HHS Public Access

Author manuscript

J Law Med Ethics. Author manuscript; available in PMC 2019 June 21.

Published in final edited form as:

J Law Med Ethics. 2019 March ; 47(1): 165–172. doi:10.1177/1073110519840497.

A Belmont Reboot: Building a Normative Foundation for Human Research in the 21st Century

Kyle B. Brothers, MD, PhD[1,2], **Suzanne M. Rivera, PhD**[3], **R. Jean Cadigan, PhD**[4], **Richard R. Sharp, PhD**[5], and **Aaron J. Goldenberg, PhD**[6]

[1]University of Louisville, Louisville, KY, Division of Pediatric Clinical and Translational Research, 231 East Chestnut Street, N-97, Louisville, KY 40202

[2]University of Louisville, Louisville, KY, Institute for Bioethics, Health Policy, and Law, 501 E. Broadway, Ste 310, Louisville, KY 40202

[3]Case Western Reserve University, Cleveland, OH, School of Medicine, TA200, 10900 Euclid Avenue, Cleveland OH 44106-4976

[4]University of North Carolina, Chapel Hill, NC, Department of Social Medicine, CB #7240, Chapel Hill, NC 27599-7240

[5]Mayo Clinic, Rochester, MN, Biomedical Ethics Research Program, 200 First St. SW, Rochester, MN 55905

[6]Case Western Reserve University, Cleveland, OH, School of Medicine, TA200, 10900 Euclid Avenue, Cleveland OH 44106-4976

Introduction

Over the past decade, awareness emerged that existing frameworks for regulation and oversight of research with human participants fit poorly with contemporary research. Although substantial and diverse literature touches on this dissonance from a variety of perspectives, the problem is illustrated most clearly by the 2011 to 2017 process undertaken to “modernize” the Common Rule, the federal regulations for the protection of human research subjects. During this process, the Office for Human Research Protections (OHRP) sought public comment on a wide array of challenges they felt were not addressed adequately in existing regulations, and that they hoped to address in proposed revisions.

The most widely debated proposal aimed to address a perception that a long-standing policy allowing the research use of nonidentified biospecimens without informed consent no longer made sense given the potential of genomic technologies to reidentify such samples.[1] OHRP, recognizing concerns that existing regulations created undue burdens on very low-risk research, also proposed a plan to allow investigators to use a decision tool to determine whether a study would be “excluded” from IRB review. Proposals intended to address these and other concerns prompted critiques in the scholarly literature and in comments submitted

*Correspondence to: Kyle B. Brothers, MD, PhD, University of Louisville School of Medicine, 231 E. Chestnut St., N-97, Louisville, KY 40202, Work Phone: 502-588-0797, Cell Phone: 502-762-8666, Fax: 502-629-5285, kyle.brothers@louisville.edu.

to OHRP during the public comment period. Ultimately, the most controversial proposals, including requiring informed consent for nonidentified biospecimens research, were not part of the final rule published in January 2017 on the final day of the Obama administration. Two years after it was published, this final rule was implemented in January 2019.

As leaders of a multi-disciplinary team working on the ethical and regulatory challenges raised by biorepository research in multi-site networks, we believe that both the controversy surrounding the OHRP proposals and the modest outcome of this six-year process are symptoms of a larger challenge. The regulatory revision process initiated by OHRP focused primarily on the transformation *of biomedical science*. Critically, however, it did not adequately consider the transformation that has occurred with regard to cultural perspectives on a range of critical issues relevant to the oversight of research with human subjects. These include, but are not limited to: changing perspectives on the right to privacy (and limits thereto), power imbalances between experts and lay people, trust in institutions, and individual ownership and control of data and biomaterials. OHRP, and the biomedical research community at large, have not resolved important questions about the oversight of human subjects research because we have not sufficiently accounted for the ways that society and societal norms have shifted since the Belmont Report was published 1979 and 45 CFR 46 Subpart A (what we now call the Common Rule) was adopted in 1981.

