Update on the NSIGHT program

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NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Update on the NSIGHT Program

- NSIGHT Program Background
- Protocols at 4 sites
- Findings to date
- Upcoming workshop

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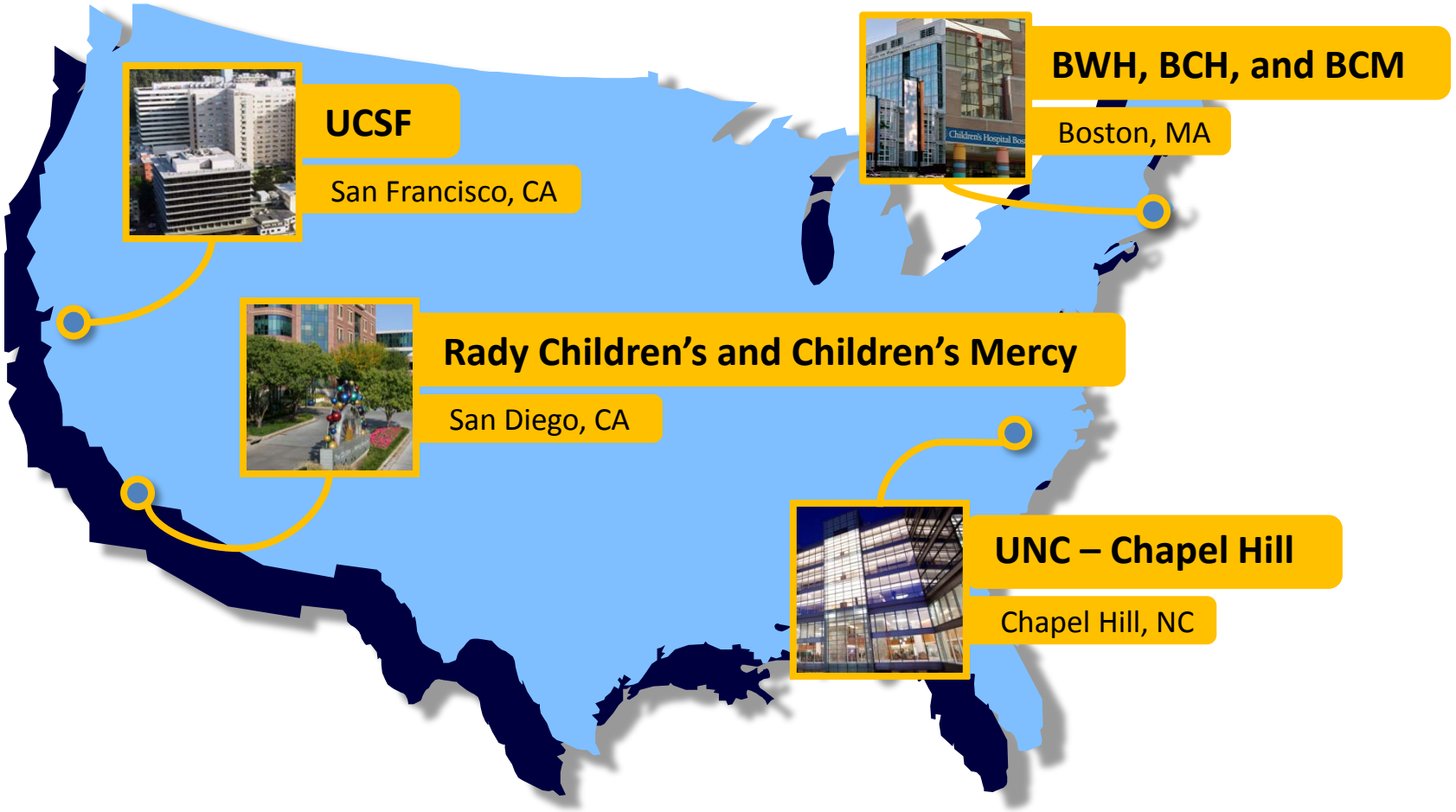
Newborn Sequencing In Genomic medicine and public HealTh (NSIGHT)



Newborn Sequencing Questions

For disorders currently screened for in newborns, how can genomic sequencing **replicate or augment** known newborn screening results?

