Active choice but not too active: Public perspectives on biobank consent models

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Purpose: Despite important recent work, US public attitudes toward specific biobank consent models are not well understood. Public opinion data can help shape efforts to develop ethically sound and publicly trusted mechanisms for informing and consenting prospective biobank donors. The purpose of this study was to explore public perspectives toward a range of consent models currently being used or considered for use among comprehensive US biobanks. **Methods:** The study used an exploratory mixed-methods design, using focus groups and telephone surveys. Eligible participants were English-speaking residents in the catchment area of a comprehensive biobank being developed at the University of Iowa. **Results:** Forty-eight participants in seven focus groups and 751 survey participants were recruited. Biobanks were unfamiliar to almost all study participants but were seen as valuable resources. Most focus group (63%) and survey (67%) participants preferred a prospective opt-in over an opt-out consent approach. Broad, research-unspecific consent was preferred over categorical and study-specific consent models for purposes of approving future research use. **Conclusion:** Many individuals may want to make an active and informed choice at the point of being approached for biobank participation but are prepared to consent broadly to future research use and to forego additional choices as a result. ***Genet Med*** **2011:xx(x):000–000.**

Key Words: *biobank, consent models, public perspectives*

Biobanks are important resources for advancing genetic and genomic research and the translation of this research into health improvements.[1,2] An estimated $1 billion has been invested in the biobanking industry within the last 10 years, and there are now at least 179 comprehensive biobanks in the United States, most of which were established in the last decade.[3] There are likely thousands of additional smaller biobanks that focus on specific diseases. Although biobanks are diversely organized entities,[4] they can be roughly defined as repositories of human DNA, RNA, tissue, blood, organs, cells, and other biological materials that can be used in a broad range of research, including genetics and genomics research.[5]

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Informed consent and biobanks

Whether informed consent is required for biobanks depends largely on how they collect and manage their data sources for research purposes. Federal regulations define a human research subject as a living individual about whom an investigator conducting research obtains (1) data through "intervention or interaction" with the individual or (2) identifiable private information.[6] Recent guidance from the federal Office of Human Research Protections indicates that studies with specimens that were not collected specifically for research purposes through an interaction or intervention with living individuals, and that are coded so that the investigator cannot readily ascertain the identity of the individual(s) to whom they pertain, do not constitute human subjects research.[7]

Interpretations of these regulations and guidelines have led to three substantively different approaches to the question of prospectively consenting biobank donors. First, there is the approach that no such consenting efforts are needed because the regulations for exemption from human subjects research are being met. This approach has been widespread in the collection and research use of newborn screening blood spots and has led to considerable controversy in recent years.[8–10]

Second, there is the approach that the regulations for exemption from human research are being met but that, nonetheless, efforts to consent individuals are needed to satisfy public and other stakeholder expectations for being informed and given the opportunity to refrain from research participation. The large-scale biobank at Vanderbilt University, BioVU, is reflective of this approach. As it collects only biological material left over from routine clinical procedures and codes all personal health information, so that investigators cannot readily ascertain the identity of sample donors, BioVU is seen as meeting the exemption criteria for human subjects research.[11–13] Nonetheless, BioVU also provides prospective donors with a variety of information about the biobank and gives them the opportunity to decline participation through an opt-out consent process, the development of which involved both the local institutional review board and public opinion data.[11,12] Opt-out consent processes generally involve providing individuals with a brief statement about the research study in question and what is being asked of them, coupled with the opportunity to signal to the investigators (usually in writing) any desire on the part of the potential research participant (PRP) to be excluded from the research.[11,14]

Third, there is the approach that biobank sample collection and research use do not fully meet the exemption criteria for human subjects research; therefore, a more traditional mechanism of prospectively consenting PRPs is needed. Opt-in consent is such a mechanism in that it is designed to provide individuals with thorough and detailed information of the relevant implications of research participation and allow them to actively signal (usually in writing) their willingness to participate in the research.[14]

Although opt-out and opt-in are both methods for prospectively consenting PRPs, there are differences between the two models that lead to arguments for and against each method. Although it is often assumed that opt-out provides far less information about the research in question than opt-in, this is not a built-in limitation. Clinical trials have used opt-out consent documents that deliver much the same amount of information as an opt-in document.[15] The BioVU repository at Vanderbilt is one example of an opt-out approach that is accompanied by patient education materials that deliver, arguably in a more accessible format, much of the same information normally found in an opt-in consent document.[11]

Although opt-in consent is widely considered better at promoting individual autonomy and active decision making than opt-out consent, many problems have been associated with opt-in consent processes, including the potential for subject burden, misunderstanding of content, sample biases, and adverse study accrual rates.[14–17] Effective opt-in consent processes are frequently resource intensive, which presents a major challenge for larger-scale research projects, including biobanks.[11] On the other hand, it can be argued that opt-in consent is better suited to some research protocols than opt-out consent, including protocols seeking to recontact, reconsent, or subsequently collect additional data from subjects.

