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Participant Engagement in Translational Genomics Research: *Respect for Persons—and Then Some*

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ABSTRACT The expansion of both formal and informal frameworks of "engaged" research in translational research settings raises emerging and substantial normative concerns. In this article, we draw on findings from a focus group study with members of a national consortium of translational genomic research sites. The goals were to catalog informal participant engagement practices, to explore the perceived roots of these practices and the motivations of research staff members for adopting them, and to reflect on their ethical implications. We learned that participant engagement is a deliberate strategy by research staff members both to achieve instrumental research goals and to "do research differently" in response to past research injustices. While many of the participant engagement practices used in translational genomic research are not new, important insights can be gained through a closer examination of the specific contours of participant engagement in this context. These practices appear to have been shaped by the professional training of genetic counselors and by the interests and needs of participants who enroll in clinical genomics studies. The contours of this contemporary application of engaged research principles have relevance not only to clinical genomics research but also to translational research broadly, particularly for how communities of clinical researchers are interpreting the principle of respect for persons. Our findings invite normative questions about the governance of these practices and sociological questions about whether and how clinical researchers in other professions are also engaging participants in translational research settings.

KEYWORDS human subjects research, translational genomics research, participant engagement, engaged research

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A developing literature attests to the growing importance of and interest in "engaging" communities, participants, and patients in the research process.[1] Several formal frameworks for what we refer to as "engaged research" have been developed and studied, including community-based participatory research (CBPR), an immersive methodology that was developed in the 1960s;[2] patient-centered outcomes research (PCOR), a health-outcomes model that positions patients and other stakeholders as advisors to ensure that health research focuses on outcomes that are important to patients;[3] and, in Europe, participant-centric initiatives (PCI), a decentralized model of engaged research that links participants and researchers as decision-makers in large dataset biomedical research with the use of social media.[4] Frameworks for engaged research share a number of drivers and perceived virtues. These include an intention to reduce the power differential between researchers and participants by reconfiguring participants as research partners, and the

METHODS, PARTICIPANTS, AND SETTING

Participant Recruitment

We recruited 10 participants from seven Clinical Sequencing Exploratory Research (CSER) Consortium sites for a two-hour focus group that was held at the 2016 spring CSER meeting in Seattle, Washington, on April 25 and 26. This was a semiannual conference hosted by the CSER Consortium. Participants were drawn from the 97 people attending the CSER meeting. Sites were asked to nominate members of their research team who had direct contact with research participants. The resulting sample included 6 participants trained as genetic counselors. The remaining 4 participants came from various educational backgrounds and identified their roles as either project managers or study coordinators. We excluded the principal investigators of the individual CSER projects because our focus group conflicted with a meeting scheduled for them. The principal investigator of the study obtained approval from the University of Louisville School of Medicine institutional review board. Verbal informed consent was reviewed with all participants prior to proceeding with the focus group discussion.

Data Collection

A focus group approach was selected so that participants would be encouraged to compare and contrast their perspectives with others, and to generate more ideas. The focus group study PI, KBB, an experienced qualitative researcher, led the focus group discussion using a discussion guide that was developed by the first author of this essay, JEC, with feedback and revisions from the CSER Informed Consent and Governance Working Group. The focus group discussion was digitally recorded. One team member, CRF, took notes, and two team members, JHY and JEC, queried participants' responses with prompts to clarify them, solicit additional information, and generate further discussion. Questions about engagement practices spanned six domains: (1) practices, (2) motivations and benefits, (3) drivers, (4) barriers and harms, (5) measures, and (6) models and sources.

Analysis

A professional transcription company transcribed the audio recording. JEC corrected transcription errors by reviewing the completed transcription while listening to the audio recording. JEC also performed open coding of the transcript based on the domains outlined in the protocol, followed by axial coding of the transcript to identify relationships between the codes. This produced code categories that fell into five provisional themes. Team members who attended the focus group then reviewed the transcripts as coded by JEC, and they met by conference call to discuss the code categories and provisional themes and their application in the transcript. Based on this discussion, additional themes were generated. To solicit input from the broader CSER community about the validity of codes, categories, themes, and the analytic approach, two team members, KBB and JEC, convened a one-hour phone meeting with members of the CSER Informed Consent and Governance Working Group, which sponsored this study. Members of the working group discussed the coded transcript and suggested additional themes based on the coded transcript. Following this meeting, team members decided upon the key themes and refined the analytical approach to an empirical and normative assessment of the data. Two team members, JEC and CRF, independently reviewed the transcript and audio recordings to verify the speaker of each extracted quotation. They then compared their speaker identification for accuracy, reconciled differences, and labeled each quotation in the manuscript with the speaker's study role.

