Sequencing Newborns

A Case for Nuanced Use of Genomic Technologies

Josephine Johnston, LLB, MBHL
Director of Research and Research Scholar

THE HASTINGS CENTER

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BIOETHICS FORUM

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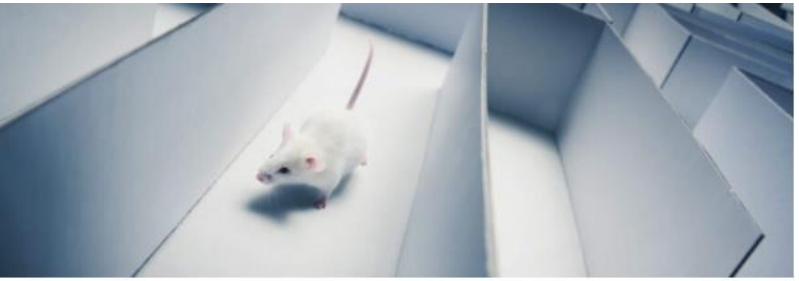

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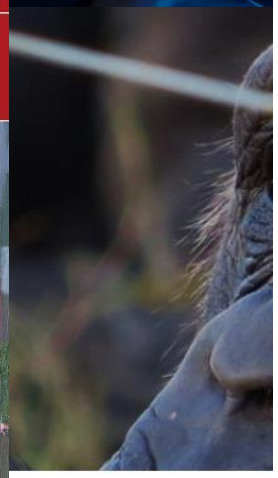

BIOETHICS FORUM ESSAY

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New Challenges

Vaccine Access, Vaccine Hesitancy: Challenges to Herd Immunity

If the United States is to achieve herd immunity, at least 75-85% of the population will need to be vaccinated, yet there are many different kinds of barriers to overcome. Some Americans are reluctant or wish to wait, because they distrust government or the safety of the vaccines or believe in widespread conspiracy theories. Views about the vaccine also differ based on religion and political party affiliation. Research shows that in communities of color and rural areas, lack of sound vaccine information and places to receive a vaccine are drivers of inequitable distribution. What are the extent and limitations of our ethical obligations to promote broad-based vaccine acceptance and to ensure access to all Americans? And what communication approaches and health policies are likely to be most effective?

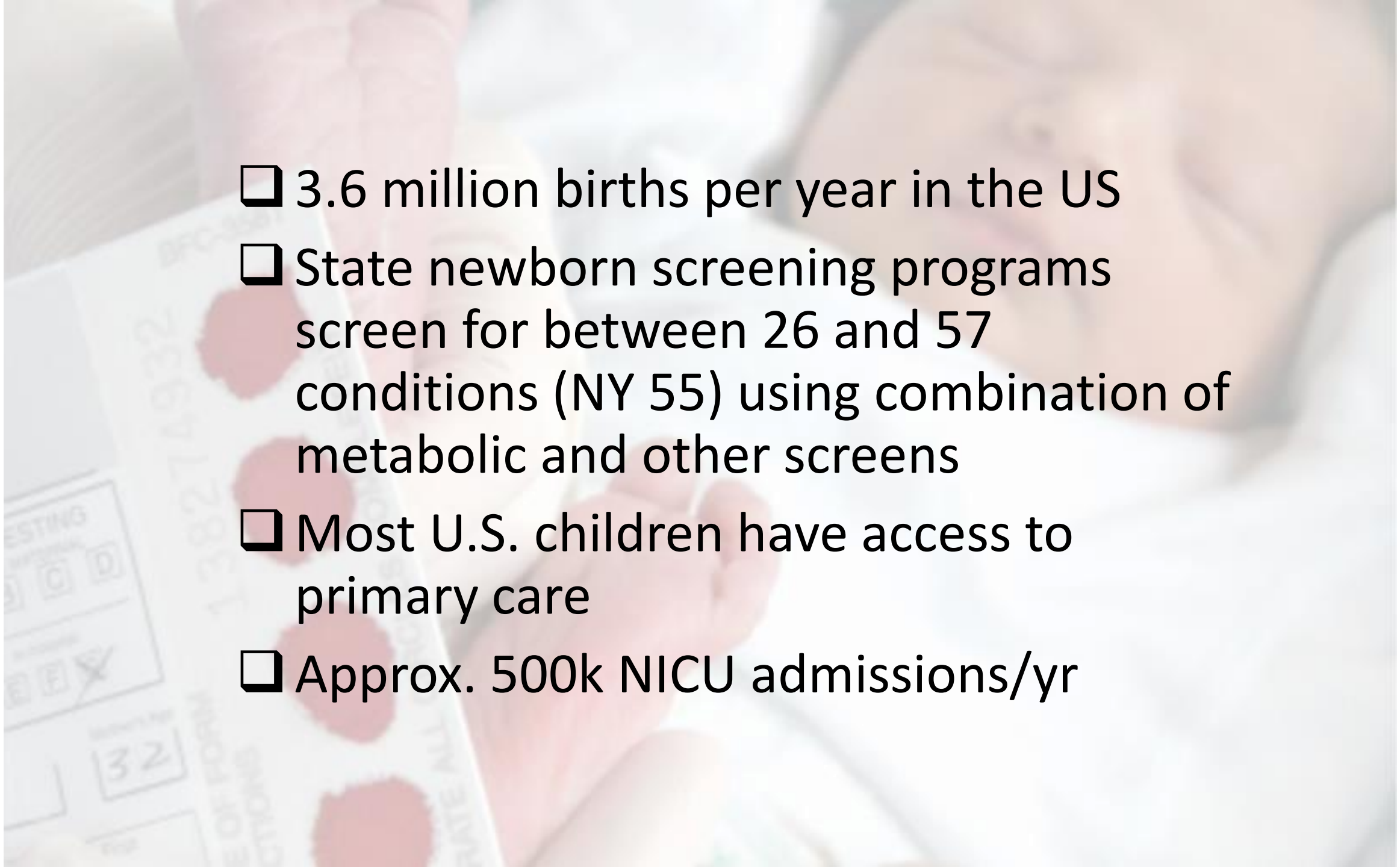
Dr. Rhea Boyd, Maya Goldenberg, and Hastings Center president Mildred Z. Solomon tackled these questions during a virtual forum on April 20, 2021

