The Future of NBS

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NEWBORN SCREENING

Disclaimers:

I do not have a crystal ball.
We are not funded/supported by industry partners.

These personal opinions are motivated by participation in national committees and workgroups.

These thoughts are motivated by the struggles, sufferings and hardships of families and patients with rare diseases.

Rare Disorders and Newborn Screening:

> 6,000 disorders

80% with genetic cause

50% affects children

> 2,400 NBS disorders

Current process is not agile enough to expand screening panels by even 10-20 disorders at once.

Ideas and Solutions to bridge gaps

Solutions from within the system

Outside solutions

The current disorder inclusion/nomination/selection process:

Incomplete and does not allow input from the entire rare disease community

- Lack of broad ideation and selection “funnels”
- Biased process shaped by special interest groups: e.g. large foundation or for-profit companies
- Often excludes payors in the decision process
- Process shaped by inefficient boundaries that prohibit efficiencies
- Strange and scientifically unsound current selection criteria

Solutions: The current disorder inclusion/nomination/selection process:

- Broad, transparent ideation and prioritization matrix (NBSTRN3.0) with timelines and regular and standardized review
- Elimination of current nomination process
- Methods of payor inclusion, real-time cost benefit assessments; Payors-driven process?
- Continuous assessments of NBS program costs

Lack of technology development and scalable technology solutions:

- Status quo dictated by few solution providers with FDA cleared methods and solutions
- Existing scalable technologies are not developed rapidly enough; e.g. LC-MSMS solutions; WGS based methods
- Technology development does not happen in NBS programs

Solutions: Public private partnerships or targeted grant programs with clear objectives

- Specific methodology development initiatives with specified outcomes: analytical targets (xx analytes) with specific performance outcomes
- Clear mandates and objectives regarding data curation

Conflict between “Screening” and “diagnostic” or “clinically actionable” results

Increasing number of disorders = increasing second tier/diagnostic requirements

→high probability that public health programs are not optimally positioned

→ Secondary cost explosions

Solutions: Public private partnerships or regionalization of resources operating under diagnostic umbrella

- Community models: e.g. COOPs
- Economic partnerships between industry partners and states

NBS and health inequities

When we expand disorders we have to be keenly aware of introducing inequities (and secondary liabilities)

Fast-tracking of disorders with very effective treatment modalities and how to deal with disorders without treatments?

Solutions: Encourage radical innovation and national coordination Efforts

Shift to:
Focus on real-time fractional Benefits-Costs analyses affecting patients with rare diseases and the public at large

Bespoke Initiative: NIH 10/27/2021

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NEWS RELEASES

Wednesday, October 27, 2021

NIH, FDA and 15 private organizations join forces to increase effective gene therapies for rare diseases

The National Institutes of Health, U.S. Food and Drug Administration, 10 pharmaceutical companies and five non-profit organizations have partnered to accelerate development of gene therapies for the 30 million Americans who suffer from a rare disease. While there are approximately 7,000 rare diseases, only two heritable diseases currently have FDA-approved gene therapies. The newly launched Bespoke Gene Therapy Consortium (BGTC), part of the NIH Accelerating Medicines Partnership (AMP) program and project-managed by the Foundation for the National Institutes of Health (FNIH), aims to optimize and streamline the gene therapy development process to help fill the unmet medical needs of people with rare diseases.

"Most rare diseases are caused by a defect in a single gene that could potentially be targeted with a customized or 'bespoke' therapy that corrects or replaces the defective gene," said NIH Director Francis S. Collins, M.D., Ph.D. "There are now significant opportunities to improve the complex development process for gene therapies that would accelerate scientific

Institute/Center

NIH Office of the Director (OD)

National Center for Advancing Translational Sciences (NCATS)

Contact

NIH News Media Branch
301-496-5787

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Complementation of Current Modes of Screening Operations

Parallel Development of complementary screening systems

Focus on Populations with high diagnostic yield

Investigate for Potential Benefits for NBS

Final Report

Period Covering July 1, 2018 – June 1, 2020

What is NICU Whole Genome Sequencing?

