

The background features a dark blue gradient with faint, light blue circular patterns and numbers. The numbers include 40, 150, 160, 170, 200, 220, 230, 240, 250, and 260, arranged in a circular fashion. There are also dashed lines and arrows forming circular paths.

THE *NEXT GENERATION OF* ETHICS IN NEWBORN SCREENING RESEARCH: INCLUDING ELSI IN NBS PILOT STUDIES

AARON GOLDENBERG, PHD MPH
CASE WESTERN RESERVE UNIVERSITY

ANTICIPATING ELSI FOR NBS CONDITIONS

- We can anticipate certain ELSI issues related to new conditions being nominated to the RUSP in the last decade (and future?)
 - Phenotypic and genotypic variation
 - Adult onset variants
 - Extremely low prevalence
 - Extremely high cost
 - New technology for screening (genomics)
 - Carrier considerations
- ***Aaron J. Goldenberg, Michele Lloyd-Puryear, Jeff Brosco et. al. GIM 2018 for the NBSTRN Bioethics and Legal Workgroup***



BACKGROUND

- Premise: decisions about RUSP/state panels could be improved with empirical data re ELSI
- GOALS
 - Encourage scholars to include ELSI research questions in pilot studies
 - Provide teams of clinicians, advocates, and investigators with sample empirical questions that could aid in identifying and assessing ELSI issues related to a specific condition
 - Allow policy-makers to maximize benefits and mitigate potential negative outcomes (Help ACHDNC weigh benefits and harms of candidate conditions)

APPROACH

- *Parent Project Muscular Dystrophy* ELSI workgroup
- Bioethics and Legal Workgroup for the NBSTRN discussed the issues/approach at length and drafted framework for NBS ELSI
- Workgroup then facilitated professional and public discussions aimed at engaging NBS stakeholders to identify important existing and emerging ELSI challenges
 - >100 Stakeholders: policy, lab directors, researchers, disease advocacy organizations
 - NBS Public Square (Genetic Alliance/Baby's First Test) provided on-line forum for additional feedback

AUTHORS

- Aaron J. Goldenberg, PhD., MPH
- **Michele Lloyd-Puryear, MD, PhD**
- **Jeffrey P. Brosco, MD, PhD**
- Bradford Therrell, PhD
- Lynn Bush, PhD
- Susan Berry, MD
- Amy Brower, PhD
- Natasha Bonhomme
- Bruce Bowdish, PhD
- Denise Chrysler, JD
- Angus Clarke, DM, FRCP
- Thomas Crawford, MD
Edward Goldman, JD
- Sally Hiner
- R. Rodney Howell, MD
- David Orren, JD
- Benjamin S. Wilfond, MD
- Michael Watson, PhD
- For the Bioethics and Legal Workgroup of the Newborn Screening Translational Research Network

RESULTS

- Nine Key ELIS questions in two broad categories:
 - Related to results of screening
 - Related to initiation and implementation at the NBS systems level

- Sample questions



RESULTS RELATED ELSI

1. What are the potential ELSI of positive screening results related to a condition?
 - Do caregivers treat an infant differently when a presymptomatic diagnosis is made?
 - What are the potential harmful or beneficial effects of an NBS diagnosis on maternal–infant bonding or other family dynamics? •

RESULTS RELATED ELSI

2. What are the potential ELSI of false positive screening results related to a new condition?

- Do caregivers treat an infant differently as a result of receiving a false positive screen result?
- Are there long-lasting psychological consequences for a positive screening test in infants who do not have a condition? What is the effect of a false positive on maternal–infant bonding?

RESULTS RELATED ELSI

3. What are the potential ELSI of false negative screening results related to a new condition?

- Do “normal” NBS results provide false reassurance to parents (e.g., cause people to ignore symptoms of serious illness? or could cause a unnecessary diagnostic odyssey for families later in life?)

RESULTS RELATED ELSI

4. What are the potential ELSI of obtaining and reporting carrier status related to a new condition?

- How does knowledge of carrier status impact the newborn/families?
- Does this knowledge lead to stigmatization, concerns about life expectancy, changes in lifestyle choices, or decisions about having more children?

RESULTS RELATED ELSI

5. What are the potential ELSI of indeterminate results related to a condition?

- Does knowledge of potential illness provide families with reassurance that they will be able to intervene at the earliest possible moment?
- Does it lead to anxiety and concern about even minor symptoms?
- Does it create “patient in waiting”?

ELSI RELATED TO NBS SYSTEM

6. What are the resource allocation implications for adding a new condition to the RUSP/state panel?
 - Are state NBS programs ready to implement the new screening test, or does it require radically new procedures, equipment, or expertise? What are the likely costs and how might it impact the programs obligation to provide screening and follow-up for other conditions?
 - What are our ethical obligations to assure kiddos can get access to short and long term follow up?

ELSI RELATED TO NBS SYSTEM

7. What are the health disparities or *equity considerations* related to adding a new condition?

- Do decisions about how to screen for a condition have implications for which populations are most likely to be diagnosed (e.g., CF screening)?
- Are population-level results of NBS likely to affect one population in particular (e.g., reveal high rates of infectious disease or stigmatizing condition)?
- What factors will influence access to confirmatory testing and treatment (e.g., health insurance, geography, culture, race/ethnicity)?

ELSI RELATED TO NBS SYSTEM

8. What are the potential implications for public/parental trust in the NBS system or health department that might arise because of adding a new condition?

- Do false negative/false positives weaken faith in NBS programs and the ability of health departments to provide accurate and helpful information?
- Is there transparency in the process of adding a new condition to a panel, the implementation of screening tests, and approach to follow-up and treatment?

