ETHICAL AND PUBLIC HEALTH CONCERNS ABOUT GENOMIC NEWBORN SCREENING

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Clinical Dream

Ethical Nightmare

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Ethical Dream
Project Goal: NBS in a Genomic Era

- HRSA funded R40 to identify and begin addressing the programmatic and policy challenges raised by the integration of NGGS technology into State NBS programs.

- Co-PI’s: Aaron Goldenberg and Beth Tarini

- 12 Focus Groups/Discussions with State NBS programs

- Working with the 7 HRSA Regional Genomics Collaboratives
The good

For Existing NBS Conditions

• Refining screening validity
• Identifying genomic variation
• Identifying modifiers
• Reduction of a diagnostic odyssey

For Adding New Conditions

• Better understanding of genotypic
• Ability to screen for a wider set of conditions for which typical assay screening is difficult
• Ability to screen for disease susceptibility genes
The Bad…Programmatic Concerns

• Storage and Management of Genomic Information
• Workforce needs
• Interpretation of Results
• Communication and Education
• Costs
The Ugly…ELSI

- Psychosocial harms associated with uncertain or ambiguous genomic data
  - Variable risk associations/Spectrum of Disease

- Parents rights to genomic information vs. “child's rights to an open future”
  - Adult Onset Conditions

- Moving us further from the core goals of NBS programs
  - Eroding the trust in the NBS program
A Spectrum of Sequencing in State NBS

- Sequencing Single Genes or Specific Genetic Variants
- Sequencing the Entire States Panel
- State Panel + known modifiers or more directed panels
- Whole Exome Sequencing
- Whole Genome Sequencing

Programmatic Complexity

ELSI Complexity
Avoiding the Mistakes of the Past

• “I think we should not repeat the mistakes of the past, because I remember when we expanded newborn screening with tandem mass spectrometry, everybody jumped the gun. So I think we need to be smart in the way that we should gather some information on those conditions, get an idea of when to start treatment, how to follow these patients before we start the [genomic] screening.”
Adjunct vs. Replacement Technology

• “I think using it as an adjunct technology would kind of ease us into it, so to speak, and you know and help us to gradually adopt it in small doses and build our knowledge and understanding and the capacity to deal with the information...As replacement technology, I feel it’s like really diving into the deep end and just feel very unprepared for that.”
Hurting the Original Intention of State NBS

• “clearly there we need to keep screening for things that have safe, effective treatment, that that’s what newborn screening is based on, and that’s finding out about all these other things that are untreatable or unknowable at this point. So I think that that clearly goes against the ethics of newborn screening.”
Potential Harms of WGS or WES

• “you really can’t put that burden on parents that we have a mandatory test with a bunch of things that we can’t figure out what’s happening with their kids ‘...I mean it’s hard enough making sure that kids are in nurturing families to suddenly throw on them that ‘We’ve mandatorily tested your child for x, y, z. We have no idea what this mean, but good luck with that,’ right...I don’t want to tell a family that ‘Your child has this late onset disorder. There’s nothing we can do for it, and shouldn’t show any symptoms ‘til maybe later on, some muscle weakness or whatever. Have fun. Good luck with your newborn...I’m not gonna do that to a parent.”
"I’m fine; I’m just waiting for my disease"

The new and growing class of presymptomatic patients

This issue of Neurology® contains a case report describing a young man with Pompe disease, a lysosomal/glycogen storage disorder caused by deficiency of the acid α-glucosidase enzyme (GAA). As a clinical case, it provides a prospective history of the early and asymptomatic years of a patient with late-onset Pompe disease. The patient described is also emblematic of a new trend that neurologists, medical geneticists, and other clinicians are facing in patient diagnosis—that is, the presymptomatic diagnosis of a serious and progressive disorder in an individual who is currently healthy and physically strong individual, before committing the patient and society to a treatment that costs about $350,000 a year for adults, requires specialized resources, has adverse effects, and will need to be provided indefinitely.

After 20 years of follow-up, quantitative muscle and strength testing have been normal, though he has reported “mild” decrease in quadriceps strength. Therefore, he and his physicians may soon be discussing initiation of ERT. Up to this point, he has enjoyed good health with no significant weakness or signs or symptoms of Pompe disease. Still, it has been
Utility of whole-genome sequencing for detection of newborn screening disorders in a population cohort of 1,696 neonates

Dale L. Bodian, PhD1, Elisabeth Klein, DNP, RNC1, Ramaswamy K. Iyer, PhD1,2, Wendy S.W. Wong, PhD1, Prachi Kothiyal, PhD1, Daniel Stauffer, PhD1, Kathi C. Huddleston, PhD, RN1, Amber D. Gaither, MD3, Irina Remsburg, MD3, Alina Khromyk, MD1, Robin L. Baker, MD4, George L. Maxwell, MD5-7, Joseph G. Vockley, PhD1,2, John E. Niederhuber, MD1,8 and Benjamin D. Solomon, MD1,3,9

Purpose: To assess the potential of whole-genome sequencing (WGS) to replicate and augment results from conventional blood-based newborn screening (NBS).

28 state-screened disorders and four hemoglobin traits were concordant for 88.6% of true positives (n = 35) and 98.9% of true negatives (n = 45,757). Of the five infants affected with a state-screened disorder, WGS identified two whereas NBS detected four. WGS yielded
Consent: The importance of Parental Choice

• 'They are scared of just even the word “DNA” being used, let alone sequencing a whole genome...There are many parents that don’t even know newborn screening happens, or they just remember, ‘Oh yeah, they took some blood, put it on a card.’ The public would have to be very, very educated that this was happening, and I think it would have to be a choice decision on the parents that they could have the normal newborn screening base, or they could have the sequencing.
Return of Results and Incidental Findings

• “We need to be very clear about like the definition of an actionable result...we would need some guidelines about ‘What are actionable results...So to understand that just because we can do the test, doesn’t mean we’re prepared to deal with the results, and maybe we shouldn’t, as Public Health systems.”

• “Ethically, I think most programs feel that they need to report what they find, and as a labratorian, you report what you find. To window something out means to me that you may be missing something that might be a very key piece of information for a family. And how do you live with that.”
The “Universal” Public Health Goals of NBS

• “I think the universality is really a baseline value that I think most Newborn Screening people share”

• “it’s one of the only places in life where there’s not healthcare [disparities]… that’s our mantra, right, is universal health? The only time in your life you really could get it [genomics], and so where can we fit in there to benefit our population?”
Universal Theme: Retirement!

- *Facilitator:* What are some of the other things that you think you would need as a State program to, you could start having these conversations or to implement some of these things?"  
  
*Participant:* “Early retirement options, like really early.”
Thank You!

• All our discussion/focus group participants!

• Amy Gaviglio, Roselle Ponsaran, Dalton Simancek

• HRSA Child and Maternal Health Bureau (R40MC268050102)