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Collecting Biospecimens and Obtaining Biobank Consent From Patients in an Academic Health Care Setting: Practical and Ethical Considerations

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Abstract

Academic health centers and health systems increasingly ask patients to enroll in research biobanks as part of standard care, raising important practical and ethical questions for integrating biobank consent processes into health care settings. This article aims to assist academic health centers and health systems considering implementing these integrated consent processes by outlining the 5 main issues—and the key practical and ethical considerations for each issue—that Indiana University Health and the Indiana Biobank faced when integrating biobank consent into their health system, as well as the key obstacles encountered. The 5 main issues to consider include the specimen to collect (leftover, new collection, or add-ons to clinical tests), whether to use opt-in or opt-out consent, where to approach patients, how to effectively use digital tools for consent, and how to appropriately simplify consent information.

Biobank recruitment has traditionally operated independently of health care, with individuals approached in a range of settings but usually not as part of standard health care. Recently, however, some academic health centers and health systems—for example, Vanderbilt Health,¹ UCLA Health,² Geisinger Health,³ Massachusetts General Hospital,⁴ Boston Children's Hospital,⁵ and Cincinnati Children's Hospital Medical Center⁶—have implemented integrated consent processes, in which patients are asked to enroll in research biobanks as part of ordinary care or in a health care setting. Such projects have successfully enrolled large numbers of people in biobanks, collecting specimens and often linking them to information stored in patients' electronic health records. For instance, over 275,000 patients have consented to be included in Geisinger Health's MyCode program as of March 2021, with nearly 200,000 specimens collected and over 140,000 patients' DNA sequenced.⁷ Other academic health centers and health systems are building similar biobanks in an attempt to replicate this success. These efforts raise important questions about best practices for addressing the practical and ethical challenges related to biospecimen collection and informed consent.

A widely cited survey from 2013 of the biobanking landscape in the United States found that more than 300 biobanks in the country were affiliated with academic institutions.⁸ In principle, any of these biobanks could pursue patient recruitment at affiliated hospitals. However, incorporating biobank recruitment into a health care setting raises important practical and ethical questions, especially for academic health centers. For instance, although academic health centers aim to both facilitate research and provide care, collecting specimens and enrolling patients into a biobank in a health care setting might blur the line in patients' minds between care and research. Moreover, the arrangements with private industry that drive programs like MyCode may be seen as inappropriate for institutions with education and community service missions.

In fall 2018, Indiana University (IU) Health, the largest health care provider in the state of Indiana, piloted a new integrated consent process for the Indiana Biobank. The Indiana Biobank was established in 2010 as a general purpose biobank for researchers. For patients who participate in the biobank, their specimens are linked to their IU Health electronic health record and subsequently made available for institutional review board (IRB)-approved studies. Building on established procedures and widespread institutional support for the biobank, a committee, including representatives from the IRB, Clinical and Translational Science Institute, pathology, community engagement, and bioethics, was formed in September 2018 to design a new integrated consent process. Overall, the new integrated consent process was considered successful in terms of enrollment and patient satisfaction. From fall 2018 to fall 2020, 11,537 participants were enrolled in the Indiana Biobank under the new process. Of 526 enrollees who were surveyed about their experiences with the new integrated consent process, 98% said they were comfortable with the process and 94% felt that they received enough information (T.J. Kasperbauer, PhD, unpublished data, 2019).

This article outlines the 5 main issues IU Health and the Indiana Biobank faced in designing the new integrated consent process, the key practical and ethical considerations for each issue, and the key obstacles encountered. We believe that summarizing our experience will be useful for other academic health centers and health systems that are considering integrating biospecimen collection and biobank consent into standard care. The points to consider for each main issue are summarized in Table 1.

Specimen to Collect: Leftover, New Collection, or Add-Ons to Clinical Tests

The specimens that are collected for the biobank significantly influence the rest of the consent process. Biobanks generally have 3 options: using leftover specimens from clinical procedures;

asking for a new, direct donation from patients; or collecting additional specimens during a procedure already being conducted for clinical care (e.g., an additional tube of blood during a clinical blood draw).

