Incorporating Biobank Consent into a Healthcare Setting: Challenges for Patient Understanding

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Abstract

Background: Biobank participants often do not understand much of the information they are provided as part of the informed consent process, despite numerous attempts at simplifying consent forms and improving their readability. We report the first assessment of biobank enrollees' comprehension under an "integrated consent" process, where patients were asked to enroll in a research biobank as part of their normal healthcare experience. A number of healthcare systems have implemented similar integrated consent processes for biobanking, but it is unknown how much patients understand after enrolling under these conditions.

Methods: We recruited patients who enrolled in a biobank while in a healthcare setting when receiving ordinary care. We assessed knowledge of consent materials using 11 true/false questions drawn from a well-known biobank knowledge test. After reviewing the results from 114 participants, we revised the consent form and repeated the knowledge assessment with 144 different participants.

Results: Participants scored poorly on the knowledge test in both rounds, with no significant differences in overall scores or individual items between the rounds. In Phase 1, participants answered 53% of the questions correctly, 25% incorrectly, and 22% "I don't know." In Phase 2, participants answered 53% of questions correctly, 24% incorrectly, and 23% "I don't know." Participants scored particularly poorly on questions about data sharing and accessing medical records.

Conclusions: Enrollees under an integrated consent model had significant misunderstandings that persisted despite an attempt to improve information specifically about those topics in a consent form. These results raise challenges for current approaches that attribute misunderstanding to overly complex consent forms. They also suggest that the pressures of the clinic may compound other problems with patient understanding of biobank consent. As health systems increasingly blend research and care, they may need to rethink their approach to educating patients about participation in a biobank.

Introduction

Biobank participants appear not to understand much of the information they are

provided as part of the informed consent process. Despite numerous attempts at

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simplifying consent forms and improving their readability, participants typically answer fewer than 80% of questions correctly on biobank knowledge tests (Eisenhauer et al. 2019). Beskow et al.'s (2010a, 2010b, 2015, 2017) process of designing and testing a simplified consent form illustrates the challenges in this area. A wide range of both laypeople and experts provided input to design their consent form and corresponding 21-item, true/false knowledge test. Beskow's team then presented the consent form and test to a sample of participants completing the test online, with plenty of time to read the material without distraction. Only 20% of individuals answered all questions correctly, with an average score of 83% correct (Beskow et al. 2017).

Comprehension is often worse in realistic consent conditions. In a study of enrollees to a breast cancer biobank, participants answered 64% of questions correctly on average after reading a simplified consent form, compared to 58% correct after reading a standard, complex consent form (Garrett et al. 2017). Even studies indicating higher levels of overall comprehension under realistic consent situations have found severe deficiencies on one or more key topics (e.g., data sharing; McCarty et al. 2015; Simon et al. 2016).

These failures in understanding raise important ethical questions about current approaches to informed consent. Persistent misunderstandings of both clinical and research procedures have long been attributed to overly complex consent forms (Corneli et al. 2017; Flory & Emanuel 2004; LoVerde et al. 1989). Consequently, proposed solutions to misunderstanding have focused on simplifying and enhancing the

readability of consent forms. Recent changes to the Common Rule formally require researchers to simplify consent materials and present information to participants in ways that facilitate comprehension (45 CFR 46.116).

However, persistent misunderstandings even under ideal conditions suggest that this approach could be misguided. As Carl Schneider (1998, 2006) has argued, attempts to achieve perfect understanding of consent forms are based on a narrow, "mandatory autonomy" conception of informed consent that requires people to make decisions based on full knowledge and reflection. An advocate of mandatory autonomy would require biobank enrollees to achieve 100% scores on biobank knowledge tests— anyone failing to meet that mark cannot enroll. Given that people fall well short of this target with even the best consent forms, one could argue that the goal of complete understanding is misconceived. Clear disclosure of risks and benefits is required, but not that participants understand them. Or perhaps we should instead significantly lower the threshold for understanding. For example, we could require that biobank participants understand that they are giving blood for research, but nothing else (e.g., who else might receive their data and for what purposes).

