Utilization of the Newborn Screening Translational Research Network (NBSTRN) in a Pilot of Severe Combined Immune Deficiency (SCID) Newborn Screening

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Newborn Screening Translational Research Network

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Presentation Overview

- Session Objectives
- Severe Combined Immune Deficiency (SCID)
- SCID Newborn Screening
- Newborn Screening Translational Research Network (NBSTRN)

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Objectives

- This session will focus on the efforts of states to implement newborn screening for severe combined immunodeficiency (SCID) and will describe related efforts to support SCID research pilots while creating a model for other candidate conditions.
- Findings from a multi-year pilot in a single state as well as results from a four-state pilot will be presented, and a quality assurance strategy for screening in premature infants will be proposed.

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Severe Combined Immune Deficiency

- SCID and related T-cell lymphocyte deficiencies are a group of disorders
- Characterized by lack of functioning immune system
- Known as the “Bubble Boy Disease”
- Babies born with SCID appear healthy
- Classic SCID is universally fatal in the first two years without immune reconstitution*

* Railey MD, Lokhnygina Y, Buckley RH. J Pediatr 2009;155:834-40

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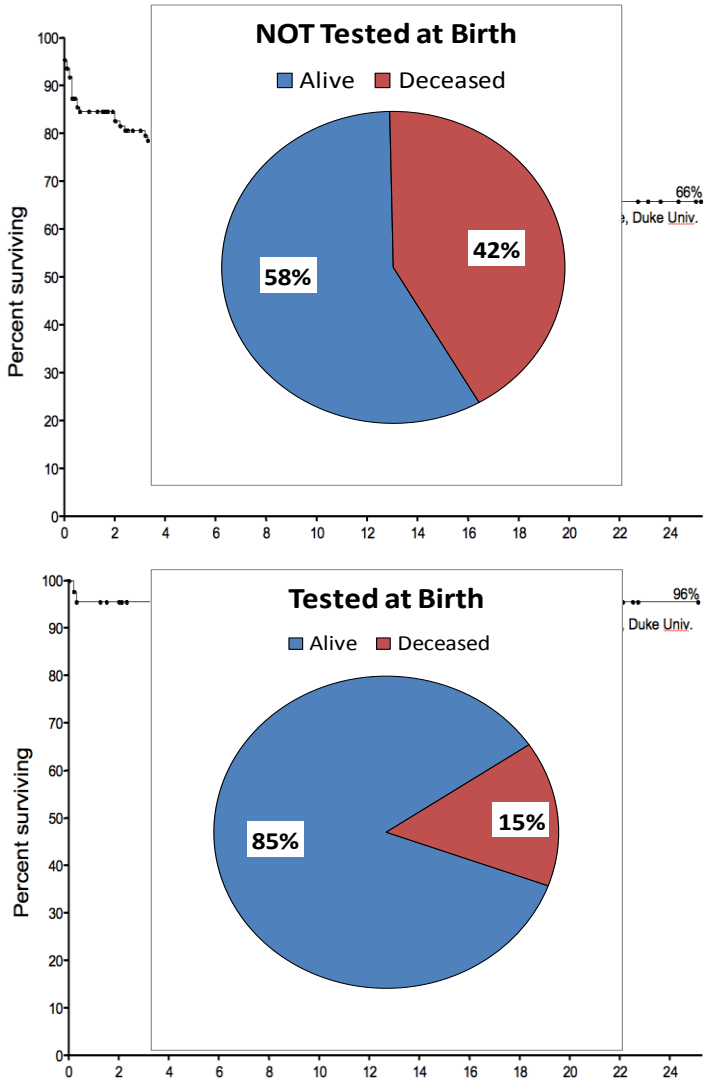
Severe Combined Immune Deficiency

- Early diagnosis is essential for lifesaving treatment
- Historically the best outcomes in siblings of deceased infant
- Many cases occur in families with no identifiable family history