- The cause of sickness is often unknown in critically ill neonates in the Neonatal Intensive Care Unit (NICU)
- Identifying the correct diagnosis may take weeks or months- *"The Diagnostic Odyssey"*
- Determining the entire genome sequence of the baby AND the parents ("Trio") has been shown to speed diagnosis and determine optimal therapies
- This technology has rapidly moved from a research to a new standard of care

From Esoteric Research to Diagnostic Care Standard

week of hospitalization, or had just developed an abnormal response to therapy. The whole cohort received RPM. There were two prespecified primary outcomes-changes in medical care reported by physicians and changes in the cost of care. The majority of infants were from underserved populations. Of 184 infants enrolled, 74 (40%) received a diagnosis by rWGS that explained their admission in a median time of 3 days. In 58 (32%) affected individuals, rWGS led to changes in medical care. Testing and precision medicine cost $1.7 million and led to $2.2-2.9 million cost savings. rWGS-based RPM had clinical utility and reduced net health care expenditures for infants in regional ICUs. rWGS should be considered early in ICU admission when the underlying etiology is unclear.

JAMA Pediatrics | Original Investigation

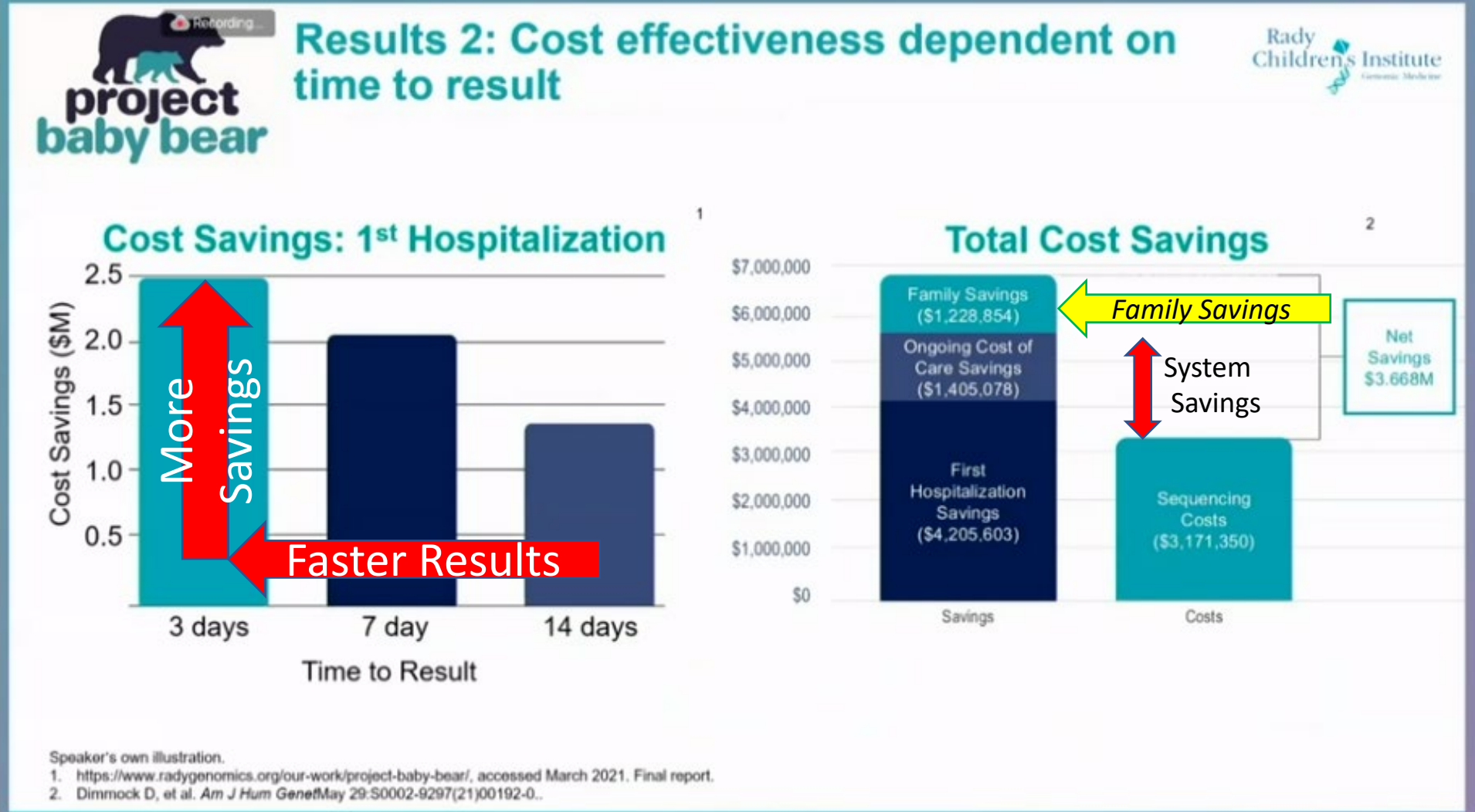
Psychosocial Effect of Newborn Genomic Sequencing on Families in the BabySeq Project