In this study, we report an assessment of the comprehension of recent biobank enrollees who consented under an "integrated consent" process, where patients were asked to enroll to a research biobank as part of their normal healthcare experience. Biobank recruitment often takes place independently from care, in a public setting, and eligibility is unrelated to where the individual receives healthcare. Integrated consent

can include a range of practices, from embedding biobank consent into patients'

consent for treatment to recruiting patients throughout their healthcare experience (e.g.,

in waiting areas or as part of scheduled clinical tests). Whichever method is used,

recruiting patients in a healthcare setting poses numerous challenges to consent.

Patients may be stressed, tired, and preoccupied with thoughts about their own health.

They may also be unfamiliar with biobanks and may interpret biobank recruitment as

part of their personal care. These obstacles only exacerbate the ethical challenges

described above with ensuring that patients understand key information about biobanks.

A number of hospitals and health care systems have implemented biobank consent

processes that are integrated into clinical care, including BioVU at Vanderbilt (Pulley et

al., 2010)[1], the UCLA Biobank[2], Geisinger Health System (Carey et al., 2016)[3], Boston

Children's Hospital (Bourgeois et al., 2017), and Cincinnati Children's Hospital (Marsolo

et al., 2012). However, it is unknown how much patients understand about biobank

participation after enrolling under these conditions. An early study of integrated consent

at BioVU found that after three years of an opt-out biobank consent process, most

patients remained unaware that the biobank even existed (Brothers et al., 2013). It is

also unclear whether iterative improvements to consent materials can overcome the

challenges of consenting in a healthcare setting. Simon et al.'s (2016) study of a

partially integrated consent found that an interactive video improved comprehension

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[1] BioVU Consent Form. Retrieved from https://victr.vanderbilt.edu/pub/biovu/?sid=220.
[2] UCLA Health Universal Consent for Biological Samples. Retrieved
from https://www.uclahealth.org/precision-health/workfiles/universal-consent-brochure-English1.pdf
[3] Geisinger Research Consent/Authorization Form. Retrieved from https://www.geisinger.org/-/media/OneGeisinger/pdfs/ghs/research/mycode/mycode-consent-v31.ashx;

compared to a standard, written consent. However, the video in this study was lengthy, causing the consent process to last more than 18 minutes, which many health systems would struggle to implement as part of standard care. Some participants still missed questions even after viewing the interactive video, again raising important ethical questions about whether full understanding by patients is achievable, or perhaps even desirable.

In this study, we tested the understanding of patients who were enrolled in a biobank at a clinical care site affiliated with a university health system [details after peer review]. They were enrolled while waiting to either see their doctor or for a scheduled clinical blood draw. The patients viewed a simplified consent form and answered a set of questions drawn from a well-known instrument used to measure knowledge of a biobank. After viewing scores from an initial assessment, we revised the consent form to enhance the salience of key information, slightly modified one of the knowledge questions, and then conducted a second round of assessment.

Methods

The process of simplifying the biobank consent form and redesigning the consent process lasted from August 2018 to October 2018. We implemented the initial consent process from October 2018 to January 2019, which we refer to as Phase 1. We developed and conducted a survey at this time to assess participants' degree of knowledge and satisfaction with the consent process.

After reviewing the results of the Phase 1 survey, we revised the consent form and one knowledge test question with the aim of improving participants' performance. To assess the effects of these revisions, we conducted a second round of survey data collection from April 2019 to June 2019, which we refer to as Phase 2. The study protocol was approved by the Institutional Review Board (IRB) at X University.

Participants

Participants were adults, at least 18 years old, who were either visiting phlebotomy services to have blood drawn or visiting a doctor as part of their normal care. Phase 1 participants were recruited from three health care locations within the state. Phase 2 participants were recruited from one of the sites from Phase 1 as well as three additional locations in the state.

The Biobank

Patients were recruited to enroll in the X Biobank as part of a precision health initiative at the X Health System. The X Biobank was established in 2010 as a general purpose biobank for researchers. Specimens from patients at the X Health System are linked to their electronic health record for research use. Biospecimens are only shared for IRB-approved projects and are available for use by researchers throughout the entire state.