It is time to undertake a different strategy for working toward the modernization of oversight and governance of research with humans. First, we need to revisit the principles articulated in the Belmont Report. If we aim to settle on an ethical framework that supports the development of policies, what ethical commitments and ideas must be included? Are additional ethical principles needed to ground this effort? Second, we need to conduct empirical research and public engagement activities to understand the views of diverse stakeholders on the ethical basis for policies on human subjects research. What implications do the Belmont principles hold for us today? Third, we need a process whereby this more contemporary interpretation of principles to guide human research ethics can be translated into policy and practice, with a focus that extends beyond the Common Rule to take a more comprehensive and global view of research oversight and governance. This work would recognize that changing societal contexts calls for changing approaches to process: a repeat of the original Belmont process would be an anachronism. While the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research successfully developed the original Belmont Report, it no longer makes sense for a small and distinguished group of scholars to gather at a conference center over a three-year period. Our proposal emphasizes a more transparent and inclusive – and thus more “modern” – process.

“Modernizing” Oversight and Governance of Research with Humans

In order to contextualize our proposals detailed below, it will be helpful to detail what issues need to be considered when working to update the oversight and governance of human research. One perspective on this issue can be found in the publications that OHRP circulated during the course of its seven-year effort to revise the Common Rule. The original 2011 publication, which utilized the Advance Notice of Proposed Rulemaking (ANPRM) mechanism,[2] suggested that the effort to revise the Common Rule was based on a desire to

"modernize, simplify, and enhance the current system." The 2015 Notice of Proposed Rulemaking (NPRM) explicitly addressed a perceived incompatibility between research regulations and contemporary research practices:[3] stating that its primary rationale for "modernizing" the Common Rule was "the changing nature of research." It identified a range of changes in research practices that pointed to a need to revise the Common Rule, such as the growing practices of data mining, the use of internet platforms and mobile devices to collect data, the expansion of data sharing, and the use of genomic technologies to generate large amounts of data. "The sheer volume of data that can be generated in research, the ease with which it can be shared, and the ways in which it can be used to identify individuals," the authors of the NPRM observed, "were simply not possible, even imaginable, when the Common Rule was first adopted."[4]

Ample evidence supports OHRP's assessment that recent scientific innovations present challenges for existing human subject research regulations. In our work on networked biorepositories, we have similarly recognized that current regulations seem out-of-sync with contemporary laboratory technologies and study designs. For example, IRBs are often unwilling to cede oversight of multi-site research studies to a central IRB. This is perhaps not surprising given that the founding concept for IRBs was that a local ethics committee, familiar with the researchers, the likely participants, and local customs and norms, would be uniquely positioned to properly protect local research subjects. Given that the original Common Rule was written with specific research transgressions in mind, including the Tuskegee syphilis study and the studies described in Henry Beecher's 1966 paper,[5] it is understandable that these regulations were designed primarily for observational or interventional studies conducted at a single site. Clearly, those who helped write the Common Rule did not anticipate the challenges that would be raised by clinical trials conducted across dozens of sites, the collection of data from a variety of sources to support big data analytics, and the networking of biorepositories to form virtual mega-collections.

Another example is the content requirements for informed consent documents. Biorepository research involves the storage of data and biospecimens for unspecified future research. Even more complex approaches recently have emerged, including iterative interventional designs which may be modified numerous times through the course of a study ("n=1 trials")[6] and a similar model that applies this research strategy across an entire healthcare system ("the Learning Healthcare System" model).[7] The original regulations were written, however, as though all relevant risks and potential benefits of research could (and should) be explained at the time of enrollment. Given that a large proportion of research today requires no direct intervention with participants and often involves risks that are not well-defined at the start of a study, the informed consent requirements of the Common Rule seem to fit poorly with these contemporary forms of research infrastructure.

These examples support OHRP's assessment that recent scientific innovations present difficult challenges for existing human subject research regulations. If we dig deeper, however, the original Common Rule seems inadequate even in situations where modern scientific techniques and practices cannot adequately explain this discontent.