Using leftover specimens is convenient since they are generally available and would otherwise be discarded. Furthermore, the regulatory requirements do not require patient consent to use leftover specimens for research if they are kept deidentified. Some have called for an expansion of current consent policies under the Federal Policy for the Protection of Human Subjects (Common Rule), such that consent would be required even to use leftover, deidentified biospecimens.⁹ Senior leadership at the National Institutes of Health have also indicated their support for such a change.¹⁰ However, currently the use of leftover, deidentified specimens is not considered human subjects research under the Common Rule.¹¹

A key downside of using leftover specimens is that it excludes patients who have not undergone relevant clinical tests. The same problem applies when collecting additional specimens from clinical testing. In addition, the exact type, quantity, and quality of leftover tissue or blood may not be optimal for research needs.

Requiring new collections results in some burden and potential risk for patients. They may be reluctant to undergo the collection procedure or to spend extra time or return at a later date to donate. Patients who are asked to provide an extra specimen during regular clinical testing may be reluctant for similar reasons. For example, if a patient is already providing multiple tubes of blood for clinical testing, it may seem onerous or uncomfortable to provide 1 or 2 more for the biobank.

Research on preferences for biospecimen donation indicate that people support both new collections and the use of leftover specimens, without a universal preference for one over the other.¹² Biobanks with integrated consent processes have used all 3 methods. For example, donors to Vanderbilt Health's BioVU consent to the use of leftover specimens from tests ordered by physicians; no additional material is requested.¹³ Geisinger Health requests that patients provide additional blood samples when their doctor orders a blood test as part of their care.¹⁴ UCLA Health's UCLA BioBank² and Massachusetts General Hospital's biobank (Mass General Brigham Biobank)⁵ take additional samples from doctor-ordered tests, as well as leftover clinical samples, which in UCLA BioBank's case includes both blood and other tissues. We chose to collect new blood samples, as an additional tube during a scheduled clinical blood draw, similar to Geisinger Health. The option of collecting leftover specimens without patient consent was not an option for the Indiana Biobank because the specimens are linked to patients' electronic health records and, thus, are not deidentified. While not yet implemented, a process is currently being considered to also obtain consent from patients to use their leftover specimens, similar to UCLA BioBank. The decision to implement a process to allow us to also include leftover specimens was made partly due to expressed patient interest in using pre-existing specimens.

Opt-In or Opt-Out Consent

A fundamental question for an integrated consent process is whether to use opt-out or opt-in consent. An opt-in consent process is typical for research: individuals are asked whether they are willing to participate and enrolled if they agree. In an opt-out consent process, in contrast, patients are automatically enrolled, and their specimens are collected and stored in the biobank unless they indicate that they do not want to contribute to the biobank. Any opt-out process must

have some mechanism for educating potential enrollees that they will be automatically enrolled unless they ask not to be. Some biobanks, like BioVU and the biobank at Cincinnati Children's Hospital Medical Center, began with an opt-out process but eventually transitioned to an opt-in process.

The main benefit of opt-out consent is convenience, for both the biobank and patients. Opt-out consent is efficient and low-effort. However, opt-out processes raise ethical and regulatory concerns about patient autonomy and control. Most importantly, patients may be completely unaware that their specimens are being entered into a biobank. Patients may not understand the purpose of the biobank or how failing to opt-out will affect them or their samples.¹⁵ If opt-out consent is used, there is a risk that patients will later be surprised to find out their specimens have been included in a biobank, which could lead to participant withdrawals, discontinuing biobank recruitment until an opt-in process can be implemented, and even lawsuits.

The main benefit of opt-in consent is that it increases the chance that patients will understand the research project they are signing up for. Although studies show that patients often do not comprehend or remember information they are given during the consent process,^{16,17} at least the key information has been actively disclosed to them in an opt-in process. Opt-in consent may also be required by research regulations if specimens are not deidentified—for instance, if they are linked to the patient's electronic health record. The main drawback of opt-in consent is that it introduces a potentially time consuming and expensive step that may slow down enrollment, possibly delaying research, while also potentially failing to significantly improve patient understanding of research procedures.