"Future-use" consent models

None of the three consent models outlined earlier necessarily take into account the question of the scope of permission to use donated samples and health information in future research. Biobank collections can be used for many years in many different kinds of research, so that a one-time "broad" (also called "general" or "blanket") consent approach, in which participants prospectively agree to their samples and health information being used in any future research deemed appropriate by a biobank and/or relevant oversight bodies, is considered by many to be well suited to the open, evolving nature of biobank-supported research.[18] However, others have argued that broad consent to future research use does not in itself meet the Common Rule benchmarks for adequately informing participants of the specific nature, risks, benefits, and other elements of this future research.[19–21] Some have insisted that broad consent should not even be thought of as "informed consent" for this reason.[19] Recent legal cases have also underscored the public confusion, misunderstanding, and mistrust associated with the use of broad consent as a permissory framework for future research use.[22,23] Despite these concerns, broad consent is widely used and supported by various experts[24] and has been recommended by many organizations.[25–27]

Alternatives to broad consent are also being widely discussed, including categorical (or tiered) consent and study-specific (or narrow) consent. In categorical consent, individuals are asked to choose from a list or "menu" of disease categories (e.g., cancer, diabetes, or mental illness) or research methodologies (e.g., genetic analysis, histological examination of tissue, or medical record review) at the time of initial consent to participate in a biobank. In an open-ended variation on categorical consent, individuals can be asked to designate in which areas of research their specimens or health information should not be used (termed "free-text consent").[28] Categorical consent has been considered by many to be a "best practice" that enhances autonomy by allowing for greater choice and control over research participation but has also been criticized for being unwieldy and burdensome.[29,30]

Study-specific consent models follow a more traditional format for obtaining informed consent, in which biobank participants would be recontacted, provided detailed information about a study for which they are eligible, and asked to consider participation in that study. To effectively operationalize study-specific consent, research participants need to be identifiable and contactable whenever researchers request specimens and/or health information for protocols requiring informed consent. Study-specific consent is preferred by some experts because it bears the traditional hallmarks of informed consent, namely the capacity to thoroughly inform individuals of the various elements of the research in question, including specifics on the potential risks and benefits of the research. However, in the evolving long-term context of biobank research, participants may need to be recontacted many times, raising questions about the cost and logistics of recontact, possible intrusiveness into people's lives, and whether recontact "defeats" the purpose and spirit of providing initial, prospective consent to biobanking.[31–33]

Table 1 provides an overview of the consent models of interest to this study.

Aims and context of study

This study aimed to explore public attitudes, preferences, and concerns toward (1) biobanking and the potential importance of biobank research; (2) prospective opt-in and opt-out frameworks for providing initial consent to participate in a biobank; and (3) consent models that address the scope of future research

Table 1 Approaches to consenting donors to biobank participation

Initial consent methods	
No consent	Participants are not approached regarding participation
Prospective opt out	Potential research participants are provided with information about the biobank and given the opportunity to signal any desire to be excluded from the research
Prospective opt in	Potential research participants are provided with information about the biobank and given the opportunity to actively signal their willingness to be included in the research
Permission for future use of samples	
Broad	Participants prospectively agree to their samples and health information being used in any future research deemed appropriate by a biobank, relevant IRB, scientific committee, and/or other entities
Categorical	Individuals prospectively choose from a "menu" of disease categories (e.g., cancer, diabetes, or mental illness) or research methodologies (e.g., genetic analysis, histological examination of tissue, or medical record review)
Study specific	Participants are recontacted and asked to consider participating in specific research studies for which they are eligible

with biobank samples and health information, including broad, categorical, and study-specific consent. Several key studies of US and Canadian public attitudes and preferences toward biobank consent models have been conducted[18,34,35]; however, no clear consent choice is evident in most of these studies. For example, Murphy et al.[18] report that 48% of their survey participants would prefer giving broad consent, whereas 42% would prefer study-specific consent. Similarly, Willison et al.[35] report that, despite support for broad, opt-in consent, no single consent approach predominated in their structured dialogs with members of the Canadian public. Similar heterogeneity has been found among public consent preferences in regions of Europe.[36]

These studies underscore the challenge biobanks face in attempting to adopt consent frameworks that align with public perceptions and preferences. Diversity in consent preferences within any given population could require biobanks to consider providing prospective participants with multiple consent options[18]; however, this step may be logistically and financially prohibitive. Our research was conducted in part to help inform the design of a consent framework for a large-scale tissue and DNA biobank being developed at the University of Iowa Hospitals and Clinics (UIHC Biobank). Several authors (J.C.M., J.L., G.W., and P.W.) of this article are involved in the planning and development of the UIHC Biobank.

The study was also conceived as a first step toward a deliberative community engagement process similar to other such processes that have been advocated for and used in the formation of biobanks, often with the use of focus groups as a preliminary step.[31–32,37] Recently, Hoeyer[4] concluded from a literature review that there exist fundamentally different types of relationships between biobank donors and researchers and that engagement with local context is essential to meet local expectations. Thus, this article has emerged out of a dual effort to help inform (1) current empirical literature on public attitudes toward biobanking and biobank consent models and (2) plans to develop a consent framework for a large-scale biobank, for which knowledge of local context and expectations is essential.

MATERIALS AND METHODS

Qualitative and quantitative methods were used to assess public perceptions and preferences surrounding consenting options for biobanks in general and for the planned UIHC biobank. The studies were facilitated by the University of Northern Iowa's Center of Social and Behavioral Research, which recruited participants, conducted the focus groups and surveys, and collected the data. Eligible participants for both the focus group and survey studies were contacted by telephone using random digit dialing to ensure representation of both listed and unlisted numbers. IRB approval was obtained from the University of Northern Iowa for both the focus group and survey studies. The University of Iowa IRB determined that the University of Iowa personnel were not engaged in research involving human subjects.