Consider the past decade's discourse on the return of genomic research results. In this debate, some scholars argue that researchers have an expansive ethical obligation to return such findings,[8] while others maintain that such an obligation, if it exists, should be constrained to a narrow set of circumstances.[9] The latter view is tied closely with a long-recognized distinction between the duties of researchers and clinicians. Clinicians have both a legal and ethical duty to place the needs of their patients before other competing interests. In contrast, the primary obligation of researchers is to generate quality research so that future patients can benefit.

It is tempting to interpret the debate over returning genomic research results as being created by new technologies and scientific approaches that could not have been anticipated at the time of the original Common Rule. Genomic technologies, with their ability to generate large numbers of results, can produce incidental findings at an unprecedented scope and scale. Additionally, this debate is tied closely to the rise of research biorepositories. In conventional clinical research, contact between the researcher and the research participant is longitudinal and the role of researcher and clinician are frequently blurred. If research results are generated that could provide a benefit to the participant, it is straightforward to conclude that the fiduciary duty of the *clinician* role obligates the clinical researcher to provide this information. In contrast, biorepository samples are frequently collected either without the knowledge of the donor (such as when leftover clinical samples are being stored)[10] or through a single contact between a researcher and research participants. This context creates a clear distinction between the researcher and clinician role, forcing the question of what obligations the researcher might have to biorepository donors who are no longer actively engaged in research.

However, the debate about the return of genomic findings to research participants also reflects a complex history of evolving values both within and beyond the scientific community. Prior to the publication of the Common Rule, foundational ethical codes recognized a limited duty of scientists to protect research participants from avoidable harms that might arise in the course of their research. The Nuremberg Code (1947) and the Declaration of Helsinki (1964) recognized an obligation of researchers to safeguard research participants' rights and welfare.[11] The Belmont Report argues that researchers "are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation".[12]

Since that time, this rather narrow conception of beneficence in research has evolved to encompass a proposed duty for researchers to provide care that is ancillary to research procedures.[13] While this proposed duty is by no means inconsistent with the ideas expressed in the Belmont Report, the idea that researchers might have an ancillary duty of care reflects a clear change in the interpretation of beneficence.

The discourse around the return of genomic research results provides hints of continuing changes in values. Several ethicists have evoked the Belmont Report's interpretation of beneficence in arguing against a duty to return these types of results to research participants, since returning results could actually create harms. And since research needs to be designed to minimize harms, investigators and IRBs should exercise caution when considering

whether genomic research results should be returned to participants.[14] Others have extended the proposed duty to provide ancillary care as a justification for returning results to participants in certain circumstances.[15]

The debate about the return of genomic research results also reveals changing ideas about the principle of respect for persons. In the Belmont Report, this principle is interpreted primarily through the lens of autonomy: the principle of respect for persons means that investigators must give participants the opportunity to consider the risks and benefits of research participation and voluntarily agree (via an informed consent process) to participate. More recently, however, research ethicists and others have argued that respect for persons also entails an obligation to return genomic research results to participants.[16] The idea that respect for persons might also entail an obligation to return research findings, especially those that carry personal utility but not medical utility, was not part of the Belmont Report. Rather, this conception seems to reflect changing ideas about the scope of this principle.

The debate on returning genomic research results also reveals that principles not mentioned in the Belmont Report might be important to contemporary conceptions of research ethics. Several commentators have argued that research participants should be treated as partners in the research process, and that returning results is an important component of this partnership.[17] Treating research participants as partners is a hallmark of community-engaged participatory research (CBPR). This research methodology emphasizes measures to engage community members as partners throughout the research process. In a 2006 study, Nancy Shore interviewed CBPR investigators to examine how they interpret the principles of the Belmont Report.[18] Shore found that CBPR researchers interpret “respect for persons” as a principle that emphasizes the duty to form partnerships with research participants and to empower research participants to participate in decision-making about research studies. Neither the Belmont Report nor the Common Rule recognize such an obligation. If views on the researcher-participant relationship have changed so significantly, contemporary policies will continue to seem out of place as long as they fail to recognize those views.

