



Public preferences and the challenge to genetic research policy

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ABSTRACT

Modern genetic research requires scientists to collect, store, and study DNA samples and health information from thousands of people. Long-standing policy allows researchers to use samples and information without a person's informed consent as long as the person's identity is protected. Under existing policy, researchers must neither disclose study results to interested research participants nor compensate people who contribute to genetic research. Research and ethics experts developed these policy approaches without input from the people whose contributions are essential to the genetic research enterprise. A growing body of evidence shows that many research participants and would-be participants disagree with the current policy approaches. For ethical and practical reasons, participants should have a greater role in determining how genetic research is conducted.

KEYWORDS: genetic privacy, genetic research ethics, genetic research policy, human subjects, informed consent, research participants

Professionals have traditionally controlled decisions about the ethics of human research. Until recently, the accepted view was that the ethical principles and practices governing research involving human subjects were properly determined by professionals, perhaps joined by a few members of the general public. Individuals with

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experience as subjects have had virtually no role in deliberations and policy-making about the ethics of human research.

This model is being challenged, however, and nowhere is the challenge more evident than in genetic research. In this field, there is a move—often supported by researchers and ethicists—to look to participants and prospective participants for ethical and policy guidance. Participants, and the researchers and ethicists supporting them, envision a new model for genetic studies that is more compatible with the ideal of subjects and investigators as partners in research.

Genetic research encompasses a variety of human studies. This essay focuses on research that involves the collection of DNA samples, or biospecimens, together with health information about the person providing the sample. Samples and information are collected in research as well as in clinical settings, where blood, tissue, and other samples are taken in the course of delivering patient care. Samples and data from both research subjects and patients are often stored in repositories known as biobanks. Those samples and data can then be used in so-called secondary research projects investigating new scientific questions. Although it is possible to protect the identity of the individuals whose materials are used in genetic research, complete anonymity or security cannot be guaranteed.¹

The move to empower subjects responds to a growing body of evidence about the views of genetic research subjects, as well as of members of the public considering research participation. Information about attitudes toward genetic research comes from personal accounts, interviews, focus groups, surveys, and studies involving actual or prospective subjects. Experienced and prospective study participants have definite views about how they should be treated in genetic research. Although public preferences are not the sole determinant of defensible research policy, some researchers and ethicists contend that the data on preferences point to ethical deficiencies in existing research approaches. These professionals also believe that the failure to address public preferences will decrease the number of individuals willing to participate in genetic research, thus threatening the public health mission of such research.

People arguing for change say that current policy and practice fail to give due regard to the concerns and preferences voiced by many individuals who have joined or are considering joining genetic studies seeking biospecimens and associated health information.² Much of the discussion addresses three topics: (1) participants' control over the research uses of their DNA samples and associated health information; (2) return of individual results to genetic research participants; and (3) compensation

¹ See Laura L. Rodriguez, Lisa D. Brooks, Judith H. Greenberg & Eric D. Green, *The Complexities of Genomic Identifiability*, 339 *Science* 275 (2013); Henry T. Greely, *The Uneasy Ethical and Legal Underpinnings of Large-Scale Genomic Biobanks*, 8 *Ann. Rev. Genom. Hum. Genet.* 343 (2007).

² Existing U.S. research regulations permit liberal research use of genetic samples and associated data without individual consent if the source's identity is protected. See Gail H. Javitt, *Take Another Little Piece of My Heart: Regulating the Research Use of Human Biospecimens*, 41 *J.L. Med. Ethics* 424–39 (2013). In a 2011 Advance Notice of Proposed Rulemaking, federal officials suggested that they might propose regulations requiring at least general consent to research use of samples and data whether or not the contributor could be identified. 76 *Fed. Reg.* 44,512, at 44,515 (July 26, 2011). But thus far they have not moved to propose such regulations. The existing regulations fail to address return of research results or compensation and profits; as a result, researchers currently have discretion over these matters.

for participants in genetic research.³ In this essay, I present empirical evidence of participants' views on these topics and describe arguments for moving toward a partnership model in genetic research.

Developments in genetic research could lead the way to changes in other types of human research, changes that would enable subjects to exercise more control over the research process. At the same time, genetic research developments reveal stakeholder conflicts and ethical concerns that may arise in the move to a more genuine partnership model.⁴

SUPPORT FOR SUBJECT EMPOWERMENT

Research participants, together with their ethicist and researcher supporters, contend that certain accepted genetic research practices fail to respect participants. Moreover, there are discrepancies between the practices that many professionals see as defensible and the practices that many participants consider appropriate. Participants and their supporters propose new research approaches that alter the status quo. These approaches give participants a much greater role in determining how their data and samples are used in genetic research.

I begin with one subject's personal account. Rebecca Fisher tells a stark and moving story about the gap between researcher and subject expectations. During the 1990s, Fisher and three of her relatives enrolled in a study that involved testing for the BRCA1 mutation, a genetic mutation associated with high rates of breast and ovarian cancer. Fisher had already had breast cancer, and the family wondered whether other family members were at risk. During the three-year study period, Fisher reported,

communication between the principal investigators and our family [was] practically nonexistent, and on those occasions when it did occur, it was almost exclusively at our behest. We received no regular status updates and, when we called or wrote to learn of any developments, our inquiries were met with annoyance, treated as an imposition—as though, once we relinquished our blood to these researchers, we were entitled to lay no further claim upon it. ...⁵

³ In August 2013, federal officials announced an agreement with the family of Henrietta Lacks, a woman whose biospecimen was taken in 1951 without her knowledge or consent and then used to develop a cell line relied on by thousands of researchers worldwide. According to the agreement, any researcher seeking access to the cell line's genome sequence must obtain permission from a committee that includes two Lacks family members. Officials explaining the agreement wrote, "the relationship between researchers and participants is evolving: seeking permission emphasizes that participants are partners, not just 'subjects.'" The agreement did not, however, include financial compensation for the Lacks family. Kathy L. Hudson & Francis S. Collins, *Family Matters*, 500 *Nature* 141, 142 (2013).