Both the focus groups and the surveys were based on an initial description of biobanking as follows:

Biobanks are typically managed by a medical center and do the following:

- Store biological samples such as blood or tissue. These samples could be left over from either inpatient or outpatient medical procedures such as blood draws, surgeries, or biopsies, or they could come from procedures such as blood draws done to get samples specifically for the biobank.
- Store a patient's medical records along with their samples.
- Provide samples and medical records to scientists to conduct medical research.
- Keep people's samples and information for many years, so research can be done on them well into the future.

Focus group participants were also told that "In other words, biobanks are a little like libraries. But instead of books, they contain biological samples and medical records. And instead of just anybody being able to access these samples and records, only researchers with special approval can get at them and use them for research." Survey participants were given more specific information about the proposed biobank at UIHC: "The University of Iowa Hospitals and Clinics is considering developing a biobank. Samples that are left over from a standard procedure, during a routine visit at the University of Iowa Hospitals and Clinics, such as a blood draw, biopsy, or surgery, that would otherwise be discarded, would instead be collected for the biobank. With the exception of those too ill to participate, all patients at the University of Iowa Hospitals and Clinics will be invited to participate. The collected samples would be linked to each patient's medical records. Both the sample and the medical record information could be used for medical research, aimed at development of possible new treatments and better understanding the causes and courses of diseases."

Focus groups

The focus groups were designed to explore issues similar to those explored by other empirical studies of biobanking, including issues of informed consent; privacy and confidentiality; future use of biological samples and health information; and return of research results.[18,34,37] A detailed discussion guide was developed to systematically explore participant attitudes and perspectives in these domains of interest (see Document, Supplemental Digital Content 1, http://links.lww.com/GIM/A177 for the focus group discussion guide). Because we could not assume that biobanks would be to any degree recognizable or familiar among study participants, we developed a set of descriptors and handouts that were provided to focus group participants at strategic points (see Document, Supplemental Digital Content 2, http://links.lww.com/GIM/A179 for the focus group handouts). On the basis of similar methods used in other focus group research,[38] we developed a series of "polling cards" to identify how many focus group participants preferred a given consent option or had no preference. The cards were distributed and completed anonymously once discussions on a particular topic had reached saturation. Finally, an anonymous survey to collect basic demographic data, including self-reported ethnicity, was administered to each participant to better describe the focus group sample. All materials were pilot tested with volunteers who were not included in the seven focus groups. The volunteers were selected by convenience sampling of friends and family of the research team who met the inclusion criteria for the focus groups. Volunteers who were expected to be more familiar with biobanking than the general population because of their relationship to the research team were excluded. The focus group process was piloted using the discussion guide, handouts, and polling cards. At the conclusion of the pilot focus group, which lasted 90 minutes, the volunteers were asked to provide feedback on the session. The final discussion guide was modified to reflect suggestions from the volunteers and observations from the moderator.

Seven focus groups, with a total of 48 participants, were conducted in April 2010, in three communities (two cities; one rural town) in the UIHC's primary, 90-mile radius, patient catchment area. A screening tool was used to promote variability in participant age, gender, education, and ethnicity and identify and exclude from the study any non-English speakers and individuals who have not used a formal healthcare service in the last 10 years. Focus groups were held in convenient, neutral locations in each community (e.g., public libraries). Each group lasted between 80 and 90 minutes. Standard focus group procedures were followed,[39] with a trained moderator and research assistant conducting and audio-taping the focus groups. All tapes were transcribed and transcriptions validated before analysis. Transcripts were managed in NVivo software and independently coded (J.L. and E.N.) into broad thematic categories, which were then refined through subcodes. All codings were verified and discrepancies reconciled through a three-way discussion (J.L., E.N., and C.M.S.). Demographic data and preference card results were managed and analyzed using Excel SP3.

Phone survey

A 49-item phone survey was developed to further explore questions posed and themes identified in the focus groups, including knowledge of and attitudes toward biobanking and biobank-supported research and options for informed consent (see Document, Supplemental Digital Content 3, http://links.lww.com/GIM/A180 for the survey script). The survey data included in this report come from a series of attitudinal measures that were administered in tandem with a brief description of the consent models of interest to the study (Table 1). After being read a description of each model, survey participants were asked to say whether they supported (strongly or somewhat) or opposed (strongly or somewhat) the model in question and were then asked to explain their answer. Participant responses were field coded into categories derived from common themes identified in the focus groups. Any responses that did not fit into one of the predefined categories were coded as "other" and recorded for qualitative analysis. After these questions were asked for the opt-in, opt-out, and no consent models, participants were asked to select the one prospective consent model they most preferred (other response options included "no preference," "none of the above," and "other"). The same approach was taken for broad, categorical, and study-specific consent.

Survey data collection began on June 17, 2010, and ended on July 25, 2010. Sampling targeted residents (1) across the state of Iowa and (2) specifically within the UIHC catchment area resulting in 751 completed interviews with the majority (n = 700; 86%) residing in the state of Iowa and the remainder in Illinois (48; 13%) and Wisconsin (3; 1%). The UIHC catchment area overlaps into several counties in Illinois and Wisconsin, accounting for the small proportion of the sample from these states. Both samples were provided by Genesys Sampling Systems.[40] The response rate for the statewide sample was 30% with a cooperation rate of 64%, and the response rate for the catchment area oversample was 28% with a cooperation rate of 60%. The response rate is the ratio of interviews to eligible numbers dialed, and the cooperation rate is the ratio of interviews to all eligible participants contacted.[41]

