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NBSTRN
NEWBORN SCREENING TRANSLATIONAL RESEARCH NETWORK

Implementation of Newborn Screening for Severe Combined Immune Deficiency

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NBSTRN-CC
February 1, 2013

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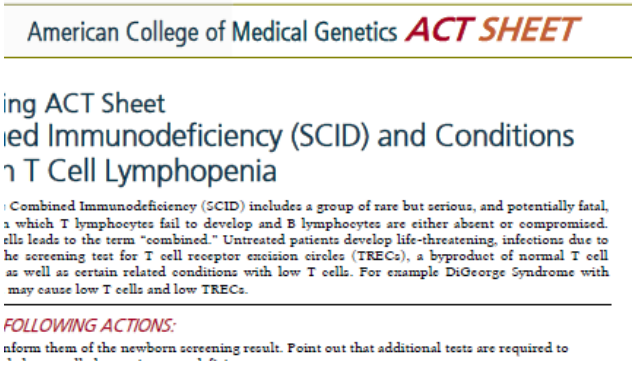
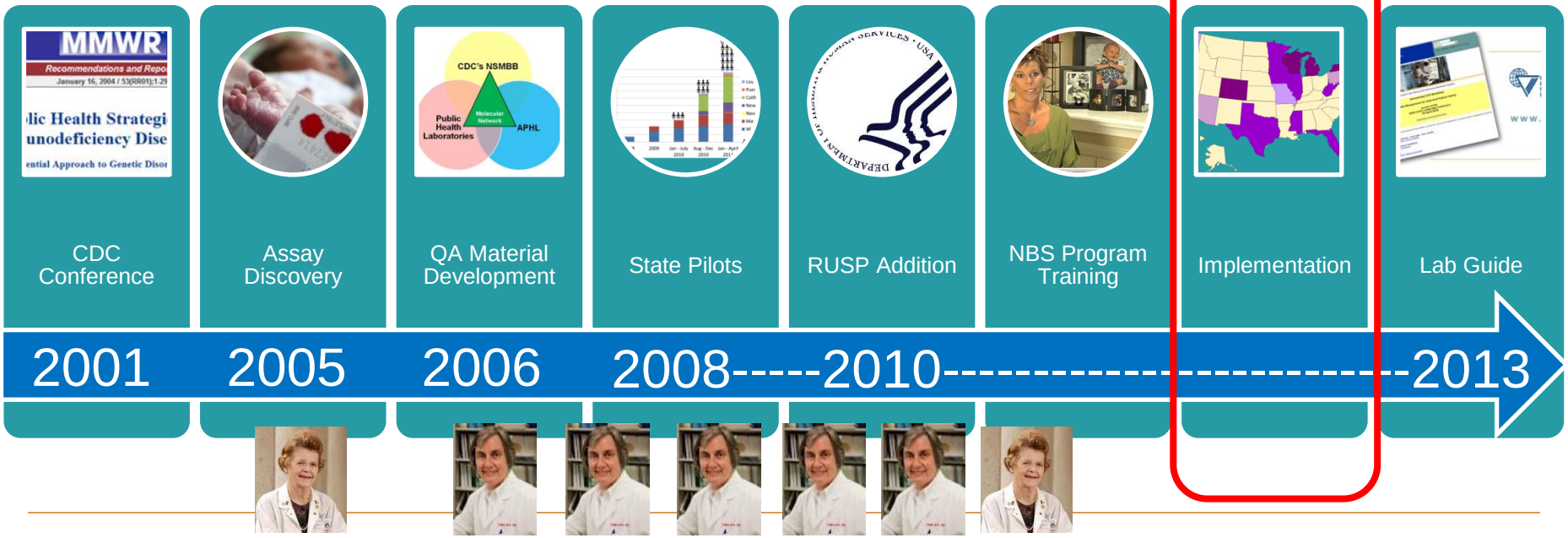
Key Events