The Biobank Consent Process

Biobank recruiters approached patients either at the phlebotomy lab or their doctor's exam room to ask if they would donate to the biobank. They briefly explained the

purpose of the biobank and the procedure for donation. Patients at the phlebotomy lab were informed that donation would require an extra vial of blood to be taken but would not require an extra needle stick. Patients seeing a doctor were told that a needle stick would be required if they were not already undergoing a blood draw that day. Those who expressed interest were handed an electronic tablet that displayed the consent materials. The recruiter remained nearby to answer questions as needed. While recruiters frequently engaged patients in a discussion about the biobank, this was not required for every patient and we did not systematically collect data about these conversations. If patients consented, an order was created for the phlebotomist to take a vial of blood for the biobank.

Simplifying the Consent Form

The existing biobank consent form was over 2600 words long, with a readability score of 12.5 on the Flesh-Kincaid scale. To improve the readability of this form, we applied a number of simplification methods used successfully by others, including shortening sentences, writing in active voice, reducing repetition, and interspersing summary statements within the text (Agency for Healthcare Research and Quality 2018; Enama et al. 2012; Grady et al. 2017b). The resulting form was roughly 1200 words long, with overall readability of 9.9 on the Flesch-Kincaid scale.

We incorporated the most essential information, including potential risks to enrollment, into an illustration presented toward the beginning of the form. The illustration depicted the process of donation and how samples would be used.

Assessing Biobank Enrollees' Knowledge

In Phase 1, biobank enrollees who provided email addresses were sent an email the day after consenting to the biobank explaining the project with a link to our survey. Those without email addresses received a phone call, and those without email or a phone number received a survey in the mail. Participants who did not respond to the email link were contacted by phone and sent a follow-up email up to two additional times. Those we could not reach on the first phone call received two more phone calls over the course of a week. The participants completed the survey by 1) clicking the link in the email and opening the survey in a web browser, 2) verbally responding to the questions read to them over the phone, or 3) completing the paper survey and returning it by mail.

We used two different recruitment procedures in Phase 2. One group of participants were recruited following the same procedures as Phase 1, which we refer to as Phase 2a. A separate group of participants only received the initial email, since we did not have the staffing to carry out follow up phone calls or emails. Those who responded to the email and completed the survey online we refer to as Phase 2b.

We assessed knowledge of consent materials using 11 true/false questions that also included an "I don't know" response option. The 11 items were adapted from Beskow et al.'s (2015, 2017) 21-item test.[4] We chose questions based on relevance to our

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[4] From Beskow et al. (2017), these were questions 2, 6, 7, 9, 10, 11, 13, 16, 17, 18, 19.

particular biobank and consent form, with the goal of shortening the length of the test as much as possible. For further guidance on selecting questions, we looked at the expert panel rankings in Beskow and Weinfurt (2019). Their expert panel was shown the results of the knowledge test in Beskow et al. (2017), and then were asked which of those topics were sufficiently important that participants had to receive additional instruction before enrolling in the biobank. The final 11 questions reflected topics that the panel thought participants must know for ethical enrollment.

The survey also included five additional questions assessing participants' satisfaction with the informed consent process, using a 5-point Likert scale, which was for internal improvement purposes. We also collected demographic information, including participants' level of education. There was also an open comment box at the end of the survey for participants to provide other feedback. The survey took approximately 2-10 minutes for participants to complete.

Revising the Consent Form and Knowledge Test

After viewing the results of Phase 1 (described below), we revised the consent form and one item in the knowledge test. During this process, we solicited feedback on the consent form from a patient advisory group, in addition to inviting commentary on the illustrations through Facebook and a Reddit research forum. Overall, we found that people were satisfied with the illustration and found it helpful in communicating the general purpose of enrollment and key risks. Based on this feedback, we decided not to make any changes to the illustration.

To emphasize important information that participants misunderstood in Phase 1, we added a list of six bullet-pointed statements at the end of the consent form. We chose this strategy based on comments from patients that the consent form still contained a lot of information that was difficult to process. Because they liked the information in the illustration at the beginning of the form, we thought it could be helpful to present some of that information again immediately prior to the final authorization. The six bulleted statements added to the consent form for Phase 2 were directly relevant to four of the questions on the knowledge test: accessing medical records, sharing data outside of the biobank, future research contact, and the unlimited duration of storage unless participants withdraw. We expected that knowledge scores would improve on each of these items as a result of our revisions.