Surveys took approximately 20 minutes to complete. All participants were first provided with a brief description of the interview purpose and informed that their participation was voluntary and confidential. All data were collected by the Computer-Assisted Telephone Interviewing system at the Center for Social and Behavioral Research at the University of Northern Iowa. Survey data were organized and analyzed in SAS using basic descriptive statistics, cross tabulations, and Pearson χ^2 test. Data from both populations were weighted to US census demographic benchmarks and combined. To determine whether we needed to report results for those participants outside of the 90-mile catchment area (noncatchment) and those within the catchment area separately, we used the Pearson $\chi 2$ statistic to compare the two samples for possible differences in responses to key survey items. No significant differences were found between the two groups in any variables of interest in this article. Hence, the catchment and noncatchment samples were combined and results analyzed with a denominator of 751 participants. Analyses involving age and income were conducted first with multiple ordered categories for age and income; after interim analyses ruled out directional association (e.g., linear trends) with key survey items, categories were combined resulting in dichotomized categories for age (18–54 years and >55 years) and income ($\leq$\$25,000 and $\geq$\$25,000) that were used in subsequent statistical tests.

RESULTS

Overview of results

In general, findings were consistent across the focus group and survey studies, with the majority of participants reporting little or no prior knowledge of biobanking, a recognition of the potential value of biobank-based research, and a preference for making a one-time active and informed choice regarding biobank participation through means of a prospective opt-in consent process. Tables 2 and 3 summarize the data on consent model preferences for the focus groups and surveys.

Focus group results

General knowledge and attitudes

A total of 48 people participated in the focus groups; the majority (58%) were female and white (88%). Table 4 summarizes demographic data for both the focus group and survey participants. Focus groups began by probing the recognizability and connotations of the word "biobank." Very few participants claimed to be familiar with the term. Associated terms that came to mind for participants included "blood banks," "organ donation," "stem cell research," and storage of "sperm" or "embryos." When given examples of the research that biobanks can support (e.g., research into the genetics of cancer; mental illness; diabetes; and infection control), participants generally agreed that this kind of research was very or extremely important. One participant said: "[if] the research can help future generations, I think it's a very important thing."

When asked whether they had any concerns about the biobank-supported research examples they were given, participants were most concerned about the possibility of misuse of samples or information held in the biobank, including insurance discrimination and whether samples would actually be used for valuable research. Participants expressed interest and excitement over the prospect of genetic research being supported by biobanks but were also concerned about the security of genetic information and insurance discrimination and the prospect of cloning.

Initial, prospective informed consent

Need for consent. There was strong agreement within and across the seven focus groups that obtaining consent for collecting, storing, and using samples and health information was important and necessary. Participants explained that it would

Table 2 Summary of survey and focus group results on initial prospective informed consent options for biobanking

Method	Survey (n = 751), % preferred (95% CI)	Focus groups (n = 48), % preferred	Common likes	Common concerns
No consent	5 (3–7%)	Discussed but not polled	Samples do not get wasted; helps research	"Not right"; might result in a negative public reaction; conflicts with cultural diversity in beliefs (e.g., on giving blood)
Opt out	18 (15–21%)	25	Provides some choice; less time and money intensive; good for sample accrual; and spurs research	Conflicts with social expectations; too passive and may not register; potentially confusing; may provide too little information
Opt in	67 (63–71%)	63	Allows for positive and active choice; more informative; will receive greater public acceptance; and fits with tradition	Potentially burdensome to participants; may lead to decreased accrual; more resources required
No preference	4 (2–6%)	12		
Either opt-in or opt-out	2 (1–3%)			
Do not know/ none of the above	4 (2–6%)			

Table 3 Summary of survey and focus group results on scope of permission for future use options for biobanking

Method	Survey (n = 751), % preferred (95% CI)	Focus groups (n = 48), % preferred	Common likes	Common concerns
Broad	41 (37–45%)	54	Allows for flexibility in research; logical given uncertainty of future research; logistically easier; spurs research and research output	Minimally informative; disallows individual control over sample and information use
Categorical	25 (21–28%)	21	Provides some level of information and choice over future sample and information use; can participate in research that has personal meaning	Categorical choices may be confusing or misunderstood; could hinder research; logistically complicated; people may not feel qualified to make selections
Study specific	29 (25–32%)	21	Promotes knowledge, choice and control over research participation; may facilitate return of research results	Recontact fatigue; may hinder research if subjects cannot be reached or if not enough people consent to a particular study; resource intensive and impractical
No preference	4 (3–6%)	4		

not be "right" to proceed without any consent; that doing research without obtaining consent might result in negative public reactions; and that permission was necessary to respect cultural beliefs that precluded donation of blood and participation in research. However, some participants did feel that a no-consent approach ensured that samples useful for research purposes would not go to waste: "But I mean these samples are valuable to the researchers, and every time you put up a barrier to say well you have to get permission first, that means there's going to be some of those samples that go to waste."

Opt-out consent. An opt-out consent approach was generally seen as an improvement over the prospect of obtaining no consent. Participants saw opt-out consent as allowing for at least some measure of knowledge, choice, and control. One person said: "I think it's a necessary option. I think if people want out, let them out." Other themes included the expectation that opt-out consent would contribute to increased biobank accrual, cost less time and money, and spur scientific progress and discovery. One participant said: "If you want to tackle serious problems like cancer and things like that, those are huge goals, so … I think the [uh] the opt-out method would get you there a lot faster."