⁴ This essay does not offer a comprehensive survey of empirical research on control over biospecimens, return of results, and compensation to contributors. Instead, it presents a selection of study findings and other information suggesting that many (not all) actual and potential research subjects favor policies that differ from those traditionally governing genetic research. As I note above, it is possible that the data on public preferences about genetic research have implications for other types of human research, and for related activities like epidemiology and public health surveillance. At the same time, the data on genetic research could be related to the special significance that many people assign to genetic information. If this is the case, public preferences about genetic research might differ from their attitudes toward other health-related activities. The societal as well as individual interests affected by activities like epidemiology and public health surveillance also differ from those affected by genetic research.

⁵ Rebecca Fisher, *A Closer Look Revisited: Are We Subjects or Are We Donors?* 14 *Genet. Med.* 458 (2012).

Fisher and her family felt used, rather than respected in the research process. They had hoped to learn information that might bear on their own health risks, but the researchers felt no obligation to respond to their questions. While researchers saw her family's blood and tissue samples as mere study materials, she and her relatives had a much different view. Although they joined the study to help others, they also assumed they would be informed of the research findings, findings that might have a bearing on their own health circumstances. But they "did not get anything back" from the study investigators, except "the sense that we were part of a machine that might ultimately churn out some useful information for someone, somewhere. . . ." ⁶ As a result of their research participation, this family experienced "frustration and bitterness," as well as "a profound sense of betrayal."⁷

Another look at subject perspectives comes from interviews with a diverse group of people asked to contribute DNA samples and health information to research biobanks.⁸ Fifty-seven people were interviewed; about half of them agreed to contribute to a biobank and half declined. Interviewers asked people about their understanding of biobank operations and their perceptions of biobank risks and potential benefits. But the interviewers also encouraged people to take the biobank discussion in any direction they wanted. The unstructured discussion allowed ethical norms and concerns to emerge from the individuals who were considering whether to contribute to the biobanks, rather than from the professionals who traditionally dominate research ethics deliberations.

Analysts reported several striking features of the interviews. Many of the prospective biobank contributors characterized their DNA "as a uniquely valuable source of information about themselves."⁹ They said that they would share that information only if researchers agreed to certain terms, such as giving contributors opportunities to learn about data produced in studies of their biospecimens. Although people gave different opinions on whether they "owned" their DNA samples, many shared one person's view that the samples were "a piece of their essence."¹⁰ The interview analysts concluded that factors like compensation and ongoing control over sample use will be required for biobanks to attract the number of contributors needed for genetic studies. This led them to endorse a novel ethical and legal approach to biobank contributions, one built on trade secret licensing.

Later I will go into the details of biobank contributor preferences; here I simply want to call attention to this project's bottom-up approach to ethical and policy inquiry. The ethicists and lawyers leading this project are among the professionals supporting greater subject involvement in decision-making about genetic research ethics. Experts have developed the existing ethical standards, they note, but this ought to change:

The rules, practices, and writings of medical and ethical experts embody and give voice to concerns that they think subjects have or, at least, ought to have. But

⁶ *Id.*

⁷ *Id.*

⁸ John M. Conley et al., *A Trade Secret Model for Genomic Biobanking*, 40 *J.L. Med. Ethics* 612 (2012).

⁹ *Id.* at 619.

¹⁰ *Id.*

there is little *a priori* reason to assume that the experts have it right, in the sense of giving accurate voice to their claimed constituency.¹¹

This group wants colleagues to abandon their habit of assuming they can speak for subjects and instead, to let subjects to speak for themselves. They propose “first, that people outside the community of sanctioned experts may have worthwhile ideas about how the practice of genetics should be carried out; and second, that those same people may prove to be competent partners in the enterprise.”¹²

This professional group is not alone in calling for a more genuine partnership in research. A growing number of researchers and ethicists are promoting genetic research arrangements that give subjects more power over how research is conducted. For example, “participant-centric initiatives” use social media technologies to give genetic research participants easy ways of locating and managing their personal data. The traditional one-time consent process is replaced with an interactive format that allows individual subjects to receive feedback on study outcomes and analysis, to learn about new studies seeking enrollment, and to communicate with researchers.¹³

Participant-centric initiatives put subjects at the center of decision-making about research. They reject the “black box” research model that so disturbed Rebecca Fisher’s family, substituting “an ongoing active interaction between participants and researchers.”¹⁴ The initiatives demand “a substantial cultural shift in current research,”¹⁵ a shift that “requires researchers to respect research participants as partners in the research rather than to see them as patients or passive providers of information and samples.”¹⁶

Another new model further blurs the conventional boundaries between researchers and subjects. “Apomediated research” removes the investigator as research intermediary, adopting instead a peer exchange system in which subjects participate in data collection, interpretation, and other tasks traditionally assigned to research professionals.¹⁷ The model relies on crowdsourcing through social media technologies and creates a framework that permits participants to organize their own research studies. For example, an online group called DIYGenomics conducted a study of the relationship between vitamin D and certain genetic mutations. People organizing the study were

¹¹ *Id.* at 613.