Other examples point to this same conclusion: debates about broad consent for biorepository research,[19] the identifiability of DNA-containing biosamples,[20] and consent of pediatric research participants upon reaching the age of majority.[21] Each of these have arisen as important controversies in research ethics in part because of new research practices and technologies that were not anticipated by the Common Rule. But we cannot adequately understand or address these challenges unless we also recognize that the values and expectations of investigators, IRB members, and research participants have changed over time. It is not just the Common Rule, but also the Belmont Report, that is in need of an update. In order to reform the oversight and governance of research with humans to meet the needs of contemporary science, we must first develop a renewed ethical foundation that reflects changing cultural contexts.

Rebooting Belmont: A Foundation for Oversight and Governance of Research with Humans

In many ways, the original Belmont process was a remarkable success. Given today's political environment, it seems incredible that a federal agency was so visionary as to recognize that a process to agree on principles was an important first step toward building a coherent set of regulations. Although we have argued that the Belmont Report is currently limited in its utility, we must acknowledge that for almost 40 years it has provided a valuable ethical framework for the protection of human research subjects.

Despite this legacy, convening a second Belmont commission to revise the Belmont Report is not the answer. The field of bioethics is relatively young, and in the 1970s there was nothing anachronistic about the idea of convening a panel of distinguished experts to develop a set of governing principles. It is no coincidence that the Belmont Report was published in the same year as the first edition of *Principles of Biomedical Ethics* by Tom Beauchamp and James Childress.[22] In 1979, the principlist framework that grounds the Belmont Report reflected the state of the art for bioethics.

A great deal has changed since then. Bioethics has grown to incorporate other frameworks including virtue ethics, communitarian ethics, and feminist ethics. The principlist approach itself also has evolved to more explicitly address the way historical and cultural contexts shape the selection and interpretation of principles. Beauchamp and Childress have revisited their *Principles of Biomedical Ethics* repeatedly, including revisions concentrating on the decisive role of context in the interpretation of the principles. Consistent with this recognition of the importance of context, bioethics also has evolved to incorporate more empirical and participatory approaches.

Revisiting the principles of the Belmont Report for the 21st century will require a process that aligns with contemporary sensibilities. We think of this process as a "reboot." This film industry analogy seems apt. When a studio decides to reboot a film series, its goal is to reimagine a beloved story and set of characters in a way that reflects contemporary sensibilities. While the actors, settings, costumes, lighting, pacing, etc. may change, reboots seek to maintain continuity with those elements of the original that make it unique. From an artistic perspective, this upholds the "integrity" of the original. Below we propose a process for rebooting the ethical foundation for the oversight and governance of human subjects research while maintaining the "integrity" of the Belmont principles.

Step 1: Building a Normative Foundation

The principlist approach has been unfairly critiqued by some commentators as a naive attempt to identify ethical guides that apply in all places at all times. Even early editions of *Principles of Biomedical Ethics* acknowledged the historical and intellectual context that made it seem important to the authors to identify consensus principles for doing ethics in biomedical settings. Nonetheless, ethical principles – whether they be Beauchamp and Childress' four principles or the Belmont Report's three principles[23] – have too often been applied in ways that ignore their historical and cultural contingency. Unfortunately, IRBs are

almost certainly one of the settings in which this reductive use of the Belmont Report principles can be observed.[24] Ethical principles, when used in specific clinical or research ethics cases, can also tend to oversimplify complex situations.[25]

Although ethical principles are a product of their time and may sometimes be misinterpreted and misused in their application to specific cases, they are often useful as a starting point for the development of policy.[26] Without guiding principles, the process of policy development can become aimless. Stakeholders may advance specific policy options, but lack an agreed-upon framework to argue for their suitability. This is exactly what seems to have happened when the effort to modernize the Common Rule resulted in significant controversy but little consensus.