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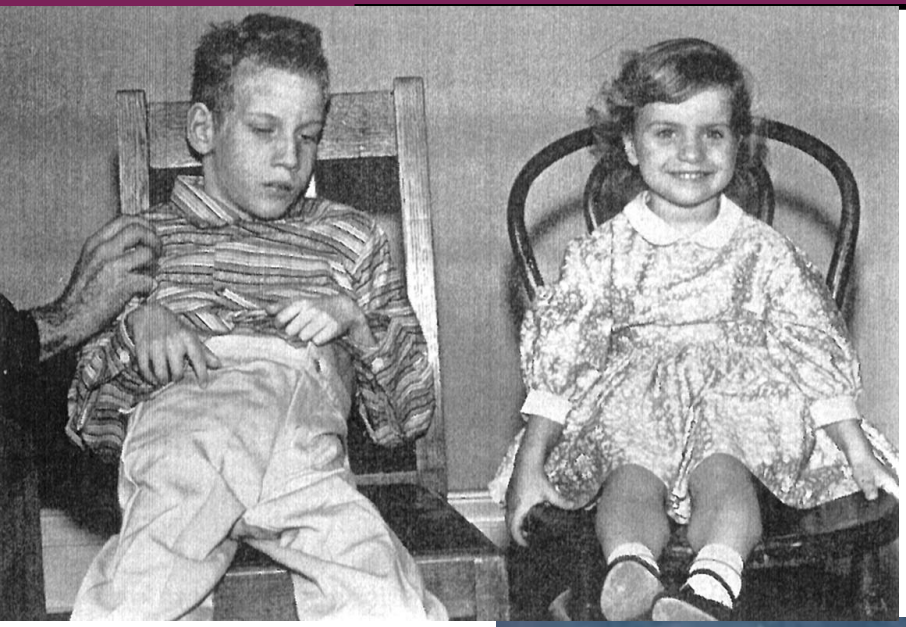
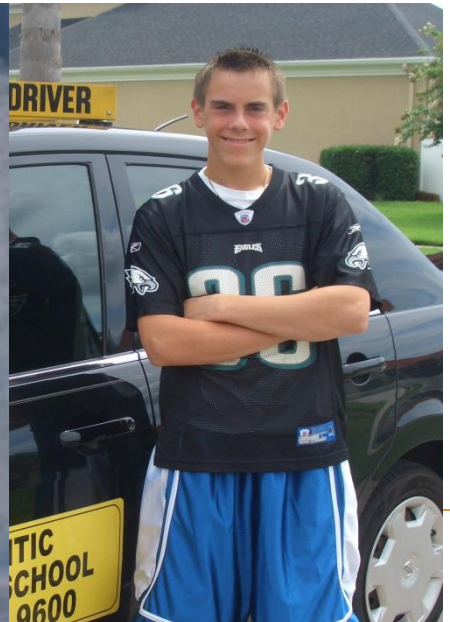
Importance of Family History





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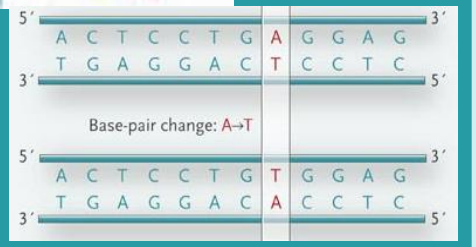
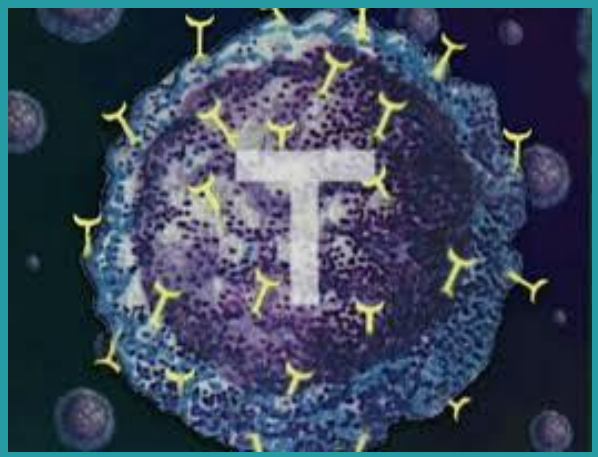
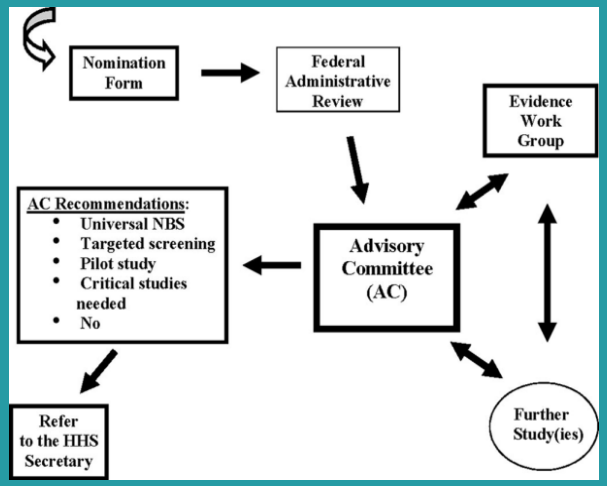
Severe Combined Immune Deficiency







