals and populations (Khoury et al. 2007)—have received little attention. Historically, efforts to ensure research is conducted in an ethical manner have largely focused on enhancing patients' autonomy by encouraging them to take on the responsibility of deciding whether research participation is right for them, typically through robust informed consent processes. While promoting individual autonomy is important, institutional trustworthiness also plays an essential role in a responsible research enterprise. Trustworthiness is not only an intrinsic ethical value, but is also of instrumental value, in that it can increase research participation and improve the public's perception of research (Callier & Bonham 2015; O'Doherty et al. 2011; Yarborough et al. 2009). One approach to building institutional responsibility is through stewardship, which has been defined in the context of large-scale biobanking as "the responsible management of something entrusted to one's care" (Fullerton et al. 2010, 3). However, Henderson and colleagues (2013) found that while many biobanks engage in at least some stewardship activities, most could do more to facilitate trusting relationships with their participants.

As data collection and sharing increase in speed and scale, it will be important to understand patients' perspectives and preferences to provide more specific guidance to research enterprises about how they should meet their ongoing ethical responsibilities throughout the course of the research relationship, beyond honoring the terms of initial informed consent. In addition, the current lack of diversity among research participants presents a major challenge (Bustamante et al. 2011, Popejoy et al. 2016). Although the historical underrepresentation of certain groups in genomic research is well documented (James et al. 2008, Haga 2010, Ford

et al. 2006), understanding why some groups' participation rate are lower than others will be necessary for precision medicine research to achieve the goal of improving the health of all Americans.

Here, we present findings from a series of focus groups with a racially and ethnically diverse group of patients, in which we used trigger videos to prompt informed discussion about key ethical concepts for precision medicine research. Previous empirical studies of patient attitudes have largely focused on issues of informed consent, results disclosure, data sharing, and/or privacy (Hull et al. 2008; Fullerton et al. 2012; Jarvik et al. 2014; Lemke et al. 2010; Lemke et al. 2011; McGregor et al. 2013; Trinidad et al. 2012). Our study focuses instead on patients' values, expectations, and concerns at the institutional level for precision medicine research enterprises. Based on our findings, we offer several considerations for institutions as they strive to develop practices that take patient values into account and support long-term, trusting research relationships.

Methods

Overview

We conducted 20 focus groups with patients at a large multispecialty group practice organization in northern California who self-identified with one of five racial and ethnic groups, which were selected based on the demographics of the greater San Francisco Bay Area: African American, Chinese, Hispanic/Latino, non-Hispanic White, and South Asian. We held four focus groups with patients from each of the five racial and ethnic groups. Focus groups were conducted in English, with the exception of two Chinese groups conducted in Mandarin and two Hispanic/Latino groups conducted in Spanish. We obtained IRB approval from Sutter Health and Stanford University.

Development of trigger videos and the library metaphor

Recognizing that patients may be unfamiliar with many of the concepts we wished to discuss in our focus groups, we worked with Booster Shot Media, a health communications media company, to develop a series of six whiteboard-animated videos, approximately 2-to-3 minutes each, to describe the concept and process of precision medicine research on health data and biospecimens. Here, we briefly describe the video development process, which is described in detail elsewhere (omitted for review).

To aid in developing our videos, we conducted two initial focus groups with patient representatives from the same health system from which we later recruited for our study focus groups. We asked patient representatives for their reactions to the term "biobank," which elicited confusion from some patients and a variety of analogies from others, including financial banks and gold mines. Because these interpretations are potentially misleading about the purpose of precision medicine research, we sought alternative terminology to effectively convey this information to patients. Collaboratively with Booster Shot Media, we identified the metaphor of a "library of medical information" to depict the integration of health record data and biospecimens in research. Features of libraries that we believed would make this metaphor effective included: (a) libraries store and share

information and knowledge for research, (b) libraries are a public good, (c) community members may voluntarily contribute resources to libraries, (d) librarians control access to the resources stored in a library, and (e) individuals may have their privileges revoked if they misuse the library's resources. In a series of pilot focus groups with patients from each of the five racial and ethnic groups in our study, we asked patients to respond specifically to the library metaphor, which confirmed that this metaphor was effective and understandable. While the library metaphor may, like metaphor of a "biobank," be open to varied interpretations, our pilot focus groups suggested that this term evoked minimal biases and effectively conveyed basic information about precision medicine research.

In these pilot focus groups and through an iterative process of storyboard drafting and research team review, we obtained feedback on preliminary storyboards and draft versions of the videos. Based on the feedback received, we revised and finalized the English versions of the videos.[1] We subsequently translated the English videos into Mandarin (with written text in Chinese) and Spanish in consultation with native speakers of each language. All written information in the videos was translated and voiceovers were re-recorded by native speakers. Prior to finalizing the translated videos, we cognitively interviewed patient representatives in Mandarin and Spanish to evaluate their effectiveness for helping participants understand key processes, concepts, and mechanisms in the precision medicine enterprise. The final videos explained six topics: (1) precision medicine biobanking as a new model for research, (2) the concept of the library of medical information, (3) the value of the library for precision medicine, (4) privacy and security, (5) information disclosure and consent, and (6) oversight and patient communication. The videos are available at http://boostershot.net/values.

Focus group recruitment

We identified patients based on electronic health record review, using the following inclusion criteria: age 18 or older; seen in a clinic within the previous 24 months; English, Mandarin, or Spanish-speaking; and with self-reported race or ethnicity of (a) African American, (b) Chinese, Chinese American, or other Chinese-speaking ethnicity, (c) Hispanic, Latino, or other Spanish-speaking ethnicity, (d) non-Hispanic White, or (e) South Asian. Patients were randomly selected within each of the five racial and ethnic groups, with a goal of achieving age and gender balance within each group. We also contacted participants who had previously indicated their willingness to participate in focus group studies, and flyers were posted in clinics and patients were able to self-refer (e.g., a spouse of an identified patient). These recruitment methods were used to ensure that we reached sufficient numbers of participants in underrepresented racial and ethnic groups and across a range of ages, based on our prior experience recruiting patients in this health system. Research staff sent a letter and email (if address was available) to identified patients describing the study and inviting them to participate, including a reply card to opt in or out to receive more information. Staff followed up with those patients who did not reply and, if

[1]For example, we attempted to address a common misconception that doctors were using the library directly to guide patient care by creating a series of images showing temporal and physical separation between the collection of samples and data, research on samples and data, and doctors learning about research findings. We also changed the narrator from a doctor character, which was contributing to conflation of research and clinical care, or a patient character, which was perceived as less effective because of a lack of authority, to a non-character-based outside voice. Additional revisions are described in [omitted for review].

patients indicated interest, confirmed whether they met inclusion criteria. Invitations were sent in waves until a sufficient number of participants were recruited for each focus group. In total, 3162 potential participants were identified, of whom 2350 could not be reached or did not reply, 432 opted out, and 380 indicated interest. Of those, 248 patients were able to be screened and met inclusion criteria and 137 were scheduled to participate in a focus group, 15 of whom were no-shows and 122 of whom ultimately enrolled in the study.