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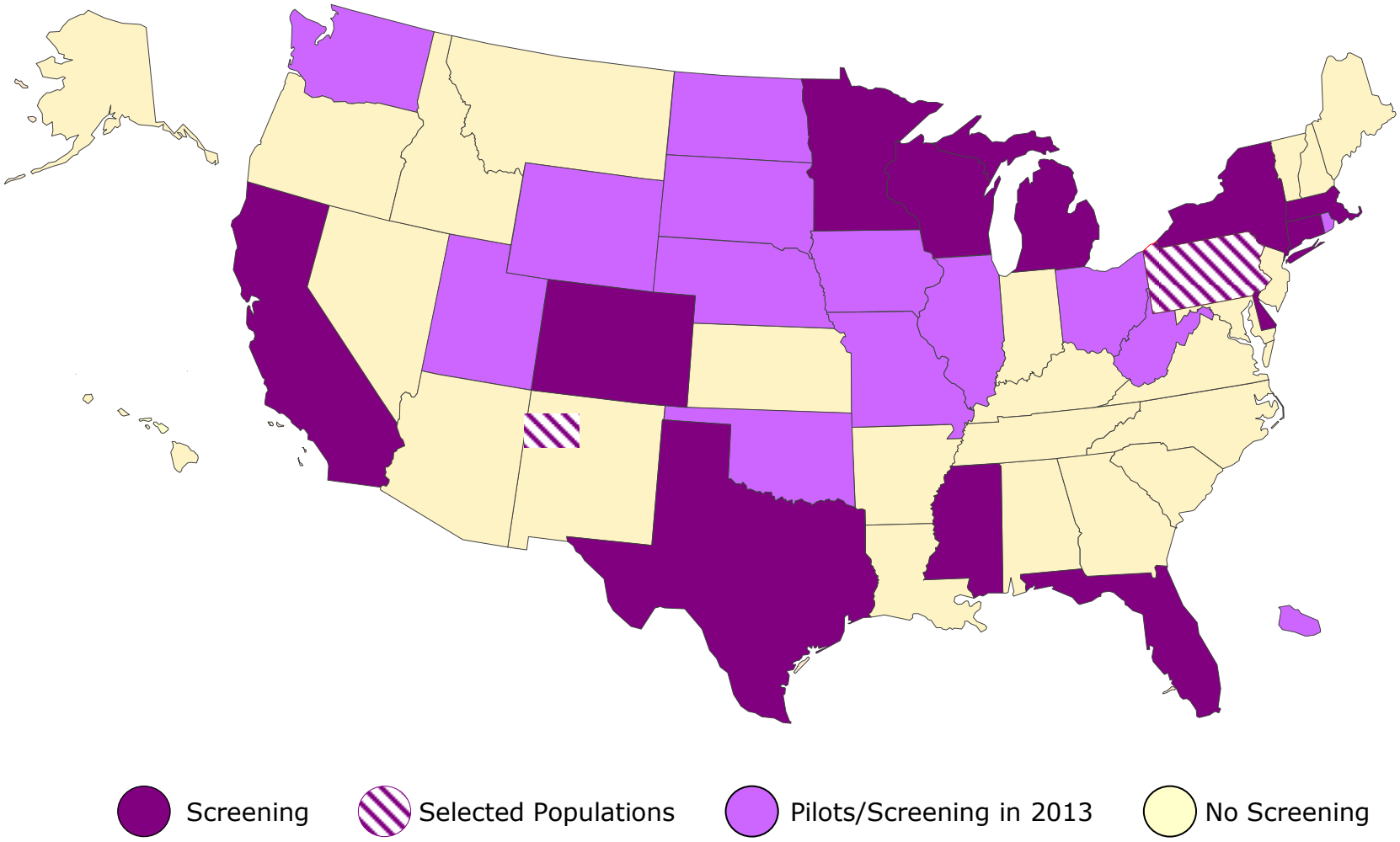
Implementation Status