Given this tension between the advantages and disadvantages of ethical principles, an effort to reboot the Belmont Report might start with a normative and conceptual effort to examine the role principles themselves might play in the development of new policies. Can we develop an account of principles for research ethics that emphasizes their interpretation in historical and cultural contexts and dispenses with the idea of timeless principles? In our 21st century context, can a finite set of ethical principles even do the ethical work that is needed to develop appropriate research policies? If not, what other types of ethical ideas or approaches might be needed?

In light of the potential advantages of the principlist approach we have identified and its familiarity to IRB members, researchers, and other stakeholders, it is unlikely that principles will be abandoned altogether. Therefore, revisiting the original principles from the Belmont Report is necessary. What historical and literary evidence do we have about the intended scope of these principles? In what ways do recent accounts of these principles reject or reinterpret these principles? A promising thread for this type of work might involve examining the “fitness” of these principles for modern needs. What would it mean for the Belmont principles to “fit” or “fail to fit” with modern needs and sensibilities? How might we evaluate this?

Critical work must also examine whether additional principles are needed to set the stage for a successful process of policy development. Which ethical commitments and ideas falling outside the Belmont principles were evoked explicitly in the debate about the Common Rule revision? Are there other important principles that were implicit in those debates? How do these principles link conceptually with one another and with the Belmont principles?

By their nature, the work to answer these questions will fall primarily to scholars in the humanities and law. In the next section, we consider how stakeholder voices from non-scholarly communities might be incorporated into this process. But that does not mean that this first step should reject inclusivity. On the contrary, efforts to reframe, reinterpret, and reorder the principles will be most successful if they embrace voices from across the humanities. Scholars skilled in the methods of history and literary analysis will prove critical in efforts to understand the efforts of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Experts in religious ethics and philosophy will need to examine the Belmont principles and to consider the potential value of including

other principles. Perhaps most importantly, scholars working from feminist and non-Western traditions should lead the way in broadening the set of ethical commitments and ideas considered relevant to policy on research with humans.

This first stage of work cannot be accomplished within the context of a single working group or grant project. Rather, it should be undertaken by a broad community in a variety of settings using a variety of methods. While aspects of this work are already being carried out by groups working on specific topics or within specific disciplines, we lack a sense of working toward a shared goal. We call on the scholarly community interested in research ethics to break out of their silos and broaden their focus. We should ask bigger questions: What normative foundation shall we build for policies on the governance and oversight of contemporary research? What are the critical ethical ideas that need to be included in this framework, and how should the overall framework be constructed?

Step 2: Expanding the Conversation

Work to build a normative and conceptual foundation will need to be tied closely with a systematic effort to empirically re-examine stakeholder views on the principles of research ethics. When the time comes to debate policies, a normative foundation will only prove useful if it accurately reflects the ethical commitments of stakeholders. Therefore, we must capture the perspectives of the many stakeholders in human participant research, and assure that the voices of those underrepresented in traditional policy-making processes have an influence on the outcome.

Since the publication of the Belmont Report, the landscape of bioethical inquiry has expanded to incorporate a variety of empirical approaches from the social sciences, including surveys, focus groups, and interviews. Of particular interest, empirical work has also illuminated our understandings of the ethical principles articulated in the Belmont Report. For example, Vitak, Shilton, and Ashtorab[27] and Nancy Shore[28] have studied researcher perspectives on the Belmont principles and their implications for ethical research practices. This excellent work has provided a starting point, but more empirical work is needed to explore the perspectives of a diverse and inclusive set of stakeholders and to allow for engagement and dialogue across the general public, including patient advocacy groups, community and religious leaders, researchers, clinicians, and others. Ideally, any engagement with the stakeholders of the Belmont Report would also include international participants, whose perspectives on solidarity and communal interests may differ from stakeholders in the United States.