Sequencing of Newborn Blood Spot DNA to Improve and Expand Newborn Screening

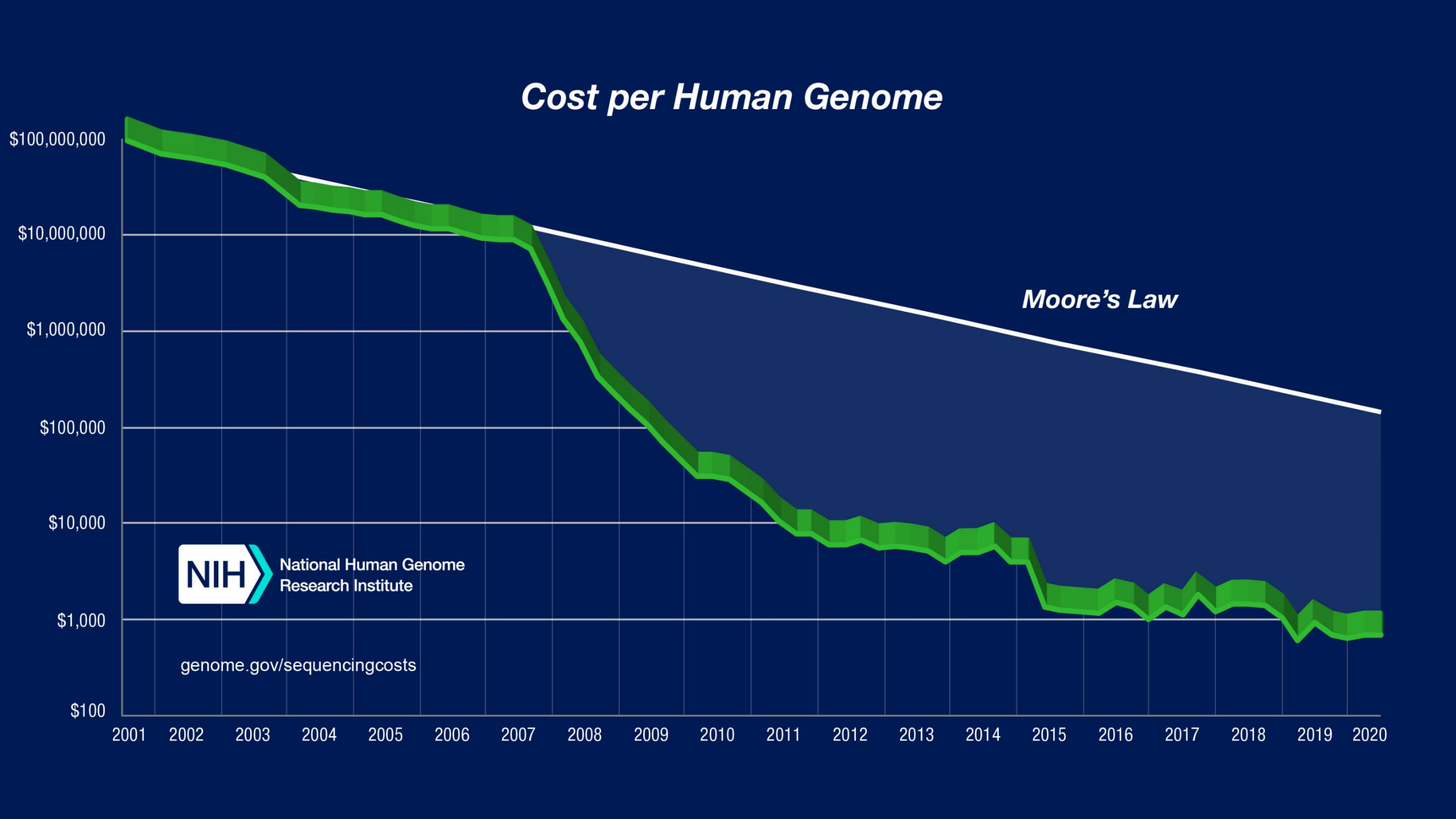
Hastings Investigators: Erik Parens and Josephine Johnston