In addition, one item in the Phase 1 test assessed knowledge of information that was not initially included in the consent form because we expected that patients would have received the information as part of their normal care. The question asks whether the patient could be contacted for future research purposes. The consent form used in Phase 2 included an explicit statement about this.

We revised the wording of one item in the knowledge test (question 6 below). In Phase 1, the item asks participants whether their health and genetic data will be "put into a database outside the Biobank." We considered that the term "database" could be

vague, and consequently changed the question in Phase 2 to ask participants whether their data would be "shared outside the Biobank."

Statistical Analysis

We used total number of items answered correctly (out of 11) as the main measure of performance on the knowledge test. To examine the effect of the revisions for Phase 2a, we used a two-sample t-test to compare the mean total number of correct answers between Phases 1 and 2a. We used chi-square tests to examine the differences between the phases on percent of correct answers to individual items. Incorrect, missing, and "I don't know" responses were combined for these analyses, as "I don't know" responses were interpreted as indicating a lack of understanding.

Noting no differences in total correct scores between Phase 1 and Phase 2a and between Phase 1 and Phase 2b (discussed in the Results section), we assessed the impact of demographic variables on overall performance post hoc, using linear regression models for multivariable analysis. For these analyses, level of education was collapsed into two groups (Bachelor's degree or higher vs. no Bachelor's degree). Race was analyzed with two groups (white and black), omitting the "other" and "more than one race" categories, as there were too few responses to provide a meaningful analysis.

Since the individuals in Phase 2b were recruited with a slightly different procedure than participants in Phase 1 and 2a (no follow up emails or phone calls), their data was considered supplementary and compared to Phase 1 separately using the same

methods as described above for Phase 2a. All statistical analyses were conducted in

SPSS version 25.0 (IBM Corp. 2017. IBM SPSS Statistics for Windows. Armonk, NY:

IBM Corp). Alpha was set at .05 for all analyses.

Results

Participant Characteristics

Two hundred and fifty-three patients enrolled in the biobank during Phase 1. Of these,

121 completed the knowledge test (48% response rate). Seven participants' data were

excluded from the analysis because they responded "I don't know" to every question.

Sixteen participants received a consent form without the NIH's Certificate of

Confidentiality. However, the survey questions were not directly relevant to the

Certificate, and subsequent analysis did not reveal any differences between these 16

and the rest of the participants, so we included them in our analysis. Thus, a total of 114

participants were included in the final analysis.

We recruited 304 biobank enrollees as part of Phase 2a, of which 149 completed the

knowledge test (49% response rate). Five participants were excluded because they

responded "I don't know" to every question, with 144 participants included in the final

analysis.

There were 201 biobank enrollees who completed the survey as part of Phase 2b, out

of 1,267 potential participants (16% response rate). Demographic information for

Phases 1, 2a, and 2b can be found in Table 1. The demographics from all phases closely matched the overall demographics of enrollees in the X Biobank.

Table 1. Demographics of survey respondents by phase

		Phase 1 n(%)	Phase 2a n(%)	Phase 2b n(%)
Age (years)	mean (range)	54 (23-87)	53 (19-79)	54 (21-83)
Sex	Female	68(62)	88(61)	131(66)
	Male	42(38)	56(39)	69(34)
	Subtotal	110	144	200
Race	White	105(92)	121(84)	176(88)
	Black	7(6)	15(10)	14(7)
	Other	1(1)	4(3)	8(4)
	More than one race	1(1)	4(3)	3(2)
	Subtotal	113	144	200
Education	Less than high school	1(1)	7(5)	4(2)
	High School	15(13)	29(20)	32(16)
	Trade/technical school or some college	38(33)	62(44)	81(40)
	Bachelor's degree or higher	60(53)	44(31)	83(41)
	Subtotal	114	142	200

* Some participants did not answer all of the demographic questions.

Most participants in Phase 1 completed the survey within six days of consenting to the biobank, and 77% completed the survey within 10 days. In Phase 2a, most participants completed the survey within four days of consenting to the biobank, and 90% completed the survey within 10 days. Most Phase 2b participants completed the survey within two days of consenting, with 98% completing the survey within 10 days of consent.

