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EDITORIAL

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Maximizing the value of human biospecimens: Lessons from coronavirus and the Seattle flu study

Collection and storage of human biospecimens for future uses has become prevalent in clinical care and clinical research. This practice has the potential to help significantly improve health and well-being. For example, research on biospecimens can help researchers to identify genetic variations associated with human diseases and develop new diagnostic tests and targeted treatments for these diseases. This practice also poses an ethical challenge. At the time biospecimens are collected, the future activities for which they might be used are typically unknown. This uncertainty has led to debate over what type of consent should be obtained to store biospecimens and use them in the future (Secretary's Advisory Committee, 2011).

Many groups and guidelines endorse "broad" consent (Grady et al., 2015), and this approach has been adopted widely (Simon, L'heureux, Murray, et al., 2011). Broad consent involves soliciting individuals' permission to retain their samples and make them available for a wide range of future research, subject to a few limitations, without further contact to obtain consent for the specific uses. This approach enhances the scientific and social value of human biospecimens over approaches that obtain consent for a narrower range of research (Table 1). For example, obtaining consent for specific types of research can prevent samples from being used in studies involving next-generation DNA sequencing techniques that were not envisioned at the time the original consent was obtained. At the same time, broad consent offers donors greater control and respect compared to blanket consent or using samples without obtaining any consent at all.

Granting its value over other extant approaches, the COVID pandemic illustrates a critical limitation of broad consent that has previously gone unrecognized. Obtaining consent to use samples for research only has the potential to limit their availability for important public health purposes, including efforts to track infection rates in the community and to explore genetic host factors that make some people more susceptible to serious disease. The present article explains this concern and argues that, in order to address it, broad consent should be replaced with broadened consent, which goes beyond broad consent to include future public health uses.

1 | SEATTLE FLU STUDY

Early in the COVID-19 pandemic, researchers associated with the Seattle Flu Study (SFS) proposed using samples, which had been collected as part of a research study on seasonal influenza transmission, to assess whether community spread of COVID-19 had begun in the United States. Repurposing the samples in this way would have provided public health officials with a critical extra few weeks of warning regarding the pandemic (Chu et al., 2020). During emerging infectious disease threats, even a few extra weeks can provide a chance to head off a disease before it begins to spread exponentially (Glanz & Robertson, 2020). Unfortunately, this opportunity was lost: Officials prevented the researchers from repurposing the samples because the consent signed by the donors was limited to research uses (Fink & Baker, 2020).

The SFS researchers eventually received permission for further testing on the samples but only on the condition that they first obtain new consent that covered public health activities. After weeks of delay, the SFS team decided to run the tests without obtaining new consent, thereby establishing that community spread was already occurring. If the original consent had included public health uses, the SFS team would not have been forced to choose between following the regulations or protecting the public's health. In addition, valuable time would have been saved, and the terrible disease burden currently being experienced in the United States might have been reduced.

2 | BROADENED CONSENT

Proponents of broad consent argue that investigators should solicit individuals' permission to store their samples and make them available for future research uses. For example, it has been argued that broad consent "serves to alert persons considering donating their biospecimens about the broad spectrum of research that could be undertaken" (Secretary's Advisory Committee, 2011). Similarly, the revised U.S. federal regulations, which now incorporate broad consent, stipulate that the consent forms must explain the "types of research" that may be conducted with the samples (45CFR46.116.d.2).

The SFS case highlights the fact that limiting consent to future research uses can prevent the samples from being available for public health purposes. Researchers might try to avoid this concern by anonymizing the samples and using them without any consent. Another option would be to code the samples and repurpose them. While these approaches make sense, they have important costs. Anonymizing samples reduces their value, for example, making it impossible to conduct contact tracing, while using samples for purposes other than those for which consent was obtained fails to respect the donors and has the potential to erode the public trust that is vital to research (Botkin, Goldenberg, Rothwell, Anderson, & Lewis, 2013).

TABLE 1 Types of consent for future use of biospecimens

Type	Obtains consent for	Advantages	Concerns
Individual study	Each study when proposed	Maximizes donor control	Increases donor burden; reduces sample value
Checklist	Specific types of research (e.g., HIV)	Enhances donor control	Uncertainty over permitted studies; reduces sample value
Menu	Donor choses type of consent	Enhances donor control	Concerns of selected approach; increases monitoring burdens
Broad consent	Broad range of research, with a few limitations	Minimizes burdens; enhances value	Donors do not know specific uses; may permit objectionable trials
Broadened consent	Broad range of uses related to health, with a few limitations	Minimizes burdens; further enhances value	Donors do not know specific uses; may permit objectionable trials
Blanket consent	Unlimited uses	Minimizes costs; maximizes value	Donors do not know specific uses; increases potential for objectionable trials
No consent	No consent obtained	Eliminates costs; maximizes value	Fails to respect donors; may undermine trust

The research use of newborn bloodspot samples without prospective consent generated significant objections. There was concern that the donors did not have a say in how the samples would be used. Moreover, genetic information obtained from the samples might be used by third parties to stigmatize or discriminate against individuals with certain genetic predispositions or markers (Cunningham, O'Doherty, Sénécal, Secko, & Avard, 2015). These concerns ultimately led to the destruction of millions of valuable samples.