Participant Characteristics and Study Limitations

Nine participants (90%) were female. We did not collect data about participants' education or certification, years of professional experience, years with their CSER site, ethnicity, or age. That the study participants were a small sample that we recruited from within the CSER community who attended the spring 2016 meeting is an additional limitation.

goal of generating scientific findings that are useful to participants and have greater congruence to the phenomena being investigated.

As ethicists and social scientists embedded in translational genomics communities, we have been struck by the emergence of a language of participant engagement at investigator meetings and national conferences.[5] The terms used in these settings—"participant engagement" and "highly engaged research," which we use interchangeably in this article—refer to unspecified practices with participants already enrolled in studies. These practices seem to contrast with community-engaged research approaches, which focus primarily on engagement with community members who are not yet enrolled in research. Of particular interest, it was unclear from discussions at the meetings and conferences how these participant engagement practices are related to CBPR, PCOR, or PCI. The CBPR model involves re-

searchers working with members of the relevant communities to identify research questions and develop the research design and also involves practices that treat research participants as experts and partners. In addition, CBPR principles and methods can inform PCOR designs.[6] Indeed, it is worth noting that, in the year after we began this study, a number of publications appeared that describe the scope, benefits, and challenges of patient engagement in health research.[7] This suggests that more health researchers are moving away from a "participants as subjects" standpoint to the practice of approaching participants as key stakeholders in clinical and health systems research, and these approaches may be informed by both PCOR and CBPR. Although references to participant engagement in translational genomics communities are neither unique nor novel, they are of interest because it is clear that they are different from formal models of engaged research, where participants are involved in some aspect of the design or execution of studies. The participant engagement practices we explore in this article are of interest from both a normative perspective and a sociological perspective. From a normative perspective, these practices provide a window into understanding how researchers comprehend their responsibilities to participants. Normative work in research ethics needs to extend beyond a conceptual account of the principles of research ethics. It also needs to account for the values and expectations of researchers and research participants.[8] Taken together, these components can serve as the basis for translational work to operationalize the principles of research ethics in actual policies and practices. From a sociological perspective, participant engagement practices offer an opportunity to explore how researchers' commitment to participant engagement has developed over time and has come to be applied in practice.

There is an important role for empirical work to elucidate these connections. By studying informal models of engaged research, we hope to illuminate grassroots interpretations of the principles of research ethics, in particular, implicit or explicit understandings of the researchers' responsibilities to research participants. Are these on-the-ground interpretations different from those reflected in current policies related to human research protections? If so, what implications should that carry for contemporary and future policies on the conduct of research with human participants?

Given the nascence of the empirical literature on participant engagement, we conducted empirical research to identify these practices and understand the associated motivations. In 2016, we held a focus group with genetic counselors and project managers from seven clinical genomics project sites that are members of the Clinical Sequencing Exploratory Research (CSER) Consortium, a national clinical genomics research network funded by the National Institutes of Health (NIH) (see the text box "Methods, Participants, and Setting"). Drawing on this extremely rich discussion, we provide a preliminary account of the practices that constitute participant engagement in this context and of the motivations identified by personnel involved in genomics research. We identify what is ethically and politically at stake in these specific practices and, by extension, insights about the broader pattern of engaged clinical research. In particular, we examine how investigators' motives for pursuing participant engagement appear to signal a change in the way genomics researchers are thinking about researchers' responsibilities to their research participants. We consider potential implications that this trend might have for the regulation of human subjects research.

CLINICAL AND TRANSLATIONAL GENOMIC RESEARCH: THE CSER CONSORTIUM

To provide a background for the perspectives shared by our focus group participants (hereafter referred to as "informants" for clarity), it would be helpful to position the CSER Consortium within clinical and translational genomics research. The first iteration of the CSER Consortium was formed in 2011 by the National Human Genome Research Institute (NHGRI) and the National Cancer Institute (NCI) as a research collaborative focused on integrating genome sequencing technologies into clinical care.[9] Four types of project teams were involved: (1) Nine projects, funded under the NIH R01 and R21 mechanisms, addressed the ethical, legal, and societal implications (ELSI) of disclosing genome sequencing results to patients and research participants. These projects primarily involved ethicists, health policy experts, and social scientists with a special interest in genomics. (2) Nine projects,

funded under the NIH U mechanism, applied sequencing technologies to specific clinical contexts and investigated how genome sequencing results were used in clinical contexts and in outcomes from this practice. These projects were led by genomics experts and medical geneticists with teams of genetic counselors, research nurses, and study coordinators who enrolled patients. Because these projects were required by the NIH to include embedded ELSI research, ethicists, health policy experts, and social scientists were also involved. (3) Another project, funded through the NIH intramural program with internal NIH investigators, also examined outcomes from using genome sequencing in a clinical context and included an ELSI dimension. (4) A final project served as the coordinating center for the CSER Consortium.