¹² *Id.* at 615.

¹³ Jane Kaye et al., *From Patients to Partners: Participant-Centric Initiatives in Biomedical Research*, 13 *Nature Rev. Genet.* 371 (2012).

¹⁴ *Id.* at 373.

¹⁵ *Id.* at 376.

¹⁶ *Id.* at 375. Responding to the evidence of participants’ desires for data control, Isaac Kohane and his colleagues proposed a collaborative genetic research regime they call the “Informed Cohort (IC).” After an extensive disclosure process, individuals could enroll in the informed cohort. Later, they could give extra health information and biospecimens if they liked, or withdraw from the cohort if they chose. They could also decide whether their contributions could be used in new studies. An oversight board would be assigned the role of communicating with cohort participants; this board would be multidisciplinary and would include participants. According to Kohane’s group, this approach would “enable patients as partners in research rather than passive, disenfranchised purveyors of biomaterials and data.” Isaac S. Kohane et al., *Reestablishing the Researcher-Patient Compact*, 316 *Science* 836, 837 (2007).

¹⁷ Dan O’Connor, *The Apomediated World: Regulating Research When Social Media Has Changed Research*, 41 *J.L. Med. Ethics* 470 (2013). See also Valerie Gutmann Koch, *PGT and Me: Social Networking-Based Genetic Testing and the Evolving Research Model*, 22 *Health Matrix* 33 (2012).

participants, too. They also designed the study, reported their test results, compiled the data, and analyzed the findings.¹⁸

These emerging models have been adopted in just a small number of studies to date. Many researchers see them as threats to the scientific enterprise.¹⁹ And as I will discuss later, studies conducted according to the new research models must still address ethical concerns about participant privacy and understanding of study information. Nevertheless, the new models are gaining public and professional attention, as well as support in some quarters. They establish a general framework for empowering research subjects and for revising the specific research principles and practices I discuss below.

CONTROL OVER BIOSPECIMENS AND ASSOCIATED DATA

Over the years, genetic researchers have at times studied people's biospecimens and health information without the informed consent or even awareness of those people. In some cases, materials that people agreed to contribute to one research project have been used in different studies. In others, specimens and data collected from patients receiving medical care have been used for research purposes.

These practices were accepted in the research community for decades, and ethicists and regulatory officials accepted them as well. A person's blanket consent to unspecified future research was seen as a sufficient basis to use their biospecimens and data in a variety of studies. Specimens and information collected in one research project could be used without consent in other studies if the sources' identities were not disclosed to the secondary researchers. Similarly, material obtained from health-related procedures could be used in research without explicit permission as long as the patient's identity was protected. Experts thought that in these circumstances, individuals would have no reason to care about what was done with their DNA samples and data.

But there is increasing evidence that this judgment is inaccurate. Litigation over sample use supplies some of the evidence. Parents have filed lawsuits challenging the research use of blood samples collected as part of public health programs that screen newborns for genetic disease.²⁰ The Havasupai Indian tribe sued an Arizona State University researcher because blood samples they thought they were contributing to a genetics study of diabetes, a serious health problem in their community, were also used in genetic studies on schizophrenia and the ancestry of tribe members.²¹

A broader picture of public attitudes comes from empirical work like the interview study I described earlier. Data from a variety of studies show that many people want to know what happens to material from and information about their bodies, and some have definite views of the research that should and should not be done with that material

¹⁸ See O'Connor, *supra* note 17, at 471, 473.

¹⁹ Sharon F. Terry & Patrick F. Terry, *Power to the People: Participant Ownership of Clinical Trial Data*, 3 *Sci. Translational Med.* 1–4 (2011).

²⁰ See Javitt, *supra* note 2, at 431.

²¹ See Michelle M. Mello & Leslie E. Wolf, *The Havasupai Indian Tribe Case—Lessons for Research Involving Stored Samples*, 363 *New Eng. J. Med.* 204 (2010). Rebecca Skloot, author of the best-selling book, *The Immortal Life of Henrietta Lacks*, reported that during her book tours, “people ask at every stop... how they can find out what is being done with the blood or biopsy they may have left at a hospital.” She told a journalist that people have “this sense of, ‘it’s a piece of my body, and I want to know what’s happening to it.’” Amy Harmon, “*Informed Consent*” and the Ethics of DNA Research, *N.Y. Times* (April 23, 2010).

and information. Although some people are satisfied with the traditional approaches to genetic research, many are not.