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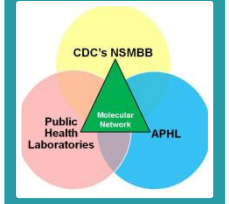
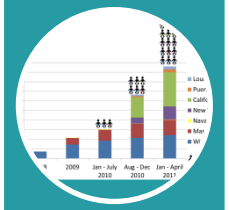
SCID Newborn Screening

CDC Conference

Assay Discovery



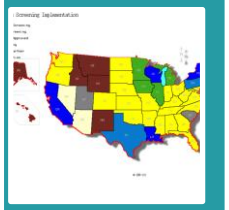
CDC's NSTRI & NSQAP



CDC & NICHD State Pilots

RUSP Addition

APHL, NNSGRC, HRSA, CDC



Statewide Adoption

CLSI

2001 2005 2008-2011 2010 2011

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Goals of the Hunter Kelly Newborn Screening Program

Identify, develop and test the most promising technologies

Increase the specificity of newborn screening and expand the number of conditions for which screening tests are available

Develop experimental treatments and disease management strategies for additional newborn screening conditions, and other genetic, metabolic, hormonal and or functional conditions that can be detected through newborn screening for which treatment is not yet available

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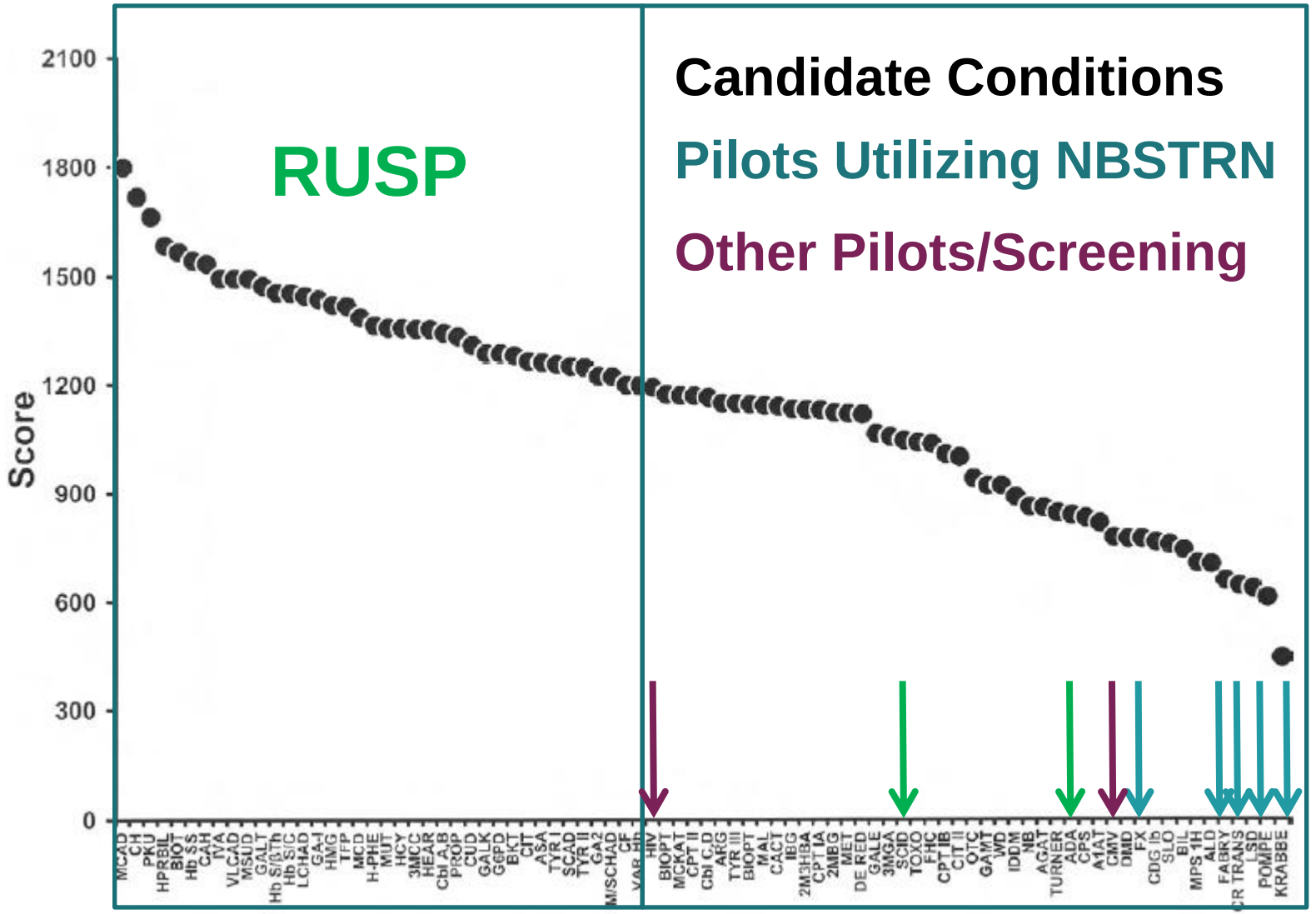
Example of NBSTRN Focus