ELSI RELATED TO NBS SYSTEM

9. Does a condition raise any concerns regarding parental permission or challenges to the ethical or social justification for requiring population-based screening?

- Does the condition have such a high benefit:cost ratio that the general public and nearly all families would agree that NBS should be universal?
- Or would many reasonable people choose to opt out (e.g., later-onset condition with ambiguous benefits of treatment)?

OTHER CONSIDERATIONS

- Need for ELSI to be condition specific
- Some questions will need longer periods of time
- Who are you trying to reach?
 - Families, NBS programs/laboratories, Clinicians/Health Care System
- Need for new collaborations
 - Academic/Research Organizations: Case, Utah, RTI
 - Professional Orgs: NBSTRN-Bioethics and Legal Workgroup



NBSTRN
Newborn Screening
Translational Research
Network



ACMG
American College of Medical
Genetics and Genomics
Translating Genes into Health

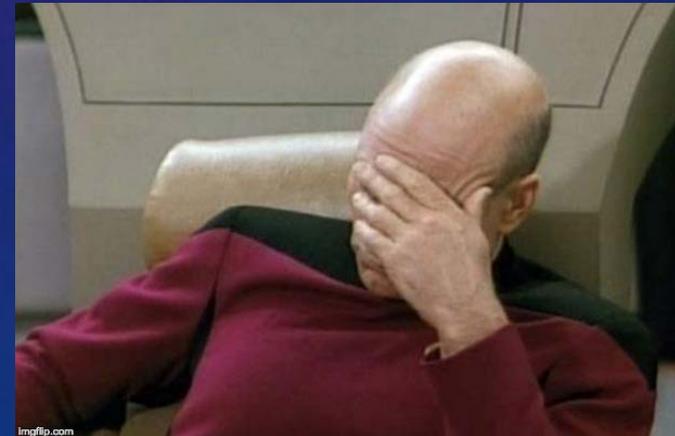


NICHD
Eunice Kennedy Shriver
National Institute of Child Health
& Human Development

This project has been funded in whole or in part with Federal funds from the NICHD, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN275201800005C.

ETHICS OF NBS PILOTS (RESEARCH ETHICS)

- **Common Rule changes**
- ***Section 12***: Defines bloodspots collected during Newborn Screening as human subjects



WHERE ARE WE? *DEFINITION OF HUMAN SUBJECT*

- Final rule ***DOES NOT*** define non-identifiable **biospecimens** as human subjects

Newborn Blood Spot

[Section 12 of the Newborn Screening Saves Lives Reauthorization Act of 2014 changed the ability of investigators to conduct certain federally funded research with newborn dried blood spots regardless of the identifiability of the blood spots. Are these requirements of the Act still in effect?](#)

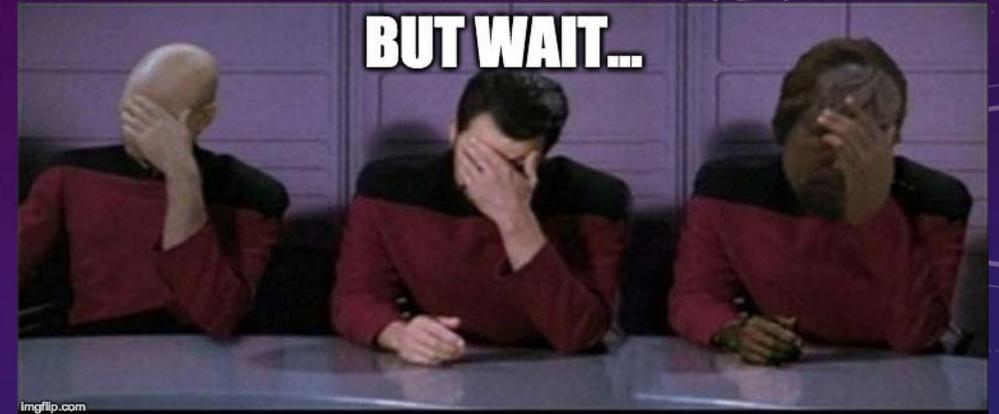
No. Research with nonidentified newborn dried blood spots, similar to other research with nonidentified biospecimens, is not considered research with human subjects under both the 2018 and pre-2018 Requirements, and thus, is not subject to 45 CFR part 46.

Although Section 12 of the Newborn Screening Saves Lives Reauthorization Act (NSSLRA) of 2014 stated that certain federally funded research on newborn dried blood spots would be considered human subjects research (regardless of the identifiability of the blood spots), and prohibited IRBs from waiving consent for such research, Section 12 applied only until changes to the Common Rule were promulgated. Thus, as of the effective date of the revised Common Rule (July 19, 2018), the requirements in Section 12 of the NSSLRA of 2014 are no longer in effect.



ETHICS OF NBS PILOTS

- **Informed Consent (parental permission)**
 - Research vs. QI/QA
 - Opt-in vs. opt-out
- **Return of results**
 - ACMG list of variants? Actionable?
 - Variants of unknown significance
 - Follow up? Availability of genetic counseling?
 - New IOM Report (Chair: Jeff Botkin)



- Recommendation 1: determine the conditions under which individual research results will be returned to participants
- Recommendation 4: ensure adequate resources and infrastructure to generate high-quality research results
- Recommendation 5: incorporate participant needs, preferences, and values in decision making about the return of individual research results
- Recommendation 7: ensure planning for the return of individual research results in applications for funding
- Recommendation 9: ensure transparency regarding return of individual research results in the consent process
- Recommendation 10: enable understanding of individual research results by research participants



THANK YOU!

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