What knowledge about **conditions not currently screened** for in newborns could genomic sequencing of newborns provide?

What additional clinical information could be learned from genomic sequencing relevant to the **clinical care of newborns**?

NSIGHT Sequencing Settings

Diagnostic

Preventive

Predictive

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Marker Paper

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Newborn Sequencing in Genomic Medicine and Public Health

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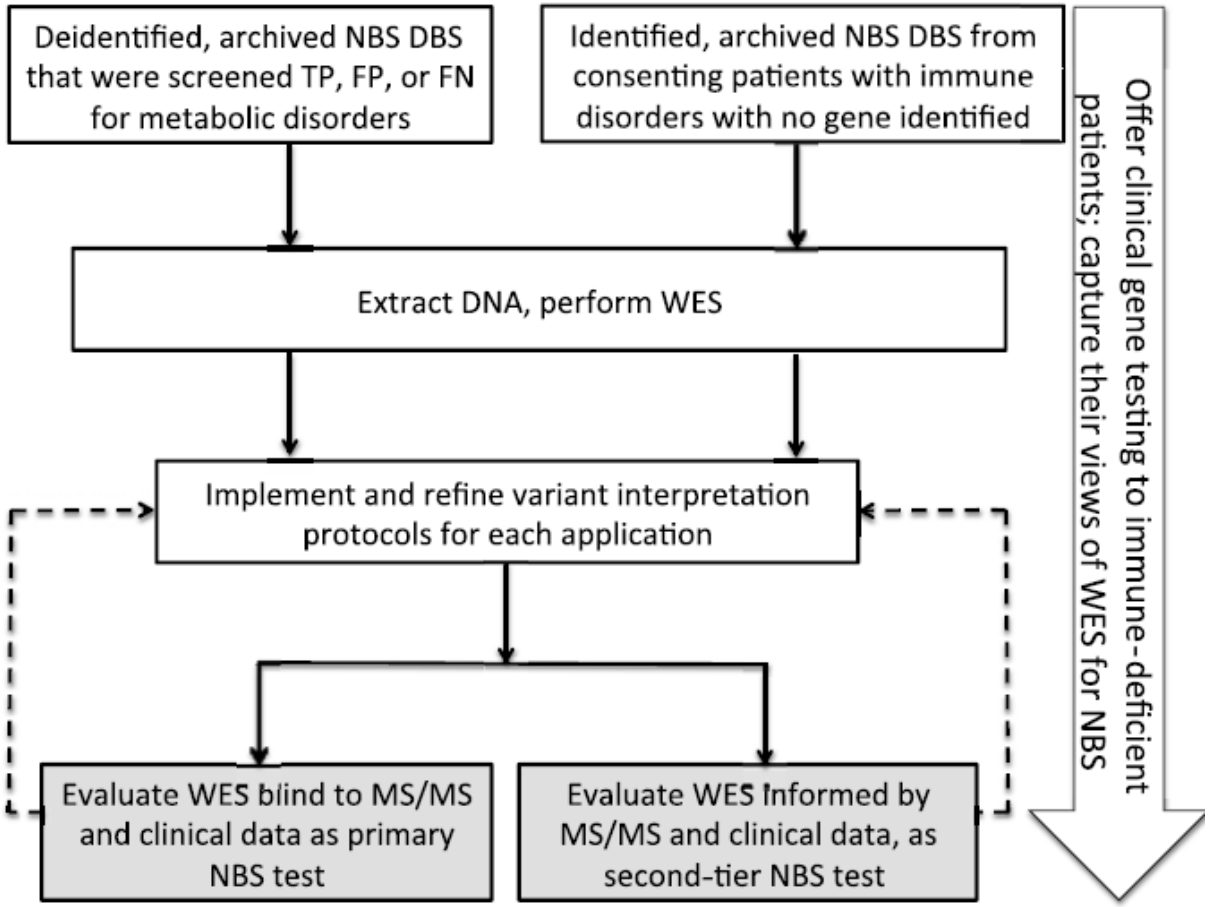
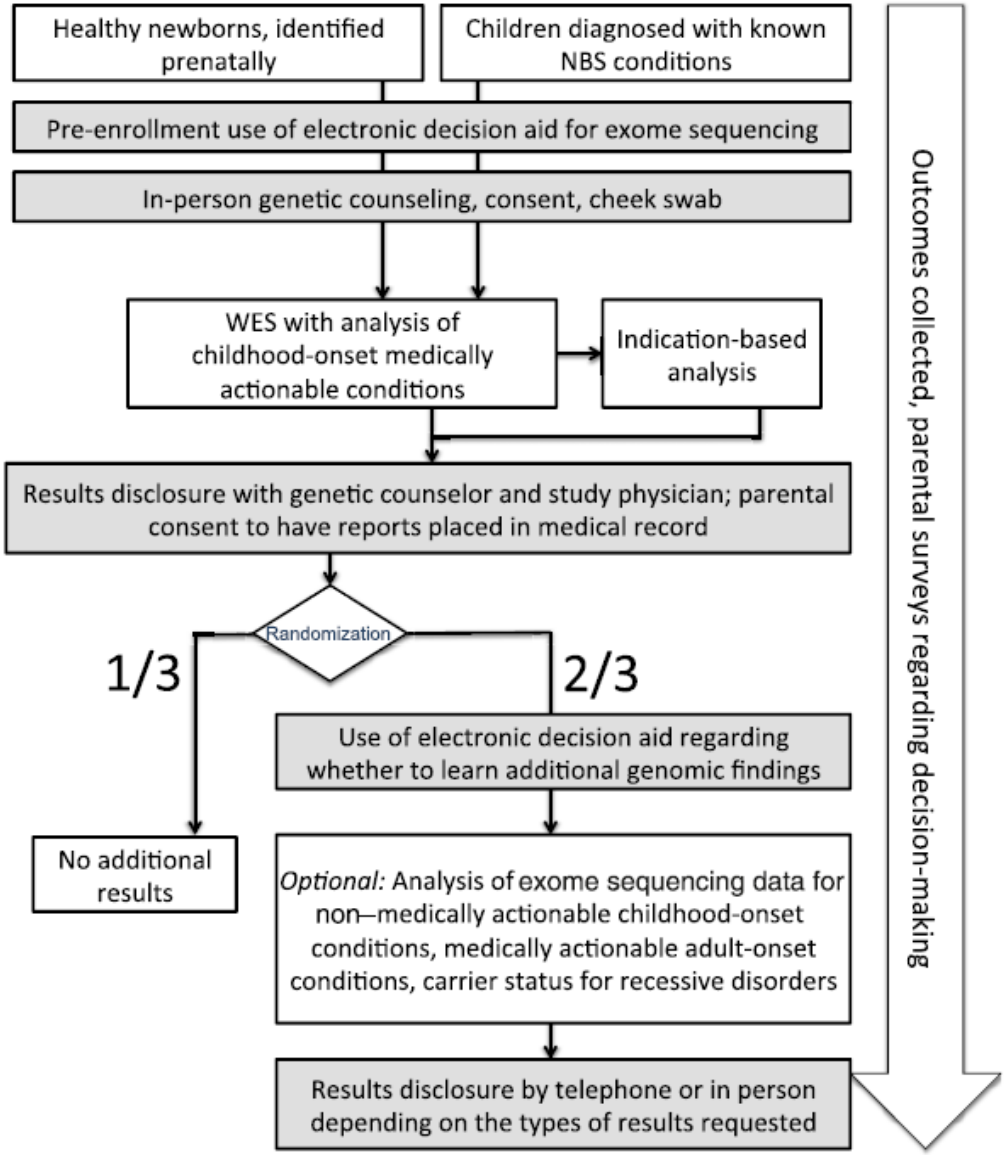
UCSF Study Design