Phase 1 Scores

In Phase 1, participants answered 53% of the questions correctly on average, 25% incorrectly, and 22% "I don't know". This translates to roughly six out of 11 questions answered correctly, on average (M = 5.81, SD = 1.99). Only 15% of participants answered more than seven out of 11 correctly, and nobody had a perfect score.

Phase 2 Scores (After Revisions to Consent Form and Test)

In Phase 2a, participants answered 53% of questions correctly on average, 24% incorrectly, and 23% "I don't know" (M = 5.77, SD = 2.21). There were again no perfect scores, and only 12% of participants answered more than seven questions correctly. Table 2 depicts the average percent correct scores for both phases. The difference in total correct scores between Phases 1 and 2a was not significant, t(256) = .136, p=.892.

Table 2. Percent correct, incorrect, and "I don't know" knowledge item responses by phase

	Phase 1 n=114	Phase 2a n=144	Phase 2b n=201
Total % Correct	53%	53%	54%
Total % Incorrect	25%	24%	22%
Total % "I don't know"	22%	23%	24%

Scores on each question also varied only slightly between Phases 1 and 2a, as shown in Table 3. None of the differences in percent correct between Phases 1 and 2a were statistically significant.

Table 3. Knowledge scores by item and phase, number and percentage correct

	Phase 1 n(%)	Phase 2a n(%)	Phase 2b n(%)
1. The materials in the Biobank will not be used for any future research. (FALSE)	73(64)	95(66)	144(72)
2. The Biobank will collect information from my medical records. (TRUE)	39(34)	51(35)	62(31)
3. Unless I decide to stop taking part, my sample and information may be kept in the Biobank for an unlimited amount of time. (TRUE)	67(59)	92(64)	122(61)
4. Researchers will be able to easily identify me using the information they get from the Biobank. (FALSE)	71(62)	87(60)	137(68)
5. Someone from the Biobank may contact me about participating in additional research. (TRUE)	41(36)	57(40)	68(34)
6*. None of my genetic or health information will ever be put into a database outside the Biobank. (FALSE)	3(3)		
6*. None of my genetic or health information will ever be shared outside of the Biobank. (FALSE)		11(8)	25(12)
7. There is a risk that someone could get access to information the Biobank has about me. (TRUE)	22(19)	37(26)	39(19)
8. Research done through the Biobank will provide me with personal health benefits. (FALSE)	71(62)	76(53)	110(55)
9. If the research leads to any new products, I will get part of the profits. (FALSE)	99(87)	112(78)	169(84)

10. I should not expect to get individual results back from research done using my sample. (TRUE)	88(77)	103(72)	149(74)
11. Once I sign up, I cannot leave the Biobank. (FALSE)	88(77)	110(76)	161(80)

* This item was modified between phases.

** In Phase 2, some questions were not answered by every participant, which was treated as an incorrect response. No item had more than three missing responses.

The supplementary analysis of Phase 2b data also indicated no significant difference in overall comprehension from Phase 1 participants, t(313) = .332, p=.71. Phase 2b participants answered an average of 55% questions correctly, 22% incorrect, and 23% responded "I don't know" (M = 5.9, SD = 2.22). There was one perfect score, and 10% of participants answered more than seven questions correctly.

One item was significantly different between Phase 1 and 2b. More participants correctly answered the revised question about data sharing in Phase 2b than in Phase 1, X^2 (1, N = 315) = 8.6, p = .003. However, the improvement was still modest (from 3% to 12% correct), indicating that comprehension remained very low.

Predictors of Performance Across Phases

Of the four demographic factors we examined (age, sex, race, education) via linear regression, only education was related to the total correct responses (Supplemental Table 1). For Phase 1 and 2a, having a bachelor's degree or higher was associated with higher test scores on average ($\hat{\beta}$ = 0.74 (SE = 0.28), t(1) = 2.67, p = 0.008). The results were similar for Phase 1 and 2b ($\hat{\beta}$ = 0.85 (SE = 0.25), t(1) = 2.42, p < 0.001).