Focus groups and analysis

We conducted 20 two-hour focus groups between October 2015 and April 2016. Focus groups were moderated by a research team member, and at least one additional team member was present for notetaking and observation. Mandarin and Spanish focus groups were moderated by native speakers on the research team. Focus group questions were developed from themes identified through literature review and team discussion and were tested and revised for clarity (Stewart et al. 2007).

All focus groups were audio-recorded with permission of the participants and transcribed verbatim, except that Mandarin focus groups were directly transcribed into English because of the complexities of translating written Chinese to written English. Spanish transcripts were subsequently translated into English. De-identified transcripts were uploaded to the qualitative software program Dedoose for data management (Dedoose 2015). Using a modified grounded theory approach, a subset of the research team developed a qualitative codebook based on *a priori* concepts from the focus group guide and *in-vivo* coding (Corbin & Strauss 2007). The coding team refined the codebook and all coders achieved an inter-rater reliability kappa ≥0.8. One research team member then divided each transcript into short excerpts, each containing the response of only one participant or similar short responses from multiple participants, and each transcript was coded by one of the coding team members. The coding team then collaboratively reviewed each code and discussed interpretation of themes in a series of team meetings (Ryan & Bernard 2003).

Results

Participant characteristics

Participant characteristics are shown by group in Table 1. Across all groups, there was an approximately even ratio between female and male participants, and a similar age distribution with an overall mean of 56. However, in the Chinese, non-Hispanic White, and South Asian groups, over 90% of participants in each group had a college degree or higher and at least two-thirds had incomes greater than $100,000. While high educational achievement and income are relatively common in the area where we recruited, these characteristics are still notably higher than average and limit the applicability of our findings across the greater U.S. population. In contrast, the African American and Hispanic/Latino groups were more comparable to the national averages of educational level and income, with the Hispanic/Latino group including half with a high school degree or less and household income of $50,000 or less, which is approximately the median income across the U.S. (U.S. Census Bureau 2015).

Overview: Building a trustworthy research enterprise

Through analysis of focus group transcripts, we identified six themes that centered on issues of trust in the research enterprise. See Table 2. Four themes elucidated factors that influence patient trust: (1) patient expectations for research benefits vary, (2) historical discrimination in healthcare and research creates distrust, (3) challenges with navigating the healthcare system influence trust in research, and (4) patients fear inappropriate data use. In addition, two themes described institutional approaches to building trustworthiness: (5) consent is necessary but insufficient, and (6) institutional trustworthiness requires robust oversight.

1. **Patient expectations for research benefits vary—**Overall, focus group participants were supportive of precision medicine research and most expressed a willingness to contribute their data and biospecimens for research. Across all groups, most participants believed research would help future patients, sometimes speaking about the benefit to society or improving medical care in general, and other times discussing helping patients who shared specific characteristics with them or their loved ones, such as disease status, race, or sex. Participants in all groups also saw value in finding ways to make the population of research participants more representative of U.S. society.

Many participants in our non-Hispanic White focus groups expressed confidence that precision medicine research would dramatically improve healthcare, making strong positive statements about its potential benefits and using modifiers such as “huge,” “enormous,” and “miraculous,” often with few qualifications. One participant described his willingness to participate by stating, *“The benefits are so enormous for everyone that there’s no downside.”*

In contrast, participants in the African American, Chinese, Hispanic/Latino, and South Asian focus groups raised questions about the value of collecting additional data:

> “I think one of the areas where I feel very uncomfortable or concerned is the pharmaceutical company looking at this data and saying that one particular drug … is not used that much, so either they increase the price to a very high level or they just say, “We’re not going to make it anymore.” … And that’s what worries me, that abundance of this kind of information.”
>
> (South Asian participant)

These participants wondered whether members of their communities would be interested in participating unless there was a clear benefit to patients like themselves. For example, several South Asian participants spoke positively about a local clinical trial focused on cardiovascular disease among South Asian immigrants, considering this type of community-based research to be an exemplar of valuable research with clear benefits to the community. While most participants in these groups said they would likely participate, many expressed their attitudes as an act of resignation, that is, accepting risks in the hope that the research would prove beneficial:

> “I will contribute, because I know that there are a lot of great benefits to it. However, this data can and will be used in a way that you don’t want it to be used, whether it be now or whether it be in the future.”

(South Asian participant)

2. Historical discrimination in healthcare and research creates distrust— Across all groups, participants' comments suggested that their willingness to participate in precision medicine research was conditional on the trustworthiness of the physicians, researchers, healthcare system, government, and corporate institutions that owned, funded, managed, or were otherwise involved with operations of the library. For example, one participant highlighted how trust in one's doctor could make someone willing to contribute:

> "I might trust my doctor to use my information more than some third, fourth, fifth party removed in some library somewhere. I know my doctor. I have trust with my doctor, and I know my doctor is going to do right by me. And so in some ways I'm like, okay doc, look if you want them to use my information to figure out something for me, I'd go at it."

(Non-Hispanic White participant)

Many also highlighted their lack of trust in particular groups, such as the government and pharmaceutical or insurance companies, as influencing their willingness to participate and noted the importance of knowing who would manage the library before enrolling: *"I would like to know who's running it and where it's located and the history."* (Hispanic/Latino participant)

Participants' perceptions of trustworthiness were closely related to their personal and cultural experiences with biomedical research and clinical care. In the African American, Hispanic/Latino, and South Asian focus groups, references to personal and group experiences with racism in these contexts figured prominently. Participants in multiple focus groups cited the Tuskegee Syphilis Study and the case of Henrietta Lacks in explaining their perceptions that certain groups have been treated unfairly by researchers:

> "So for example, with Johns Hopkins, they used to advertise because they had so many African Americans in Baltimore that they were a testing population for researchers. And so the way minorities have been used in research in the country and that history kind of still definitely permeates … like the way colonial medicine was used as well…associating research with being essentialized and just domination."