A number of studies have been conducted on attitudes toward DNA sample use in research; I will describe a few of them here. A project involving a large survey of and focus groups with members of the general public found majority support for requiring parents' informed permission to store blood samples obtained in newborn genetic screening programs for future research use.²² In another project, a team conducting telephone interviews with 1193 patients at academic medical centers found that 72 per cent of the patients wanted to know about research uses of their leftover clinical samples even if they would remain completely anonymous to the researchers.²³

More information about public attitudes comes from telephone surveys involving 751 people living in the vicinity of a biobank being developed in Iowa. The biobank planned to collect biospecimens left over from medical tests and procedures; the specimens would be linked to patients' medical records, but data would be coded to protect patients' identities. Ninety per cent of survey respondents said that some form of consent was required to store clinical samples and records. A majority also wanted some say about how their contributions would be used. Twenty-nine per cent wanted the opportunity to consent to each specific study of their contribution and another 25 per cent wanted the chance to give "categorical consent," which allows individuals to decide which kinds of studies would be permissible. Forty-one per cent preferred the option of giving one-time blanket consent to all research uses.²⁴

A separate national survey conducted in 2007–08 examined public attitudes toward research uses of biospecimens and health data. The survey team asked nearly 5000 people whether they would want the opportunity to decide about each specific research use of their contributions. Although 90 per cent said that they would be willing to contribute samples and data to a research biobank, nearly half wanted the power to decide about each specific research use of their contribution.²⁵

Similarly, in focus groups with members of a Seattle-based health care delivery system, a research team found few people satisfied with the option of giving blanket consent to future research. Many focus group participants wanted the option of consenting to different categories of research, and nearly all thought that "researchers should seek study subjects' consent prior to implementing a substantive change in study procedures—for example, if data were to be used to study a different disease or if data were to be provided to a for-profit entity that had not been named in the original consent."²⁶

People with actual experience as subjects in genetic research also want information about how their biospecimens and health information could be used in future research. A University of Washington group surveyed 365 people enrolled in a genetics study

²² Jeffrey R. Botkin et al., *Public Attitudes Regarding the Use of Residual Newborn Screening Specimens for Research*, 129 *Pediatrics* 231 (2012).

²³ Sara Chandros Hull et al., *Patients' Views on Identifiability of Samples and Informed Consent for Genetic Research*, 8 *Am. J. Bioeth.* 62 (2008).

²⁴ Christian M. Simon et al., *Active Choice But Not Too Active: Public Perspectives on Biobank Consent Models*, 13 *Genetics in Med.* 821 (2011).

²⁵ Juli Murphy et al., *Public Perspectives on Informed Consent in Biobanking*, 99 *Am. J. Pub. Health* 128 (2009).

²⁶ Susan Brown Trinidad et al., *Informed Consent in Genome-Scale Research: What Do Prospective Participants Think?* 3 *AJOB Prim. Res.* 3 (2012).

on dementia to determine their views about sharing de-identified data with other researchers. Eighty-six per cent of the survey respondents were willing to have their data shared, but nearly all of them wanted an opportunity to decide the matter themselves. Ninety per cent said that it was important for investigators to ask contributors for permission to share the data. Forty per cent objected to an opt-out system that would allow data sharing unless a contributor affirmatively objected to sharing. Seventy per cent objected to data sharing without notice or permission.²⁷ Although most agreed to the data sharing, many expressed concerns about whether their privacy would be sufficiently protected and whether the data would be used to advance the commercial interests of for-profit entities.²⁸

Although quite supportive of the genetic research effort, most of these participants thought that people ought to be asked about wide data sharing. As the Washington group reported, “[b]eing given a choice about uses of their data that were not contemplated at the time of original consent was important ... because the request represented a tangible demonstration of the researchers’ trustworthiness and regard.”²⁹

Other empirical studies have produced similar findings.³⁰ Although some genetic research subjects and prospective subjects don’t object to the traditional approaches, a sizable number do object. Many people considering whether to contribute to genetic research want information about the potential research uses of their biospecimens and data, as well as the authority to decide what uses are permissible. They want this information and authority when studies use leftover clinical samples and when their identities will be concealed from researchers. A significant number of people care about what happens to material that comes from their bodies and the genetic and health information associated with that material. These findings suggest that a successful genetic research effort may require changes in conventional practices governing research use of biospecimens and associated health data.

RETURN OF GENETIC RESEARCH RESULTS

Like other forms of research, genetic research is conducted to advance knowledge. Although people enrolled in studies sometimes receive personal benefits as a result of their participation, the purpose of research is to generate information that could improve future health care. In accord with the research mission, researchers in the past felt no obligation to give genetic study subjects information about study results. The professional community of scientists and physicians were seen as the proper audience for such results. Subjects had no special entitlement to learn about either aggregate study findings or their individual findings.

By the 1990s, professionals’ views about disclosure of aggregate research findings began to change. The change was partly a result of pressure from community and indigenous groups seeking greater control over research data produced in studies

²⁷ S. B. Trinidad et al., *Research Practice and Participant Preferences: The Growing Gulf*, 331 *Science* 287 (2011).

²⁸ Evette J. Ludman et al., *Glad You Asked: Participants’ Opinions of Re-Consent for DBGAP Submission*, 5 *J. Empir. Res. Hum. Res. Ethics* 9 (2010).

²⁹ Trinidad et al., *supra* note 27, at 288.

³⁰ E.g., B. A. Tarini et al., *Not Without My Permission: Parents’ Willingness to Permit Use of Newborn Screening Samples for Research*, 13 *Pub. Health Genom.* 125 (2010); Kieran C. O’Doherty, Alice K. Hawkins & Michael M. Burgess, *Involving Citizens in the Ethics of Biobank Research: Informing Institutional Policy through Structured Public Deliberation*, 75 *Soc. Sci. Med.* 1604 (2012).

involving those groups.³¹ Although some researchers and ethicists took a paternalistic view, claiming that disclosure of even aggregate results might trigger unwarranted anxiety among subjects and lead them to seek unnecessary medical interventions, others came to believe that researchers had a responsibility to provide a summary of research results to interested participants.³² By 2009, an international survey of 343 genetic researchers found 90 per cent agreeing that they had a duty to offer subjects aggregate research results.³³ Recognition of such a duty is consistent with the partnership model of human research, in which both researchers and subjects have a stake in the outcome of the study to which they have contributed.