NSIGHT Project Principal Investigator: Barbara Koenig, University of California, San Francisco

Funder: Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Human Genome Research Institute



- 3.6 million births per year in the US
- State newborn screening programs screen for between 26 and 57 conditions (NY 55) using combination of metabolic and other screens
- Most U.S. children have access to primary care
- Approx. 500k NICU admissions/yr


Cost per Human Genome
$100,000,000
$10,000,000
$1,000,000
$100,000
$10,000
$1,000
$100
Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
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I am almost certain…that whole-genome sequencing will become part of new-born screening in the next few years…It is likely that within a few decades people will look back on our current circumstances with a sense of disbelief that we screened for so few conditions.

-Francis Collins, *The Language of Life: DNA and the Revolution in Personalized Medicine* (Profile Books, 2010, p. 50)

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, M.D., Ph.D, Director, National Institutes of Health, Wall Street Journal July 7, 2014

I tested my son as soon as he was born and I tested my daughter's amniotic fluid [while she was in the womb] … Genetic testing is a responsibility if you are having children.

--Anne Wojcicki, 23andMe, *The Observer* (2016)

Parents are interested in newborn genomic testing during the early postpartum period

Susan E. Waisbren, PhD[1–3], Danielle K. Bäck, BS[3,4], Christina Liu, BS[4], Sarah S. Kalia, ScM, CGC[4], Steven A. Ringer, MD, PhD[3,5], Ingrid A. Holm, MD, MPH[1,3,6] and Robert C. Green, MD, MPH[3,4,7]

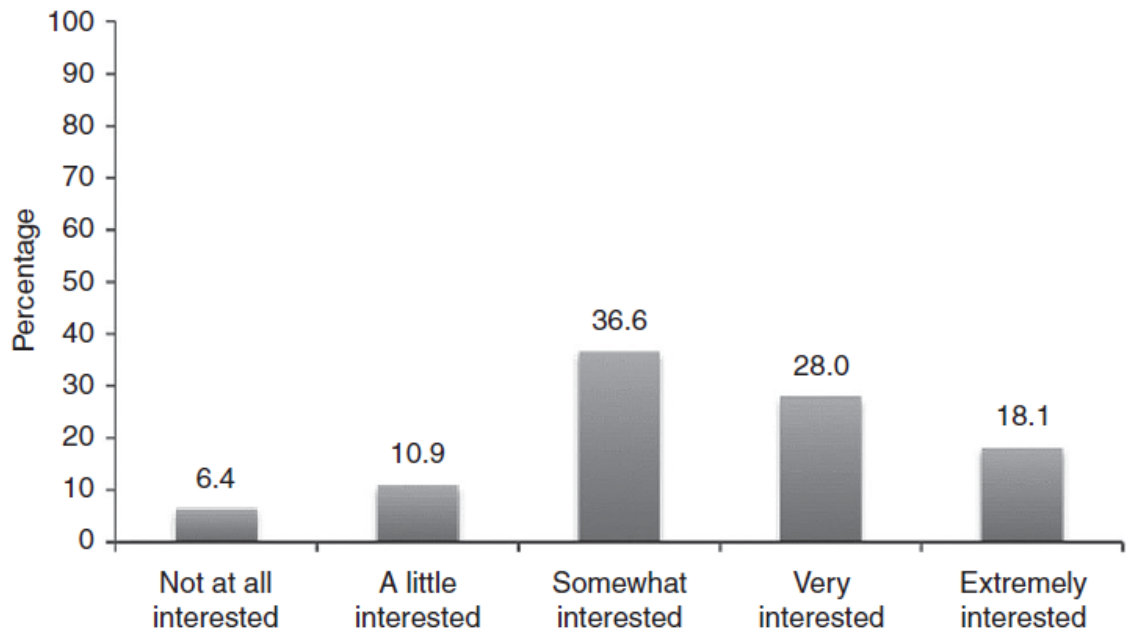


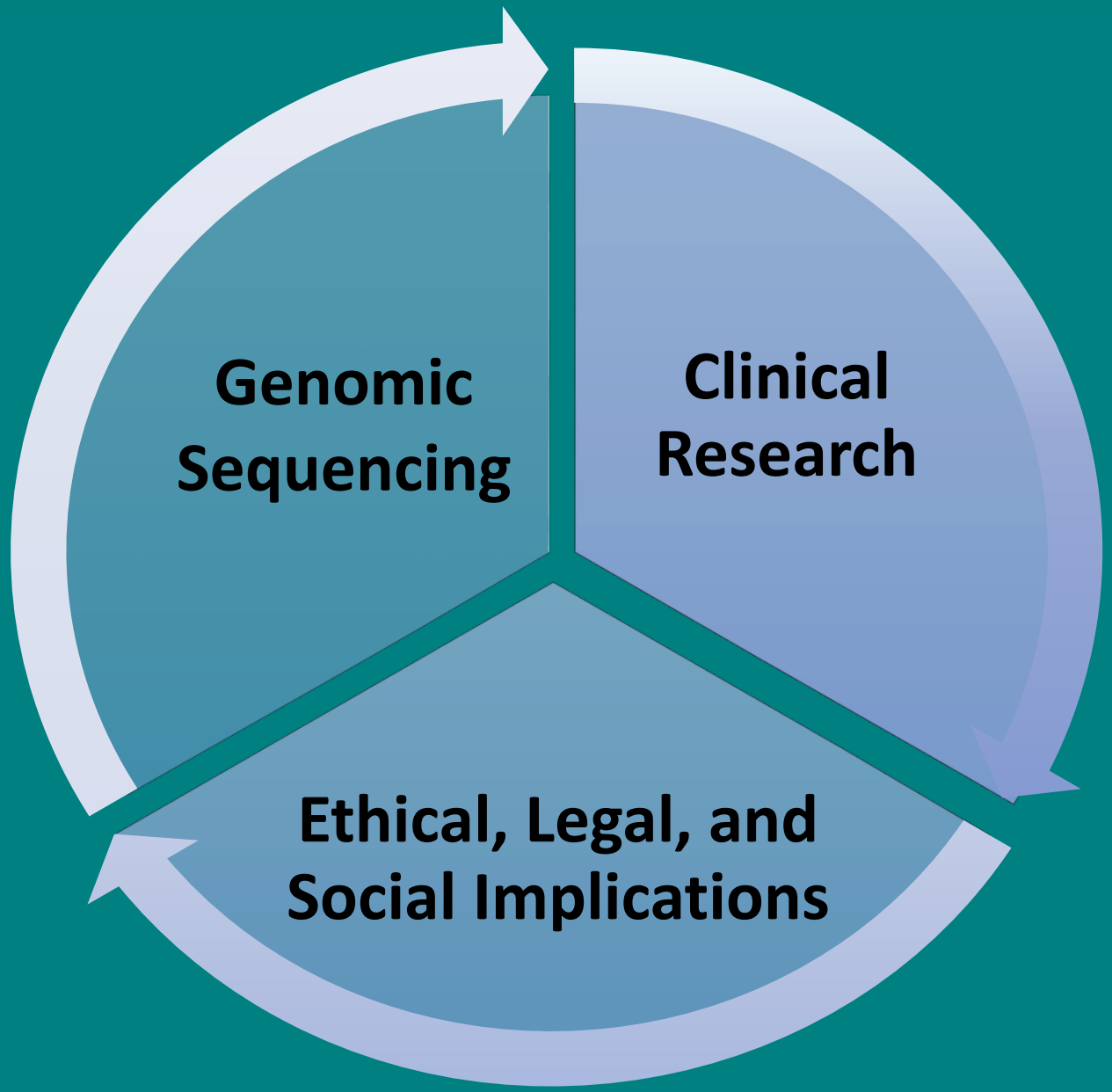
Figure 1 Parental interest, immediately after birth, in hypothetical newborn genomic testing for their newborns as part of a research study.

2010 NIH Workshop

- New, sophisticated and increasingly cost-effective techniques for DNA-based sequencing and analysis may make it possible to expand newborn screening in the future and substantially expand its clinical and public health value.
- To identify elements of a trans-NIH research agenda that could inform the possible application of new genomic concepts and technologies to newborn screening and child health.

www.genome.gov/pages/policyethics/staffarticles/newborn_screening_meeting_summary.pdf

Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) Program



NSIGHT Projects

Principal Investigators	Institutions	Title
Robert Green Alan Beggs	Brigham and Women's Hospital Boston Children's Hospital	BabySeq: Genome Sequence-Based Screening for Childhood Risk and Newborn Illness
Stephen Kingsmore	Rady Children's Hospital, San Diego Children's Mercy Hospital, Kansas City	Clinical and Social Implications of 2-day Genome Results in Acutely Ill Newborns
Jennifer Puck Barbara Koenig Pui-Yan Kwok	University of California San Francisco	NBSeq: Sequencing of Newborn Blood Spot DNA to Improve and Expand Newborn Screening
Cynthia Powell Jonathan Berg	University of North Carolina at Chapel Hill	NC NEXUS: North Carolina Newborn Exome Sequencing for Universal Screening

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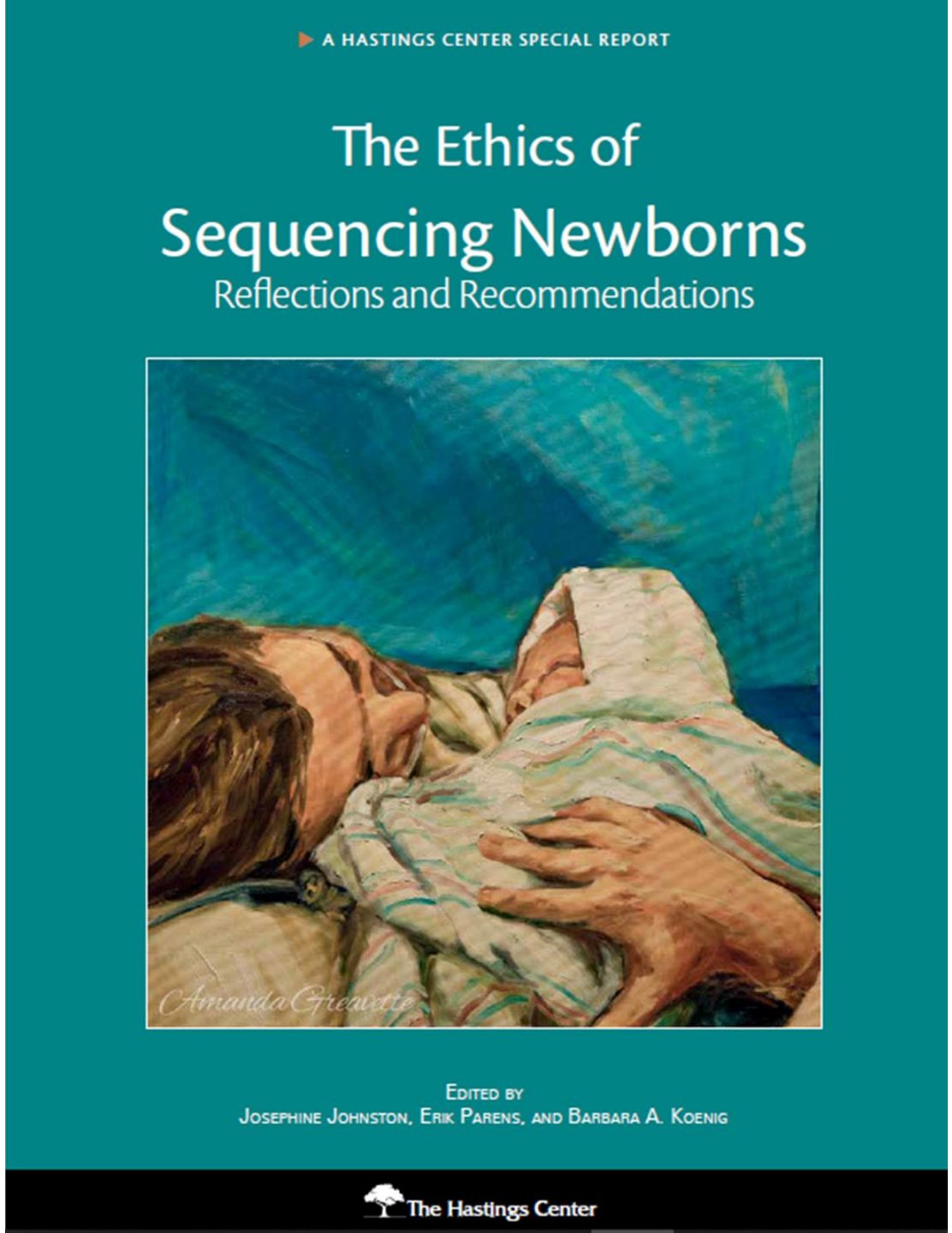
Cynthia M. Powell
Jennifer M. Puck
Scott Roberts
Monica E. Smith
Stefan Timmermans
Rachel L. Zacharias

Plus, invited guests

Guiding Questions

- Which contextual forces shape our discussion of the utility of sequencing in newborns?
- Under what circumstances should newborns be sequenced?
- How should state-mandated newborn screening programs use sequencing?
- What role should parents play in determining how sequencing information about their infant is used and stored?
- Should sequencing be part of routine pediatric practice?



Lead article by:
Josephine Johnston
John D. Lantos
Aaron Goldenberg
Flavia Chen
Erik Parens
Barbara A. Koenig &
members of the
NSIGHT Ethics and
Policy Advisory Board

Plus: 12 essays by
members of the
NSIGHT Ethics and
Policy Advisory Board

Project’s Findings

Analysis

2 Reasons

- ❑ Diagnosis
- ❑ Screening

2 Types of Sequencing

- ❑ Targeted
- ❑ Whole-exome or whole-genome

Analysis

3 Contexts

- ❑ Clinical Contexts
  - Sick newborns, e.g. in NICU
  - Routine primary care
- ❑ Public Health
  - In the US, state newborn screening programs
- ❑ Direct-to-Consumer
  - E.g. BabyGenes, 23andMe

Analysis

Ethical, legal and social implications—for whom?

- ❑Newborns
- ❑Families
- ❑Clinicians
- ❑Researchers
- ❑State newborn screening programs
- ❑Genetics/DTC companies
- ❑Society

Varies by context

Structure of Ethical Analysis

Just Distribution of Benefits

- ❑Time to diagnosis
- ❑Improved care
- ❑Benefits to family

Protection from Harms

- ❑Unnecessary follow-up and expense
- ❑Uncertainty
- ❑Self-determination

Varies by context

Special Considerations: Public Health

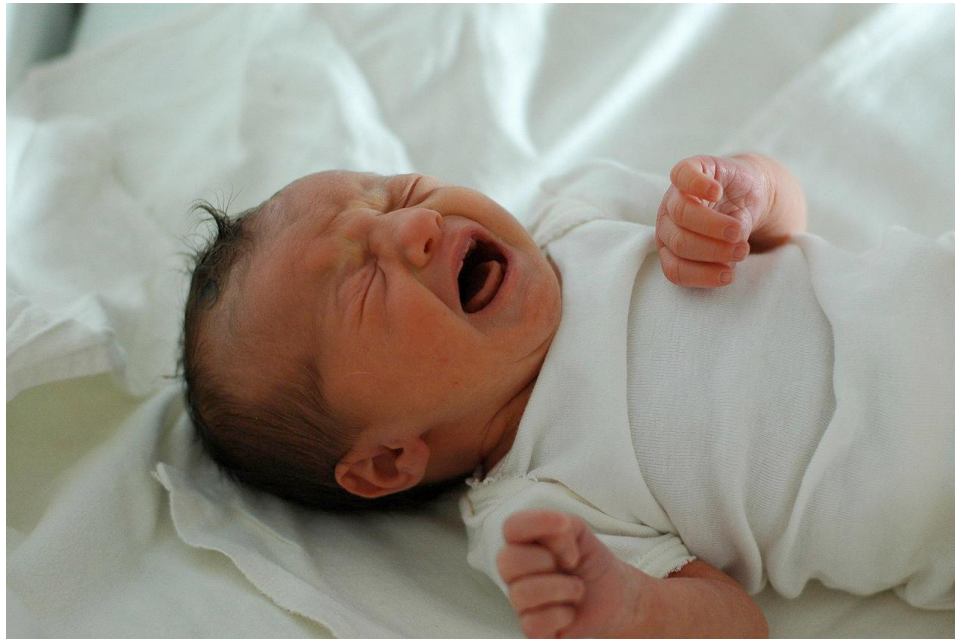
State newborn screening programs

- ❑ Goal: Testing and follow-up care available to all
  - Refusal not in infant's best interests
  - Precious public health $ (see COVID)
- ❑ Existing screening criteria are strong:
  - Evidence for benefit of early identification
  - States are able to screen for this important health problem
  - Effective treatments are available

Recommendations

Clinical Contexts

- ❑ Use targeted or whole-genome sequencing for diagnosis
  - With parental permission, genetic counseling, follow-up care
  - Return results that may benefit infant and/or family members
- ❑ Not ready to use for screening
  - Limited usefulness in asymptomatic infants
  - Concerns over storage of results
  - Concerns over discrimination or insurance uses
  - Results could create unnecessary distress
  - Results could generate unneeded follow-up care and monitoring
  - Children may wish for self-determination regarding certain results



Recommendations

Public Health Context

- ❑ Do not use targeted or whole-genome sequencing as sole screen
  - Cannot replace existing screening tools
  - Concerns over storage of results
  - Concerns over discrimination or insurance uses
  - Potential for results to generate unnecessary distress
  - Potential for results to require counseling and generate unneeded follow-up care and monitoring
- ❑ OK to use targeted sequencing
  - As a secondary test following a positive screen
  - As a primary screen to detect conditions that meet all screening criteria

Recommendations

Direct-to-Consumer

- ❑Parents should not use DTC sequencing for diagnosis or screening

- ❑Health care professionals should recommend against DTC sequencing in infants and children

Editorial

THE LANCET

www.thelancet.com Vol 392 September 8, 2018

Are we ready for universal genomic sequencing for newborns?

