



Not a Simple Story: Contextualizing Opt-Out in U.S. Biobanks

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Collaborators on U.S. Biobank Study

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Consent for Biobank Specimen Contributors

- Biobanks facilitate the collection of specimens and associated data for future unspecified research

Opt-in informed consent:

- Potential research participants provided with information about the biobank and given the opportunity to actively signal their willingness to be included in the research.
- Criticized as not fitting broad biobank model, logistically difficult

Opt-out:

- Potential research participants provided with information about the biobank and given the opportunity to signal any desire to be excluded from the research.
- Criticized as undermining contributors' autonomy

Consent for Biobank Specimen Contributors

- Europe turned to broad or general opt-in consent
- The U.S. turned to de-identification (not human subjects) in 2004, but this and other options continued to be controversial, and we are now debating changes to the Common Rule

“Reforms would require written consent for research use of biospecimens, even those that have been stripped of identifiers. Consent could be obtained using a standard, short form by which a person could provide open-ended consent for most research uses of a variety of biospecimens.” (ANPRM, 2011)

What do U.S. Biobanks Actually Do? (our study)

Creation of database of ~700 biobanks

- Multi-faceted search strategy addressed lack of census
- Eligibility criteria: Web presence, located in US, contact information found

National Biobank Survey: recruited all identified banks

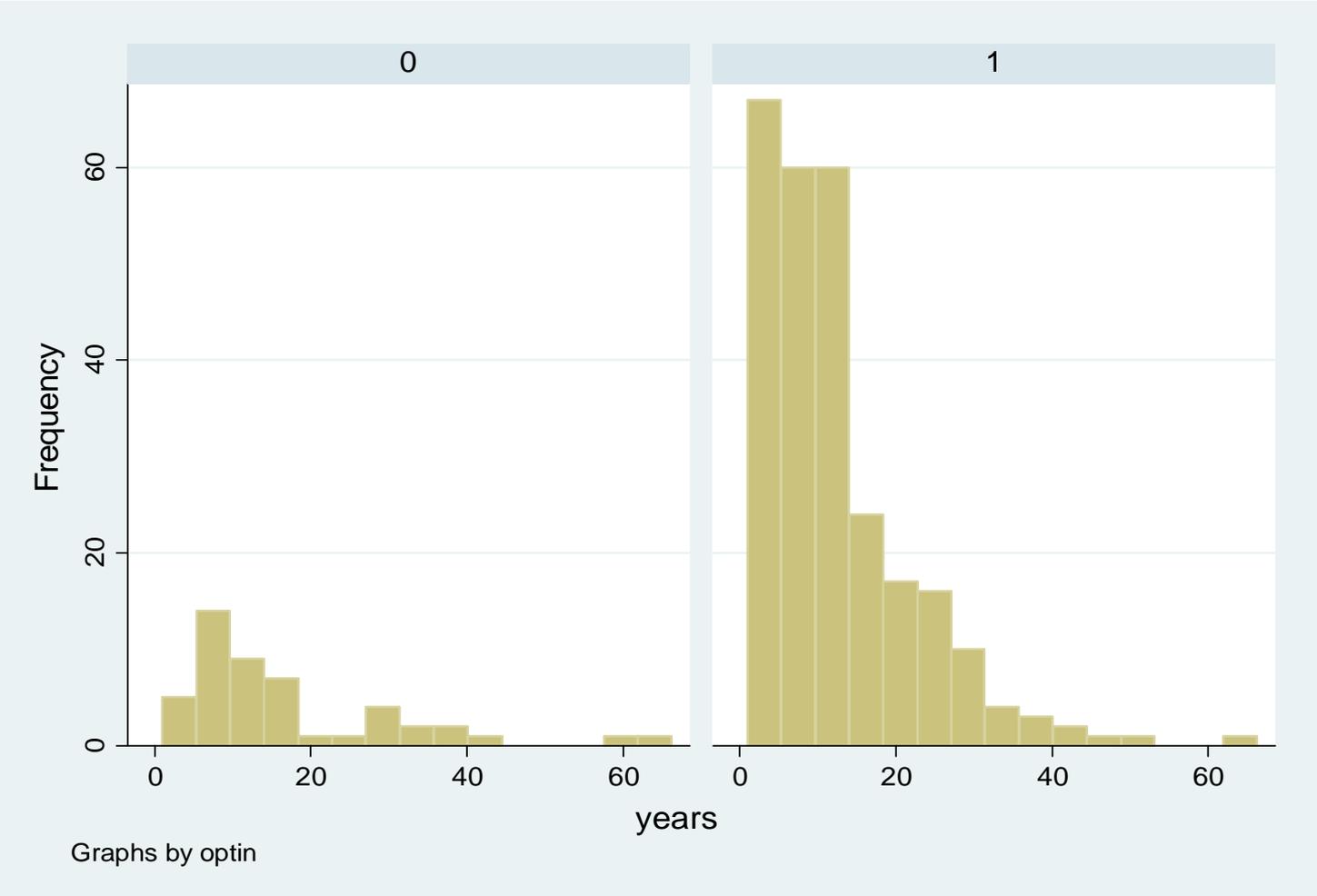
- Pilot, July 2011, N=100, 79% response rate
- Full survey, March-April 2012, N=662
62% response rate (72% among 523 previously contacted)