The configuration of the CSER Consortium is important because it produced two critical opportunities for this analysis of participant engagement. First, the Consortium was intentionally constructed to create collaborations among scientists with expertise in genome sequencing technologies, clinicians and research staff members with experience in clinical research, and ELSI researchers. The conference calls and in-person meetings of the CSER Consortium offered those of us with interests in bioethics and the social sciences of biomedicine many opportunities to observe translational researchers as they discussed their research strategies and approaches. It was in these conversations that we first became attuned to the language of "engaged research" and "participant engagement." Secondly, the collaborative nature of this consortium, which held two meetings each year, gave us the opportunity to invite research staff members from multiple projects across the country to take part in a focus group study.

PARTICIPANT ENGAGEMENT: PRACTICES AND MOTIVATIONS

We opened the focus group by asking informants to describe the practices they associate with participant engagement. In their responses, informants offered insight into their own motivations for adopting these practices and why participants welcome, desire, and at times even solicit these practices. From this discussion, a portrait emerged of participant engagement practices that are characterized by relationship-building with participants, strongly motivated by respect for participants as persons with a wide range of motivations for enrolling in studies, and flexible and responsive to the logistical needs of the study and to a broad array of participant needs beyond their role as research participants. We classified the practices that informants described into two categories: instrumental engagement and engagement for its intrinsic value. While these categories are not at all exclusive—both include practices that research staffs use to make participation in studies meaningful, for example—instrumental engagement practices address research staff members' needs to successfully conduct their studies, whereas engagement for its intrinsic value reflects an acknowledgment by research staff that participants are whole persons who warrant respect and care, and not simply research subjects. The interplay between these two sets of participant engagement practices generates some important ethical tensions, which we will discuss later.

> The pursuit of less asymmetrical relationships is perceived to carry both instrumental and intrinsic value in translational research.

Engagement for its instrumental value. Retention of research participants is critical to study success for all research teams, but clinical genomics researchers face additional retention challenges due to the long duration of studies (often five years, and longer if renewed), the possibility that participants may be enrolled in more than one study, and the loss of interest by some participants if not selected for the sequencing arm of a trial or, alternatively, if their sequencing findings have little or no clinical utility. Given these complexities, informants feel that they cannot take for granted that participants will stay enrolled in a study and will complete study tasks across the entire course of the study. Informants therefore perceive that their teams must devise strategies to encourage participants to remain enrolled and "engaged." The informants' responses indicate that they are sensitive to the fact that participants enroll and re-

main in translational genomics studies for a wide range of reasons, and they try to tailor their strategies to these motivations. These motivations include receiving incentives (for example, parking passes and Amazon.com gift cards), having a chance to undergo sequencing, and feeling altruistic (desiring, for instance, to contribute to science or drug development or to help someone else's child).

Research staff members use a range of communication practices to convey to participants that they are vital to the study's success and to encourage them to remain in the study. These include sending birthday cards and newsletters with study updates and organizing social and educational events. As one genetics counselor explained,

> I work on a different research study that's been related to kids with a birth defect for a genetic research study. And we want to follow with them for five years. We sent out birthday cards. They get holiday cards. They get a newsletter once a year. And they're people who really appreciate that. (Participant 6, genetic counselor)

A related goal for research staffs is encouraging participants to complete study tasks, such as returning surveys and attending appointments. Research staff members will call and email participants with reminders, but sometimes more is required. One informant described how participants in the control arm of a study (who thus did not receive sequencing) were angry with the surveys that team members sent to them because the surveys focused on study results that were not relevant to them:

> We had to respond to the control participants at some midpoint in the study, because they were actually really annoyed with the surveys that we were giving them. We had to stop the study and completely revise our surveys to be more broad. All of our questions were framed around study results, and they were mad. We got really good feedback from them, but we basically had to stop the study, change everything, and go to this vague description of, "Tell us how you know about the information you just discussed with your doctor." But it worked, and actually I don't think we have a huge dropout rate. (Participant 1, senior project manager)

The team took these steps, the informant said, both out of concern that participants would leave the study and to increase the likelihood that they would complete the surveys.