(South Asian participant)

Some African American participants referenced historical mistreatment regarding healthcare in particular. One participant stated that his *"generation really is the first generation for African Americans that have been able to receive different types of medical care."* Another explained the potency of these memories, saying: *"There have been tests done on our population that's been secretive and hasn't been to our benefit. So it could be some seeds of that still in my memory bank somewhere."*

3. Challenges with navigating the healthcare system influence trust in research—Participants also described how challenges with accessing and understanding healthcare could affect trust. For example, several participants in the Hispanic/Latino focus

groups linked recent U.S. immigrants' unfamiliarity with navigating the medical system to decreased trust in research:

> "The whole medical system here and the whole ecosystem surrounding medicine here, with insurance and everything, is very difficult for someone from our system to navigate through. They're not used to that back home. And that automatically creates a lack of trust…. Knowing that you could in effect be denied treatment if you have a medical condition because of economic reasons."
>
> (Hispanic/Latino participant)

Others described how differences in language and accent can create barriers and a sense of alienation:

> "If I ask my parents' generation why they would like to not participate, it's the exposure. The language, the American accent. My mom is not very comfortable around American accents. Sometimes she feels inferior because she doesn't understand."
>
> (Hispanic/Latino participant)

Another participant cautioned that ignoring local language could engender conflict between groups: *"[Some communities are] very strict about the slang they use. If you don't speak their slang, you're nothing.… You're the enemy."* (African American participant)

Several focus groups also emphasized the importance of building relationships locally and improving communication with participants within their communities. Across multiple groups, participants expressed greater trust in local institutions tied to their communities than in those without local ties. One African American participant explained, *"I have family that's in Atlanta, Georgia, and they have two great medical facilities…. But the African Americans will still go to Grady [public, community based hospital]. They will not go to Emory. They will go to Grady because that's where they feel comfortable."* These participants recommended including researchers with whom participants could identify and hiring individuals from participants' local communities:

> "So, you being Caucasian going to an all African American audience would get a different reaction, would get a different acceptance level, if you will, versus an African American – a known African American doctor, somebody who would be trustworthy. Guarantee it. And I think that's not just the African American community. I think it happens in the brown community and the yellow community and the red community as well. I think that people relate to people that look like them. They trust people that look like them more."
>
> (African American participant)

4. Patients fear inappropriate data use—Participants in all of our focus groups had strong views about who would have access to their data and biospecimens, including how users would be authorized or credentialed, and were particularly concerned about inappropriate access. Participants described a range of examples of inappropriate access, including: law enforcement or government agencies misusing patient information for

forensic or surveillance purposes; pharmaceutical or insurance companies using the library to develop costly treatments, raise rates, or deny coverage; and information being shared with researchers outside the U.S. without global ethics standards in place. Many also raised a general concern about profit-motivated uses of patient data and biospecimens, leading patients to request transparency about funding, ownership, and management of the library.

The potential for research to result in racial discrimination was one of the most frequently cited risks, particularly in the African American, Hispanic/Latino, and South Asian groups. Participants in these focus groups raised the risk of being denied healthcare due to research results that would create or affirm racial stereotypes by associating certain groups with disease. One African American participant worried about the creation of racially determined "bubbles," predicting that research would result in *"everybody in a bubble. … This is the Caucasians' path. This is the Asians' path. This is the African Americans' path. Everyone has a different pathway based on ethnicity. Is that the right way to treat a person?"* Other participants expressed fear that these associations would be used by insurers and employers to deny coverage or employment, resulting in racial discrimination:

> "I don't want to read in the newspaper a headline saying, 'Oh, research said that Hispanics are prone to be the ones with the highest level of depression,' and then that information taken into then the government making specific policies or health policies. …. Is that going to help us, or is that going to then allow people to see a specific population as weaker? … It has been done before in this country and in other places."
>
> (South Asian participant)

Participants in multiple groups also raised specific concerns about government access to patient data. Several participants referenced the history of racial tensions in the U.S., and the 2016 presidential election cycle in particular, in raising the potential for the government to cite national security interests to justify targeting certain racial and ethnic groups in ways unforeseen by patients who donate biospecimens and data for research purposes:

> "It all depends on what kind of policy the government has and how they're going to use the data. I would imagine, if you are talking about ethnicity and if I identify myself as from the Middle East or maybe religion, Muslim, and so on, that may be one factor that the government wants to access for whatever purpose. It may not be a good one."
>
> (Chinese participant)

Additionally, some participants raised issues related to cultural beliefs to underscore the importance of addressing diverse attitudes on the donation of data and biospecimens. These participants stressed the importance of understanding religious guidance on the care of the body in disclosing details of research participation and raised questions about how biospecimens would be stored, cared for, and used, including issues of profit-making and benefit-sharing. For example, some Hispanic/Latino and South Asian participants noted strict religious guidance forbidding the exchange of biospecimens "for money." In contrast, some non-Hispanic White participants argued that individual donors should be entitled to compensation if their samples were successfully commercialized: *"If they're going to pick*

fifty samples and yours happens to be one of them and they discover some world-saving drug and they make a trillion dollars, where's your share of that because you helped do that."

5. **Consent is necessary but insufficient—**Despite general willingness of participants in all groups to participate, they also felt it was important to be notified about the possibility of contributing their data and biospecimens for research and to have the opportunity to actively opt into research by providing their individual informed consent. They saw this as demonstrating a basic sense of respect for patients and contributing to the ongoing relationship between patients and the healthcare system:

> "You will get more people [to] participate [in an opt-out system] but lots of them are not willingly, they probably didn't notice this request, right? They don't remember to choose to opt out, so for people who set this [library] up, they will get more data, but I think this is not respectful enough to patients. Because this issue is quite personal, it should let everyone think carefully, give them a chance."
>
> (Chinese participant)

However, participants expressed skepticism about some aspects of the consent process. For example, some wondered whether they would receive truthful information from the research institution, assumed that research is already being done without their knowledge, or worried that, even if they elected to opt out, their data and biospecimens would still be included in the library against their wishes. Others highlighted concerns about being asked to give consent while in a vulnerable state, such as in an emergency medical situation, and many worried that patients would lose track of email or mail notifications if the institution did not take care to notify them in a way that would ensure they were aware of study updates. In raising these hesitations, participants demonstrated a strong preference for institutions to address the potential inadequacies of consent and to ensure appropriate ongoing management through robust oversight and governance.

Importantly, however, participants did not see oversight and governance as substitutes for consent, or vice versa. In all focus groups, the dominant opinion was that individuals should be asked permission as to whether and how their data and biospecimens are used and viewed oversight and governance as necessary institutional obligations that supplement, rather than replace, consent because each serves a different function. One participant elaborated on these different functions:

> "You need both, because the oversight committee just defines the guidelines, the boundaries of the database and who gets access to it. But the individualized [consent] gives each patient the ability to control their fate, whether or not they want to opt in or if they want certain people to access or not. So you do need both because one defines the database, the other one controls their own access."
>
> (Chinese participant)

6. **Institutional trustworthiness requires robust oversight—**Across all groups, most participants assumed that there would be some sort of oversight system of the library in place and viewed its existence as central to their trust in the research enterprise. Participants

linked trust to the existence and quality of oversight, and some noted that trust in ongoing oversight processes is necessary because conditions in the library change over time:

> "Something happens and then all of the sudden these people have rights to the library and it's no longer used for its intended purpose. Again, how long will they hold on to things, how will it be disposed of, is there expiration, I don't know, just all those things."
>
> (African American participant)

Transparency and public accountability were of key importance, with participants in all groups expressing a desire for ongoing communication and feedback about research using their data and biospecimens, including who accessed them and for what studies. Participants also wanted assurances that the research would yield medical advances that would benefit all patients. Many liked the idea of opting in initially but being able to change their mind and withdraw after seeing what kind of studies are being done, or simply because they no longer want to participate: "*I might agree now, but in some years it may be I don't want to do that anymore, and if there's a way to just say pull me out. Pull all my records out right now. Delete for good. Bam."* (Non-Hispanic White participant) Others wanted periodic updates or check-ins, or a repository where they could look up their individual data or studies of specific interest.