Preliminary Findings

- Organizational form (academic, gov't, for- and not-for-profit) inadequate to predict diversity of biobank work and policies
- Variable work and policies: Many banks combine specimens from different sources, studies, locations, and populations; some collections are small, underutilized, with uncertain funding; some banks have a high degree of formalization, business plan, oversight committees, and policies
- **Variation in Consent Policy:**
 - 74% opt-in (incl. 76% broad consent)**
 - 14% opt-out**
 - (12% mixed)



Opt-out & Opt-in by Number of Years in Existence





What Explains the Choice of Opt-Out?

- Informed consent is embedded in a larger set of policies and organizational features of biobanks—related to why they are originally created, what challenges they face, and how they adapt over time.
- We argue that the diversity of solutions adopted by biobanks to address relationships with specimen contributors cannot be understood apart from the people and the organizations that do the actual work.

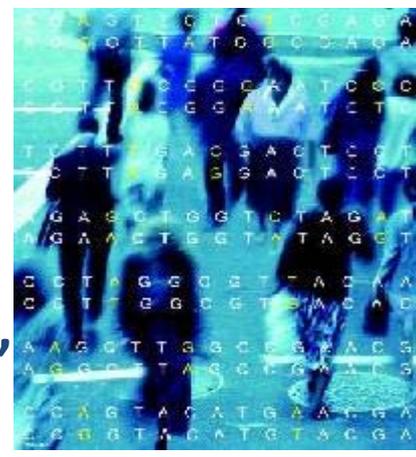
Illustration from Biobank Case Studies

As part of our larger project, we conducted 6 case studies with banks selected for diversity in creation stories, conducting interviews with 3-6 individuals at each bank

De Novo: 1) a government population collection for gene-environment studies; 2) a community study funded by philanthropic gift, through university

Network: 1) an NIH funded, linked disease-specific collections at 8 med centers; 2) Centralized support from disease-advocacy organization

Re-purposed: 1) University Biobank (UB) hospital/clinic specimens and EMR data; 2) State Neonatal Bank (SNB) re-purposed state-owned newborn blood spots for health research



1. University Biobank: 2004 “Discovery Machine”

UB bioinformatics experts developed a sophisticated one-way de-identification algorithm that theoretically ensures no human can use medical record data to correctly identify the individual contributing sample, enabling the biobank to qualify as doing “non-human subjects” research.

“We proposed a novel method of building a biobank that involved both an informatics technology of de-identification and a community engagement model that was an opt-out for a de-identified non-human subjects resource... an ‘all-comers’ biobank that was capable of supporting disease-oriented research in virtually any disease... and float the boats of dozens if not hundreds of investigator grant submissions... any faculty member at the institution... (but) the very first grant that came in paid for the entire institutional investment...” (UB PI)



Centralized closed system for researcher access

UB has access to specimens and patient medical records from the associated university hospital.