Participants also viewed opt-out as too "passive" and not reflective enough of social expectations to be informed and to actively choose research participation. One person said: "In a transparent society you're better off asking people to reach into the goodness of their heart to participate." Another participant said: "I do view [biobank research] as different than going to a

Table 4 Demographics of focus group ($n = 48$) and survey respondents ($n = 751$)

Demographics	Focus group, %	Survey, % (SE)
Gender		
Male	41.7	37.0 (2.1)
Female	58.3	63.0 (2.1)
Age (yr)		
Mean	52.5	58.4
Range	18–92	18–94
Ethnicity		
White	87.5	96.9 (0.7)
Other	12.5	3.1 (0.7)
Income[a]		
$25,000 or less	—	19.5 (1.9)
$25,001–$50,000	—	22.2 (2.1)
$50,001–$80,001	—	28.6 (2.3)
$80,001 or more	—	29.7 (2.2)
Education[a]		
Not a high school graduate	2.1	4.9 (1.0)
High school graduate or GED	14.6	32.7 (2.0)
Some college or 2-year degree	22.9	25.7 (1.8)
4-year college graduate or more	60.4	36.8 (2.0)
Religious preference[a]		
Religious	—	85.1 (1.6)
Nonreligious	—	14.9 (1.6)

[a]Income ($n = 540$), education ($n = 747$), and religious preference ($n = 732$).

doctor for a procedure that directly involves your health, this is some other thing, this is a research deal. [M]y body parts are my body parts, and … I don't want [them] to end up there through the back door."

Opt-out consent was associated with a potential for misunderstanding and confusion. One person likened it to "taking a test with double negatives—you have to constantly figure out what the real question is." Environmental factors added to this concern. As one person put it: "[When] you come into the hospital or even a doctor's appointment, there's so many things on your mind … the opt-out paper might not fully register with you."

Participants were concerned that an opt-out approach would result in people receiving too little critical information, which could be:

> "… scary in the sense that when you go in because you have an infection they might be, you know, drawing blood and using that for genetic testing because you have this opt out, [but] you don't know what they're using it for, [or there is] the potential for a big database with you know … long histories and (and) tracking things that nobody knows about."

Participants also worried that an opt-out process would present more comprehension issues for certain groups such as immigrants, the elderly, and the lesser educated, when compared with an opt-in process. For example, one person said: "I worry with an opt-out versus an opt-in process that people with lesser education are less likely to fully understand."

Opt-in consent. An opt-in consent approach to biobanking was preferred by the majority of focus group participants. It was viewed as a more active decision-making framework, when compared with opt out. One participant said: "Either way you get a choice, but I think [opt in] is more of a positive choice." Participants also viewed opt-in as a publicly more acceptable option. As one participant said: "You're not going to have as much opposition down the road, people saying, 'I didn't know'." An opt-in approach was also seen as more informative than an opt-out approach, for example: "The benefit of having the opt-in [is] you would maybe actually sit there and read it and know a little bit more about it." Others liked it because it is the "traditional" way that people participate in research.

At the same time, focus group participants were concerned that opt-in consent materials would be significantly longer, more complicated, and difficult to read than opt-out consent material. Participants questioned how understandable information would be if opt-in consent meant that significantly more information would be conveyed to subjects, and they were concerned that an opt-in process would be more cumbersome and inefficient: "There's a lot of resources involved in this kind of permission … to have those people come in and explain it or take nurses time away from patients or whatever they're doing, to explain all of this and try and get them to sign on the dotted line." Participants were also concerned that an opt-in consent process might be too time- and resource-intensive to ensure that all eligible patients would be approached for consent or that some patients might be scared off as a result of the time commitment involved.

Scope of permission for future use

Broad consent. Of the three options for consenting to future use of samples and health information, broad consent received the strongest support in both the focus group discussions and responses to the polling cards. Participants felt that broad consent would provide the biobank with the necessary flexibility to support important research. As one participant said, "it unties the research." Participants speculated that broad consent might result in a larger and more diverse collection of samples and thus provide researchers with "a broad amount of people of different backgrounds and … more to choose from." Broad consent was seen as an appropriate response on the part of a biobank to the ongoing uncertainty regarding what kind of future research might be conducted with its samples and health information. As one person put it: "You could ask someone to give you permission for certain things, but then you don't know what it's going to be for in the future, so [broad consent] gives you the option to grow with the research as the research grows." Participants felt that broad consent would also be less costly, require less effort, and be less burdensome for biobank participants. One person said, "Just have a [broad] approach to it. No use pestering people all the time."

Although their perspectives on broad consent were generally very favorable, participants did express some concerns over the model. They recognized that biobank participants would have little choice or control over the kind of research their samples would be used in and that they would need to trust the biobank to appropriately manage researcher access to their samples and

health information. One participant explained, "It's a big step of trust, I think, to hand over [broad] permission just not knowing what it could be used for." Another participant said: "It'd be nice if you had some knowledge of how [a donated sample] was going to be used in general, but not to, you know, have to be giving permission for everything. I would be inclined to trust science and you know assume that they'd be handling it, you know, pretty responsibly and very well."

Categorical consent. Although more participants expressed a preference for broad consent, categorical consent was favorably perceived on several accounts. Most notably, it was associated with a greater degree of choice and control than broad consent. As one person said: "It gives a patient a choice, and people like to make their own decisions. And they get to pick and choose, rather than someone tells them." Another said, "I think it's very empowering to the person who's making the donation." Categorical consent was also viewed as inherently more informative than broad consent as it would list multiple categories of research that a patient's sample and health information could be used for. Having this information was considered potentially very meaningful as it would allow biobank participants to match their donation to research studies that "are close to their heart that they want research done on."