The debate over returning individual genetic research results is more divided; however. Many researchers and ethicists worry about psychological and other harms that could materialize if subjects became aware of their individual results. Some oppose any return of individual results and others want to return only “clinically actionable” results, which applies when “there are established therapeutic or preventive interventions or other available actions that have the potential to change the clinical course of the disease.”³⁴ But empirical studies of people considering research participation find that most think they should have an opportunity to learn a broader array of individual results.

The large 2007–08 U.S. survey I described earlier asked people about their attitudes toward return of individual results in a proposed biobank project that would examine how genetics and other factors affect disease risk. Survey respondents said that they would be most willing to join a study that returned such results. The team conducting the survey reported that “[n]ine in ten respondents agreed that they would want to know their individual research results, and 91% wanted their individual research results about health risks “even if there was nothing they could do about them.”³⁵

More details come from 16 focus groups considering the same proposed biobank project. Focus group participants said they wanted accurate, valid, and actionable results information, but many adopted a much broader definition of actionable than the definition endorsed by professional groups. Not surprisingly, most participants wanted information relevant to potential medical treatment and disease prevention. But they expressed interest in receiving information relevant to other kinds of risks, too, such as risks potentially applicable to family members and risks affecting reproductive decisions. Focus group participants thought that information about currently untreatable

³¹ REBECCA DRESSER, WHEN SCIENCE OFFERS SALVATION: PATIENT ADVOCACY AND RESEARCH ETHICS 22–43 (2001).

³² Ann H. Partridge & Eric P. Winer, *Informing Clinical Trial Participants about Study Results*, 288 JAMA 363 (2002).

³³ Fiona Alice Miller, Robin Zoe Hayeems, Li Li & Jessica Peace Bytautas, *What Does “Respect for Persons” Require? Attitudes and Reported Practices of Genetics Researchers in Informing Research Participants about Research*, 38 J. Med. Ethics 48 (2012). Despite the apparent widespread acknowledgment of a duty to return aggregate results, “return of aggregate results is still an uncommon practice in the United States.” Lynn G. Dressler, *Disclosure of Research Results from Cancer Genomic Studies: State of the Science*, 15 Clinical Cancer Res. 4270 (2009).

³⁴ Richard R. Fabsitz et al., *Ethical and Practical Guidelines for Reporting Genetic Research Results to Study Participants*, 3 Circ. Cardiovasc. Genet. 574 (2010). Another expert group took a similar position on return of results in studies using biobank contributions. Susan M. Wolf et al., *Managing Incidental Findings and Research Results in Genomic Research Involving Biobanks and Archived Data Sets*, 14 Genet. Med. 361 (2012).

³⁵ David Kaufman, Juli Murphy, Joan Scott & Kathy Hudson, *Subjects Matter: A Survey of Public Opinions about a Large Genetic Cohort Study*, 10 Genetics in Med. 831, 835 (2008).

and preventable conditions could also be useful, given that future research advances could change the medical situation. Such information could help with financial planning, as well, and could prompt them “to live life to its fullest now.”³⁶ The information might also lead them to enroll in studies of the relevant condition and become active in efforts to address environmental factors contributing to the condition. Comments like the following were common: “I’m volunteering some of my flesh for you to evaluate me. Tell me what’s wrong with it. Not that you could do something about it necessarily, but at least let me know.”³⁷

Another set of focus groups that met in 2009 and 2010 expressed similar views. People in these focus groups offered many reasons for wanting results that fall short of the professional standard for clinical utility. They said that knowing about such results would empower genetic research contributors, give them a sense of control, help their families, demonstrate researchers’ respect for them, and lead them to feel more involved in the research. Some said the results “belong” to the research contributors, which makes it “unfair or wrong for researchers to know a person’s [individual research results] without sharing them.”³⁸ Many said that they understood that the health significance of results is often uncertain and can change over time. They nevertheless “felt that the validity or reliability of the information was less important than researchers’ transparency about their level of certainty about each result.”³⁹ At the same time, although some focus group participants expressed interest in receiving information about genes related to appearance and other nonmedical conditions, most called such results “frivolous.”⁴⁰

These surveys and focus groups tell us what members of the public believe they would consider in deciding whether to contribute samples and information for use in genetic research. Studies of actual research participants report similar findings. For example, a survey of people, who had permitted samples to be stored for future research, found a substantial portion saying that they would want to know the results of a genetic study evaluating their risk of Alzheimer disease, a condition that is largely untreatable at this time. One person commented, “the researcher would do us a disservice not to let us know, not to do so would be like the over-protective mother who doesn’t let kids grow up.”⁴¹

Rebecca Fisher, the research subject I described earlier, also makes a compelling case for giving subjects the option of learning their individual results. Her contribution to research was motivated by altruism, yet she also expected something in return. She urges researchers to develop “a more fulsome understanding of what ... altruism means to

³⁶ Juli Murphy et al., *Public Expectations for Return of Results from Large-Cohort Genetic Research*, 8 Am. J. Bioethics 36, 40 (2008).

³⁷ *Id.* at 40.

³⁸ Juli Murphy Bollinger, Joan Scott, Rachel Dvoskin & David Kaufman, *Public Preferences Regarding the Return of Individual Genetic Research Results*, 14 Genet. Med. 451, 456 (2012).