People have the “prerogative not to have their blood used... even though they cannot be identified... it’s not their DNA, it’s some hypothetical human being who looks a lot like them..” (PI)

All work is done in-house.

The bank’s resources are only available to university’s researchers whose use of data can be audited.

It’s an enforceable infrastructure. It’s restricted to university research faculty and staff because we need to be able to fire somebody who does not follow the acceptable use policy.” (PI)

Pay to play

UB pays capital expense of genotyping core services and researchers pay for samples, and agree to return unused specimens and research results to UB

130,000 specimens collected/year

Oversight: All uses of the specimens and data are audited.

“More advisory committees per kilogram than any project I’ve ever done... and we have tensions among our advisors”

The trade-off

*“I will be honest with you. Our success in the opt-out process and our success in getting the brochures out and stuff is less than perfect, and you know we have to sort of scream about that from time to time, and if I were not as confident about the robustness of our de-identification protocol and of our security protocols, I would be more concerned than I am, but I truly believe that the risk of re-identification is breathtakingly low.”
(Ethics Oversight Committee)*



2. State Neonatal Bank:

Sample collection is done through the state's newborn screening system. All ~120,000 children born each year added unless parents opt out (~4.5 million samples stored).

Creation of the SNB

In 2000, commission encouraged the state to utilize the stored bloodspots for health research and to store the samples indefinitely.

In 2009, SNB was established as a separate non-profit run through a local university. The state contracts with SNB to catalogue, store, and distribute bloodspots to researchers.

Opt-out → Opt-in?

OHRP was asked if an opt-out procedure for the SNB was consistent with federal regulations.

OHRP response: Because the state knew that samples were going to be put into a research biobank, even if not the primary purpose of collection, then the collection itself constituted a human research activity, & need IRB review.



State internal IRB review concluded:

Samples collected previously were exempt from consent requirements – provided that SNB advertise its existence and have a clear way for parents or children to have their sample removed and destroyed.

Prospectively, at the time of screening, all parents must receive a special brochure explaining the SNB and then sign a consent form either allowing or not allowing residual sample storage and use.



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SNB

Admin. Use Only

Baby Name _____

Affix Label Here if Desired

Information Provided to Parent

Parent Declined

You should have been given the booklet, "After Newborn Screening". If not, please ask for it. This booklet describes the State Neonatal Bank and how dried blood spots (DBS) could be used for medical research after newborn screening is complete. Please read this booklet and if you have any additional questions, you may call the Newborn Screening Program at 1-866-673-9939.

- Participation in the State Neonatal Bank is completely voluntary.
 - If I say "yes" now I may change my mind at any time and ask that my child's DBS not be used for research by calling 1-866-673-9939.
 - When my child is 18 he or she can ask that their DBS not be used for research.
 - There is no penalty from not allowing my child's DBS to be used for research.
- I voluntarily agree to allow my child's DBS to possibly be used for medical research after newborn screening is complete. My permission applies to any blood spots obtained for newborn screening.



Parent Signature _____ Date _____

Dept of Community Health Laboratory Copy

Remove. Discuss with parent. If granted, collect parent signature and submit original signed copy to MIDCH Laboratory. Give the parent this copy.

1F



Do not send specimens in plastic bags.

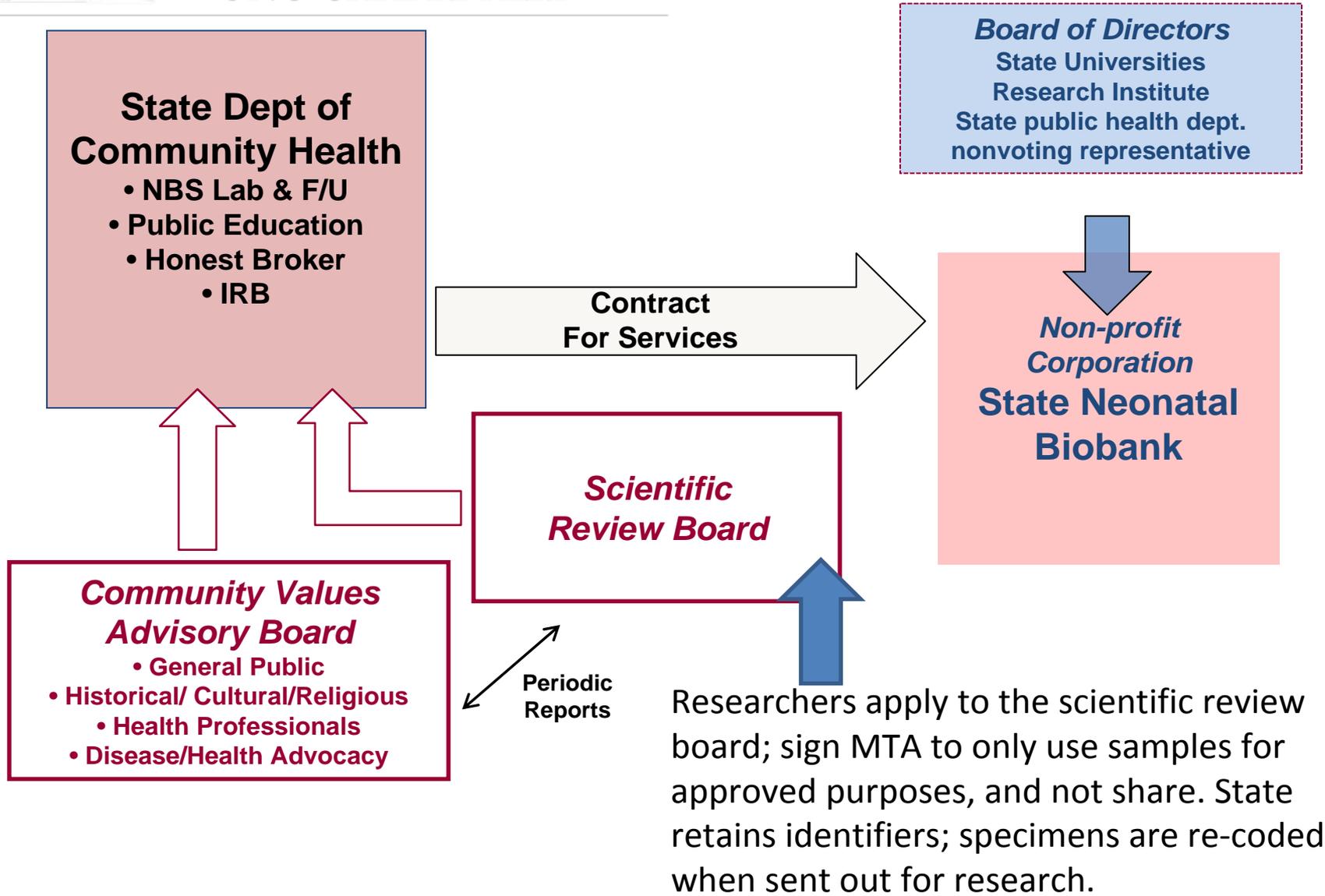


See attached instructions for specimen collection and sending. Allow blood to dry for 3-6 hours using the overlay for support. Close the overlay when dry. Send within 24 hours of collection.

DO NOT REMOVE OVERLAY



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Context of the decision to use NBS for research: Controversies in other states.



“[If] we had a court order to destroy all the DNA samples like that terrible story in Texas... to destroy the biologic samples. I said ‘Holy Christ. This is like burning books.’” (another case study PI)

SNB: “Hold in trust, to benefit citizens of the state”

PI of SNB described preserving the “last drop” to be “held in trust,” in the name of children and parents (rather than in order to make it accessible to scientists).

Conclusions

- Biobanks have different missions/goals and different ways they build their collections.
- Their diverse organizational cultures have shaped differing conceptualizations of tissue and data, relationships with researchers and the community of specimen contributors, and concerns with privacy and identifiability.
- While actors at each biobank might pursue what they see as ethical ends differently, all express a sense of responsibility for the specimens they store... which can never be abstracted from the context of their collection, storage, and use.



Thank you!