Discussion

We found that biobank enrollees did poorly on a knowledge test of topics covered in a biobank consent form, even after an intervention aimed at improving understanding of specific items. The average score of 53% correct was far below the commonly used 80% standard for adequate knowledge (Eisenhauer et al. 2019). These results raise the concern that consenting within a healthcare context compounds other problems with biobank enrollees' understanding of consent materials. Previous studies have found poor knowledge in donors to a breast cancer biobank (Garrett et al. 2017; 58% correct with complex consent and 66% with simplified consent) and in non-biobank participants who just read the consent form and answered knowledge questions (Beskow et al. 2017; 83% correct). Ours is the first study of enrollees' knowledge under an "integrated consent" model and the first to use Beskow et al.'s survey with actual biobank enrollees.

Particularly concerning were the three questions where participants scored below 50%, regarding access to medical records (question 2), sharing data outside the biobank (question 6), and the risk of others accessing personal information about enrollees (question 7). We expected larger improvements on the questions about medical records and data sharing, given the changes to the consent form made in Phase 2, as well as items about the unlimited duration of storage (question 3) and future research contact (question 5). It is nonetheless noteworthy that at least two-thirds of participants answered certain items correctly across all phases, including regarding research usage of data, individual financial benefit, return of results, and ability to withdraw from the biobank. Despite significant shortening of the consent form, and a relatively simple

consent process in a potentially distracting setting, many participants still understood these important features of enrollment.

Possible Explanations for Poor Knowledge Scores

A possible explanation for poor performance on the knowledge test is that the consent form is still too complex. Multiple comments from participants suggested that certain sections were too wordy. The reading difficulty score is also higher than that of Beskow et al. (2017) and other biobank consent forms that have undergone simplification processes. While recruiters did engage with participants to answer questions, it is also possible that the use of a tablet reduced the face-to-face interaction that could have otherwise helped reduce the complexity of the information. However, overall complexity of the consent form cannot explain why the concise bullet-pointed statements failed to improve scores. The bullet points succinctly stated that patients' medical records would be accessed and that data would be shared outside of the biobank, yet most participants answered questions about those topics incorrectly.

Another possible explanation is that participants did not read the consent form carefully. Because of the context of the consent process (in a health care setting, while waiting for other tests), participants may not have paid close attention to details, perhaps because they felt rushed or assumed that what they were being requested to do was low risk. For example, one participant commented, "The day I participated I had 3 doctor & lab appointments. The first was delayed and so I felt very rushed while I was in the lab."

Another reported, "I acted too quickly" in reading the form but "I'm all for helping in any research I can."

Numerous participants also commented that they trusted their doctor (or the health system) and consequently did not read the form closely. One stated that they had been with the health system for 20 years and "didn't think anything of it." We are currently conducting follow-up studies to further explore the role of trust and other factors that might lead people to ignore crucial information. However, this explanation also fails to explain why participants scored so poorly on specific questions. If they had not paid close attention to the forms, and were just guessing at the correct answer, they should have guessed correctly more than 3-12% (question 6) of the time.

Low scores on the question about data sharing can perhaps be explained by the inherent difficulty of the topic. Only 43% of participants in Beskow et al. (2017) correctly answered that question (item 6 in Table 3), and fewer than half of the participants correctly answered similarly worded questions correct in Garret et al. (2017), Simon et al. (2016), and Ormond et al. (2009). This suggests that participants find information about data sharing particularly challenging in the context of biobank research.

Accessing medical records and risks of identification may have been especially confusing topics. We speculate that participants interpret "collecting" information from their medical record as only something health care providers do. They may understand that the biobank is sharing information from their medical record, but distinguish this

from the sort of access they observe during a doctor's appointment. Similarly, the item about risk of identification is potentially confusing because "risk" has a strong negative connotation. Even if participants believe that others could access their information, they may not believe it presents any danger to them in this context. The integrated consent process used in this study may also exacerbate these confusions by blurring the line between healthcare and research, which could explain why participants in other studies have not struggled with these topics to the same degree.

Ethical Issues in Responding to Poor Knowledge Scores

An important ethical question raised by this research is what should be done when participants demonstrate a lack of understanding about the basic elements of biobanking. This dilemma is not unique to biobanking; setting an appropriate threshold for understanding is a problem for consent in all areas of medicine. However, this question is especially important when considering the novelty of integrating biobank consent into ordinary patient care. Our results suggest that the pressures of the clinic may negatively influence patient understanding of biobank consent materials. As health systems blend research and care, they may also need to rethink their approach to educating patients through the consent process.