³⁹ *Id.* at 456.

⁴⁰ *Id.* at 454–55.

⁴¹ David Wendler & Rebecca Pentz, *How Does the Collection of Genetic Test Results Affect Research Participants?* 143 Am. J. Med. Genet., Part A 1733, 1736 (2007). See also David Shalowitz & Franklin Miller, *Communicating the Results of Clinical Research to Participants: Attitudes, Practices, and Future Directions*, 5 PLoS Med. 714 (2008).

the giver.”⁴² People who contribute to genetic research have “an entirely appropriate sense of entitlement” to learning what is discovered in the study, she declares, even if the results are of uncertain clinical significance. Fisher makes this appeal to researchers: “Tell me what you know ... even if you do not know what it means. Tell me because we are both human beings, and the new marketplace in which we suddenly find ourselves trades on the ultimate currency: our own cells.”⁴³

Misha Angrist, another genetic research participant, labels the return of results a “moral imperative.” Angrist is both a research subject and a research professional—he has a Ph.D. in genetics and a master’s degree in genetic counseling, and was also an early contributor to the Personal Genome Project, a research project aimed at learning more about how genes and environment contribute to human traits.⁴⁴ In an article on returning results, Angrist says it is “paternalistic and hypocritical” for researchers to refuse to return a broad range of results to interested participants. Experts worried that participants will inflate the significance of genetic information have only themselves to blame, he contends, for the research community is largely responsible for the public’s unrealistic expectations about the implications of genetic findings. Moreover, he argues, worries about psychological harm, genetic discrimination, and unnecessary medical procedures are based on assumptions rather than evidence.⁴⁵ Angrist proposes that returning research results is a way to show respect for the autonomy of participants, as well as a way to promote their engagement in research and “a true abiding partnership between researcher and participant.”⁴⁶

Fisher, Angrist, and others voice strong opposition to unilateral professional control over the disclosure of research results. According to the empirical evidence, many of the people who have joined genetic studies or are prospective research contributors want to decide the matter for themselves. And their conception of useful information often goes beyond the narrow conception endorsed by many professional groups. As researcher Lynn Dressler observes, subjects who “consider themselves not just patients, but partners in research may consider return of results as a form of benefit-sharing or reciprocity not hinging on relevance to health.”⁴⁷

⁴² Rebecca Fisher, *A Closer Look: Are We Subjects or Are We Donors?* 8 Am. J. Bioethics 49 (2008).

⁴³ *Id.* at 49.

⁴⁴ The project is described at www.personalgenomes.org (accessed 7 December 2013). Angrist also wrote a book about the project and his experience as a participant. MISHA ANGRIST, *HERE IS A HUMAN BEING: AT THE DAWN OF PERSONAL GENOMICS* (2011).

⁴⁵ Because the issue of returning individual research results is relatively new, few teams have evaluated the effects of disclosure on participants. One group that evaluated a disclosure program reported that participants were highly satisfied with the disclosure process and reported no significant psychological harm three months after they learned their results. Kurt D. Christensen, J. Scott Roberts, David I. Shalowitz et al., *Disclosing Individual CDKN2A Research Results to Melanoma Survivors: Interest, Impact, and Demand on Researchers*, 20 Cancer Epidemiol. Biomarkers Prev. 522 (2011).

⁴⁶ Misha Angrist, *You Never Call, You Never Write: Why the Return of “Omic” Results to Research Participants is Both a Good Idea and a Moral Imperative*, 8 Per. Med. 651 (2011). In his book about the Personal Genome Project, Angrist comments, “Scientists who do human subject research spend so much time writing grants, crafting consent forms, collecting samples, experimenting on and analyzing those samples, and then looking for more, that most of us don’t have a clue as to how it feels on the other end of the phlebotomist’s needle.” Angrist, *supra* note 44, at 30.

⁴⁷ Dressler, *supra* note 33, at 4275.

COMPENSATION FOR CONTRIBUTIONS

Money is at the heart of a third set of genetic research issues. Should people contributing DNA samples and health information be paid? When their materials are used to develop a commercially valuable cell line or other product, should they receive a portion of the profits? Traditionally, few contributors to genetic research received payment in any form, and courts have rejected research contributors' claims to a share of the profits from commercially lucrative research.

Many researchers and others argue that we should preserve and promote the system that relies primarily on altruistic sample donation.⁴⁸ They recognize that it is acceptable, and sometimes necessary, to compensate patients and healthy volunteers for any extra time and effort they devote to providing samples and information for genetic research. But money should not be paid for the samples and information alone, they say. According to this group, turning sample contribution into a clear economic exchange would dampen the altruism that often underlies the choice to contribute.

Payment to genetic research contributors could be structured in different ways. One option would be to pay all contributors a small amount when their samples are taken. When a sample is given, no one knows whether it will be one of the very few that lead to a valuable product. Payment for samples would have to be quite small if this approach were adopted, because only a tiny number of samples actually lead to revenue-generating products. Another option would be to pay only the contributors whose samples actually lead to valuable products.