Additionally, participants in all focus groups wanted detailed information about data de-identification and security, and for oversight committees to ensure robust authorization processes for all users. However, participants also expressed resignation that, no matter what security measures were in place, there would always be a threat of data breaches in the library: *"It'll happen. Over years that corruption is going to happen there, here. It's gonna happen. … That's just the way this world works."* (African American participant) Many referred to recently publicized hacks of financial or other online data as evidence of the potential risk. Nevertheless, most participants felt the benefits of research outweighed the risks and were hypothetically willing to participate so long as they had adequate assurances of transparency and trusted that their concerns would be addressed on an institutional level. Participants viewed it as the institution's responsibility to make a good faith effort to put in place the best security possible, even when they accepted the likelihood of an eventual breach or misuse of data:

> "The idea would be to take as many precautions as possible and general protocols to have in place. Nothing's 100 percent. I mean, you can go out to dinner, and someone can take your credit card information. But we don't worry about that, right? Like, we go out and still eat. It doesn't stop us from eating in a restaurant. So, I think you just trust whoever's in charge of it, and you hope that they're doing their best to protect your information."
>
> (Hispanic/Latino participant)

Another important oversight function noted by participants in all groups was the ability to strictly enforce rules and punish violators. Many viewed enforcement power as a critical function, in light of their resignation that no security measure could be 100% effective. Others highlighted the importance of harsh punishment, asking whether the oversight

committee would *"have some oversight to send [a] person [who broke the library's rules] to prison? It's a big deal. If a person should do that, the penalty should be real, real high, and it should be real, real effective."* (African American participant)

In terms of composition of oversight committees, participants in all focus groups identified expertise as essential for addressing concerns over data quality, research rigor, security, and privacy, adding that committees should incorporate a diversity of opinions and experience including patients as well as clinical, research, technical, legal, and ethics experts. Many also noted that, while it is valuable to include patient representatives, patients may not have sufficient knowledge or expertise to play a major role in oversight. Furthermore, participants discussed the importance of establishing processes to create what several described as a "checks and balances" system to prevent the concentration of power and mitigate any conflicts of interest, whether financial or non-financial:

> "I think it's most important to set up the rules, because you need to clearly understand what the data is going to get used for. I guess it's like checks and balances, right? So, maybe there's two committees, one to set up the rules, from like medical professionals and researchers, and one is actually an independent committee that says, okay, who is following the rules—I mean, who is not following the rules? What are the consequences?"
>
> (Chinese participant)

Participants were particularly opposed to having representatives from the pharmaceutical and insurance industries take part in oversight, but they were also skeptical about the vested interests of patient representatives such as, for example, a patient with a focus on a particular disease or way of thinking.

Discussion

From individual consent to institutional trustworthiness

Our findings are consistent with prior work that has shown that a substantial proportion of patients are hypothetically interested in participating in biobank research, contingent on institutional trustworthiness (Brothers et al. 2011; Kaufman et al. 2009; Lemke et al. 2010; Rahm et al. 2013). Specifically, we found that patients expect research institutions to engage in outreach and oversight practices that cultivate long-term, trusting research relationships. Trusting research relationships are built on participants' willingness to make themselves vulnerable to researchers, and on researchers' promises not to betray that vulnerability through either malevolence or negligence (Kass et al. 1996; Levi & Stoker 2000; Platt & Kardia 2015). Indeed, research relationships depend critically upon the willingness of participants to entrust some aspects of their well-being to researchers (Richardson & Belsky 2004; Richardson & Cho 2012), especially in the context of long-term or ongoing researcher-participant relationships (Olson 2015; Resnik 2009). Therefore, it is not surprising that we found that patients view institutional trustworthiness as an ethical responsibility of researchers if patients are to entrust them with their data and biospecimens.

In highlighting the importance of institutional trustworthiness, our findings challenge the current model of research ethics that focuses primarily on supporting individual autonomy. Informed consent is an important part of demonstrating respect for patients and has been shown to increase satisfaction and willingness to participate (Holm et al. 2015). Yet while some describe consent as an agreement to enter into "a regime of governance" (Mehlman et al. 2014), others have argued that it is inappropriate to rely so heavily on initial disclosure when patients lack agency over ongoing decisions (O'Doherty et al. 2011). In fact, although Henry Beecher noted the importance of informed consent in his influential article on ethics in clinical research, he prioritized researchers' ongoing ethical responsibilities by arguing that to protect participants, "the more reliable safeguard [is] the presence of an intelligent, informed, conscientious, compassionate, responsible investigator" (Beecher 1966, 1360). Nonetheless, even the recently revised Common Rule continues to focus on individual consent, allowing the option of broad consent for secondary uses of biospecimens and emphasizing the importance of privacy protections but not detailing other institutional responsibilities (§ __.116.d) (OHRP 2017). In the context of precision medicine research, responsible researchers and institutions are increasingly important given the longitudinal nature of their relationships with participants and the uncertainties about the future state of research. Our focus group participants expressed a desire to take part in long-term research relationships if they were founded on ongoing transparency and accountability, beyond the information provided in an initial informed consent discussion. This finding aligns with prior work that has suggested that disclosure at the time of consent cannot adequately address patients' desire for ongoing communication and feedback (Spencer et al. 2016) and that initial consent alone cannot achieve the transparency needed to address patients' moral, religious, and cultural concerns about uses of their data (DeVries et al. 2016). As a result, robust institutional oversight that acknowledges patient values and experiences is essential to demonstrate trustworthiness.

Additionally, participants in our focus groups expressed a desire for communication and transparency with researchers, but they did not view the existing model of simply including patient representatives on oversight committees as sufficient. Rather, they were skeptical about the motivations and representativeness of all committee members, including patients. These concerns align with those identified in the literature about the difficulty in achieving true representation of the entire community of patients (Kendell et al. 2014; Koay & Sharp 2013) and patient representatives' susceptibility to biases and conflicts of interest (Rose 2013). Tools like deliberative democracy—a methodology that relies on community engagement to evaluate ethical issues—have the potential to integrate patient voices into, and therefore increase the legitimacy of, the design and structure of biobanks (Longstaff & Burgess 2010; McWhirter et al. 2014; O'Doherty & Burgess 2009). While these tools can certainly play an important role in bringing patient voices to the forefront, our findings suggest that it is critical for engagement efforts to be accompanied by institutional commitment to diversity, inclusion, and responsible oversight in order to adequately address concerns about ongoing enforcement and other longitudinal needs in the context of precision medicine research.