Research staff members were also responsive to participants who were disappointed that they might not receive actionable clinical results about themselves or family members. Participants' views on this issue may, however, not reflect significant complexity about the actual value of receiving these types of results.[10] One informant explained why participants valued sequencing results: "At my site, they are very invested because they're cancer patients. And so they really want to be involved in this. They were sometimes coming in and asking me, 'Where are my results? How come it's taking so long?'" (Participant 8, project coordinator).

Informants described two strategies to retain participants and sustain their commitment to completing the study, both of which are responsive to participants' desire for sequencing and their disappointment if not randomized to the sequencing arm of a trial. A project manager explained that one strategy they use is to explain the scientific value of completing the surveys to participants:

> We enroll both patients with conditions and also patients that are healthy. Then we randomize them, because not everyone even gets sequenced. So, it has been very interesting to sort of look at [how] a lot of people who didn't receive sequencing were kind of disappointed. Our research assistants did try to follow up with them a little bit more to nudge them to do the surveys, explain to them why they thought it was important, and why it really was still meaningful for them to participate, because they didn't get sequenced. (Participant 4, project manager)

Another strategy is to reward participants with sequencing. Informants described this as a technique they employed to maintain interest, by offering participants a chance to undergo sequencing even if they had not been assigned to the sequencing arm. For example, one team implemented a sequencing lottery, which allowed some participants from the control arm to win entry into the whole-genome sequencing arm.[11] Staff members were not the only team members offering sequencing to participants to maintain their interest. According to one project manager, physicians on some study teams did this as well:

> Some of the physicians emphasized that a lot more than others. I read all the disclosure sessions, and some of the physicians didn't really mention it, and other [physicians] were like, "You really do have a chance," because

> people were disappointed. Our cardiomyopathy cohort, they were promising [participants], "Well, we're going to get you into another study that involves the sequencing." (Participant 4, project manager)

Engagement for its intrinsic value. Discussion about participant engagement turned to the obligations that informants felt toward participants, to offer them "something" in exchange for their time, effort, and commitment to the study. Informants repeatedly stated they were motivated to make participants feel valued even in the absence of tangible benefits such as sequencing results, so that they did not feel that the benefits of research flowed only in one direction. As one project manager said,

> I think that's a big part of patient engagement. What can you do to make them feel like they are meaningful, even if they're not getting exactly what they want? And showing them how they're either beneficial to you, or like you were beneficial to them in some way. (Participant 7, genetic counselor and project manager)

A surprising number of practices centered on providing clinical care to participants in the absence of significant individual findings, even when this care was not a required component of the study. According to one informant, "They want to talk about their clinical testing and their clinical results, because most of them, there's nothing on their exomes [reports]" (Participant 7, genetic counselor and project manager).

Providing clinical care was explained by informants as an activity that fills a need created by the limited availability of specialized care. One informant stated that she had a duty to make herself accessible to patient participants because she knows that health care providers are not providing this care for them. Another said, "If they really wanted to talk about their child's heart condition for the next 30 minutes, they had an hour with us, then that's what they had to talk about" (Participant 5, genetic counselor).

Other forms of clinical care that research staff members provided to participants included accompanying them as they received their sequencing results, talking with them about the significance of their sequencing findings, and discussing family history reports with them. As one informant pointed out, "We spend way more time on family history reports than I have ever done as a clinical genetic counselor in my whole life, so that they feel like they are getting something, because they're not getting their whole genome sequenced" (Participant 7, genetic counselor and project manager).

ENGAGEMENT IN TRANSLATIONAL RESEARCH

To frame the implications of these focus group findings for normative issues in research ethics, it will be helpful to first examine two overarching themes that link many of the practices and motivations that our informants shared: the particular asymmetries that are generated by participant engagement practices and the blurring of distinctions between research and clinical care. These themes are not novel to our work, obviously. Both have received extensive attention in the normative literature on research ethics,[12] and there has even been some empirical work examining these phenomena.[13] Of importance here, however, are the contours of these themes that have emerged in translational research that pursues engagement in an informal way, that is, without the adoption of a formal model of engagement.

The asymmetries of participant engagement. If asymmetry in research staff–participant relationships falls on a spectrum, with the highly asymmetrical relationships attributed to traditional research approaches at one end and more symmetrical relationships such as those considered ideal within the CBPR and PCOR models at the other, our informants reported relationships that fell near the middle. The space that separates the practices and motivations described by our informants from either end of that spectrum has been of crucial interest.

Our informants have adopted participant engagement practices with the goal of building and maintaining relationships with participants. Relationships not only facilitate participants' completion of study tasks; they are also a means to value participants' contributions. In this context, however, these relationships are not well-defined prospectively. Unlike the explicit frameworks for CBPR and PCOR, the participant engagement strategies described by informants do not involve a stated intention to form specific types of relationships (such as a partnership).