The effort to empirically study perspectives on the ethical principles relevant to research with humans will need to focus on not only collecting data, but also engaging stakeholders in meaningful dialogue about these principles. Therefore, we must look beyond the traditional methodologies utilized in bioethics and the social sciences. While surveys and interviews are effective methods for assessing perspectives and attitudes, their utility may be limited in contexts where respondents lack adequate background information. Perspectives on research ethics is likely a topic that will benefit from the use of other methods, like deliberative democracy and the Delphi approach, that integrate more educational opportunities and that invite stakeholders to engage in discussion with one another.[29]

These methodologies help shift the locus of "expertise" away from academic perspectives, facilitate the integration of new community voices into this process, and place a high value on the experiences of research participants to guide and move the dialogue. This approach is epitomized in the community-based participatory approach to research, which emphasizes the collaboration and participation of community members at all stages of the research process, including the framing of study questions, the collection of data, and the interpretation of research results. These methodologies are especially salient when trying to engage community members who are not only underrepresented as research participants, but also underrepresented in the scholarly communities that would participate in this process.

While empirical approaches will be crucial to a Belmont reboot, they have limitations. First, our proposed strategy would not capture the perspectives of every stakeholder. Even though community leaders may raise important concerns shared by their constituents, they should not be seen as representing the perspectives of all members of a population group. Second, while gathering public perspectives is crucial to an effort to reboot the Belmont Report, these voices must be integrated into a larger process that accounts for the full range of ethical and policy considerations. The relationship between a normative critique and any empirical methods must be a two-way street, with one approach necessarily informing the other in order to produce ongoing dialogue. Third, the utility of a process to empirically examine public and professional perspectives may be limited if the results from these activities are not effectively communicated to the narrower set of stakeholders responsible for designing and enacting new policies. While empirical studies may encourage *engagement and dialogue* about the Belmont principles, these studies must be paired with mechanisms to allow others to *hear* those messages as a part of a process to operationalize findings from this work into policy assessment and development.

Some of these limitations might be addressed by additionally engaging the public in meaningful discourse about Belmont beyond the framework of empirical research, including through public discussion groups, town hall meetings, and the use of online forums. These might provide important opportunities to engage a broader range of stakeholders, some of whom may not be interested in participating in a formal research study.

Step 3: Transcending the Regulations

The final step in our three-part proposal is perhaps the most radical: an explicit call to disentangle policy making from ethical decision making. While we support the eventual development of a new set of regulations to govern research with human participants, and believe the way to pursue this goal is to build those regulations on the foundation provided by a new consensus around normative ethical principles, these policies will still not be sufficient to address all the challenges that will face researchers, IRBs, and study participants in the 21st century. The regulations governing human research do not decide for us what is right or wrong. We will continue to require approaches to operationalize moral decision-making when situations arise that the regulations do not or cannot govern. This means we need to develop and promote best practices beyond that which may be required by regulations[30] with a focus on both administrative practices and behavioral norms.[31]

These sorts of practices are already under development in a number of contexts. Consider, for example, that biorepositories have been utilizing oversight boards and community advisory boards for a number of years. These practices were certainly not envisioned, much less obligated, under the Common Rule, but they have created important opportunities for stakeholders to make ethical decisions in ways that augment the functions of IRBs. During the effort to modernize the Common Rule, OHRP proposed a "broad consent" solution that would have refocused governance of this type of research on individual consent. However, public comments about this policy made it clear that we lack a shared understanding about what a reasonable person might want to know about potential future uses of their clinical specimens *and* that neither legal precedent nor the Belmont principles provide a solution. In some ways, the failure of this proposal reinforces the importance of extending the governance and oversight of biorepository research to include stakeholders beyond the IRB.

More is at stake in a reboot of the Belmont Report than simply reforming the Common Rule. If we are to truly modernize the oversight and governance of research with human participants, we will need to expand the scope of policies that will receive attention in this broad effort. As we have noted, biorepositories often delegate ethical decisions to advisory committees with broad stakeholder representation. In community-based participatory research, participants themselves are asked to make decisions like which research questions will be studied and how the research results will be disseminated. As a modern consensus about the ethical foundation for research with humans emerges through normative and empirical work, it will become necessary both to re-evaluate existing practices and to innovate new governance practices.