To be clear, our findings do not suggest that informed consent or community and patient engagement should be disregarded. On the contrary, our findings suggest that consent and

relationship building play distinct roles, both of which are critical for the success of precision medicine research. A robust consent process allows patients to provide their individual permission and enter into a forward-looking relationship with the research enterprise. Subsequently, the research enterprise is responsible for proving itself worthy of research participants' trust.

Beyond consent: Considerations for cultivating trust in research relationships

Our findings, when taken alongside findings from previous studies, point toward several approaches that researchers and institutions seeking to engage in precision medicine research can consider in order to cultivate long-term patient trust. By taking deliberate steps to build relationships with participants, institutions can promote a culture of trust in research (Yarborough et al. 2009). Here, we describe three overarching issues for institutions to consider to better address the histories and cultural perspectives of diverse patients, followed by a description of key features of oversight mechanisms to be built upon these foundational considerations. The fundamental issues we discuss are not intended only to apply in the setting of a specific research project, but instead to incorporate as institutions build relationships with patients over the long term and work to create an overall environment of trust. While addressing each of these considerations will have costs and challenges in practice, those costs must be balanced against the costs of failing to build trusting relationships or enroll diverse populations. Further research should be done to evaluate their efficacy in practice.

(1) Address the role of history and experience on trust—It is important to recognize that many patients' experiences with the healthcare system lead them to start from a point of mistrust, or at least skepticism, about research. Trust depends on patients' past experiences and the accountability and reputation of the research institution (Platt & Kardia 2015), and is known to vary across racial and ethnic groups (Boulware et al. 2003). Our study is consistent with several previous studies that have shown that historical events such as the Tuskegee Syphilis Study and the case of Henrietta Lacks contribute to mistrust of biomedical research not only among African Americans (Corbie-Smith et al. 1999; Shavers et al. 2000; Freimuth et al. 2001; Buseh et al. 2013), which is well documented, but also among Chinese, Hispanic/Latino, and South Asian patients. For patients of diverse backgrounds, these historical events can serve as powerful, cautionary reminders of the potential for exploitation in research. In fact, many participants expressed a sense of resignation even though they ultimately indicated they would be willing to participate in research, which indicates that even among a population that recognizes the value of research, there are many lingering concerns that have not been fully erased from memory.

We also found that personal experience and the history of racism in clinical care can significantly influence how patients perceive the potential risks of research. Participants discussed personal and familial experiences with inequity in access and quality of care and expressed concerns that the benefits and risks of precision medicine research would be unequally distributed across populations. This extrapolation from clinical experiences to research underscores the "spillover effect" (Platt & Kardia 2015), which suggests patients who trust their individual healthcare provider tend to have higher levels of trust in their

healthcare system. Others have demonstrated this effect from clinical care to research (Brothers et al. 2011; Rahm et al. 2013), reflecting the importance of recognizing that the trustworthiness of research is inextricable from patients' clinical experiences. Our findings suggest that negative experiences or low levels of trust in clinical care or the healthcare system can have a similar "spillover effect" on how patients view research, with low levels of trust transferring into concerns about the value and potential risks of participation.

This spillover effect also relates to our findings that some patients, particularly recent U.S. immigrants, may not feel comfortable navigating the healthcare system. Our findings indicate that some immigrants may not understand not only how research activities are translated into clinical care, but also how research participation affects their ability to receive care. Researchers should invest in appropriate support mechanisms to improve basic understanding among immigrant patients of precision medicine research and its relationship to clinical care. This should include clear explanation of the process by which research findings are incorporated into clinical care and discussion of whether participation will affect any aspect of access or provision of services.

(2) Engage concerns about potential group harm—Our findings indicate that non-White patients have concerns about the potential for precision medicine research to lead to racial profiling and discrimination. This is consistent with other studies of African American patients' perspectives on genetic research (Bussey-Jones et al. 2010; Halbert et al. 2016). Our study suggests that these concerns are not limited to African Americans, but also extend to other minority groups. In particular, our study suggests that minority patients may have concerns about government access and use of patient data for non-health related purposes and the possibility for group harm that results in racial targeting and discrimination.

Addressing concerns over the potential for group harm is essential for building trustworthy research enterprises. Recent events, including the demand for the return of genetic samples by the Havasupai Tribe, underscore the importance of addressing the current deficiency of mechanisms dealing with ethical issues related to population-level risk. This work should begin by identifying how group harm might be addressed in the current consent process. This would require thinking beyond the individual as the unit of analysis and addressing how risks may accrue unevenly to socially identified groups. However, addressing group harm cannot be limited to the specifics of consent, and alternative mechanisms that engage the views and interests of participants and their communities should be developed.

(3) Address cultural values and communication barriers—Our participants identified cultural differences and challenges associated with language as potential barriers to certain groups' participation. Our finding that patients prefer researchers who not only speak their language, but also are familiar with their communities, is consistent with previous studies of mistrust in medical research (Braunstein et al. 2008; Lang et al. 2013). Our findings suggest that building trust with underrepresented research participants will require high standards of translation and effective communication, including attention to local dialects and styles of communication, in order to mitigate feelings of alienation. It will also depend on careful selection and training of those who engage patients beyond the point of consent, throughout the research process. For example, including community and

religious leaders as team members may help patients understand how medical advances fit within the context of local values or religious teachings (Zdechlik 2017).

Addressing these sociocultural dimensions is particularly important when engaging individuals from groups with historically low research participation rates. Previous research indicates greater skepticism among racial and ethnic minority patients about benefits of genetic testing and genetic research (Dye et al. 2016). Given the additional complexities of precision medicine research, including the breadth of data required and broad scope of data sharing, engaging historically underrepresented groups will demand clear communication of the value of unrepresented minority groups in the research, as well as the specific risks and benefits that relate to their communities. Incorporating these approaches was perceived as instrumental to not only establishing trusting relationships between participants and researchers, but also creating trustworthiness in the research enterprise broadly.

(4) Integrate patient values and expectations into oversight and governance structures—For research institutions that have built a foundation of trust with their patients by addressing the considerations described above, our findings suggest that robust, thoughtfully designed, and ongoing oversight and governance may help mitigate, at least to some degree, patients' concerns about precision medicine research in ways that the consent process cannot. Participants expressed skepticism about the fidelity of informed consent, and desire for an "escape mechanism" in the event that institutions did not honor the terms of the consent. This perspective is consistent with proposals for dynamic, process-oriented governance models (Fullerton et al. 2010; Henderson et al. 2013; Kaye 2012; O'Doherty et al. 2011), which can play an important role in continuing to foster institutional trustworthiness (Kerasidou 2016; Moodley & Singh 2016; Platt & Kardia 2015; Yarborough & Sharp 2002). Our findings suggest that oversight committees should be built on three key elements: transparency, accountability, and checks and balances.