From the perspective of our informants, research participants have an ambiguous status. They are neither full collaborators in the research process, nor are they "guinea pigs" or "research subjects." On the one hand,

our informants did not seek to make participants into collaborators, as they might in formal frameworks of engagement. Participants enrolled in the studies that our informants managed have limited agency to advocate for their values and interests. Their power to shape study procedures lies in their ability to practice limited forms of resistance.[14] Examples of resistance include expressing displeasure about study tasks to team members, ignoring requests to complete tasks, and withdrawing from the study. While research staffs, for their part, attempt to accommodate participants' preferences and wishes, they retain the power to determine the study design, tasks, and execution.

On the other hand, our informants gave voice to a number of differences that separated their approach from the asymmetry attributed to traditional research. They saw their approach as a new-school way of conducting research with human participants, even if it does not follow the formal models of engaged research. There was an animated discussion by informants about the role of participants in research, and agreement that it is evolving. As one project manager explained,

> So, [these relationships] are not quite collaborations, but they want to feel like they're partners in this, not just in the old-school-way model of guinea pigs. They want to feel like they're participating in a different level. I heard a family with a daughter with Down syndrome who said, "My daughter is a participant and not a patient." (Participant 1, senior project manager)

We do not, however, possess enough empirical data to substantiate their intuitions. Are these practices really new in any substantive way? Several members of the working group that contributed to the analysis of our data observed that virtually none of the engaged research practices reported by our informants are novel. They observed that practices such as sending birthday cards to participants, emphasizing the scientific importance of receiving completed questionnaires, and offering ancillary care can all be found in clinical research practices going back decades.

Whether these practices are new or well established, the critical insight provided by our informants is that the pursuit of less asymmetrical relationships is perceived to carry both instrumental and intrinsic value in translational research. Our informants believe that within the specific context where they engage in research, they have a duty to develop fair, reciprocal relationships with their participants. As we will discuss in more detail, this is a critical insight because it points to on-the-ground understandings of the research staff–participant relationship that are significantly more expansive than those ensconced in current research policies, which focus primarily on human research *protections*.

Blurring research and clinical care. Informants reported being responsive to participants' requests for clinical care and information in ways that exceed their roles as research staff members. They saw this as a way to foster the commitment of participants and build relationships with them. As one genetic counselor explained,

> I will answer an email from any research participant because I want them to answer my emails. So they can send me whatever it is. They're looking for a genetic counselor for X, Y, or Z, and I'm going to—I mean, I do that for all my patients too, but I think there are certain health care providers that are not doing that for them. So we're very accessible. (Participant 5, genetic counselor)

Informants characterized this accessibility as a way of "fixing" the limitations of standard modes of health care delivery. One informant described the care and attention that genetic counselors can offer participants as a surrogate for the responsiveness that has traditionally been expected in patient care:

> I think in health care, their doctor was their community doctor. Their doctor did everything, and they were part of their family. And that's just not the way American health care is very often anymore, especially in big cities. It is different. I don't know whether that was a better or worse time. I think we're better in that we have specialized [care], but not better in that we don't know the lives of our patients and what best suits them. So maybe this is how we fixed it. You have to make them feel engaged, where, before, you just were engaged, because they were your patients and you had this interaction with them. (Participant 4, project manager)

It is tempting to interpret these care practices as setting the stage for therapeutic misconception. Such a reading would see participants as demonstrating a misunderstanding about the aims of the research, and research staff members as believing that they are obligated to provide clinical benefits to participants. The development of therapeutic misconception in translational ge-

nomics research would certainly not be a surprise, given that CSER studies are explicitly designed to test the use of sequencing in clinic-like situations, with the return of results to individual participants.[15] On the basis of our empirical evidence, however, it is unclear whether these practices create a therapeutic misconception. To better understand this, we would need to conduct further research with participants themselves. Given the aims of CSER, which focuses on translational research in clinical settings, it is unclear whether the perception of a therapeutic role would either be a misconception or pose a risk to ethical research.