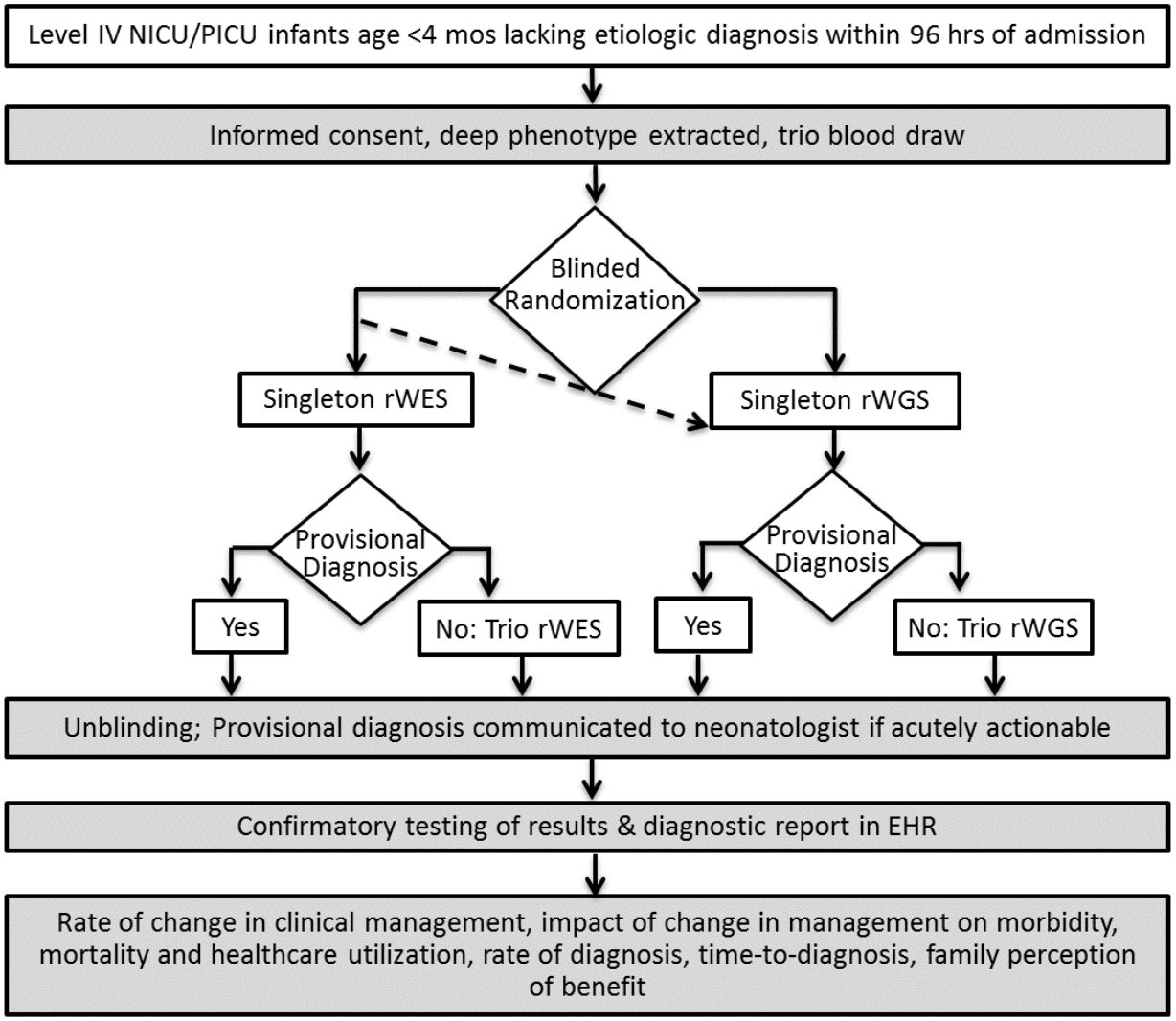
- Dried blood spots, no population bias
- Newborn screening and patients with immune disorders
- Exome seq
- Evaluate seq for newborn screening - focus groups and legal