First, oversight committees should provide both substantive and process-oriented transparency. Participants in our focus groups, as well as in previous studies (Anderson & Edwards 2010; Damschroder et al. 2007), expressed a desire to know where and how their data are used. This aspect of transparency is distinct from the desire to receive individual clinical results, instead reflecting a more socially oriented desire to know how their data are contributing to the progress of research. By receiving this type of feedback, patients can better understand the value of the research and understand whether and how their contributions are making a difference (Spencer et al. 2016). In addition, patients should be offered process-oriented details about committee activities and decision making, including reporting on who accesses and uses patient data and biospecimens and what policies govern those decisions. These sorts of disclosures, which can be made through, for example, newsletters or websites (McCarty et al. 2012; Sudlow et al. 2015), can increase patients' trust in the research institution (Damschroder et al. 2007) and allow them to engage in an active research partnership (Kaye 2012).

Second, oversight committees should not only strive to be accountable to patients, but also demand accountability from those who access patient data and biospecimens. Accountability is particularly important in light of the fact that patient data and biospecimens will be shared

with unspecified future researchers, whom patients cannot vet on an individual basis and can only rely on the research enterprise to oversee (Fullerton et al. 2010). Specifically, participants in our focus groups viewed robust security processes, policy enforcement, and punishment for violators as critical elements of research oversight, all features that Damschroder and colleagues (2007) considered necessary elements of a trustworthy research institution. These security processes could include, for example, data de-identification, contract restrictions for data users, or scientific misconduct penalties for misuse. Even though such processes cannot be perfectly effective in preventing unauthorized use of patient information, the implementation of strong security and enforcement processes would make the research enterprise more deserving of patients' trust; moreover, the existence of these processes can demonstrate to patients that the research enterprise is committed to building and maintaining their trust.

Third, oversight committees should seek to neutralize vested interests and accumulation of power by setting up structures to manage conflicts of interest and including diverse membership in terms of expertise, interests, and patient populations. Participants in our study described the importance of a system of checks and balances to prevent any conflicts of interest, whether financial or otherwise, from influencing research oversight. Our findings, like those in other studies, make clear that patients have serious concerns about conflicts of interest, particularly when it comes to research that is managed or funded by government or industry (Frye et al. 2015; Kaufman et al. 2009; Lemke et al. 2010; Spencer et al. 2016). However, the participants in our study further clarified that, while these organizations may pose the greatest concerns, no person or committee is immune from biases. Consequently, oversight and governance mechanisms should have systems in place, such as deliberate strategies for determining committee composition, to ensure diversity of background and experience and to assess and avoid any potential biases. By managing potential conflicts carefully and responsibly, as O'Doherty and colleagues (2011) argue, institutions can prevent tensions between the purported values of the research enterprise and those espoused by the people or organizations who manage it.

Strengths and limitations

The strengths of our study include the diversity and number of our focus group participants, which allowed a wide range of perspectives that are more representative of the general patient population, as well as the population that the *All of Us* initiative seeks to enroll, than the leadership of typical patient advocacy groups. Because we had separate focus groups for patients who identified with each racial or ethnic group, participants had space to openly discuss their perspectives on issues of race and ethnicity in precision medicine research, although this may have resulted in an overemphasis of such issues relative to other potential benefits or concerns. Furthermore, our use of trigger videos to spark discussion helped provide all focus group participants with the same point of reference and allowed discussion of topics that might not have arisen without prompting, such as the specifics of oversight committees.

The limitations of our study include the possibility of selection bias among participants in our focus groups. Despite our efforts to achieve diversity in race and ethnicity, age, and

gender, those who responded to our invitation were probably more willing to participate in research in general and more likely to perceive research initiatives as valuable. Relative to the U.S. population, our participants—particularly those in the Chinese, non-Hispanic White, and South Asian groups—also had higher educational levels and incomes, which is somewhat more representative of the geographic region and the health system from which we recruited but makes our findings ungeneralizable to the broader U.S. population. We note that our African American and Hispanic/Latino focus group participants had a wide range of educational levels and income. Nevertheless, our findings regarding concerns about and distrust of research among racial and ethnic minorities in the U.S. are corroborated by the literature. Furthermore, while recruiting from this population limited the socioeconomic diversity of our study, it allowed us to include participants of a wide range of racial, ethnic, linguistic, and immigration backgrounds. We hypothesize that many of the concerns identified by these groups are similar to those of more socioeconomically diverse patients, but future studies should examine the extent to which our findings hold true for patients from a broader range of socioeconomic backgrounds.

Another limitation is that the considerations we present do not incorporate feedback regarding cost and feasibility from the perspective of research institutions, particularly in the setting of networked research where institutional structures and local communities are varied. In addition, our focus groups were only able to assess participants' stated preferences, not their actual willingness to participate in precision medicine research. Despite our efforts to develop unbiased trigger videos that provided a balanced perspective, our videos might have influenced participants' attitudes. In particular, our use of the library metaphor differs from other studies that typically use the term biobank, which could limit our ability to make comparisons between our and others' findings. Our focus group testing of this term suggests that it effectively conveyed the general meaning and key components of precision medicine research to patients, but further work should be done to evaluate the efficacy of this and other potential metaphors. Finally, in an effort to present an unbiased perspective on precision medicine research, our videos highlighted potential security and other risks of research, which may have caused participants to perceive these risks as greater than they are in practice. Because focus group conversations encourage participants to build on each other's comments, our results may overemphasize the extent of patients' concerns about some potential risks and the actual value of proposed oversight mechanisms.

Future directions

Future studies should evaluate the extent to which addressing each of the considerations described in this paper would increase patient trust, build a sense of inclusion, demonstrate respect for patients, and affect participation rates in precision medicine research, particularly among socioeconomically diverse patients. It will also be important to understand patients' perspectives on the meanings and implications of trust, inclusion, and respect and how these might vary across patient populations, disease contexts, and institutional settings. In addition, our findings suggest that the political climate influences patients' perspectives on the risks associated with research, including the possibility of data sharing with governmental entities. Future research should probe how changing policies on issues related to health insurance, immigration, and national security affect patients' willingness to

participate in research that requires collection of in-depth personal health information and the extent to which the "spillover effect" affects recruitment of historically underrepresented groups.

Conclusion

As the *All of Us* initiative and other efforts to integrate health data and biospecimens for research continue, the current approach of relying on consent and patient engagement will be insufficient for the institutions engaged in these research projects. To build long-term research relationships, institutions must look beyond supporting individual decisional autonomy; they must also take on the responsibility of addressing sociohistorical experiences of diverse populations, creating community-centered communication approaches, and establishing robust oversight practices that are responsive to patient values. By meeting patients' expectations and addressing their concerns, institutions embarking on precision medicine research can work toward building long-term, trusting relationships with the patients who are integral to their research agendas.