We believe there is something more taking place here, and that is an *ethic of care* in genomics research that draws in large part from the training and professional culture of genetic counselors.[16] We observed three dimensions to this ethic of care. First, there was enthusiastic agreement among informants that genetic counselors are a different kind of provider. For example, a project manager with graduate training in genetic counseling said,

> I do think some of that is innately in the master's training I had. You respect your patients, and you respect their autonomy. They are the people that are in power. You're trying to support them, right? So I think I've always felt this way, because that's how I was trained to be a provider. (Participant 4, project manager)

A second dimension of this ethic of care is a powerful awareness among genetic counselors of past research injustices, coupled with a determination to not replicate these injustices. To execute these commitments, they strive to develop relationships with participants that go beyond what is considered minimal respect for persons. This involves adopting practices that convey appreciation for participants' contributions to research and accommodating their preferences where possible.

A third dimension of this ethic of care is professional refusal.[17] Informants in our focus group voiced social critiques about the erosion of primary care for participants with rare disorders. In the face of growing pressures that threaten the provider-patient relationship, research staff members who are genetic counselors—that is, clinicians—are able to provide a more intensive level of care to participants in research settings, where time and financial resources might be divided among fewer "patients." Most participants value this dimension of being part of the research. They can receive clinical services through research that they would not be able to access through traditional clinical contexts, including direct access to a genetic counselor and genetic sequencing.

Both research staff members and participants see the blurring of clinical care and research as a desirable "feature" of participant engagement in translational research and not a "bug." While the CSER studies were intentionally constructed to bridge clinical care and research in that they were designed as trials to test the clinical outcomes from genome sequencing, informants also emphasized the "care" aspect of clinical care. They were concerned with caring for their participants in myriad ways, not just testing the outcomes of existing clinical processes. It is thus critical to understand the intentions of research staff members if we are to determine whether the insertion of clinical care into genomics research should be considered, from a research ethics perspective, to represent a therapeutic misconception, or instead to represent a (semi)intentional blending of research and clinical care. While there may still be important normative reasons to use research and consent strategies that minimize the therapeutic misconception, these efforts will need to account for the fact that both researchers and participants seem to be actively blurring the distinctions between these two domains of activity.[18]

For our informants, the principle of respect for persons—a principle of research ethics—implied an obligation to adopt practices that look a great deal like clinical care.

An analysis of the distinction between therapeutic misconception and intentional blending can also be informed by an analysis of the sources of these practices. When we asked informants to explore the possible sources for their perspectives on participant engagement, they singled out CBPR as the primary source of these practices. This suggests that the principles and

values that inform the CBPR framework are leaking into other domains of health research. Informants also noted that these practices derive from their own experiences with problematic informed consent practices in public health research and are connected to the entry of social scientists with CBPR experience into clinical research. When we suggested that PCOR initiatives or the individual laboratory cultures created by specific PIs might be driving interest in participant engagement, informants emphatically rejected these possibilities.

Another important source of these practices is the research participants themselves. Informants told us that some participants with prior experience in other studies had developed expectations about the conduct of research that in turn shaped how the research staff treated them and other participants. Moreover, participants sometimes requested that research staff members engage with them outside of the study setting. For example, one informant described receiving invitations from participants who are active in disease advocacy organizations to attend their educational events. She experienced ambivalence about whether to identify herself as a member of a genomics research team at these events and where she should draw the line on her time outside of the study. These expectations by participants for "excursions" that involve staff engagement outside of study settings indicate that changing perspectives on the relationships between research teams and participants are not being driven exclusively by research staffs. Rather, participants are developing their own expectations and are speaking out when research staff members do not meet them—or perhaps when they see opportunities to benefit their interests beyond the scope of a study. Participating in these extramural activities may appear to level the asymmetries inherent to the relationships between staff members and participants. It may also alter the dynamics of those relationships within the bounds of the study in unknown ways.

IMPLICATIONS FOR THE GOVERNANCE OF HUMAN SUBJECTS RESEARCH

There are important normative implications for understanding participant engagement as a set of practices characterized by an ethic of care. The idea that research participants deserve respect is, of course, not a new idea. *The Belmont Report*, which provided the normative foundation for the Common Rule (the U.S. federal regulations governing research with humans), emphasized *respect for persons* as one of the three fundamental principles of research ethics in the context of human subjects research. *The Belmont Report* specifically focuses on two implications that the principle of respect for persons carries for research. First, because potential participants in research deserve respect, researchers are obligated to provide them with enough information to make an autonomous decision about such participation. This also means that information about research participation should not be withheld from participants unless there is a compelling reason to withhold it. Second, respect for persons implies that individuals who have constraints on their autonomy should receive special protections.