Beskow and Weinfurt (2019) recently explored this question by presenting the knowledge test scores from Beskow et al. (2017) to the panel of experts who previously helped develop the corresponding consent form. Upon seeing the results, about half of the panel supported requiring participants to review items to improve their

understanding, and the other half supported allowing enrollment without further review. Only a small minority supported preventing enrollment when patients answered questions incorrectly, despite the experts having previously identified the items as essential knowledge.

These results created a vigorous debate about ethical enrollment in biobanks (Wieten et al. 2019). Some argued that evidence of misunderstanding cannot be ignored; individuals should not be enrolled in biobanks unless they can pass a knowledge test, even if that requires repeated instruction and re-testing. For example, Pope (2019) questioned whether even enhanced biobank consent forms are "really the best we can do" (p. 28). He argues, "we should first redouble our efforts at achieving understanding" before questioning whether the goal of understanding is misconceived. Directly relevant to integrated consent, Appelbaum (2019) argued that the threshold for understanding must be higher when consenting for research that patients might falsely believe will impact their care.

Our results suggest that doubling down on improving consent forms is unlikely to be successful. If misunderstanding was due to poor consent forms, our participants should have shown much higher understanding in both phases, as would participants in Beskow et al. (2017) and many other studies. Persistent misunderstanding should lead us to question whether consent forms are really the problem. As others argued in response to Beskow et al.'s research, patients and research participants often use a "trust heuristic" to make decisions, where they look for indicators of trustworthiness

rather than studying detailed consent materials (Burgess & O'Doherty, 2019; Kasperbauer & Schwartz, 2019). Given the low risks of biobank research, these commentators argue, participants should be free to decide how much they want to know and how much they would like to defer to trusted institutions. From this perspective, the key ethical obligation is disclosure of information that is understandable, but people should not be forced to understand.

At the same time, there are certain areas where misunderstanding is particularly problematic. For example, numerous studies indicate that potential biobank participants are concerned about privacy and data sharing risks (De Vries et al. 2018; Kaufman et al. 2009; Kraft et al. 2018; Lee et al. 2019; Sanderson et al. 2017; Warner et al. 2018). It is therefore concerning if participants do not understand that their data will be shared with researchers outside of the biobank, as it seems our participants did not.

Innovative approaches can perhaps be used to improve participant understanding in cases where widespread misunderstanding is deemed unacceptable. Various technologies now exist to make participant education less cumbersome and resource intensive than in the past. Video consent, e-consent, and patient portals can be leveraged to improve patient understanding over time (Grady et al. 2017a; Kraft, Garrison & Wilfond 2019). For example, the National Institute of Health's All of Us program has done this at a national level (All of Us Research Program Investigators 2019; Wilbanks 2018). Their e-consent portal utilizes short, simple videos as well as interactive quizzes that people can complete on their own time. Boston Children's

Hospital and other health systems have also shown that biobank consent materials can be successfully incorporated into patient health portals (Bourgeois et al. 2017, Boutin et al. 2016).

Video consent and e-consent portals can also incorporate corrective feedback techniques. Beskow et al. (2017) and Simon et al. (2016) both successfully improved potential enrollees' understanding by informing them of incorrect responses, along with simple clarifying explanations on the topic. Such techniques could perhaps be integrated into patient portals, which would allow patients to learn about biobanks both before and after enrollment. More broadly, any approach could aim to provide ongoing education and engagement with biobank participants, instead of relying on a single interaction to ensure adequate understanding. It is important, with any of these methods, to actively engage with potential participants to help convey basic information about their enrollment.

Conclusions

Patients who consented to a biobank during ordinary health care seemed to have significant misunderstandings about their enrollment. Participants scored particularly poorly on questions about data sharing and accessing medical records. These misunderstandings persisted despite an attempt to improve information in the consent form about those topics. This persistent misunderstanding may further strengthen challenges to the goal of ensuring understanding in biobanks and other low risk research. Innovative solutions can be pursued, perhaps especially when integrating

research consent into ordinary patient care. But given the low risk of biobanks and the

freedom of participants to decide how much they want to know, we should consider

whether other patient approaches to consent, such as relying on trust rather than full

understanding, are ethically acceptable.

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