Research on patient enrollment preferences at BioVU found that people were generally supportive of opt-out processes, even though the biobank eventually transitioned to an opt-in process.^{18,19} Other studies have confirmed that patients support opt-out processes but have also found that if given the choice, people prefer opt-in processes.²⁰ For example, 63% of focus group participants and 67% of survey participants in Simon and colleagues' study preferred opt-in consent, with focus group participants favorably citing the more active and informed choice provided by opt-in consent.²¹ A patient advisory group at Cincinnati Children's Hospital Medical Center ultimately favored an opt-in over an opt-out process because it would provide patients with more explicit control over their enrollment.⁶ So while participants may like the convenience of an opt-out process, they generally seem to prefer having a more active choice in enrolling in biobanks.

Due to the above ethical and regulatory concerns and data on patient preferences, the Indiana Biobank chose to implement an opt-in consent process. Patients are asked whether they would like to enroll in the biobank and explicitly informed that their participation is voluntary and that declining to participate will not affect their care. Our opt-in consent process also allows patients to provide Health Insurance Portability and Accountability Act (HIPAA) authorization, so that the biobank can link specimens to the patient's electronic health record. As mentioned above, 94% of participants surveyed indicated that they received enough information through the opt-in consent process (T.J. Kasperbauer, PhD, unpublished data, 2019).

Where to Approach Patients

Patients can provide their consent to participate in a biobank in a wide range of possible clinical situations. We primarily considered 2 potential places to seek consent for participation in the biobank: at registration (or the waiting room) and at the phlebotomy lab.

For efficiency, arguably the best course is to integrate biobank consent into registration procedures. Patients are already familiar with completing paperwork when they enter the clinic, so they may be more willing to review biobank consent materials at that time. This is also a natural context to present biobank information if there will be a link to the patient's electronic health record.

A related method would be to approach patients while they are in the waiting room. Patients could be directed to another area where the consent process could be conducted privately.

Separating the biobank consent discussion from other clinical paperwork could highlight that the biobank consent is for research and distinct from their clinical care. Waiting until patients have completed other paperwork also gives biobank recruiters time to verify whether the patient should be approached at all (e.g., they already declined to contribute to the biobank or are visiting for a procedure that would prevent biobank donation).

However, approaching patients during registration procedures or while in the waiting room can be problematic for clinical staff, especially given the variety of clinical operating styles. Many clinics lack the staffing to incorporate a new biobank consent process into these steps. Clinical staff may also lack the expertise required to answer questions patients might have about the biobank. Indeed, many Clinical and Translational Science Institutes find it challenging to train clinical staff to conduct biobank consent processes.²² Any consent processes, and any added burden on clinical staff, must be assessed to ensure that they do not disrupt normal operations. Because the Indiana Biobank collects samples via an extra tube during a clinical blood draw, we decided to approach patients at the phlebotomy lab prior to getting blood drawn. This guaranteed that blood would be drawn immediately after patients consented to participate in the biobank. It

also minimized issues involved in alerting phlebotomists to draw an extra tube, since they could be informed directly by the biobank recruiter.

The main disadvantage to approaching patients in the phlebotomy lab is that many patients do not need to visit the phlebotomy lab, decreasing the number of potential participants. The lab can also be a challenging context in which to obtain consent because many patients are in a rush and may be reluctant to spend additional time undergoing an extra blood draw. The Indiana Biobank's recruitment team has observed patients being called for their exam just as they start reading the consent form. These patients are put in a difficult position to either make a quick decision or promise to return later. Neither option is desirable for patients or biobank recruiters, so Indiana Biobank recruiters avoid it as much as possible.

Effective Use of Digital Tools for Consent

Many have noted that consent for medical research is going digital, replacing the paper forms that were standard in the past.^{23,24} These paper forms are being replaced in many contexts due to the ease of record keeping and flexibility in presentation style that e-consent and digital tools (e.g., videos and interactive software) provide. E-consent and digital tools also have the potential to increase engagement with and understanding of biobank consent materials. At the Indiana Biobank, we chose to use tablets to present materials in a form that resembled a paper consent form (i.e., the tablet materials generally used the same text and figures as the paper consent form) and to have a biobank recruiter available to answer questions and certify the identity of potential participants. In the future, we hope to also incorporate videos presenting consent information and other automated processes (see below).

The first step in building an e-consent process is to provide consent materials on an electronic device (e.g., a tablet). At the Indiana Biobank, we use a simplified version of the traditional Paper consent form (explained below), which was converted to a tablet format. Biobank recruiters can present the tablet directly to potential participants, as done at the Indiana Biobank, or the tablets can be incorporated into registration procedures.