Critics object to both options. Small payments to all sample contributors "might not merely fail to incentivize patients, but might actually be scorned as an unfair or token reward."⁴⁹ And large payments to the lucky few whose samples are used to develop valuable products would also be problematic. Such an approach would not only be difficult to administer, given the many years it can take to produce a profit-making product, it would also be unjust to the many people who made equal contributions but failed to hit the genetic product jackpot.⁵⁰

But concerns about the negative effects of adding money to the system are not shared by many potential research contributors. The individuals and patient groups asserting commercial interests in products developed from their DNA samples clearly don't share these concerns.⁵¹ And empirical research reveals that many potential contributors want to receive compensation for what they consider to be valuable materials, materials that are undeniably vital to the genetic research enterprise.

Compensation was a common topic in the previously described interviews with fifty-seven people considering whether to contribute to genetic research biobanks. As a group, these interviewees "saw in their DNA something of unique value in the 'business' of medical research."⁵² And a number of them said that "easy money was their primary

⁴⁸ See, e.g., Robert D. Truog, Aaron S. Kesselheim & Steven Joffe, *Paying Patients for Their Tissue: The Legacy of Henrietta Lacks*, 337 *Science* 37 (2012).

⁴⁹ *Id.* at 38.

⁵⁰ *Id.*

⁵¹ Jon F. Merz, David Magnus, Mildred K. Cho & Arthur L. Caplan, *Protecting Subjects' Interests in Genetics Research*, 70 *Am. J. Hum. Genet.* 965 (2002).

⁵² Conley et al., *supra* note 8, at 622.

motivation” for agreeing to participate in a biobank offering \$20 for their DNA sample.⁵³

The 2007–08 national survey described earlier asked people how compensation would affect their willingness to contribute samples and information to a large biobank. Seventy-five per cent said that monetary compensation was very or somewhat important to their choice whether to participate. Survey respondents were also asked about two payment options. One offered \$50 for a half-day of giving blood and other samples and filling out questionnaires. The other offered \$200 plus \$20 for each completed questionnaire. The higher compensation rate was a strong factor influencing willingness to participate.⁵⁴

Other indications of contributor attitudes come from a Canadian project consulting members of the public about the “core values that should guide biobanking.”⁵⁵ Participants spent four days learning about and discussing various issues, including payment to people contributing samples. Individuals proposed a variety of ways to compensate contributors, including fixed fees, a percentage of the proceeds from profitable research, and salaries for limited-term employment during the time samples are under study. The group eventually settled on a different arrangement: all tissue contributors should receive tax credits and relevant health information based on the research findings.

More information comes from a *Science* poll asking readers whether researchers should be required to pay patients for tissue removed for clinical reasons. Members of the research community are the primary readers of this journal, so it was surprising that 30 per cent of the respondents thought that patients ought to be paid. One reader made the following comment:

When we recycle our trash at the curb, we receive a little kick-back on our trash costs. A decrement in our cost of medical services—certainly equal to the apportioned cost of tissue disposal—would psychologically have the same effect. We want a sense of control, courtesy, and justice, not an incalculable and probably unrealizable market value⁵⁶

In a letter to *Science* addressing the payment question, two economists contested the claim that payment would have a detrimental effect on altruism. Instead, they contended, “[T]he great majority of patients would likely be willing to donate waste tissue in exchange for either a fixed fee or a chance to share in the rewards of financially successful research.”⁵⁷ They proposed that such arrangements would induce more individuals, both altruistic and non-altruistic, to contribute. Purely altruistic contributors could maintain their altruism by donating their payments to a good cause. Moreover, they observed, “[B]lockbuster cell lines” produce great wealth for some researchers while many other researchers don’t receive great financial rewards for their work. If this

⁵³ *Id.* at 620.

⁵⁴ Kaufmann et al., *supra* note 35, at 835, 838.

⁵⁵ Heather L. Walmsley, *Stock Options, Tax Credits, or Employment Contracts Please! The Value of Deliberative Public Disagreement about Human Tissue Donation*, 73 *Soc. Sci. Med.* 209 (2011).

⁵⁶ Heidi Draffin, *Readers’ Poll Results: Paying for Tissue*, 338 *Science* 328 (2012).

⁵⁷ Scott D. Kominers & Gary S. Becker, *Paying for Tissue: Net Benefits*, 337 *Science* 1292 (2012).

sort of differential treatment is acceptable, they asked, why isn't differential treatment acceptable for DNA contributors, too? And in what way would "such a system be less fair to patients than the current system, under which all revenues from tissue lines... accrue to the medical community?"⁵⁸

So it appears that a significant number of people think that compensation for their DNA samples and associated information should be part of the genetic research system. Many see their samples as essential to the research advances that improve health care and sometimes confer wealth on researchers and their employers. They don't necessarily expect to receive large payments, and altruism remains a major motivation for their research contributions. But they do want recognition that their contributions have value, and payment would constitute this recognition. Their views deserve consideration in the compensation debate.

CONCLUSION

Experts in science and ethics have adopted genetic research practices and policies with little input from research participants and the public. As a result, conventional approaches to consent, return of results, and payment fail to reflect the views of many actual and would-be research contributors. Thus far, many experts have been reluctant to give research contributors a role in decisions about genetic research policy. But this stance is increasingly challenged by members of the public, as well as the research community.

Added costs and burdens for researchers are the major impediments to change. Measures giving people more control over research use of their materials, access to individual results, and compensation will be expensive and time-consuming. Contributor-centered policies will require research teams to establish communication systems that facilitate interactions between contributors and researchers. Tracking and distributing biospecimens according to contributors' research preferences also present logistical challenges. Researchers will spend more time communicating with subjects than they normally do, discussing ongoing studies, new enrollment opportunities, and study results. Researchers providing individual research results must set aside money to cover high-quality genetic testing and professional time devoted to the discussion of results. Increased compensation to research contributors will add to research budgets, and any effort to share profits with contributors could be difficult to implement.