However, participants were very concerned about the potential difficulty of understanding categorical choices and the possibility of feeling unqualified to make selections from a categorical format. As one participant put it, "I personally don't think I'm as knowledgeable as I would need to be to fill that out, so I'd prefer to have someone that's knowledgeable pick it more than myself." A related and predominant concern was that categorical consent would be time consuming, cumbersome, and potentially counterproductive to the goals of advancing research in a timely and effective way. One participant summed up this concern as follows:

> "You know, being a patient or something and having to fill out, 'well do I want it done for this, and this, and this, I've been here for an hour already and I want to get out of here,' and you don't really care anymore, and then on the researchers side, going 'okay, can we use it for this' or, you know, 'do we have enough of that?' It just seems like it would be really cumbersome to have."

Others had concerns that categorical consent might hinder research if participants do not agree to research for which they qualify. One participant said: "Researchers may want something else that is more important than what [was] checked on that box …. [I]t could be really beneficial and then they couldn't use it because [participants] said they couldn't use it." Another participant concluded that categorical consent would be "useless" for this same reason. "If they took your sample and they wanted to use it on something you didn't check, then it's no good to them because you didn't check it."

Study-specific consent. When discussing this consent option, participants again emphasized the value of having prior knowledge of the research in question, choice, and control over how samples and health information would be used. For example, participants said: "Well, I do like the fact that … there's less opportunities for surprises with this option" and "people that want more control certainly would have total control." In addition, participants felt that study-specific consent would facilitate return of individual-level research results and allow one to "pass on that information to your children and their children too, you know, in case they're studying something that's important and they find something out …."

However, study-specific consent generated a number of concerns, particularly around the question of how burdensome to research participants this model may be. Participants cited a number of burdens:

> "Too much paperwork."
> "Too much information too."
> "We have enough telemarketers without getting more phone calls."
> "I would get irritated and say give it back to me I'm tired of this."
> "Way too time consuming."
> "I'd get sick of being contacted."

Another perspective was that study-specific consent provided too much control to research participants: "Well, the control thing … that's a little bit over the top. If you want that much control, just don't [participate]." Participants felt that the progress of important research could be hurt if biobank participants could not be contacted for individual studies or if insufficient numbers of people agreed to participate in certain studies. A study-specific consent approach was considered impractical and likely to stretch biobank resources given the "time" and "money" that many focus group participants felt would need to be invested in this approach.

Survey results

General knowledge and attitudes

Survey participants (n = 751) were 58.4 years of age on average (range: 18–94 years) and were predominantly female (n = 488; 63%) and white (n = 725; 97%). Table 4 summarizes demographic data for both the focus group and survey participants. Most survey participants (n = 645; 86%) reported never having participated in a medical or clinical research study before, and slightly fewer (562; 74%) reported not having ever heard of a "biorepository" or "biobank" before the survey. When asked to rate on 5-point scale how valuable they thought a biobank might be based on the description they were given, most survey participants felt it would be very or extremely valuable (n = 632; 84%). This question was asked again near the end of the interview, with little change in response (n = 679; 90%).

Initial, prospective informed consent

Proportionately more participants preferred an initial opt-in (n = 503; 67%) consent framework, when compared with opt-out (n = 142; 18%) or no (n = 39; 5%) consent. A small number (n = 31; 4%) had no particular preference. As in the focus groups, survey participants valued the prospect of having a choice over whether samples and health information were included in a biobank. Most (n = 367; 90%) survey participants who said they opposed a no-consent framework said it was because they wanted a choice over whether their leftover samples would be used in research. Opt-out consent was supported (as opposed to preferred) by 584 (78%) participants. The most frequently (n = 396; 67%) named reason for supporting opt-out was that it provided at least some level of choice over whether samples would be included in biobank research. Those who opposed opt-out were concerned that they might not be given the opportunity to opt-out (n = 67; 41%) or thought that opt-out would be too confusing (n = 37; 26%).

Scope of permission for future use

The survey results were roughly consistent with the focus group findings on the question of broad, categorical, and study-specific consent. Broad consent was preferred by more ($n = 301$; 41%) survey participants, when compared with those preferring categorical consent ($n = 185$; 25%), study-specific consent ($n = 215$; 29%), or those who had no preference ($n = 35$; 4%). When participants were asked their reasons for supporting broad consent, the most-to-least frequently cited reasons were that (1) "the research would help others" (39%); (2) "I would only have to sign the paper or be asked about the research once" (23%); (3) "broad consent allows for research in the future that might not have been considered yet" (14%); and (4) "broad consent allows my sample(s) to be used for the projects they are most appropriate for" (13%). Participants opposed categorical consent because they "don't feel qualified to choose what samples are used for" ($n = 26$; 26%); "it would be too burdensome to choose from all of the categories" ($n = 26$; 24%); or because samples may not be used in appropriate future research ($n = 18$; 17%). The most cited ($n = 266$; 79%) reason for opposing study-specific consent was that it would be "too burdensome."

We also considered how respondent preferences for opt-in and opt-out consent matched up with preferences for broad, categorical, and study-specific consent. Survey participants who preferred opt-out consent more frequently preferred broad consent, but this difference was not significant.

