NEXT-GENERATION GENOMIC SCREENING IN NEWBORNS: *Key Questions And Important Distinctions*

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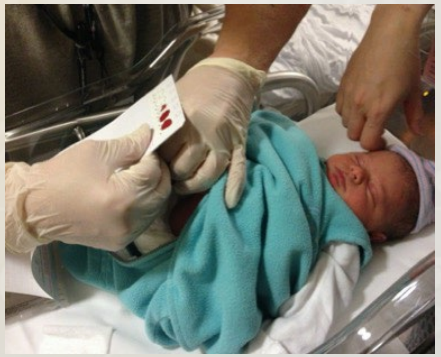
NASEM: Next-Generation Screening – The Promise and Perils of DNA Sequencing of Newborns at Birth: A Workshop

DISCLOSURES

I have nothing to disclose

Newborn Screening ⟷ **Sequencing Newborns**

- Genomic sequencing integrated into Public Health NBS:
  - Adjunct Technology
  - Replacement Technology
- Need to distinguish between *public health based NBS* and *other pathways* to sequencing in newborns:
  - Clinical (NICU, Peds)
  - Direct through Providers
  - Direct to Consumers
- Implications for consent, return of results, follow up



HOW DID WE GET HERE?

2010: NICHD/NHGRI symposium to develop a research agenda for the "application of new genomics concepts and technologies to newborn screening and child health"

2013: NIH funds four NSIGHT projects to explore "the implications, challenges and opportunities associated with the possible use of genomic sequence information in the newborn period."

2014: "Over the course of the next few decades, the availability of cheap, efficient DNA sequencing technology will lead to a medical landscape in which each baby's genome is sequenced, and that information is used to shape a lifetime of personalized strategies for disease prevention, detection and treatment." (Francis Collins, Wall Street Journal)

Today: Multiple programs using genome sequencing to screen healthy and sick newborns for a wide range of conditions (Research, Clinical, Commercial)

PROJECT	LOCATION
BabySeq2	US
Baby Beyond	Australia
BeginNGS	US/Greece
EarlyCheck	US
Genomics England	UK
GUARDIAN	US
NBSeq	US
NC Nexus	US
Screen4Care	Europe

* Table and timeline not exhaustive

SCOPE OF SCREENING

What newborns?

"Healthy"

ick Newborns

What results should we return (and when)?

Everything

Over Time

HEALTH

A deep dive into newborns' DNA can reveal potential disease risks — but is the testing worth it?

https://www.pbs.org/newshour/science/a-deep-dive-into-newborns-dna-may-reveal-potential-disease-risks-but-is-the-testing-worth-it

- What are the benefits and harms of these approaches?

UTILITY CONSIDERATIONS

When are findings useful?

Diagnostic Odyssey ⟷ **Therapeutic Odyssey**

- How can we acknowledge the continuum that parents experience?

What do we mean by actionability?

Clinical Utility ⟷ **Personal Utility**

- How can acknowledge the spectrum of potential uses of genomic information?
  - Pharmaceutical/Surgical
  - Other Services: ex. Physical/Occupational Therapy
  - Educational/Behavioral Interventions

UNCERTAINTY CONSIDERATIONS

What do findings tell us?

Pathogenic Likely Pathogenic **VUS** Likely Benign **Benign**

- How is uncertainty impacted conducting WGS in "healthy" vs. symptomatic children?
- Are we creating to many "patients in waiting"?

What is the impact of uncertainty?

Diagnostic Uncertainty **Prognostic Uncertainty**

- How to assess the harms/benefits of uncertainty?
- What kinds of support do families need?

EQUITY CONSIDERATIONS

Availabilit

Accessibility

Accessibili

Equity

AJOB EMPIRICAL BIOETHICS
https://doi.org/10.1080/23294515.2023.2209747

"I Have Fought for so Many Things": Disadvantaged families' Efforts to Obtain Community-Based Services for Their Child after Genomic Sequencing

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ABSTRACT

Background: Families whose child has unexplained intellectual or developmental differences often hope that a genetic diagnosis will lower barriers to community-based therapeutic and support services. However, there is little known about efforts to mobilize genetic information outside the clinic or how socioeconomic disadvantage shapes and constrains outcomes.

Methods: We conducted an ethnographic study with predominantly socioeconomically disadvantaged families enrolled in a multi-year genomics research study, including clinic observations and in-depth interviews in English and Spanish at multiple time points. Coding and thematic development were used to collaboratively interpret fieldnotes and transcripts.

Results: Thirty-two families participated. Themes included familial expectations that a genetic diagnosis could be translated into information, understanding, and assistance to improve the quality of a child's day-to-day life. After sequencing, however, genetic information was not readily converted into improved access to services beyond the clinic, with families often struggling to use a genetic diagnosis to advocate for their child.

Conclusion: Families' ability to use a genetic diagnosis as an effective advocacy tool beyond the clinic was limited by the knowledge and resources available to them, and by the eligibility criteria used by therapeutic service providers' – which focused on clinical diagnosis and functional criteria more than etiologic information. All families undertaking genomic testing, particularly those who are disadvantaged, need additional support to understand the limits and potential benefits of genetic information beyond the clinic.

KEYWORDS

Genomics; ELSI; ethnography; pediatric; developmental conditions; utility; therapeutic odyssey

LEGAL/POLICY CONSIDERATIONS

- Evolving Genetic Privacy Concerns
- Storage and Use of Samples and Data
- Trust, Trustworthiness, and Accountability
- Changes in Human Subjects Protections

https://www.aclu.org/news/privacy-technology/widespread-newborn-dna-sequencing-will-worsen-risks-to-genetic-privacy

Need for Ethical Stewardship

OTHER CONSIDERATIONS FOR TODAY

- ***Promote*** regulatory structures and health systems that support the equitable translation of research to practice
- ***Build*** robust educational/engagement strategies to hear from parents
- ***Avoid*** "giving in" to an inequitable health care system or assume that all families will "eventually" have access *("trickle-down equity")*
- ***Establish*** a culture where equity and ethics are foundational and fully integrated into research, translational, and care pathways
- ***Challenge*** our own assumptions….

THANK YOU!

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