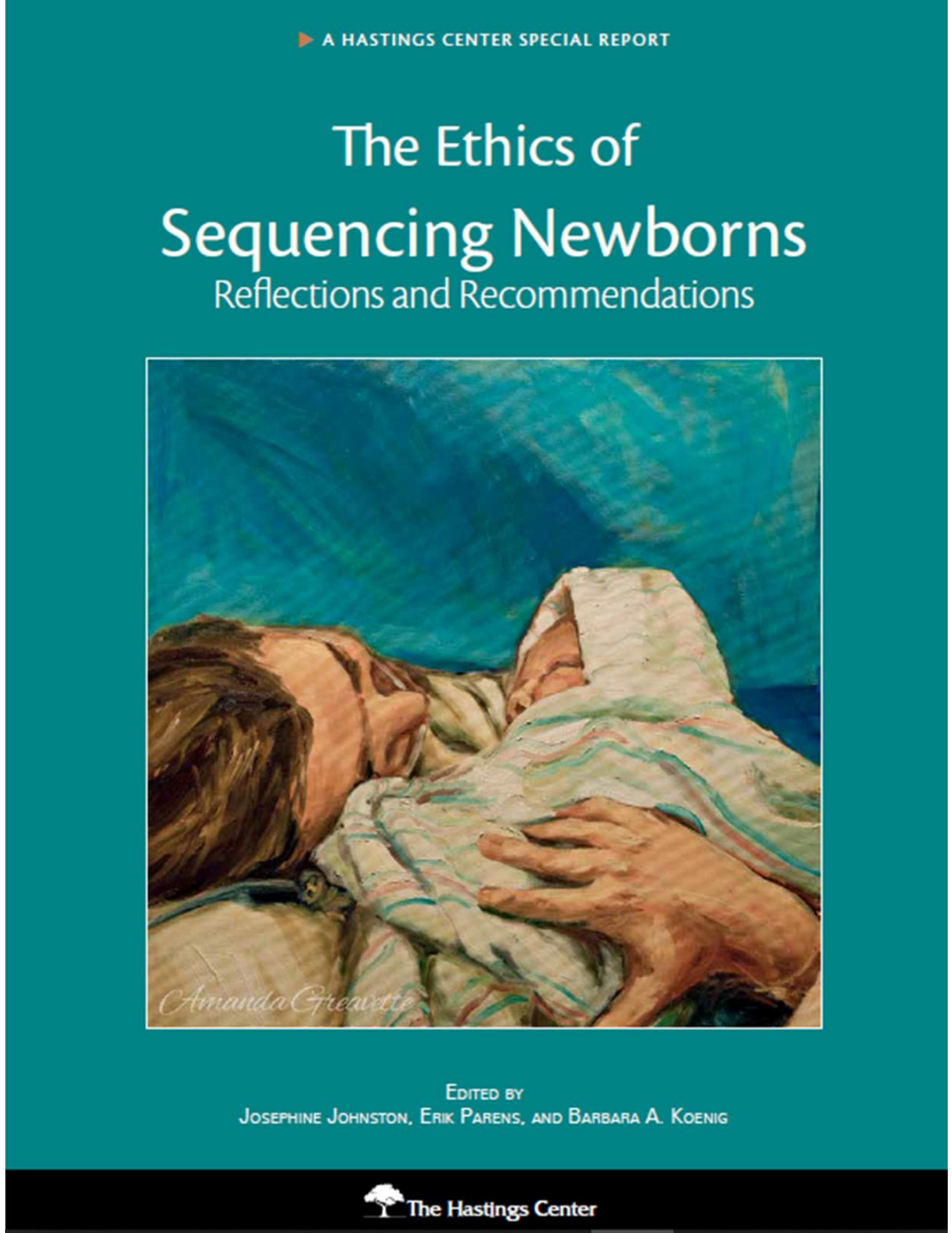
Jessica Bordeau/BSIP/Science Photo Library

"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", said Francis Collins—the current director of the US National Institutes of Health (NIH) in 2014. However, after a 4-year research process funded by NIH, such optimism is not shared in the latest report—*Sequencing Newborns: A Call for Nuanced Use of Genomic Technologies*—released by The Hastings Center, a US-based, non-partisan, bioethics think tank, last month.

The report proposes a nuanced approach to genome sequencing, which means different recommendations for the use of two kinds of genome sequencing (targeted and genome-wide sequencing) in newborns for two purposes (diagnosis and screening) and across three contexts: clinical practice, public health, and direct-to-consumer service. For example, targeted sequencing of a specific genomic region, whole exome, and genome sequencing can be used to assist in the diagnosis of symptomatic newborns, but whole-exome and genome sequencing should be used neither as screening tools for newborns, nor integrated into routine primary or paediatric care. Health-care professionals should recommend against direct-to-consumer sequencing of newborns. Indeed, the recommendations are largely aligned with the opinions of other bioethics groups from Europe and the UK, because current knowledge does not justify universal neonatal screening by genomic sequencing.

There are important unresolved scientific and ethical concerns for the use of genomic technologies. Given the great potential to improve health care, particularly in personalised medicine, and its soon to be increasingly expanded use in both medical and non-medical contexts, it is crucial to develop more robust research globally to further understand scientific complexities and uncertainties in sequencing. As the report concludes—"research continues to determine the best applications of sequencing technology in newborns". ■ *The Lancet*

For **The Hastings Center Report** see https://onlinelibrary.wiley.com/doi/epdf/10.1002/hast.874



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THANK YOU

I look forward to your questions