Other variables of significance

Age. We found a significant difference in the distribution of preferences for broad, categorical, and study-specific consent when comparing individuals aged 18–54 years and those 55 years and older. Broad consent was still preferred by proportionately more individuals in both these age groups, when compared with the other two consent models; however, more people in the younger group preferred categorical consent, when compared with the older group ($\chi^2 = 5.04$, $P = 0.002$).

Income. Although opt-in consent was generally preferred over opt-out consent, participants who reported a household income of $25,000 or less were less likely to prefer an opt-in ($n = 62$; 68%) consent approach, when compared with those reporting a household income of $25,000 or more ($n = 299$; 81%) ($\chi^2 = 7.29$, $P = 0.01$).

Other demographic variables (e.g., gender, education, ethnicity, and religious preference) were not significantly associated with any consent preferences.

DISCUSSION

In aggregate, this study found that (1) members of the public in the study region had limited knowledge of biobanks; (2) biobanks were not only valued for the advances in research and treatments they promoted but also generated concerns about possible sample misuse, risk of unauthorized participant identification, and insurance discrimination; (3) individuals preferred making an informed and active choice with respect to the initial request to participate in a biobank; and (4) broad consent to future research use of biobanked samples was preferred by proportionately more participants than either categorical or study-specific consent, with the majority, however, preferring to have some input on the use of samples.

Other studies have identified a similar trend in limited public knowledge of biobanks, particularly genetic and genomic-oriented biobanks,[34] suggesting an ongoing need for public and community education and engagement on issues surrounding biobanking. In our survey study, the perceived value of biobanks increased only slightly over the course of the telephone survey, in which descriptive material and questions about biobanking may have had an educational effect. The relationship between public education, perceived value, and willingness to participate in biobanks needs further investigation.

The preference for opt-in consent in our study is consistent with findings from several recent studies,[18,35,42] suggesting that opt-in consent may align most closely with wider public expectations of how biobanks ought to obtain consent for collecting and storing samples and information. At the same time, this finding needs to be balanced against the sizeable number of individuals who preferred opt-out consent (25% in our focus groups, 18% in our surveys). Conceivably, the kind of concerns raised by members of the public with respect to the potentially burdensome, intrusive, and confusing nature of opt-in consent may push certain groups, such as patients with breast cancer facing surgery, to prefer briefer, streamlined opt-out consent processes.[43] Moreover, as our study suggests, certain consent options may be preferentially associated with socioeconomic indicators such as income. Further research is needed to identify how consent preferences for biobanking are moderated by diagnostic, environmental, social, economic, and other factors.

Broad, categorical, and study-specific consent

The preference for broad consent in our study seems relatively clear-cut at first glance. In our study and others, the preference for a broader scope of consent is consistent with assumptions that the research institution and/or the biobank will take responsibility for the proper use and care of the tissue and information and that the donation will be used for advancing science and medical treatments.[44] However, a different interpretation of our data is possible if the frequencies for categorical and study-specific consent were to be combined on grounds that these models promote some degree of control and choice over future research participation, whereas broad consent promotes little or none. In this case, 54% of our survey and 42% of our focus group participants could be seen as preferring a control/choice-promoting model (e.g., categorical or study-specific consent) over a control/choice demoting model (e.g., broad consent).

Rearranged this way, our data would suggest that the majority of our survey participants and a large proportion of our focus group participants want ongoing choices and control over the inclusion of their samples and information in research. However, this rearrangement of data does not take into account that categorical and study-specific consent are markedly distinct from one another and from broad consent. As explained earlier, categorical and study-specific consent are geared to different levels of detail about research and occur at very different time points. Categorical consent is a one-time event (with the potential for renewal), whereas study-specific consent recurs with some frequency. These differences seem to have been recognized by our focus group and survey participants who were concerned, for example, that people may feel underqualified to make categorical choices, whereas the need to recontact individuals in study-specific consent was seen as intrusive and burdensome. Furthermore, the scope of consent to future use of research samples should not be considered in isolation from obtaining of initial, prospective consent to participate in a biobank. The step of trust that many focus group participants evidently would take in their preference for broad consent may be directly linked to the reassurance that would be provided to them by a prospective opt-in consent process. In other words, it

is possible that the amount of control afforded by an initial prospective opt-in process may satisfy people's need for some decision-making control, whereas giving permission for broad future use limits the level of burden on the individual in the future. Further work is needed to explore these interdependent dimensions of informed consent and decision making for biobanking.

Public preference data for future-use consent models can look markedly different depending on whether categorical and study-specific consent are treated separately or combined. More research is needed in this area to develop robust constructs of these consent models that take into account not only just their choice or control-promoting dimensions but also their timing, format, content, and context of delivery. Until such time, we recommend that broad, categorical, and study-specific consent be treated separately, as distinct consent models that cannot be conceptually combined on the basis of only a single commonality.