Fortunately, there is a better approach: Individuals could be asked for prospective consent that covers public health uses. In particular, standard broad consent wording regarding possible future uses of individuals' biospecimens could be broadened as follows (additions in italics): "If you agree, your biospecimens will be stored and may be used in future research *or other efforts, such as public health activities*, that are designed to promote health and well-being."

Replacing broad consent with broadened consent in this way could be problematic if individuals opposed these additional uses. However, empirical studies find that individuals overwhelmingly support the use of their samples in projects that have the potential to promote health and well-being (Grady et al., 2015). That is, individuals' support is not limited to research uses. While these data do not support using samples for activities unrelated to health and well-being, they do support public health uses.

Broadened consent might also be problematic if it increased the risks to donors. For example, commentators point out that advanced genetic technologies make it possible to reidentify genetic samples in ways that may harm the donors. However, safeguards that are commonly adopted in the research setting can be implemented in the context of public health activities as well, suggesting that the expansion of possible future uses to include public health activities does not increase the risks to donors.

Finally, replacing broad consent with broadened consent would obviate the need to rely on the new and untested regulatory mechanism, which regards certain public health activities as not constituting human subjects research (US Department of Health and Human Services, 2018). This is especially important given that it may be interpreted narrowly so that it does not cover repurposing samples that were originally collected for research.

3 | A WAY FORWARD

As its proponents emphasize, provision of broad consent does not constitute blanket permission for investigators to use donated biospecimens in any way they like. Instead, proposed uses should undergo independent review to ensure that they are consistent with the original consent, as well as being ethical and socially valuable. A similar approach should be used for broadened consent as well. In particular, it will be important to ensure that public health uses are sufficiently valuable to justify any opportunity costs that arise from samples not being available for research purposes.

Review of proposed research uses is frequently conducted by an institutional review board. While reliance on an institutional review board could be used for public health activities as well, their expertise focuses on research. Hence, it may make sense to establish a review process specific to public health uses. Whatever form it takes, a reliable and independent review process is important to respect donors and maintain public trust that donated biospecimens are being used for legitimate purposes. Independent review also helps to ensure samples are being used for valuable purposes, thereby maximizing the value of donors' contributions.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest with respect to the present work.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

Botkin, J. R., Goldenberg, A. J., Rothwell, E., Anderson, R. A., & Lewis, M. H. (2013). Retention and research use of residual newborn screening bloodspots. *Pediatrics*, *131*, 120–127. https://doi.org/10.1542/peds.2012-0852

Chu, H. Y., Englund, J. A., Starita, L. M., Famulare, M., Brandstetter, E., Nickerson, D. A., … Seattle Flu Study Investigators. (2020). Early detection of covid-19 through a citywide pandemic surveillance platform. *New England Journal of Medicine*, *383*, 185–187. https://doi.org/10.1056/NEJMc2008646

Cunningham, S., O'Doherty, K. C., Sénécal, K., Secko, D., & Avard, D. (2015). Public concerns regarding the storage and secondary uses of residual newborn bloodspots: An analysis of print media, legal cases, and public engagement activities. *Journal of Community Genetics*, *6*, 117–128. https://doi.org/10.1007/s12687-014-0206-0

Fink, S., & Baker, M. (2020). It's just everywhere already: how delays in testing set back the U.S. coronavirus response. *New York Times*. March 10, 2020. Retrieved from https://www.nytimes.com/2020/03/10/us/coronavirus-testing-delays.html.

Glanz, J., & Robertson, C. (2020). Lockdown delays cost at least 36,000 lives, data show. *New York Times*, May 20.

Grady, C., Eckstein, L., Berkman, B., Brock, D., Cook-Deegan, R., Fullerton, S. M., … Wendler, D. (2015). Broad consent for research with biological samples. *American Journal of Bioethics*, *15*, 34–42. https://doi.org/10.1080/15265161.2015.1062162

Secretary's Advisory Committee on Human Research Protections. (2011, 20 July). FAQs, terms and recommendations on informed consent and research use of biospecimens. Secretarial Communications. Retrieved from http://www.hhs.gov/ohrp/sachrp/commsec.

Simon, C., L'heureux, J., Murray, J., Winokur, P., Weiner, G., Newbury, E., … Zimmerman, B., (2011). Active choice but not too active: Public perspectives on biobank consent models. *Genetics in Medicine*, *13*, 821–831. https://doi.org/10.1097/GIM.0b013e31821d2f88

US Department of Health and Human Services. 2018 Protection of human subjects. 45 CFR § 46. Retrieved from https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML.