Tools for Public Education about Research Ethics

JEFFREY R. BOTKIN, M.D., M.P.H.

PROFESSOR OF PEDIATRICS AND MEDICAL ETHICS

ADJUNCT PROFESSOR OF HUMAN GENETICS



Disclosure

I serve on the Ethics Advisory Committee for Illumina Corporation with compensation

Objectives

Review a controversial issue in population screening and biobanking

Provide an overview of selected educational tools for the general public used in our research involving genetic screening

History

➢ The National Human Genome Research Institute (NHGRI) has set aside 5% of its budget for scholarship on the ethical, legal, and social issues in human genetics (ELSI)

The only NIH institute or center to formally devote significant funding to ethical, legal, and social issues

Centers of Excellence for ELSI Research (CEER)

- Current CEERs at Johns Hopkins, Columbia, Vanderbilt, Oklahoma, Utah
- ➢ UCEER: Funded by the NHGRI in 2016 for 4 years (2016 − 2020) with one renewal opportunity for another 4 years (2020- 2024)
- Each center has a primary focus. UCEER's primary focus is genetic screening in the healthcare of women and children
 - Newborn screening
 - Prenatal screening
 - An emphasis on informed consent and patient education

Why focus on population screening?

- 1. Screened individuals do not consider themselves ill or at risk
- 2. Screening engages large numbers of individuals, complicating informed consent
- 3. High ratio of false to true positive results
- 4. Individuals and healthcare providers often poorly prepared to manage positive results
- 5. Often identifies people with mild variations of conditions that wouldn't have been identified clinically.

A public policy question

- All states conduct newborn screening
 - Is it ethically appropriate for state health departments to save residual bloodspots after newborn screening for biomedical research?
 - How much should parents know about this practice?
 - Should parents be asked their permission?





Dried Blood Spot Retention Time



From: NewSTEPS, Sontag, August 2015

Newborn Screening Dried Bloodspots

Obtained without parental knowledge or consent in most states

- Because NBS is conducted without parental consent
- NBS brochures may contain a sentence about secondary uses of DBS
- ➢ Research with DBS is almost always conducted with deidentified bloodspots
 - Traditionally, research was no longer human subjects research
 - Many states conduct IRB review of protocols anyhow



Bloodspot Litigation

Minnesota suit based on state genetic privacy law

- *Bearder v. State*, 806 N.W.2d 766 [2011]
- Settled => state now requires consent for storage and secondary uses

Texas suit based on constitutional claims regarding illegal search and seizure

- Beleno v. Texas Dept. of State Health Services, U.S. District Court, Western District of Texas, SA09CA0188 [2009]
- Settled: state destroyed 5 millioDBS and now requires consent
- Illinois suit alleging constitutional violations
 - Doe v. VanNess, Marion County Superior Court, 49D011409CT031[2014]
 - Suit dismissed

A Research Agenda

- Assumption: Public attitudes are a critical element in developing acceptable and effective public policies
- How do we foster knowledge and understanding of complex issues in biomedicine?
- How do we garner informed public attitudes?
- What contemporary tools are useful for promoting informed choice?
- What weight should be given to public attitudes in policy decisions?



Federal Regulations Governing Biospecimens



➢ If biospecimens are not readily identifiable to the investigator, the research is not considered human subjects research and falls outside the regulations

HIPAA may apply in covered entities unless de-identified by HIPAA standards

Identifiable specimens: consent can often be waived if an IRB determines that the 4 criteria are met

Consent can be simplified/altered if research meets the 4 waiver criteria

Waiver/Alteration Criteria (45CFR46.116(d)

Minimal risk research

➢Will not adversely affect the rights or welfare of subjects

>Not practicable to obtain consent

➢When appropriate, subjects given pertinent information after participation

Biospecimen-based research



>Ethical and regulatory issues arise because

- Research with biospecimens is removed in time and place from the source individual
 - Downstream uses cannot be predicted at the time of acquisition
- Public sensitivities about the personal nature of biospecimens ("Its part of me.")
- High scientific yield
- Low risk

Risks Associated with Biospecimen Research

➢No instances of welfare harms from biospecimen research

Several instances of "dignitary harms"

- Henrietta Lacks story
- Havasupai Tribal case
- The Moore case
- Newborn screening lawsuits

Henrietta Lacks

Newborn Screening Dried Bloodspots

Used for a wide variety of purposes

- •QA/QI purposes
- Forensic purposes
- Biomedical research
 - Genetic epidemiology
 - Metabolic disorders
 - Endocrine disorders

Infectious diseases

Toxicology

Are Dried Bloodspots Useful for Research?

Scoping review of the international literature from 1973 –2017

- 654 articles identified
- For US studies, 80% for research, 20% for QA/QI.
- >Leading titles(citations)
 - Neonatal cytokines and coagulation factors in children with cerebral palsy (368)

• Prevalence of HIV infection in childbearing women in the United States. Surveillance using newborn blood samples (243)

> Rothwell, Johnson, Richie, Botkin. Secondary research uses of residual newborn screening dried bloodspots: A scoping review. <u>Genetics in Medicine</u> (2018) https://doi.org/10.1038/s41436-018-0387-8

The Cost and Burdens of Consent



➢ Post partum period is short, hectic, and with many clinical and personal priorities

- Consent process likely to result in a substantial decrease in available DBS for research
 - In several studies, uptake drops to about 60% when an informed consent requirement is implemented
 - Primarily due to administrative burdens and barriers, NOT due to parents who decline consent
 - The value of the biobank is severely diminished if it does not represent the whole population

Assessing Public Attitudes

Our team developed a "deliberative discussion focus group" approach

Detailed information provided in 90 – 120 min focus groups with diverse participants

Educational presentation (video) followed by group discussion led by a facilitator with a guide and a subject matter expert to answer questions

Rothwell, E., Anderson, R., & Botkin, J.R. Deliberative discussion focus groups. <u>Qualitative Health Research</u> 2015 Jun 15. pii: 1049732315591150.

What do Parents Want to Know?

Two short videos developed on newborn screening and residual bloodspot retention

- Focus groups with 128 participants from 4 states
- Couples who were pregnant or had a child <5yrs of age
- 55% women, 32% white, 34% Latino, 28% African-American

Botkin JR, Rothwell E, Anderson RA, Goldenberg A, Kupperman M, Dolan SM, Rose NC, Stark L. What parents want to know about the storage and use of residual newborn *blood spots*. <u>Am J Med Genet</u> A. 2014 Nov;164(11):2739-44





Carnitine palmitoyltransferase I deficiency (CP Carnitine palmitoyltransferase type II deficience Classic galactosemia (GALT) Maple syrup urine disease (MSUD) Carnitine uptake defect (CUD) Glutaric acidemia, type II (GA-2) The Seven Things Parents Should Know about Residual Dried Bloodspots

- 1. Some states save leftover bloodspots after newborn screening is complete.
- 2. Leftover bloodspots can be used to improve the public's health in many ways.
- 3. No extra heel pricks are done to collect blood for other potential uses of the spots.
- 4. Safeguards are in place to protect the privacy of babies and families and to ensure the ethical conduct of research.
- 5. The baby's name or other identifiable information is not attached to the leftover bloodspots used in most research.
- 6. Because most research with leftover bloodspots is done anonymously, parents will usually not get results back from the research.
- A parent may request that their baby's bloodspot not be used in research after newborn screening.

Challenges with Public Education

How to present complex information in a brief (5 min) video

- Keeping text information at an appropriate reading level
 - Narration of text reduces challenges with low literacy
- Balance, balance, balance
 - How to keep our personal biases out of the educational materials
 - People have concerns about privacy. Should risks to privacy be highlighted when the track record is remarkably good?
- Will more information make people more or less supportive of newborn screening?

Research on Parental Attitudes NHGRI R01

Methods for promoting public dialogue on the use of residual newborn screening samples for research" (PI - Botkin)

Respondents

Group	N (%)			
Focus Groups (n=15)	128 (3%)			
Surveys (paper/phone)	1368 (37%)			
Knowledge Networks	2309 (60%)			

Respondents

Group	N (%)		
Video	1769 (47%)		
No Video	2036 (53%)		

Respondents

Group	N (%)
White – Non-Hispanic	1795 (61%)
African American	774 (24%)
Hispanic	701 (22%)
Mothers of children < 1 yr	414 (12%)
Native American	121 (4%)
Mountain States Region	2313(60%)

Gender	N (%)
Male	1404 (36%)
Female	2401 (64%)

Selected Core Questions

Did you know that these [NBS] tests were done?



How supportive are you of Health Departments doing these blood tests on all new babies?



Do you think it is alright that these tests are done without permission from the parents?



How concerned would you be if Health Department saved the leftover blood samples from babies after the tests are done?



Do you think it would be alright for these leftover blood samples to be used for important research on diseases that affect mothers and babies?



What do you think is the best thing to do?



General Findings

Enhanced education is associated with *increased* support for retention and use

- ➢ The public is generally supportive of the retention and use of residual newborn screening bloodspots
 - A substantial number of individuals have significant concerns about this practice
- >The public wants information about this practice
- An element of choice is expected
 - Opt-in preferred over opt-out

Public Attitudes on Research Access to Tissues and Medical Records

- ➢ Botkin et al. Public attitudes regarding the use of electronic health information and residual clinical tissues for research <u>J Community Genet</u>. 2014 Jul; 5(3): 205−213
 - 12 focus groups (131 participants) in Utah, Washington, Arizona and Minnesota
 - Participants informed of current practices regarding the secondary research uses of clinical records and residual biospecimens
 - Informed that the University was considering an information and opt-out approach and asked whether this was acceptable
 - The large majority of participants supported the proposed approach

Summary of the broader literature on biobanks

- The majority of individuals support the secondary use of clinical biospecimens for research use
- ➢ People want to know about this practice
- People want a choice about whether their biospecimens are used
 - Opt-in > opt-out



Collaboration with Michigan Biotrust

Michigan has established the BioTrust to retain and manage residual NBS bloodspots. Parental consent is required.

>NIH/NICHD Grant – Erin Rothwell and Botkin PIs

➤<u>Title</u>: R01 Video Informed Consent Information (VICI) for Residual Bloodspot Biobanking <u>Description</u>: To develop and formally assess a video informed consent tool and an interactive application for biobanking of residual bloodspots for the Michigan Biotrust

- Information delivered in the post-partum period via iPad
- Compared to current informational brochure

BioTrust Brochure

What are the risks if your baby's blood spots are used for research?

The risk is that your baby's blood spot could be identified. The chance this will happen is very low. Many steps are taken to protect privacy.

What steps are taken to protect privacy?

There are many levels of security at the Michigan Neonatal Biobank where blood spots are stored. They are stored using a code and not your child's name. Details that could identify a child or family are removed. MDHHS has taken steps to keep blood spots secure. The highest level of protection, a "Certificate of Confidentiality" from the United States Department of Health and Human Services has been granted. Details are below:

Certificate of Confidentiality

- US Department of Health and Human Services http://grants.nih.gov/grants/policy/coc/
- It gives the BioTrust the right to refuse a court subpoena, in any federal, state, or local, civil, criminal, administrative, legislative, or other proceedings. The BioTrust will exercise that right.
- It cannot be used to resist a demand for information from personnel of the U.S. Government. It cannot be used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the FDA.
- It does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you give an insurer, employer, or other person your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Will you or your child benefit from blood spot research?

Most likely you or your child will not benefit. You will not be paid if your child's blood spots are used. Your family will not get money if products (such as new drugs) ever come from the research. You will help ensure the BioTrust represents all of the groups of people in our state. This ensures no group is left out of research. You, or a family member, may also be helped by research looking at new ways to diagnose, prevent or treat disease.

What are your choices for blood spot research?

You can say "yes" or "no" to blood spot research. You will be asked to check a box and sign a form found in your baby's newborn screening card. If you say "yes", all blood spots taken for newborn screening may be used, except for the blood spot saved for your own use if needed. If you say "no", blood spots will be stored but not used for research. You must contact MDHHS if you do not want blood spots stored for any reason after newborn screening.

Can you change your mind?

Yes. You can call MDHHS at any time if you change your mind about blood spot research. After turning 18, your child must make this request.

What do you need to do?

ASK if you have questions.

VISIT www.michigan.gov/biotrust to read more about consent options.

CALL MDHHS if you still have questions about blood spots.

MARK your choice for blood spot research use on the BioTrust consent form and sign it.

<u>GET</u> your pink copy of the BioTrust consent form to take home.

MDHHS Newborn Screening Program

Telephone: (Toll Free) 1-866-673-9939

Email: newbornscreening@michigan.gov

Website: www.michigan.gov/newbornscreening

For questions about your research rights or whom to contact in case of a research-related injury: please call the MDHHS IRB at 517-241-1928



MDHHS is an equal opportunity employer, services and program provider. 100,000 printed at \$0.04 each with a total cost of \$3,776.30 12/15

After Newborn Screening





Learn More About the Facts and Choices You Need to Understand

BioTrust Consent Document

	-		
Before you sign this form please read, <i>Your Baby's Blood Spots</i> . It explains in more detail how your baby's blood spots may be used in health research through the Michigan BioTrust for Health. If you still have questions, please call the Michigan Department of Health and Human Services (MDHHS) toll free at 1-866-673-9939.	prochure. this copy.	0	GRAZAHOIB
Yes, my baby's blood spots may be used for health research through the BioTrust. By checking this box you understand:	BioTrust b ive parent	0	plastic bags.
• Unused blood spots are stored using a code and not your child's name. The spots are stored forever at a secure site (Biobank) unless you, or your grown child, change your mind.	It to read IDHHS. G	0	Do not send specimens in
• Stored blood spots may be used by the state lab to help ensure that newborn screening detects those at risk. Stored blood spots may also be used for research approved by MDHHS. Blood spots can only be used for studies to better understand disease or improve the public's health	ruct parer form to N	0	A A A A A A A A A A A A A A A A A A A
 Many types of laboratory methods are used to study biological factors like DNA or environmental factors like metals and toxins. 	orm. Instr consent	0	Send within 24 hours of collection.
 The risk for using your baby's blood spots in research is that it could be identified. This risk is very low. Many steps are taken to protect privacy. Details that could identify your child or family are removed before your child's blood spots are given to a researcher. 	consent f eted white	0	the overlay. When dry.
 Most likely you or your child will not benefit from blood spot research. Participation is voluntary. You can call MDHHS at any time if you change your mind. There is no penalty or loss of benefits for saving no or changing your mind. 	the white urn comple	0	hours using the overlay for support. Close
No, my baby's blood spots may not be used for health research.	he back of ature. Ret	0	Milow blood to dry for a for a of 3
Blood spots will be stored forever but not used for research. These stored blood spots may still be used by the state lab to help ensure that newborn screening detects those at risk.	label on t	0	collection and sending.
	ix patient t decision	0	specimen specimen
Big Parent Signature Date Your choice applies to all blood spots collected for newborn screening. Please visit <u>www.michigan.gov/biotrust</u> for further information	sired, affi ect parent	0	YAJAJVO
including research updates. For questions about your research rights or whom to contact in case of a research-related injury, please call the MDHHS IRB at 517-241-1928.	If de Colli	0	DO NOT



VICI Study

- ➢ 532 new mothers randomized in three Michigan hospital-based birthing centers to brochure, video, or interactive computer app
 - Interventions offered by research coordinators not hospital staff
- Knowledge on 20 items was significantly better with video and interactive app compared to brochure
- Satisfaction was significantly better for video & app
- > Participants rarely used interactive feature of the app

Support for NBS and Biotrust was high overall and highest in the video group

VICI Results - Challenges

Intervention was employed by research staff – clinical staff were too busy to assist

- Uncertain whether routine use by clinical staff will improve the efficiency and efficacy of the consent process
- Signatures for consent must be on the NBS card that goes to the lab
 - Cannot employ a fully electronic consent process

> We need more robust implementation science component!

VICI Continuation

➤ We are currently seeking funding to continue the research with the collaboration of Texas and Michigan to implement and evaluate routine use in newborn nurseries

Overall Conclusions

Video and interactive tools can significantly enhance understanding of complex and controversial issues

Enhanced understanding is associated with increased support for these programs

People want to be informed and they want a choice

Videos are time-consuming and relatively expensive to produce

Videos are challenging to implement in the real world of clinical medicine

 Many opportunities to engage people at home and through their devices

Other Genetic Education Projects

➢<u>NIH R21 HD083832-01 (Rothwell, PI)</u> Improved Prenatal Genetic Screening Decision Making through Interactive Technology

➢<u>NIH R01 HD069045-01 (Swoboda, PI) Pilot newborn screening project for</u> identification and prospective follow-up of infants with spinal muscular atrophy

➢<u>NEA Grant</u>: (Gretchen Case/ Sydney O'Donnell – PIs) Development of an educational intervention (CRiTICS) for providers' communication of a positive prenatal genetic screening result.

UCEER Grant: Comic Book to Increase Health Literacy about Carrier Screening (Botkin PI)

Links to Our Videos and Brochures

Newborn Screening Videos <u>https://uofuhealth.utah.edu/uceer/nbs-videos.php</u> <u>https://vimeo.com/showcase/3301573</u>

Newborn Screening Brochures <u>https://uofuhealth.utah.edu/uceer/nbs-brochures.php</u>

Utah Genome Project – Education and Consent

https://uofuhealth.utah.edu/uceer/research/recent-relevant-research/ugp-movies.php

Carrier Screening Video

https://uofuhealth.utah.edu/uceer/research/recent-relevant-research/carrier-screening.php

The Team -- Thank You!

>Utah Center of Excellence for ELSI Research

- Rebecca Anderson
- Shakila Nawaz
- Erin Johnson
- Erin Rothwell
- Jim Tabery
- Nancy Rose
- Bob Wong

- Leslie Francis
- Louisa Stark
- Teneille Brown
- Kim Kaphingst

11

- Avery Holton
- Lauren Clark
- Karen Dent
- Gretchen Case
- Sydney Cheek-O'Donnell

- Roger Altizer
- Heather Canary
- Jose Zagal
- Richard Nelson

Thank You!