Implications for biobanks and biobank participants

Our findings have a number of implications for biobanks and biobank participants generally and for the comprehensive DNA biobank (UIHC Biobank) being planned at the University of Iowa specifically. First and most fundamentally, the findings suggest that biobank participants need to be informed and consulted at some level about their participation in biobank-based research. Biobanking specimens and using them for research without any effort to inform individuals and/or obtain their permission is not a viable option from a public standpoint. Together with other published data, the study findings also suggest that biobanks and members of the public would be potentially well served by a prospective opt-in informed consent process. Although opt-out consent approaches may be appealing for reasons that members of the public recognize, such as their relative efficiency and conduciveness to rapid recruitment, opt-in consent may be an ultimately better option given how strongly it is associated with making an informed, active, and positive choice, and, as a result, with the joint principles of respect for persons and autonomy. Adoption of an opt-in consent framework will also, however, present biobanks with significant effectiveness and efficiency challenges. Participants in our study were concerned about the burden of comprehension, time, and need for resources that opt-in consent processes may impose. In the case of large-scale biobanks such as the planned UIHC Biobank, these concerns are likely to grow given plans to ultimately recruit participants across a comprehensive spectrum of clinical and medical departments and services. It can be expected that conditions and opportunities for making an informed, active, and positive choice about biobank participation are likely to be very different, for example, in the case of a patient with breast cancer scheduled or being admitted for surgery, when compared with a healthy patient being seen for a routine checkup. Biobanks need to consider the limits of portability and applicability of a standardized opt-in informed consent process across different clinical and medical settings. They may need to develop creative ways to address the contextual, financial, and practical constraints of seeking an informed, active, and positive decision about biobank participation. Some of the options that biobanks might consider and that deserve further research include simplified consent forms with available supplemental information as described by Beskow et al.,[45] multimedia consent approaches, and addendums to existing consent forms to allow participants to enroll into disease-specific and broad biobank research.

Combined with other published data, our study findings also suggest that the utilization of a broad prospective consent model would seem to align favorably with the perspectives of many, although not all, members of the public on the question of how biobanks should obtain permission for enabling the use of donated biospecimens in future research. Study participants viewed broad consent as less burdensome on research participants and more likely to support flexibility, progress, and efficiency in research. However, their concerns also point to the possible need for biobanks to consider and be responsive to the minimally informative nature of broad consent and its tendency to disallow individual control over sample and information use. Broad consent has been considered ethically valid provided that personal information related to research is handled safely; prospective participants are granted the right to withdraw consent; and new research studies or changes to the legal or ethical authority of a biobank are approved by an ethics-review board.[24] However, these provisions do not address the potential unease that individuals may experience over the minimal information and control afforded by broad consent and that may be counter productive in the broader effort to conduct biobank research with the trust and support of participants, as well as the wider public. It may be possible to assuage some of this unease by combining broad consent with some version of categorical consent and by using online and other resources designed to keep biobank participants informed of evolving research. Biobanks would do well to preemptively consider their options in this respect and to consult with IRBs, ethics experts, and other sources with a view to addressing the compromises to autonomy and respect for persons that necessarily follow from obtaining of broad, research unspecific consent. Community engagement in early stages biobank development is needed to take into account the demographic and cultural contexts in which the biobank is being planned, as well as the type of biobank involved. Participants in disease-specific biobanks, who donated samples specifically for research, may have very different views than those whose samples were obtained for clinical purposes and are now going to be used in a broad population-based biobank.

Other considerations

Finally, although other studies have found little association between age, income, and consent preferences for biobanking, our study provides some evidence of variability in consent preferences based on income and age. These findings add to the study conducted by Murphy et al.,[18] in which race was the only demographic identified to influence preferences for consent. In our study, lower income was associated with an increased preference for opt-out consent, although the majority still preferred opt-in; however, education showed no association to any consent preference. Our study also suggests that younger people may prefer having more choice or control over ongoing participation in biobank-supported research. This finding is consistent with other studies suggesting that the desire for decision-making control over biobank participation tends to decrease with age.[36]

Limitations

This study considered a common array of consent models for biobanking and how they were perceived among members of the public in the US Midwest. Results may not be representative of public perceptions in other regions of the United States, although some overlap with other study results is evident.[18,34] Our findings are also circumscribed by the fact that the research was conducted with members of the public and not with actual biobank participants. In some cases, attitudes and concerns

between these two groups markedly differ.[34] In other cases, both members of the public and individuals with experience participating in a biobank share very similar perceptions and preferences.[46]

Our study findings are also largely specific to whites and English speakers. Murphy et al.[18] has found that preferences for consent models may vary based on ethnicity. Apart from other minority groups, there is a rapidly growing Spanish-speaking population in the state of Iowa, whose perspectives may need to be taken into account in efforts to incorporate public preferences into biobank consent design. Our population was generally an educated, somewhat older, mostly white group of participants, so further research may be needed to reflect the preferences of other populations. Finally, the study also addressed only the issue of consent for a competent adult, not the surrogate consent that would be given for use of newborn screening cards or other pediatric populations, or for impaired adults.

CONCLUSION

The process of seeking informed consent for medical research involving human participants is widely accepted and enshrined in law. Informed consent enables individuals to decide whether to accept certain risks of biobank participation and acknowledges the relevance of the Belmont principle of respect for persons to biobanking.[10,18,20,44] However, no overarching policy exists with respect to the type(s) and timing of informed consent needed in the case of biobanking with biospecimens and health information. Both initial, prospective opt-in and opt-out consent frameworks have been considered legally and ethically defensible for purposes of collecting and storing coded biospecimens and health information. Compelling arguments have been made for and against broad, categorical, and study-specific consent formats for the purposes of informing individuals about and obtaining their permission for the use of their biospecimens and health information in future research.

Our research suggests that many members of the public support the prospect of making an active and informed initial decision about biobank participation but that they have concerns about the need for and potential adverse impact of future-use consent mechanisms such as categorical and study-specific consent. It is also possible that, if thoroughly and appropriately conducted within the context of a well-governed biobank, a prospective opt-in consent process will nurture the level of individual understanding, decision-making confidence, and general reassurance needed to enable ongoing, ethical research access to biospecimens and health information through the mechanism of broad consent.

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