UNC-CH Study Design



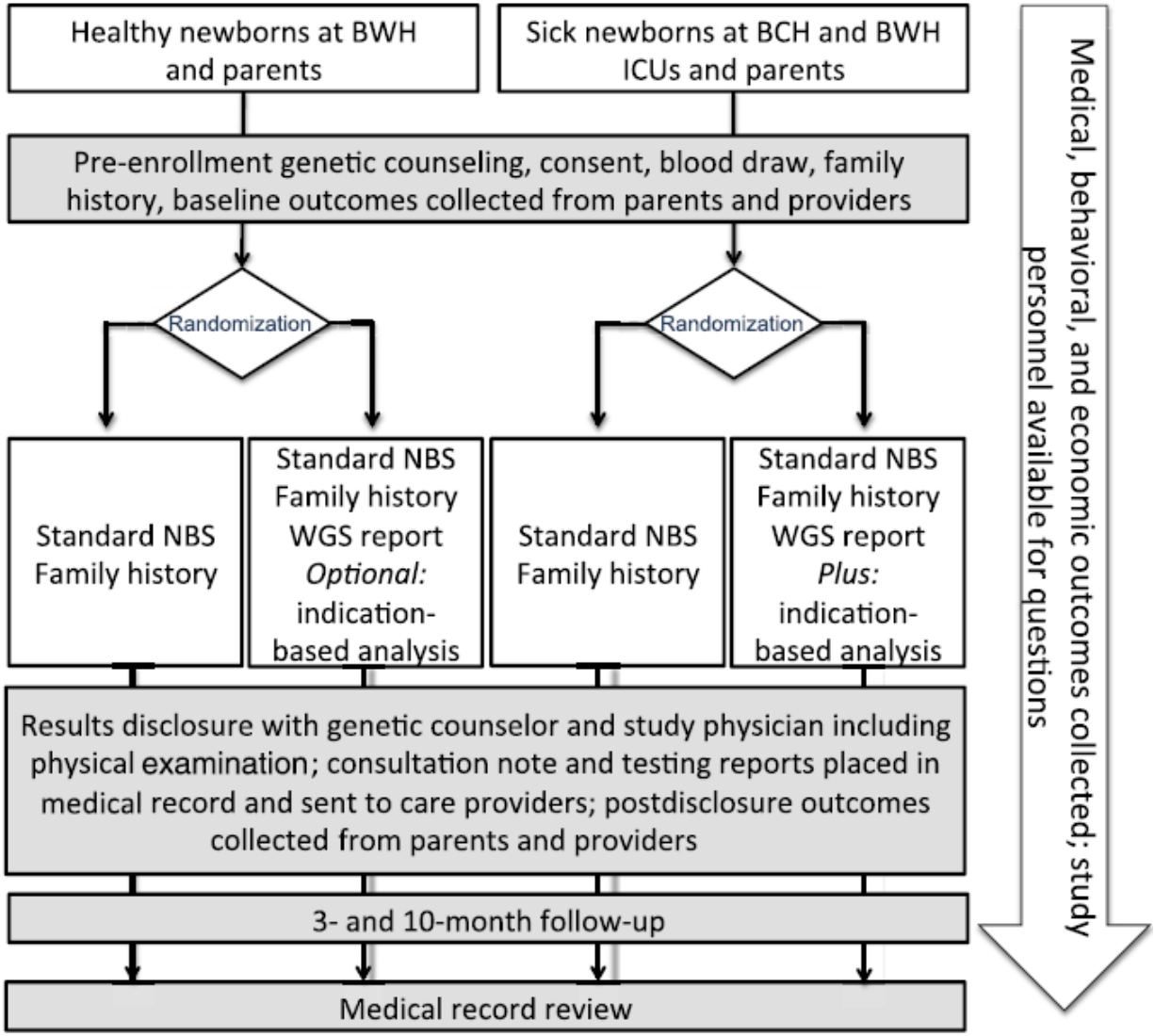
- Healthy and diagnosed with newborn screening conditions
- Saliva samples
- Electronic decision aid
- Randomized decision making for 3 additional types of genomic findings
- Parental follow-up surveys on decision making