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Expansion of SCID Newborn Screening Pilots

- **NIH initiated project to enable additional states to pilot screening**
  - National SCID Pilot Study
- **Key Features**
  - Initiates pilots in high number birth states (New York, California)
  - High capacity assay development (New York, California)
  - Regionalization model
    - Puerto Rico → Massachusetts
    - Louisiana → Wisconsin
  - CDC quality assurance program
  - Utilize NBSTRN

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National SCID Pilot Study


Dr. Michele Caggana, PI

- **Deliverables**
  - **Analytical**
    - Technology ✓
    - Protocols ✓
    - Analysis Tools ✓
    - Quality Assurance Methods
    - Pilot data set ✓
  - **Clinical**
    - System of referral for follow-up and treatment ✓

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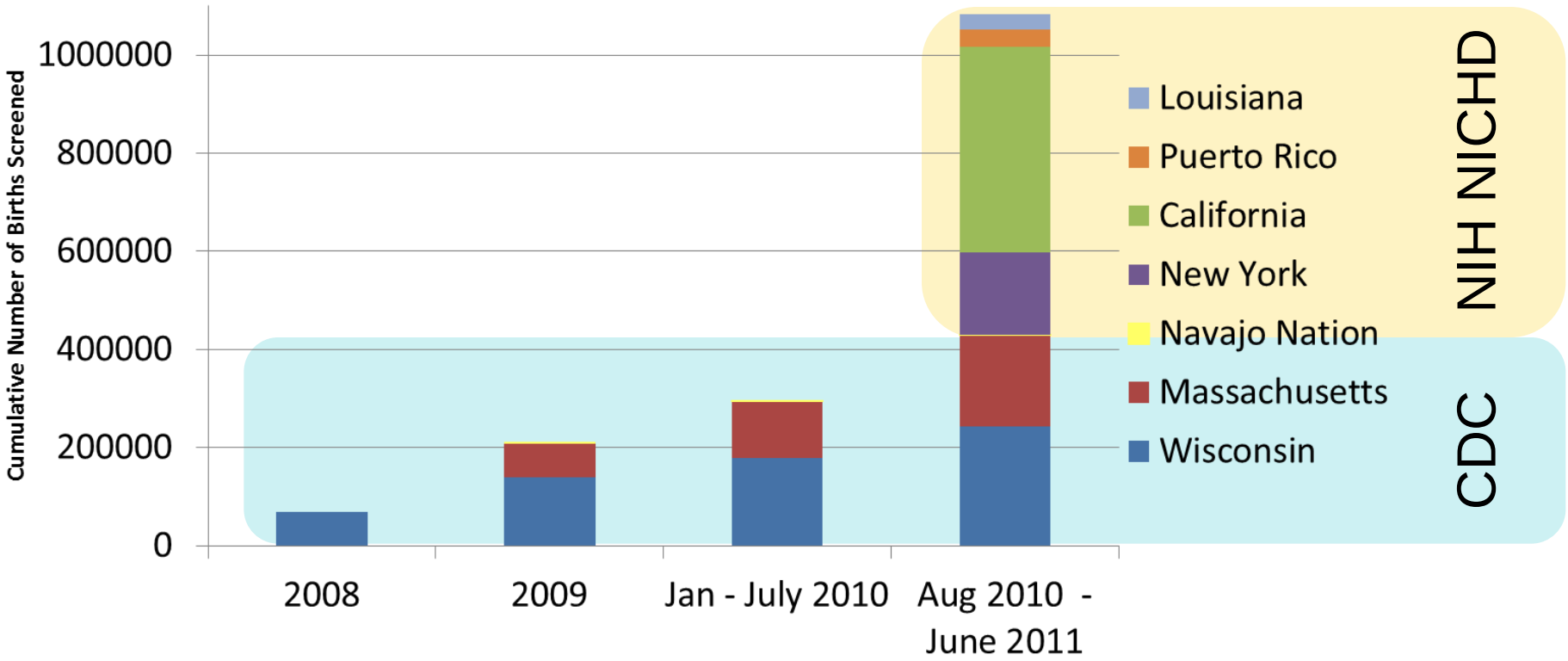
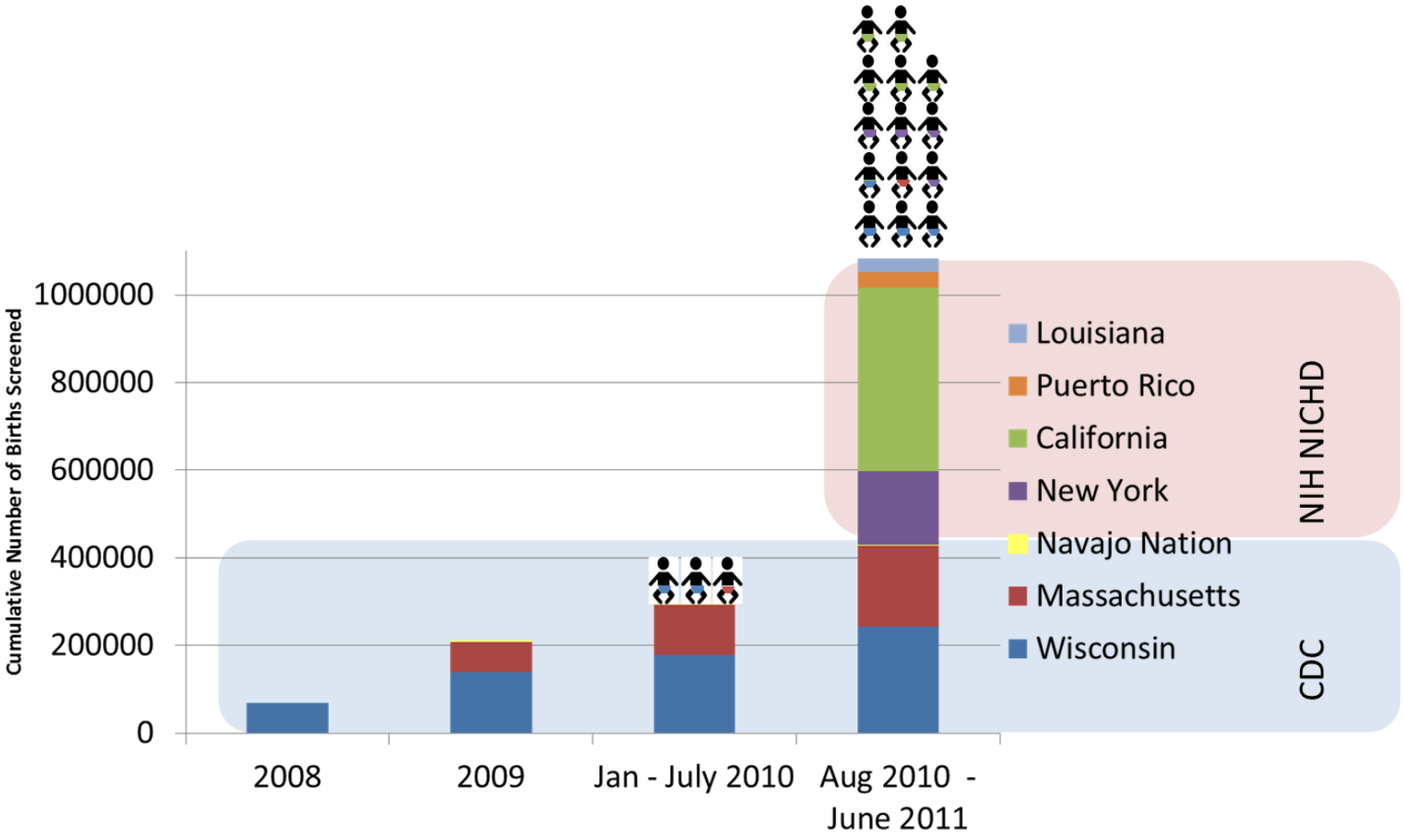
State-wide Screening Pilots