These practices are likely to continue to include group decision-making, but also might include decision-making by individuals. Current policies create numerous opportunities of this sort: Research coordinators often need to decide how to proceed when they encounter potential participants who appear not to comprehend an informed consent document. Pathologists who operate a biorepository make important decisions about specimen collections. What types of ethical decisions should continue to fall to individuals, and what ethical guidance do they need to make ethically appropriate decisions?

Conclusion

Given that 2019 marks the 40th anniversary of the Belmont Report, now is an excellent time to revisit this document. Other teams have proposed alternative methods for marking this occasion.[32] We have proposed a "reboot" of the Belmont Report, so it seems appropriate to close by again taking a cue from the film industry. The Academy of Motion Pictures engages in ongoing debate about whether the process for selecting Oscar winners needs to be changed. In 2018, the Academy engaged in a public discourse about the need for a new category for popular movies. The superhero movie *Black Panther* reshaped the culture and economics of Hollywood, but it had emerged from a genre that significantly decreased its chances for appropriate recognition by the Academy. So the Academy changed the Oscar process through a process that was itself open for debate within the community.

It is time for the golden statues of our field – the Belmont principles – to receive the update they deserve. We have proposed three steps that might be followed by the community to reconsider the ethical basis for policies on research with human participants, and then eventually to reconsider the policies themselves. However, the ideas we have outlined here are just a beginning. This process should itself be open for debate within the community. More important than any particular step is the goal itself: to engage the community around a shared purpose. Together, we respect the integrity of the Belmont Report by recognizing the context that led to its creation, and then by considering carefully our own contemporary context that demands a reboot.

Acknowledgements

This work was supported by the National Human Genome Research Institute (NHGRI/NIH) under award number 1R01HG008988. The authors would like to acknowledge the following collaborators who participated in formative conversations and provided comments on drafts of this manuscript: Mark Rothstein, Eric Juengst, and Gail Henderson.

References

1. Cadigan RJ et al., “Public Comments on Proposed Regulatory Reforms That Would Impact Biospecimen Research: The Good, the Bad, and the Puzzling,” IRB 37, no. 5 (2015): 1–10; S. M. Rivera et al., “CTSA Institution Responses to Proposed Common Rule Changes: Did They Get What They Wanted?,” Journal of Empirical Research on Human Research Ethics 12, no. 2 (2017): 79–86.
2. Department of Health and Human Services, “Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators,” Federal Register 76, no. 143 (2011): 44512–31.
3. Department of Health and Human Services, “Federal Policy for the Protection of Human Subjects,” Federal Register 80, no. 173 (2015): 53933–4061.
4. Id., at 53938.
5. Beecher HK, “Ethics and Clinical Research,” N. Engl. J. Med 274, no. 24 (1966): 1354–60. [PubMed: 5327352]
6. Lillie EO et al., “The N-of-1 Clinical Trial: The Ultimate Strategy for Individualizing Medicine?,” Personalized Medicine 8, no. 2 (2011): 161–73. [PubMed: 21695041]
7. Glasgow RE et al., “National Institutes of Health Approaches to Dissemination and Implementation Science: Current and Future Directions,” American Journal of Public Health 102, no. 7 (2012): 1274–81. [PubMed: 22594758]
8. Wolf SM et al., “Managing Incidental Findings and Research Results in Genomic Research Involving Biobanks and Archived Data Sets,” Genetics in Medicine 14, no. 4 (2012): 361–84. [PubMed: 22436882]
9. Clayton EW, “Incidental Findings in Genetics Research Using Archived DNA,” Journal of Law, Medicine & Ethics 36, no. 2 (2008): 286–91.
10. Roden DM et al., “Development of a Large-Scale De-Identified DNA Biobank to Enable Personalized Medicine,” Clinical Pharmacology and Therapeutics 84, no. 3 (2008): 362–69. [PubMed: 18500243]
11. Nuremburg Code, “Trials of War Criminals before the Nuernburg Miltary Tribunals under Control Council Law No. 10: Nuernburg, October 1946-April 1949,” (1947); World Medical Association, “WMA Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects,” (1964).
12. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, “The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research,” (1979).