A Randomized Clinical Trial

Stacey Pereira, PhD; Hadley Stevens Smith, PhD, MPSA; Leslie A. Frankel, PhD; Kurt D. Christensen, PhD; Rubaiya Islam, BA; Jill Oliver Robinson, MA; Casie A. Genetti, MS; Carrie L. Blout Zawatsky, MS; Bethany Zettler, MS; Richard B. Parad, MD, MPH; Susan E. Waisbren, PhD; Alan H. Beggs, PhD; Robert C. Green, MD, MPH; Ingrid A. Holm, MD, MPH; Amy L. McGuire, JD, PhD; for the BabySeq Project Team

andomized clinical trial of nGS, there was no persistent negative psychosocial effect on families among those who received nGS nor among those who received a monogenic disease risk finding for their infant.

Gene-Targeted Therapies: Early Diagnosis and Equitable Delivery (Day 2)



Project Baby Bear Key Outcomes & Relevance

- 178 babies in less than 2 years
- 43% received a diagnosis
  - 35 cases were rare
  - Incidence less than 1 in a million
- 31% changed management

- *Small number of cases*
- *57% may yet be diagnosed*
  - *rWGS data can be re-analyzed as future genotypic diagnoses are discovered*
- *Fewer* procedures and tests

MDHHS
Michigan Department of Health & Human Services

Medical Services Administration
BULLETIN
MSA

Bulletin Number: MSA 21-33

Distribution: Hospitals, Laboratories, Medicaid Health Plans

Issued: August 17, 2021

Subject: Coverage of Rapid Whole Genome Sequencing (rWGS) Testing

Effective: As Indicated

Programs Affected: Medicaid, Healthy Michigan Plan, MIChild, Children's Special Health Care Services (CSHCS)

Note: Implementation of this policy is contingent upon approval of a State Plan Amendment (SPA) by the Centers for Medicare & Medicaid Services (CMS).

Commercial Payors Recognize the Need for rWGS

- Blue Shield CA policy effective July 1, 2019

> "…rapid whole genome sequencing… considered medically necessary for the evaluation of critically ill infants or children less than 18 years of age in neonatal or pediatric intensive care with illness of unknown etiology"

- BCBSA has adopted a similar policy recommendation to its Plans and 10 have currently adopted

Policy link:
https://www.blueshieldca.com/bsca/bsc/public/common/PortalComponents/provider/StreamDocumentServlet?fileName=PRV_WholeExome_Sequen.pdf

Closing the Loop: Building technology for NBS

Diagnostic NICU sequencing is fast, could complement NBS
2nd tier testing workflows
NICU babies: Symptomatic populations with high diagnostic yield
Benefits for rare disease community: stepwise bridging the gap, coverage for early onset disorders
Expandable to other areas: developmental delays patients

NICU Sequencing and Impact for NBS

Technology that can augment NBS

- From the Perspective of rare disease community
- From Perspective of Technology development

Thank you

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