Classic SCID Cases



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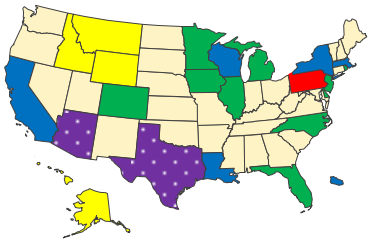
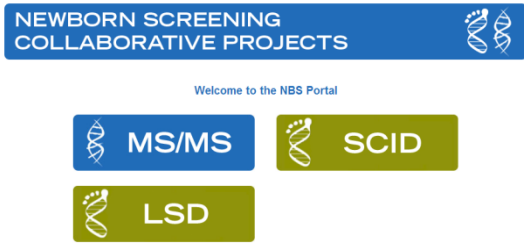
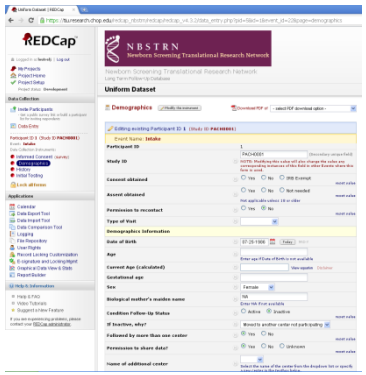
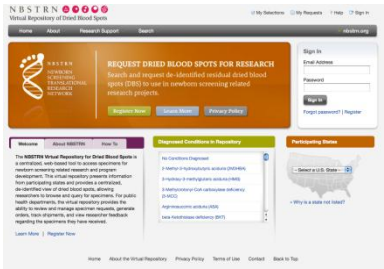
NBSTRN Role

- Convene Experts
- Facilitate and Host Monthly National Calls
- Develop Analytical Tools
  - R4S
  - LTFU
- Develop VRDBS and Sample Banks
- Disseminate Findings









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SCID Data Portal

- Goal was to collect, aggregate and analyze de-identified screening data generated during the pilot
- Enables real-time laboratory performance quality improvement
- Stores laboratory protocols
- Facilitates tracking of emerging findings
- Provides disease definitions
- Available to any newborn screening program and or researcher

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Emerging Findings

- Screening technology is a robust biomarker for SCID and profound T cell lymphopenia
  - Future investigations of this valuable biomarker will accelerate research in immunology.
- Majority of classic SCID cases have zero TREC
- Molecular etiology of low TREC cases is varied
- Incidence rates different from published findings
- Incidence rates vary by race and ethnic categories

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Tools and Resources Developed

QA Program

- Dried blood spot reference materials
- Available to any laboratory
- 11 labs – 100% sensitivity, >99% specificity

Data Portal

- Clinical validation through data sharing and analysis
- Available to any interested stakeholder
- Novel disease categories – SCID, SCID Variant, Non SCID

Laboratory Protocols

- Pilot state instruction manuals for implementing SCID newborn screening
- Available to any interested stakeholder
- Four independently validated laboratory developed tests

Information Sharing Resource

- Monthly conference calls to share expertise and discuss issues
- Available to any interested stakeholder
- 16 states, families, researchers, industry, advocates, foundations

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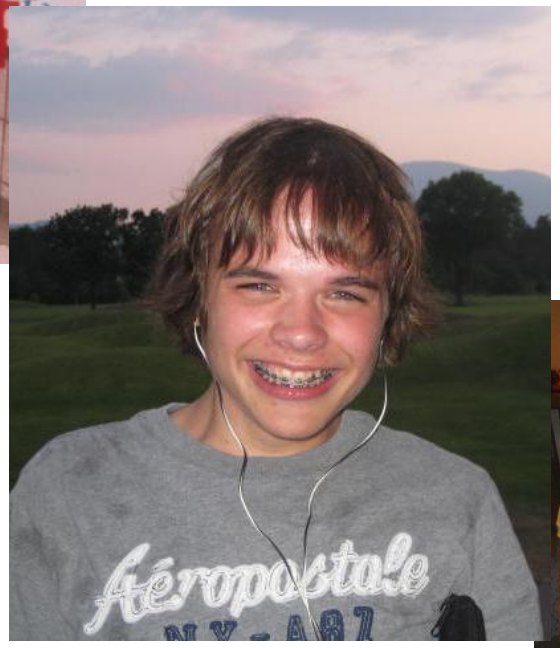
Thank You!



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SCID Trial -HHSN267200603430