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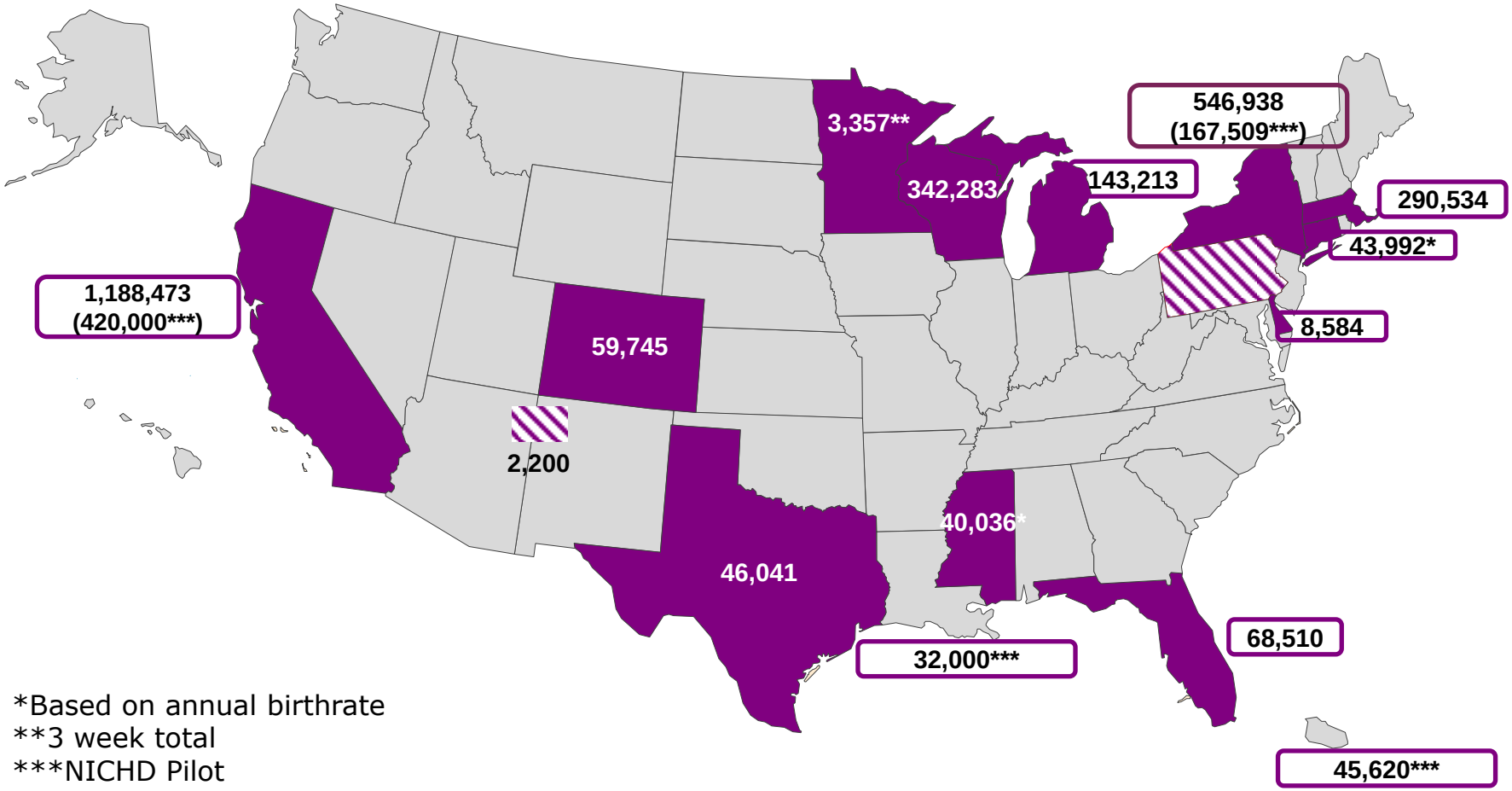
Estimated Newborns Screened Through December 31st 2012



*Based on annual birthrate
**3 week total
***NICHD Pilot

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Selected Stats

Total Number of Newborns Screened by 12/31/12	Percentage of Births Screened	States Planning Pilots or Screening in 2013	Estimated Percentage of Births Screened by 2014	Clinically Diagnosed Cases Since RUSP Addition in Non-screening States
2.85 M	45%	12	62%	15

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Resources for NBS Laboratories

- **CDC**
  - Conduct Individualized Laboratory Training
  - Support Laboratory Test Development
  - Supply Quality Control Reference Materials
  - Provide Proficiency Testing through NSQAP
- **NICHD**
  - National Pilot Protocols and Algorithms
  - R4S SCID Data Portal through NBSTRN
  - Monthly Stakeholder Calls through NBSTRN
  - Information Resource through NBSTRN

CDC Update

- **Clinical Laboratory and Standards Institute (CLSI) Guideline ILA-36**
  - "Newborn Blood Spot Screening for SCID by Measurement of T-cell Receptor Excision Circles"
  - Approved Dec 2012; Publication scheduled for May 2013
  - Addresses laboratory operations, instrumentation, TREC assay protocols, automated methodologies, diagnostic tests, short-term and long-term follow-up.
- **CDC Cooperative Agreements**
  - Oct 2011-Sep 2013
  - Michigan: More than 150,000 screened; 4 SCID found
  - Minnesota: Completed method development; began screening Jan 2013

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R4S SCID Module

- **NBSTRN funded the SCID module for R4S**
- **Facilitates analytical validation of screening assay**
- **Collects clinical information**
- **Tutorials can be arranged at any time**
- **Co-curators**
  - **Roshini Abraham, PhD**
  - **Fred Lorey, PhD**