13. Richardson HS and Belsky L, “The Ancillary-Care Responsibilities of Medical Researchers: An Ethical Framework for Thinking About the Clinical Care That Researchers Owe Their Subjects,” Hastings Center Report 34, no. 1 (2004): 25–33. [PubMed: 15098404]
14. See E. W. Clayton, supra note 9; Burke W, Evans BJ, and Jarvik GP, “Return of Results: Ethical and Legal Distinctions between Research and Clinical Care,” American Journal of Medical Genetics Part C: Seminars in Medical Genetics 166, no. 1 (2014): 105–11.
15. Beskow LM and Burke W, “Offering Individual Genetic Research Results: Context Matters,” Science Translational Medicine 2, no. 38 (2010): 38cm20.
16. Shalowitz DI and Miller FG, “Disclosing Individual Results of Clinical Research: Implications of Respect for Participants,” Journal of the American Medical Association 294, no. 6 (2005): 737–40. [PubMed: 16091577]
17. Wolf SM, “Return of Individual Research Results and Incidental Findings: Facing the Challenges of Translational Science,” Annual Review of Genomics and Human Genetics 14(2013): 557–77.
18. Shore N, “Re-Conceptualizing the Belmont Report,” Journal of Community Practice 14, no. 4 (2006): 5–26.
19. Grady C et al., “Broad Consent for Research with Biological Samples: Workshop Conclusions,” American Journal of Bioethics 15, no. 9 (2015): 34–42.
20. See R. J. Cadigan et al., supra note 1.
21. Brothers KB et al., “When Participants in Genomic Research Grow Up: Contact and Consent at the Age of Majority,” The Journal of Pediatrics 168(2016): 226–31.e1. [PubMed: 26477867]
22. Beauchamp TL and Childress JF, Principles of Biomedical Ethics (New York: Oxford University Press, 1979).
23. Beauchamp and Childress proposed autonomy, beneficence, non-maleficence, and justice as the four primary principles for bioethics. The Belmont Report proposes respect for persons, beneficence, and justice as the three principles that should ground human research ethics. There is significant overlap in these accounts, however. The discussion of respect for persons in the Belmont Report highlights that this principle encompasses autonomy. Similarly, non-maleficence can also be understood as a dimension of the principle of beneficence.
24. Vanderpool HY, The Ethics of Research Involving Human Subjects: Facing the 21st Century (Frederick, MD: University Publishing Group, Inc, 1996).
25. Churchill LR, Fanning JB, and Schenck D, What Patients Teach: The Everyday Ethics of Health Care (New York: Oxford University Press, 2016).
26. Id.
27. Vitak J, Shilton K, and Ashktorab Z, “Beyond the Belmont Principles: Ethical Challenges, Practices, and Beliefs in the Online Data Research Community,” abstract from presentation at 19th ACM Conference on Computer-Supported Cooperative Work & Social Computing, printed in Proceedings of the 19th ACM Conference on Computer-Supported Cooperative Work & Social Computing (2016): 941–53.
28. See N. Shore, supra note 18.
29. Elster J, Deliberative Democracy, vol. 1 (New York: Cambridge University Press, 1998); H. A. Linstone and M. Turoff, The Delphi Method (Reading, MA: Addison-Wesley, 1975).
30. Rivera SM et al., “Modernizing Research Regulations Is Not Enough: It’s Time to Think Outside the Regulatory Box,” American Journal of Bioethics 17, no. 7 (2017): 1–3.
31. King NM, Henderson G, and Stein J, Beyond Regulations: Ethics in Human Subjects Research (Chapel Hill, NC: UNC Press Books, 1999).
32. Friesen P et al., “Rethinking the Belmont Report?,” American Journal of Bioethics 17, no. 7 (2017): 15–21; E. Y. Adashi, L. B. Walters, and J. A. Menikoff, “The Belmont Report at 40: Reckoning with Time,” American Journal of Public Health 108, no. 10 (2018): 1345–48.