One option that we considered, but have not used to date, is to create a consent process that participants can access on a device of their own, potentially from their home. For example, the National Institutes of Health's All of Us Research Program developed an interactive e-consent process that can be accessed either on their website or through an app.²⁵ To ensure that people engage with the most important information, the program poses questions at key moments and, if needed, provides participants with corrective feedback about topics they have misunderstood. An ongoing challenge with such programs is to overcome limitations and inequalities in health literacy and in access to electronic devices and a reliable internet connection.

Patient portals can also be useful in presenting consent materials. Boston Children's Hospital and Massachusetts General Hospital have successfully incorporated biobank consent materials into their health portals.^{5,26} Patients receive an email link prior to a doctor's appointment, which brings them to information about the biobank and the consent form, linked to their patient portal. While very few people make a decision based on the electronically provided information alone (only 1% of those who receive the email), the information helps prime patients to receive the material again when they visit the hospital. In principle, patients could receive emails, notices in their patient portal, and a direct request either in their doctor's office or at the phlebotomy lab.

Any of these options can also incorporate videos to improve the delivery of consent information.

The All of Us Research Program uses short, 1–3-minute videos to explain key topics.²⁵

Similarly, researchers at Stanford University collaborated with a health communications company to develop a series of 2–3-minute animated videos explaining the concept of biobanks and how they contribute to research.²⁷ It is also possible to turn the entirety of written consent materials into videos, as UCLA BioBank has done.²⁸ Mass General Brigham Biobank pursued a more moderate approach, with a 3-minute video introduction to the biobank included alongside the full online consent form.²⁹

However, videos are often resource intensive to create. Additionally, it can be difficult to include all of the necessary information to receive IRB approval in short videos, which can lead to long videos that frustrate patients. For example, Simon and colleagues translated the University of Iowa's 9-page biobank consent form into a 16-minute video with illustrations of key concepts.³⁰ The video successfully improved comprehension, compared to traditional paper consent forms, by almost 2 percentage points. However, on average, it also took participants 5 minutes longer to complete the video than the paper consent. Shorter videos would be preferable, as long as they do not significantly compromise comprehension.

Appropriate Simplification of Consent Information

There has long been a movement to simplify the information presented to patients as part of consent processes for research participation.^{31,32} Fitting with these long-stated but long-delayed goals, the Common Rule modifications enacted in 2018 require that consent forms present information concisely and in a way that facilitates understanding of the reasons for research participation.¹¹ To meet these requirements, many institutions are simplifying their consent

forms to enhance their readability. Simplification is known to boost enrollment rates in addition to making consent forms easier to read.^{16,17}

As part of the Indiana Biobank's project to create a new integrated consent process, our committee completely rewrote the existing 7-page consent form. We simplified the form by shortening sentences, using active voice, reducing repetition, and emphasizing the main takeaways in bullet points at both the beginning and end of the form. The institution's IRB and HIPAA compliance staff partnered and coordinated with the committee to ensure the resulting language met all regulatory requirements. As a result, the readability of the consent form dropped from a 12th- to a 9th-grade reading level on the Flesch–Kincaid scale. By applying similar techniques, BioVU and the UCLA BioBank were able to reduce their consent forms to just over 2 pages. The Indiana Biobank continues to look for ways to improve the form's readability and reach the recommended 6th- to 8th-grade reading level.³²

Shortening and simplifying a consent form raises important challenges related to the dangers of oversimplifying information (e.g., eliminating essential information) or minimizing real risks that potential participants should consider. Despite extensive discussion and effort, we found no obvious way to simplify the description of risks without minimizing them, as illustrated in the following 3 areas:

1. *Risks of sharing data:* The Indiana Biobank's consent form states that people outside of IU could access participants' data, including a brief outline of the types of organizations those people might come from (e.g., government agencies and private companies).

However, the consent materials provide few other details about data sharing. Previous studies have found that biobank participants often do not understand that entities outside of the biobank might receive their data, despite explicit statements that these entities

could receive their data.^{16,17} Patients and research participants also often object to sharing their specimens and associated data with commercial entities.^{33,34} We are currently conducting research to identify effective ways to highlight how data might be shared without overly complicating the consent form.

