Including ELSI research questions in newborn screening pilot studies

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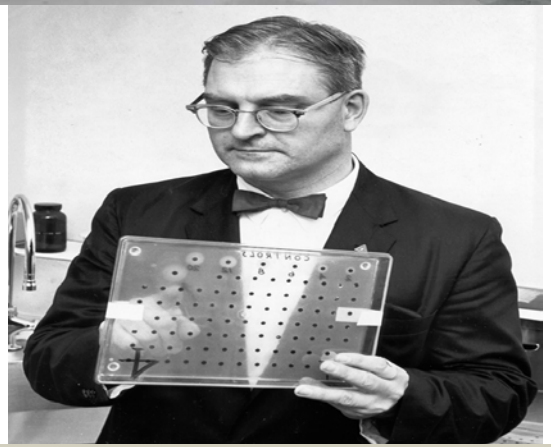
NBS in the 1960s



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ELSI as NBS for PKU began in early 1960s

- False negatives (move from hospital to state-legislated)
- Few/No concerns about parental consent
- Few/No concerns about “genetics”

ELSI after 1 million screened – in late 1960s

- Indeterminant values (who to treat)
- How to treat (what level of Phe ok)
- When to stop treatment
- False positives (few physical harms)
- “Iatrogenesis: The PKU Anxiety Syndrome”

(Rothenberg, J. Am Acad Child Psych., 1968)

Background

- Based on our experience with NBS over the last 50 years, we can anticipate certain ELSI
- Conditions being nominated to the RUSP in the last decade (and future?) are even more complex
  - Phenotypic and genotypic variation
  - Adult onset variants
  - Extremely low prevalence
  - Extremely high cost
  - New technology for screening (genomics)
  - Carrier considerations
  - Social media, public opinion

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
- N.B. specific ELSI questions will vary based on the condition being studied (e.g. x-linked condition)

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

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Results

- Two broad categories of ELSI issues
  - Related to results of screening
  - Related to initiation and implementation at the NBS systems level
- Brief description of 9 key ELSI questions
- List of data/approaches to addressing each of the 9 ELSI questions
- Sample questions/hypotheses

Results - Related ELSI

1. What are the potential ELSI of *positive screening results* related to a condition?
2. What are the potential ELSI of *false positive* screening results related to a new condition?
3. What are the potential ELSI of *false negative* screening results related to a new condition?
4. What are the potential ELSI of obtaining and reporting *carrier status* related to a new condition?
5. What are the potential ELSI of *indeterminate results* related to a condition?

ELSI Related to NBS System

6. What are the *resource allocation* implications for adding a new condition to the RUSP/state panel?
7. What are the *health disparities or equity considerations* related to adding a new condition?
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?
9. Does a condition raise any concerns regarding *parental permission* or challenges to the ethical or social justification for requiring population-based screening?

Key ELSI questions	Potential data sources	Sample ELSI research questions
Issues related to NBS results		
What are the potential ELSI of positive screening results related to a new condition?	•Families •Clinicians •Administrative databases	•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? •Are there potential harms from subsequent diagnostic testing (which may be invasive) and treatment and how do these harms impact the net benefits of screening? •What are the financial costs of diagnosis and follow-up? What is the system-wide cost?
What are the potential ELSI implications of false positive screening results related to a new condition?	•Families •Clinicians •Administrative databases	•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? •Are there potential harms from subsequent diagnostic testing? •What are the financial costs of diagnosis and follow-up? What is the system-wide cost?
What are the potential ELSI of false negative screening results related to a new condition?	•Families, clinicians	•What is the preventable morbidity and mortality related to false negative screening results? •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?)
What are the potential ELSI of obtaining and reporting carrier status related to a new condition?	•Families •Clinicians •Administrative databases	•How does knowledge of carrier status impact the newborn/families? What is the cost/ benefit to the newborn? To the family? Of disclosing carrier status? ◦Does knowledge of carrier status improve understanding the risk of developing diseases? ◦Does this knowledge lead to stigmatization, concerns about life expectancy, changes in lifestyle choices, or decisions about having more children? Does it affect other family members?

		◦What are the financial costs of follow-up? What is the system-wide cost?
What are the potential ELSI of indeterminate results related to a condition?	•Families •Clinicians •Administrative databases	•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? •Are there potential harms from subsequent diagnostic testing and follow-up? •What are the financial costs of diagnosis and follow-up? What is the system-wide cost?
What are the cost or resource allocation implications for adding a new condition to the RUSP or a state panel?	•State NBS programs •Public health departments, other state agencies •Clinicians, professional organizations, health care organizations, general public	•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 (including case follow-up)? •What are the opportunity costs, if any, of expanding to include the new condition? •Is there a sufficient number of clinicians trained to treat the condition? What is their geographic distribution? •What is the system-wide financial cost of diagnosis and treatment? •Are the prevalence and impact of the condition sufficient to justify the cost? Are there plans for long-term follow-up to judge impact of programs?
What are the health disparities or equity considerations related to adding a new condition to the RUSP or a state panel?	•NBS programs, families, NBS researchers, general public, health care organizations	•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)?

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?	•NBS programs, families, clinicians, general public, health care organizations	•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?
Does a condition raise any concerns regarding parental permission or challenges to the ethical or social justification for requiring population-based screening?	•NBS programs, families, clinicians, general public	•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)?

Conclusion

- Integrating ELSI questions into pilot studies for NBS (candidate) conditions
  - Help ACHDNC weigh the benefits and harms of candidate conditions
  - Help NBS programs to better understand the potential impact of screening for a new condition on newborns and families
  - Allow policy-makers to maximize benefits and mitigate potential negative outcomes

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