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Appendix A. Focus group questions

After Videos 1, 2, and 3

1. Based on the videos, what is a Library of Medical Information?
    - Based on the videos, how do patients participate in a library?
    - Based on the videos, how is research conducted using a library?
    - Based on the videos, what kinds of questions can this research answer?
    - Were you aware that this type of research was being conducted?
    - What surprised you about this research approach?
2. In your opinion, what is the value of this type of research?
    - In your opinion, who do you think would benefit from this research? (probe: immediate vs. long term)
    - Do you think you would directly benefit from this research?
    - How likely do you feel it is that you or someone like you would benefit from this type of research? (probe for: different groups within community by r/e, disease, age, etc.; probe for expected timeline of the benefits)
3. How would you feel about your EHR data being used for this type of research?

- Are there certain types of data you would be less willing to offer for research? For example, how do you feel about sharing nonmedical, information such as billing information or different types of medical information, such as history of mental health, drug abuse.
- A lot of people are not comfortable with sharing their (what group identified x) data and as a result we know little about how to treat (x). Is there a way of doing the research that would make you more comfortable about sharing this information?

4. Now, instead of EHR data, we want to ask you specifically about biological samples. How would you feel about your biological samples being used for this type of research?

- What are your feelings about your genetic information being used for research?
- Are there certain types of samples (e.g., blood, tissue, urine, saliva) that you feel less comfortable being used?

5. How do you feel about your data and samples being used by different types of researchers/institutions?

- Are there certain types of research or researchers who you would not like using your data? What types of researchers do you feel comfortable with?
- How would you feel about this research if only researchers in this health system and their collaborators had access to data and samples?
  - Explain: if insurers or pharma got access to data, they would have had to do so illegitimately.
- How would you feel about having your data going to government databases (but not the samples)?
  - Explain that NIH funded researchers often use databases for research
  - Probe for feelings about genetic data.
- What if partnering with (named researchers) was the only way the research could be conducted, would there be ways of making this research acceptable to you?
- Do you feel differently depending on whether they are using data or samples?
- What are your thoughts about your data/samples moving between institutions?

6. How would your family or members of your community feel about this type of research?

- Do you think that your family members or members of your community would feel comfortable sharing their EHR data? How about their biological samples, like DNA?
- Do your family members or community hold cultural beliefs about certain biological samples that would raise concerns about this research? (probe for stigma; cultural meanings attached to certain bodily parts)

7. How likely would you be to participate in a Library of Medical Information?

- Whose opinion would be important to you in deciding whether to participate? (probe: family, friends, physician, religious leaders)
- What concerns you about participating in this research?
- If the study was focused on participants of your racial or ethnic background, would you be more likely to participate?

After Video 4

8. What concerns if any do you have about the issues raised in Video 4?

9. What questions would you ask about data security?

- How do these concerns about security compare with your concerns about other types of data you have online, e.g., financial, Facebook images?

10. How important are issues of privacy for you in deciding whether to participate?

11. Given that the health records that are being used are already electronic, would you be more or less (or equally) concerned about data security if you knew that it was also being used for research?

After Videos 5 and 6

12. Assuming that only the types of researchers that you personally feel comfortable with would have access to the data, how do you feel about each of the following scenarios? (note: all probes are important)

Scenario 1: Your healthcare system notifies you that your EHR data are going to be used in research in general.

- How would you respond to this notification?
- What do you see as the benefits of this approach? What are the drawbacks?
- What if this also included taking a sample of your blood for use in research?
- Would it matter how you received the notification (email/letter/provider/public posting)?

- Would you agree to this system if it meant that otherwise the research could not be conducted?

Scenario 2: What if your healthcare system notified you that your EHR data would be used in research unless you responded to opt-out.

- How would you respond? Would you opt-out?
- What are the benefits of this approach? What are the drawbacks?
- Would you feel differently if this also included taking a sample of your blood for use in research?
- How would you prefer to receive this communication and/or how would you like to be able to opt-out?
- Would you agree to this system if it meant that otherwise the research could not be conducted?

Scenario 3: What if your healthcare system notified you that your EHR data could be used in research only if you respond and opt-in. If you don't respond, your data will not be used.

- How would you respond? Would you opt-in?
- What are the benefits of this approach? What are the drawbacks?
- Would you feel differently if a sample of your blood would also be taken for use in research?
- How would you prefer to receive this communication and/or how would you like to be able to opt-in?
- Would you agree to this system if it meant that otherwise the research could not be conducted?

- For the various options above, would you be okay with general permission, or would you require specific permission?
  - If you require specific permission, would you be fine being contacted each time even if it meant an email every week?
  - Even if it meant that less research would be conducted?
- Which approaches to enrolling patients in this type of research do you feel most comfortable with for yourself?
- Which approach to enrolling patients do you think would allow researchers to get the most benefit out of the library?
- Which of these approaches would present greater challenges for a family member or your community?

13. What do you feel are the most important issues for oversight?

- Should oversight focus most on whether data is accessed for research, how it is used, or how it is shared and why? Which types of people would you like to be in charge of oversight?
- What type of responsibilities would you want these people to have? (probe for: create rules, enforce rules, types of research allowed, types of data collected, assess clinical relevance)
- What roles or responsibilities of an oversight committee are most important to you?

Tradeoff Scenario: Deferring to Community Based Oversight in lieu of Consent/Specific Consent (Revisit consent preferences)

If you could create an oversight committee that was empowered to address the most important issues you have identified such as (x), e.g., making sure that researchers maintained data security, de-identified data, reported back findings to patients and could be represented by the people you have listed

- Would you be willing to accept general notification where patients would be informed that the research is occurring, but would not be asked for their permission?
- Would you be willing to have an “opt-out” system instead of “opt- in”?
- Would you be willing to give general permission instead of specific permission for each study that wanted to use your data?

14. I asked you this question earlier, but I’d like to know whether your views have changed. How likely would you be to participate in a Library of Medical Information?

15. Non-White racial and ethnic groups sometimes do not participate in biomedical research. Do you have any ideas about why that is?

- Do you think that is a problem, and why or why not?
- What do you think would improve participation?

16. Are there any other issues that should be considered in doing this type of research using a Library of Medical Information?

17. We are still in the process of improving our videos. What are ways we could make these better?

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Table 1.