In this discussion, we are primarily interested in the first implication of respect for persons. In both *The Belmont Report* and the Common Rule's requirements, respect for persons is expressed primarily through the informed consent process. Excellent normative work in recent years has added a dimension to this framework by emphasizing that informed consent (and implicitly respect for persons) should be thought of as a longitudinal process that begins with recruitment efforts and continues throughout a participant's involvement with a study.[19]

Our findings reveal, however, that research staff members have developed a more expansive and dynamic interpretation of the obligations demanded by the principle of respect for persons. Informants repeatedly emphasized the importance of seeking trust from participants and demonstrating respect for them. This is a fundamentally relational orientation to participant engagement that transcends instrumental goals. Staff members who practice participant engagement are motivated by a sense that participants deserve respect and that the resulting duty obligates them to adopt specific practices. Their intuitions about this obligation are bolstered by their perception that research participants likewise expect to be treated with respect in the form of specific engagement practices such as providing sequencing results, providing counseling related to these and other results, and keeping them informed of the study's progress.[20]

For our informants, there was an inherent link between the principle of respect for persons and the intentional blurring of research and clinical care. For them, the principle of respect for persons—a principle of research ethics—implied an obligation to adopt practices that look a great deal like clinical care. From one ethical perspective, some of these efforts would be considered transgressions since they risk contributing to a therapeutic misconception. Consider, for example, that some informants reported that they provided counseling on medical issues that fall outside the scope of the study. For these informants, that practice represented an obligation created by the principle of respect for persons.

Although we have focused on this interpretation in only one domain of human subjects research—translational genomics research—similar views on appropriate ways to demonstrate respect for persons are features of the other models of engaged research that we have outlined (CBPR, PCOR, and PCI). In a 2006 study by Nancy Shore, investigators who performed CBPR were interviewed to identify their views on the principles of *The Belmont Report*. These CBPR researchers provided an interpretation of the principle of respect for persons that emphasizes the formation of partnerships with research participants and a commitment to empowering research participants to have a say in decision-making about the study.[21] The explicit frameworks of CBPR, PCOR, and PCI—as well as this empirical work with CBPR researchers—seem to share an assumption that the duty to treat research participants with respect creates more expansive obligations that are not reflected in the current requirements of the Common Rule.

Given the growing use of models for engaged research, including participant engagement within genomics research, it is important to consider the implications of these practices for research governance, including oversight by IRBs. In other words, how should our sociological understanding of the evolving commitments of researchers and research participants influence our normative expectations about the obligations of researchers? Even though many of the practices described by our informants are not required under current regulations, IRBs in the U.S. are empowered to apply community values in their review of proposed research projects. Because Shore's earlier work focused on a group of experts—CBPR researchers—it is not at all clear that the values of those specialists reflected the types of community values that IRBs should explicitly consider. In our focus group, however, we were able to gain insight into the values of researchers who are not committed to a formal framework of engaged research and into their perceptions of the expectations of research participants. Our informants' values seem to reflect values that are emerging in broader communities. As community adoption of these values becomes more apparent, including through ongoing empirical work, IRBs may expect studies to adopt engaged research practices on the grounds that they are required by the principle of respect for persons. We have already begun to see this trend in relation to the return of research results, where some IRBs advise (or even require) that studies performing sequencing for research purposes should return results to participants.[22] However, it should give us pause that this expansive interpretation of respect for persons could be adopted as a standard for evaluating all research studies, as this trend raises important normative and practical challenges.

First, the open-endedness of this construct could create substantial challenges. There are clear historical lessons about the ethical wrongs committed when respect for persons is absent. But in the context of different communities and different types of research, what does it mean to demonstrate respect for persons? Answers to this question turn on developing relationships with participants so that research practices reflect the expectations, interests, and needs of participants. In other words, respect for persons might be a nonnegotiable principle of clinical research, but within the specific *culture* of participant engagement in genomics research, it is interpretative and dynamic. This means that research staffs may need to interpret and demonstrate respect for persons in ways that vary widely from one study to another. This is not so problematic if studies are held to a standard that centers around a process where research staff members are expected to build relationships with participants and elicit their perspectives on the practices the study should adopt. But if IRBs come to expect that studies adopt specific practices that are regarded as respectful because they have been adopted in other contexts, then much of this effort will miss the mark in terms of responding to participants' actual expectations.

Second, it remains unclear whether participant engagement would be scalable across the spectrum of human subjects research that is performed at research institutions. The process of building relationships with participants that allow for flexible interpretation of engagement requires substantial time and skill. With CSER studies, these efforts were explicitly required by the funding opportunity announcement and received concomitant funding. If all funding opportunities included a participant engagement component, the number of other research activities that could be funded could be substantially decreased.