RCHSD and CMH Study Design



- NICU infants
- Suggestive of genetic disease
- Randomized to rapid genome seq
- Cross-over allowed
- Parent and clinician follow-up surveys
- Equipoise

BWH, BCH, and BCM Study Design



- Healthy and sick infants
- Randomized to genomic seq
- Optional indication based analysis if genome seq
- Parent and physician follow-up surveys

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Replicate or Augment Newborn Screening

For disorders currently screened for in newborns, how can genomic sequencing **replicate or augment** known **newborn screening** results?

- Exome sequencing currently cannot replicate known newborn screening results – **of 182 exomes, 12.3% FN**
- Exome sequencing useful to augment newborn screening – **can identify gene**

Science 28 Oct 2016:
Vol. 354, Issue 6311, pp. 398-399

Knowledge on Conditions Not Screened

What knowledge about **conditions not currently screened** for in newborns could genomic sequencing of newborns provide?

- Develop electronic Decision Aid for parents informed decision-making and evaluating outcome
  - All – **childhood onset medically actionable conditions**
  - Randomized – **childhood onset *not* medically actionable; adult onset medically actionable; and/or carrier status**

Lewis et al. *Pediatrics*
January 2016, VOLUME 137 / ISSUE Supplement 1

Clinical Care of Newborns

What additional clinical information could be learned from genomic sequencing relevant to the **clinical care of newborns**?

- NICU sequencing leads to diagnoses and changes in clinical management
  - **20 out of 35 (57%) infants diagnosed**
  - **13 out of 20 (65%) diagnoses impacted acute clinical management** such as: change in medication, palliative care, or reproductive genetic counselling

Willig et al. *The Lancet Respiratory Medicine* Volume 3, Issue 5, May 2015, Pages 377-387

Unanticipated Findings

Enrollment and understanding reasons for decline

- Much lower than anticipated based on survey data – **46% reported "very", or "extremely" interested in newborn genomic testing**
- At first only 7% enrollment – **24 of 345 sick NICU infants, and 138 of 2062 healthy babies**
  - Noted logistical concerns on 1st approach
  - After GC meeting privacy, unclear results, and insurance discrimination concerns noted

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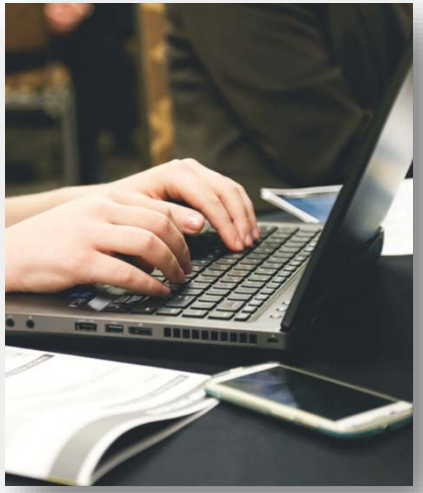
http://www.genomes2people.org/babyseqproject/

Network-wide Working + Writing Groups

NBSTRN
Newborn Screening Translational Research Network

NBSTRN provides coordinating center services to NSIGHT

- **Working Groups:** Common Data Elements and ELSI
- **Writing Groups:**
  - Enrollment
  - NSIGHT FDA Investigational Device Exemption Investigator Experience
  - Variant Interpretation



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Planning New Joint Workshop

With success of NSIGHT, NHGRI and NICHD exploring opportunities for further collaborations

- Anticipated workshop Spring 2018
- Evaluate gaps and emerging opportunities

Nick Youngson

Acknowledgments

Thank you to the NSIGHT participants and their families!

NHGRI
Joy Boyer
Sarah Gould
Ellen Howerton
Lu Wang

NICHD
Melissa Parisi

Newborn **S**equencing **I**n **G**enomic medicine and public **H**eal**T**h (NSIGHT)

Any Questions?

THANKS!