Condition Types
SCID
Leaky SCID/Omenn Syndrome
Variant SCID
Syndromes with T cell impairment
Secondary T cell lymphopenia other than preterm alone
Preterm alone

Conditions by Flow Phenotyping
T-B+NK-
T-B-NK-
T-B-NK+
T-B+NK+
Other

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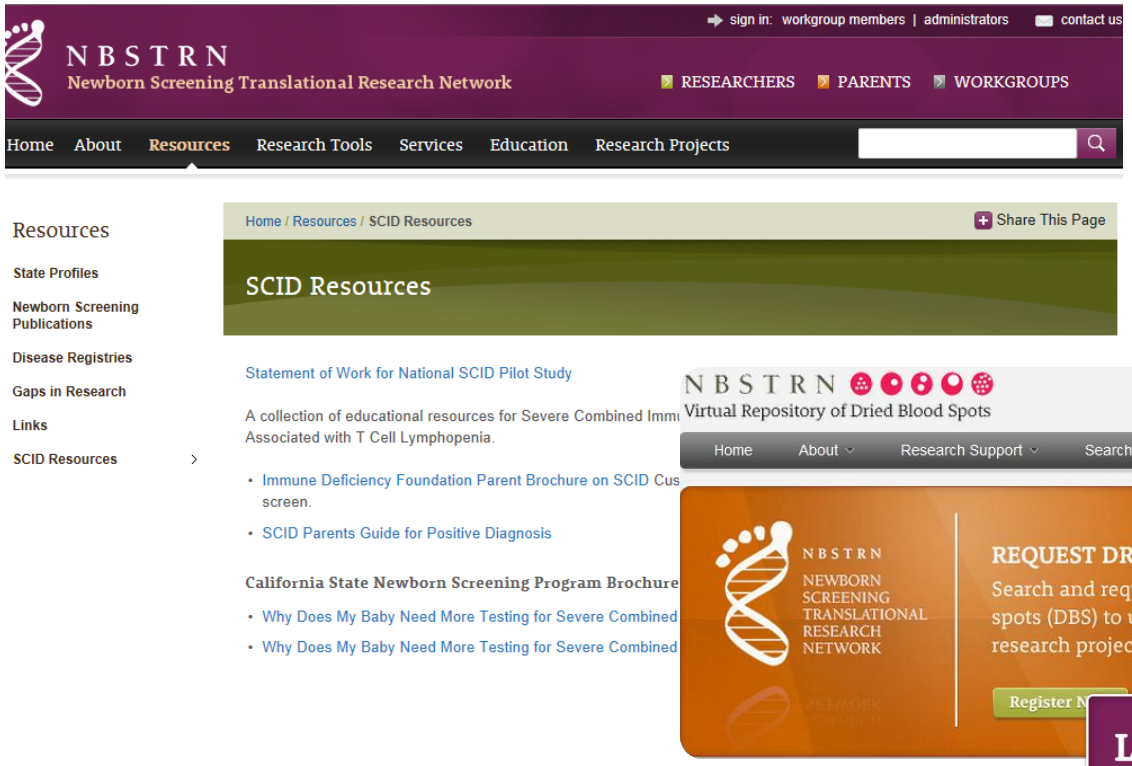
Resources for Health Care Providers

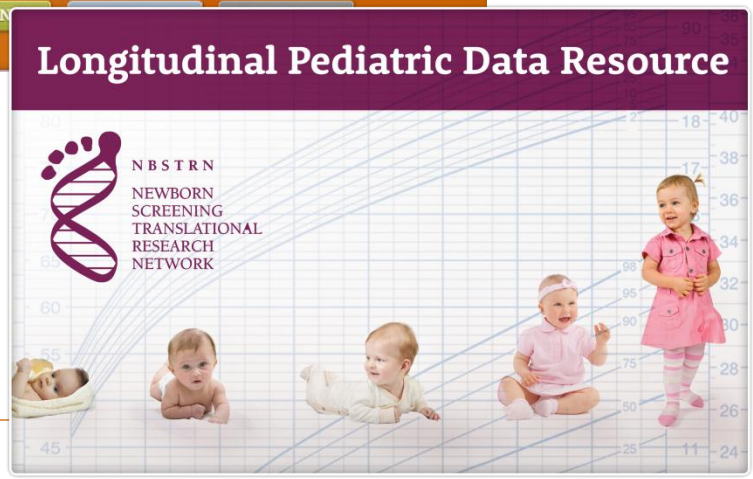
- **HRSA, ACMG**
  - Clinical Decision Support Materials
  - ACT Sheets
  - Available online
- **Immune Deficiency Foundation**
  - SCID Newborn Screening Toolkit for Advocates
  - Rotavirus Vaccine Pamphlet
  - Parent Education Materials
- **CDC, APHL, and Jeffrey Modell Foundation**
  - Two-year fellowship for post-doctoral candidates
  - Newborn screening research including immune deficiencies