Characteristics of focus group participants (n=122)

	Overall (n=122)	African American (n=23)	Chinese (n=28)	Hispanic/Latino (n=20)	Non-Hispanic White (n=26)	South Asian (n=25)
Sex						
Female	65 (54%)	11 (48%)	14 (50%)	11 (55%)	15 (58%)	14 (56%)
Male	55 (46%)	12 (52%)	14 (50%)	7 (35%)	11 (42%)	11 (44%)
No response	2 (2%)	0 (0%)	0 (0%)	2 (10%)	0 (0%)	0 (0%)
Age (years)						
Mean (SD)	56	57 (15)	57 (19)	55 (14)	60 (17)	50 (17)
Range	20–95	23–82	20–87	31–80	24–95	22–81
No response	4 (3%)	1 (4%)	0 (0%)	0 (0%)	1 (4%)	2 (8%)
Education						
High school degree or less	15 (12%)	5 (22%)	0 (0%)	10 (50%)	0 (0%)	0 (0%)
Some college or technical school	14 (11%)	5 (22%)	2 (7%)	4 (20%)	1 (4%)	2 (8%)
College degree	41 (34%)	7 (30%)	11 (39%)	2 (10%)	11 (42%)	10 (40%)
Graduate degree	52 (43%)	6 (26%)	15 (54%)	4 (20%)	14 (54%)	13 (52%)
Gross annual income						
$50,000 or less	29 (24%)	6 (26%)	6 (21%)	11 (55%)	1 (4%)	5 (20%)
$50,001 to $100,000	24 (20%)	8 (35%)	3 (11%)	5 (25%)	5 (19%)	3 (12%)
$100,001 to $200,000	41 (34%)	3 (13%)	13 (46%)	4 (20%)	11 (42%)	10 (40%)
$200,001 or greater	25 (18%)	4 (17%)	6 (21%)	0 (0%)	9 (35%)	6 (24%)
No response	3 (2%)	2 (9%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)

Table 2.

Representative quotes

Theme	Representative Quote
(1) Patient expectations for research benefits vary	
Willingness to participate	"I definitely believe that in this case the whole is greater than the sum of the parts. That my contribution would be infinitesimally small, but … collectively it's a big thing." (Chinese participant)
Potential for benefits	"This is huge… This is really a revolution in medicine… There's a lot of promise here with recent work in genetics, databases, electronic reporting of medical records, so I think the benefits are pretty present and pretty clear." (Non-Hispanic White participant)
Skepticism about benefits	"I would say the most complete amount of information you can get on someone's life and all the things is probably the most useful, but it's the most – it's the scariest, right? And so, I think you'd have to have a leap of faith that, yes, I want to contribute to this. People say it's the right thing to do, and I think that it can benefit me and benefit many people, humanity, but I want to know that it's not gonna come back to maybe negatively influence me." (Hispanic/Latino participant)
(2) Historical discrimination in healthcare and research creates distrust	
Trust and willingness to participate	"I trust my doctor. I have a good relationship there. I'd want to know, what do you think about this? What are the benefits? What are the not-so benefits?" (African American participant)
Historical discrimination	"None of us even were born in a hospital. And when we were in the South, … all the black folks were kept in the basement of the hospital. That's where our beds were. And everyone else was either on top, 'cause this was in Ringgold, Georgia, right outside of Chattanooga, Tennessee. So there was different methods of how African Americans were treated when they went to the hospital. Like I said, my generation is now the first one where we can openly walk into a hospital and receive treatment without fear of being told that you have to go through the back door or go down the stairs." (African American participant)
(3) Challenges navigating the healthcare system influence trust in research	
Challenges navigating the healthcare system	"Lack of trust. That's simple because most of the people, immigrants, have come to this country. They'll not really trust the whole system.… There's a basic sense of insecurity, 'cause you have come to a different country." (Hispanic/Latino participant)
Language barriers	"It has to be very clear, and it has to be in a language that people understand. And if they are going to be translated, the translations need to be accurate, because it's awful when you read those translations in Spanish and they don't make sense. I'm from the Dominican Republic and Spanish is my first language, and sometimes you read stuff and you don't understand what those forms say. So, if you're going to do translations, you have to make sure that they're correct. If they're confusing, then it's not even valid." (Hispanic/Latino participant)
Cultural competence	"It's extremely important to be sensitive to cultural groups and to slowly build up that trust and confidence in the system. And I think, also, it helps when there are more researchers who are from different cultures, you know, like people who are doing the outreach itself. When they can identify with the people, I think there's a higher level of trust." (South Asian participant)
(4) Patients fear inappropriate data use	
Racial discrimination and government access	"Certain ethnic, religious, cultural groups were targeted for certain hate crimes, or what certain countries do to certain different types of demographic groups, as far as exploiting them or treating them differently or not treating them fairly. It's like, that information is giving those government agencies more substance how to attack your certain group or how to discriminate against a certain group." (South Asian participant)
Cultural differences about donating biospecimens	"I was raised Muslim, and so there are very clear guidelines on how to conduct yourself medically. For example, you're allowed to give a kidney because that benefits someone else. Usually you're supposed to bury a body within 24 hours, but you can hold it for more than 24 hours if there needs to be autopsy or that person elected to be an organ donor, and being an organ donor is okay, because that benefits the rest of society." (South Asian participant)
(5) Consent is necessary but insufficient	
Importance of consent	"If you look at the history, a lot of things have happened scientifically in which populations have been used for research and science in a way they did not consent to be used and in ways that it was not even ethical. And the researchers at the time made decisions in the name of science. … So, those are my concerns. I want the patients to have the control over what is it they're doing with their data." (Hispanic/Latino participant)
Skepticism about consent	"If you're alert, if you're knowingly getting into something, you will feel comfortable that, yes, I walked into it because I was aware of it…I knew what it was leading to. But there are some ways where there are loopholes. Like the path leads into something else that we're not aware of, and that makes us

Theme	Representative Quote
	uncomfortable. And that's a very day-to-day thing these days, unfortunately. So that makes you lose trust in whatever next step might come your way." (South Asian participant)
(6) Institutional trustworthiness requires robust oversight	
Ongoing communication	"Who's going to be using it? Who's going to access it on their end? How long they're going to be accessing the data? And whether or not they're going to be sharing the results or not sharing the results, things like that. And then they can see an ethical report card of said company or said agency. Are they known for using data and manipulating it for negative reasons? Or does their research actually have a benefit to public health or benefit for the health care industry?" (South Asian participant)
De-identification and security	"Actually, this could be the solution. You've got a library of data, and you've got different security levels, and then you categorize the research people: who can come in to access, and for what use? And that should follow certain processes and procedures. And if the insurance company comes in and says, hey, I want to look at the data and try to change my pricing, I'd say nope, you're not doing the right research." (African American participant)
Enforcement and punishment	"You give them such a big financial penalty that they'll never do it again, because that's the only way you're going to stop it. It doesn't matter how many locks you put on it. People will find a way to open those locks." (South Asian participant)
Diversity and expertise	"I think that you have to have knowledgeable people, professional people also on that oversight committee to determine whether or not these are valid reasons for researchers accessing that information. So, I think you do need a greater percentage of professional people than patients." (Hispanic/Latino participant)
Checks and balances	"I guess have checks and balances in the leadership of those people that have access so that one person doesn't have all the access or like have all the power…. Not just one person overseeing it, because then that's like they have all the power. So, checks and balances, basically." (South Asian participant)