2. *Risks of individuals being re-identified from sharing genetic information:* Beskow and colleagues' survey of biobank experts found that 83% wanted a statement in consent forms indicating that "There is a small chance that someone could trace my information back to me."³⁵ However, we had numerous discussions about whether this was ethically required, how much detail to provide, and how to compare the identification risks from direct identifiers (like someone's name) to the risks from indirect identifiers (like someone's genetic information).³⁶ Ultimately, we decided to emphasize that direct identification would be prevented by removing personal information like names and contact details. Thus, our consent form does assert that identification from DNA is a possibility but does not frame it as a fundamental risk of enrollment.
3. *Accessing patient electronic health records:* We also grappled with how to communicate the fact that the Indiana Biobank links information from participants' electronic health records with their biobank specimens. In Beskow and Weinfurt's survey of experts' opinions on information in consent forms, access to electronic health records was considered one of the most essential pieces of information that participants had to understand for ethical enrollment.³⁷ To meet this goal, concise, direct statements about the link to the electronic health record were placed at both the beginning and end of the Indiana Biobank consent form. However, many enrollees still misunderstand this link,³⁸ so we are conducting additional research on how understanding might be improved.

To further simplify the content of our consent form, the committee designing the new consent process included experts in visual communication and human-centered design who optimized the layout, typography, and imagery used in the consent form. A major part of this effort involved designing an infographic, shown in Figure 1, to illustrate the main features of enrolling in the biobank without downplaying the risks. The infographic was presented at the beginning of the form and provided a quick snapshot of the most essential information.

We had significant debate about how much text to provide alongside the illustrations in the infographic. To improve the infographic, we solicited feedback from patient advisory groups, as well as through an online survey sent out to the public via Facebook and Reddit. Overall, the survey found that the illustrations were fairly successful in communicating on their own but that some text was needed to ensure people did not miss important details or make incorrect assumptions. Because each step in the specimen donation process entailed specific risks, we decided to highlight one main risk for each step in the infographic.

Conclusions

Incorporating biobank consent into a health care setting raises many difficult practical and ethical questions. As academic health centers and health systems aim to increase biobank enrollment through integrated consent processes, they will likely confront the main issues we have discussed here. While there are few obviously correct or simple choices in this area, academic health centers and health systems must continue developing morally responsible consent processes to ensure that research biobanks can continue to serve as essential resources for medical researchers long into the future.

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Figure Legend

Figure 1

Infographic used as part of the consent form for enrolling in the Indiana Biobank (IB). ©

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Table 1**Practical and Ethical Considerations When Integrating Biobank Consent Into Standard Care**

Issue	Practical and ethical points to consider
Specimen to collect: leftover, new collection, or add-ons to clinical tests	• Using leftover specimens increases the rate of collection, as they are generally available, but may not be optimal for research needs • New collections and add-ons to clinical tests provide fresh material but can result in some burden and potential risk for patients and face stricter consent requirements
Opt-in or opt-out consent	• Opt-in increases the chance that patients will understand the research project but introduces a potentially time consuming and expensive step • Opt-out is convenient but raises ethical and regulatory concerns about patient autonomy and control • Studies have shown that participants generally prefer opt-in over opt-out
Where to approach patients	• Integrating consent into registration procedures streamlines the process for patients • Approaching patients during registration procedures or while in the waiting room requires additional training to prepare clinical staff on biobank consent processes • Approaching patients at the phlebotomy lab minimizes disruption of clinic processes and allows immediate collection of specimens after consent is given but excludes patients who are not undergoing relevant clinical tests
Effective use of digital tools for consent	• E-consent has the potential to increase patient engagement with consent materials and can provide corrective feedback • Patient portals provide a promising mechanism to present consent materials but yield low uptake without follow-up, in-person enrollment • Video consent increases engagement but videos are often resource intensive to create and it can be difficult to include all of the necessary information in short videos
Appropriate simplification of consent information	• Studies suggest that simplifying consent can boost enrollment and does not impair understanding of consent information • Simplified consent may eliminate essential information or minimize real risks • Infographics and other visual elements in consent forms can concisely communicate key information

Figure 1