The research community may resent the added burdens, especially at a time of funding cutbacks. But what researchers regard as costly and time-consuming frills are seen as basic necessities by many research contributors. For example, after some focus group participants learned that returning research results would make research more expensive, they replied that researchers should simply conduct smaller studies and use the savings to return results to contributors.⁵⁹ Supporters of change also have a variety of ideas about manageable ways genetic researchers can extend more control to

⁵⁸ Id. See also John C. Bear, "What's My DNA Worth, Anyway?" *A Response to the Commercialization of Individuals' DNA Information*, 47 *Persp. Biol. Med.* 273 (2004).

⁵⁹ Bollinger et al., *supra* note 38.

contributors, offer them individual results, and compensate them without unduly compromising the research mission.⁶⁰

It is also possible that at least some of the added costs will be offset by savings in other areas. Based on the empirical data I have described, many people considering genetic research participation will react positively to the revised policies. As a result, research recruitment could become easier and cheaper. And people who choose to contribute to research might feel more involved and appreciated in studies that offer them more information, control, and compensation, which could in turn decrease drop-out rates. The opportunity to receive individual research results will give some participants an added incentive to complete study participation. Higher retention rates would allow studies to be completed faster and at less cost.⁶¹

Indeed, several commentators think that that moving toward contributor-centered arrangements is in the research community's self-interest. In proposing the return of at least some individual research results, law professor Hank Greely writes:

Consider what happens after the first lawsuit by the bereaved family of a research subject whose life would have been saved had researchers revealed a risk they discovered. Whether or not the plaintiffs win, those researchers and their institutions will be branded as heartless, interested in subjects only as laboratory animals, and all biomedical research will feel the fallout.⁶²

Similarly, ethicist Tom Tomlinson predicts that increased public trust in and support of biobank research will follow if biobanks establish a system that gives contributors more information and control over research uses of their materials.⁶³ Misha Angrist suggests that researchers will gain an advantage "in the marketplace for research participants" if they "proactively engage their participants, respond to their queries and make themselves available."⁶⁴

Publicity about the Henrietta Lacks case has heightened general awareness of research with DNA samples, and this awareness could affect the public's response to genetic research requests. Like it or not, many people probably won't be willing to join studies unless they are given control of personal data, personally meaningful research results, and reasonable compensation for their contributions.

This is not to say that changes in genetic research practices would be completely beneficial for contributors. Some people could permit wide sharing of identifiable samples and information without understanding the potentially harmful consequences, such as privacy violations and insurance consequences.⁶⁵ Some could overestimate the benefits of genetic knowledge, while some could experience confusion or undue distress when

⁶⁰ See, e.g., Kaye et al., *supra* note 13; Kohane et al., *supra* note 16; Greely, *supra* note 1; J. Scott Roberts et al., *Returning Individual Research Results: Development of a Cancer Genetics Education and Risk Communication Protocol*, 5 J. Empirical Res. Hum. Res. Ethics 17 (2010); Merz et al., *supra* note 51; Bear, *supra* note 58.

⁶¹ See Kaufman, *supra* note 35; Ludman, *supra* note 28; Christensen, *supra* note 45.

⁶² Greely, *supra* note 1, at 360.

⁶³ Tom Tomlinson, *Respecting Donors to Biobanks*, 43 Hastings Center Rep. 41 (2013).

⁶⁴ Angrist, *supra* note 46, at 652.

⁶⁵ See O'Connor, *supra* note 17; Misha Angrist, *Eyes Wide Open: The Personal Genome Project, Citizen Science and Veracity in Informed Consent*, 6 Per. Med. 691 (2009).

they learn their research results.⁶⁶ Effective education and counseling will be needed to address these problems.

It is also possible that some paternalism in research is a defensible response to the expertise gaps, power differentials, and economic disparities that often characterize subject–researcher relationships. Moreover, the interests of the research community and the broader society must be taken into account in decisions about the best ways to respect research participants’ preferences.

The task going forward is to determine where limits on contributor preferences are defensible, taking into account the views of not only researchers and ethicists, but the individuals most personally affected by research practices. What practices do contributors see as justified by concern for contributor protection? What level of individual control over biospecimens and associated data would satisfy contributors while minimizing burdens on researchers and biobanks? What is a reasonable concept of personal utility to guide the return of individual results? What approaches would enable researchers to return research results in a meaningful yet affordable way?⁶⁷ What are fair and workable compensation arrangements?

As Rebecca Fisher reminds us, participants are “fully one-half of the interaction” in genetics research.⁶⁸ For ethical and practical reasons, participants should have a greater role in determining how genetic research is conducted. Through becoming more inclusive, researchers, ethicists, and policymakers can develop defensible policies that give due regard to the views of everyone whose personal commitments are necessary to a successful genetic research endeavor.

⁶⁶ See Ellen Wright Clayton & Lainie Friedman Ross, *Implications of Disclosing Individual Research Results of Clinical Research*, 295JAMA 37 (2006).

⁶⁷ One group reported that a research results disclosure program that received high satisfaction rates from participants “required more than 2 hours and 30 minutes and more than \$1,300 per completed disclosure to execute.” See Christensen et al., *supra* note 45.

⁶⁸ Fisher, *supra* note 5, at 459.