Moreover, participants' capacity to develop substantive relationships with researchers is limited. Research fatigue is a well-recognized phenomenon in which participants become less willing to participate in research because study tasks are too demanding or they are asked to contribute to research too frequently. Engaged research strategies have been explored by CBPR and PCOR researchers as a solution to address the former problem, as these approaches can help rekindle participants' interest in the value of research participation. Requiring that every study adopt these strategies, however, would likely exacerbate the latter problem by increasing the time and effort required for participation in each study.

Given these limitations, it would be premature for IRBs to begin evaluating studies based on the expectations expressed by our informants in the context of translational genomics research. Even if these approaches were to prove highly effective for improving the quality and acceptability of research, requiring all studies to take them would likely represent too much of a good thing. Instead, IRBs should encourage continued innovation for all levels of research engagement. For studies that will depend on a one-time informed consent process, the focus should fall on making this process as transparent and accessible as possible. For investigators wishing to pursue more substantive relationships with participants, IRBs should permit a variety of approaches so that participant engagement activities are as congruent as possible with the expectations of participants, the capabilities of the study team, and, always lurking in the background, the constraints of the research budget.

THE FUTURE OF PARTICIPANT ENGAGEMENT

From the perspectives of our informants, some of the features of CBPR have migrated into the work practices of translational genomics research, generating a set of expectations and values that are distinct from those attributed to conventional research approaches. In addition, the specific training and culture of genetic counselors as clinicians appears to foster an ethic of care in research settings. Genomics research participants, too, bring their experiences and expectations for reciprocity into studies.

These dynamics are of fundamental interest to both research ethicists and social scientists of biomedicine. Formal models of engaged research—including CBPR, PCOR, and PCI—seem to be built on a set of shared or overlapping principles and values about the proper relationship between investigators and research participants and about the purpose of research. The informants who participated in our focus group provided some preliminary but tantalizing evidence that translational genomics research has embraced some of the same principles but has started to apply them in less formal and more fluid ways. From a sociological perspective, this suggests a trend toward a new set of stakeholder expectations for the way human subjects research is conducted and provides a clue that we may be observing the effects of a set of social changes that are not limited to the research community.

The increasing importance of participant engagement indicates a need for scholarly work in both the social sciences and research ethics. For social scientists, participant engagement raises fascinating questions about how these principles are being adopted and applied across biomedical research. Are there practices we have not identified in our preliminary work, and do they vary among fields of human subjects research? Of particular note, our focus group centered on engagement with research participants only. Are researchers in these fields also adopting engaged practices such as working with communities to identify research questions or interpret and apply research findings? What are the professional and cultural sources of these principles and practices? Are genomics researchers early adopters of these principles beyond formal models of engaged research as a result of the prominent role genetic counselors play in this research?

Our study has focused exclusively on the perspectives of research staff members. We did not include principal investigators due to a scheduling conflict, although these and other stakeholders in translational genomics research may have different perspectives. We also did not speak directly with CSER participants, although our focus group participants represented the perspectives of participants to us in their focus group narratives. This raises questions about the experiences of participants in engaged research. Our findings have raised the possibility that there is a spectrum of how participants navigate the asymmetries of their relationships with research staff members. Empirical research is needed to understand their perceptions of their roles and agency as well as the benefits and burdens associated with taking part in highly engaged research.

For research ethicists, there is a critical need to examine the implications of highly engaged research for the normative standards that govern human subjects research. Our preliminary empirical findings point to an important tension. On the one hand, research staff members are interpreting the principle of respect for persons in a far more expansive way than originally envisioned in *The Belmont Report*. On the other hand, both research staff members and participants seem to be seeking types of relationships very much like those that have in the past been subject to critique for perpetuating the therapeutic misconception. These practices also threaten to overburden both research staffs and participants. Careful normative work, informed by new empirical work, should consider the risks and benefits of participant engagement, along with other forms of engaged research. Will engagement in human subjects research lead to a more robust set of obligations for all researchers to demonstrate respect for persons? Or will it instead threaten the potential for participants to make an informed and voluntary decision to participate in research as a commitment made independent of access to clinical care? Although more work is needed, our initial findings indicate that these two dimensions of participant engagement—a more expansive interpretation of respect for persons and a further blurring of research and clinical care—are two sides of the same coin. As translational research increasingly uses highly engaged practices, it will become important to pursue normative work that examines these trade-offs.[23]

Our data indicate that translational research models seem to have entered a liminal state, particularly in genomics. It remains to be seen where these practices are heading and what ethical and regulatory implications they may carry. We call on ethicists, social scientists, and health policy experts to turn their attention to these issues, and join us as we sit, perhaps uncomfortably, with the tensions being created by highly engaged research practices. ♦

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