Immune Deficiency Foundation Update

- **IDF offers educational resources to families and state**
  - **IDF SCID Newborn Screening Campaign website and blog**
  - **Educational guides to be of use to the states in their follow up protocols for SCID screening**
  - **Two educational guides for parents have been developed by IDF and experts in SCID with the help of the New York-Mid-Atlantic Consortium for Genetic and Newborn Screening Services (NYMAC).**
  - **Targeted advocacy actions**
  - **IDF will be holding the IDF 2013 National Conference in Baltimore, MD June 27-29, 2013**

Resources for NBS Researchers





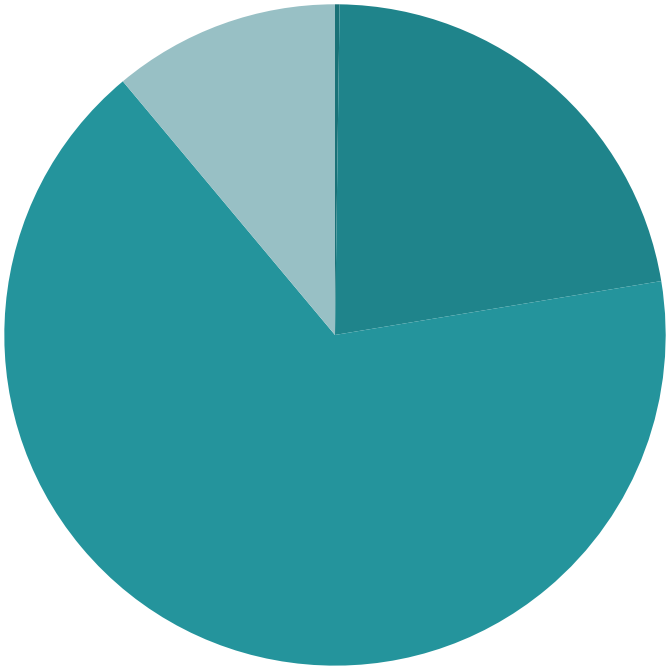
https://www.nbstrn.org/resources/scid-resources

Expansion of SCID Newborn Screening Pilots

- NIH initiated project to enable additional states to pilot screening – Dr. Michele Caggana, PI
- 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
  - SCID data portal
  - Monthly conference calls to share expertise

Characteristics of SCID Cases Race or Ethnicity

New York and California Pilots
N = 9



Asian

African American

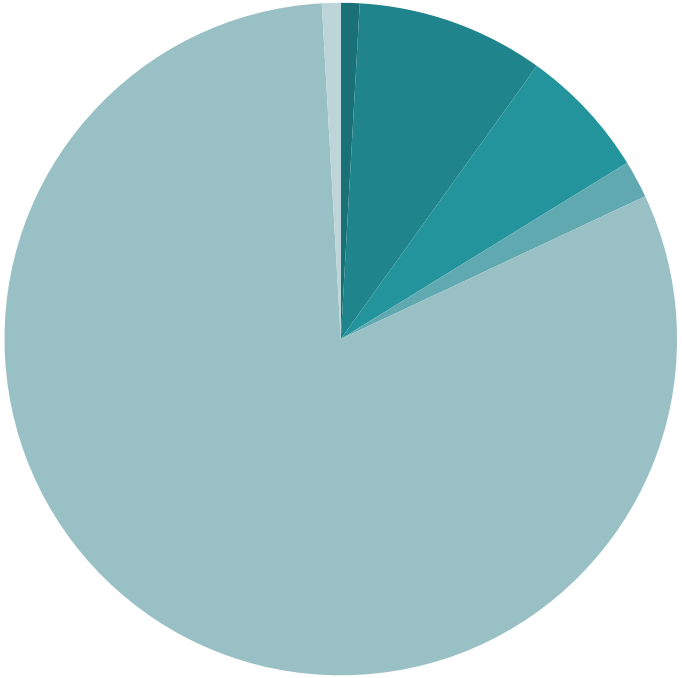
Hispanic

American Indian

Caucasian

Arabic

Duke Retrospective Study
N = 111



LPDR

SCID

ID _____

Source of information _____

State _____

Birth weight _____

Neonatal complications ☐ Unknown ☐ Yes ☐ No

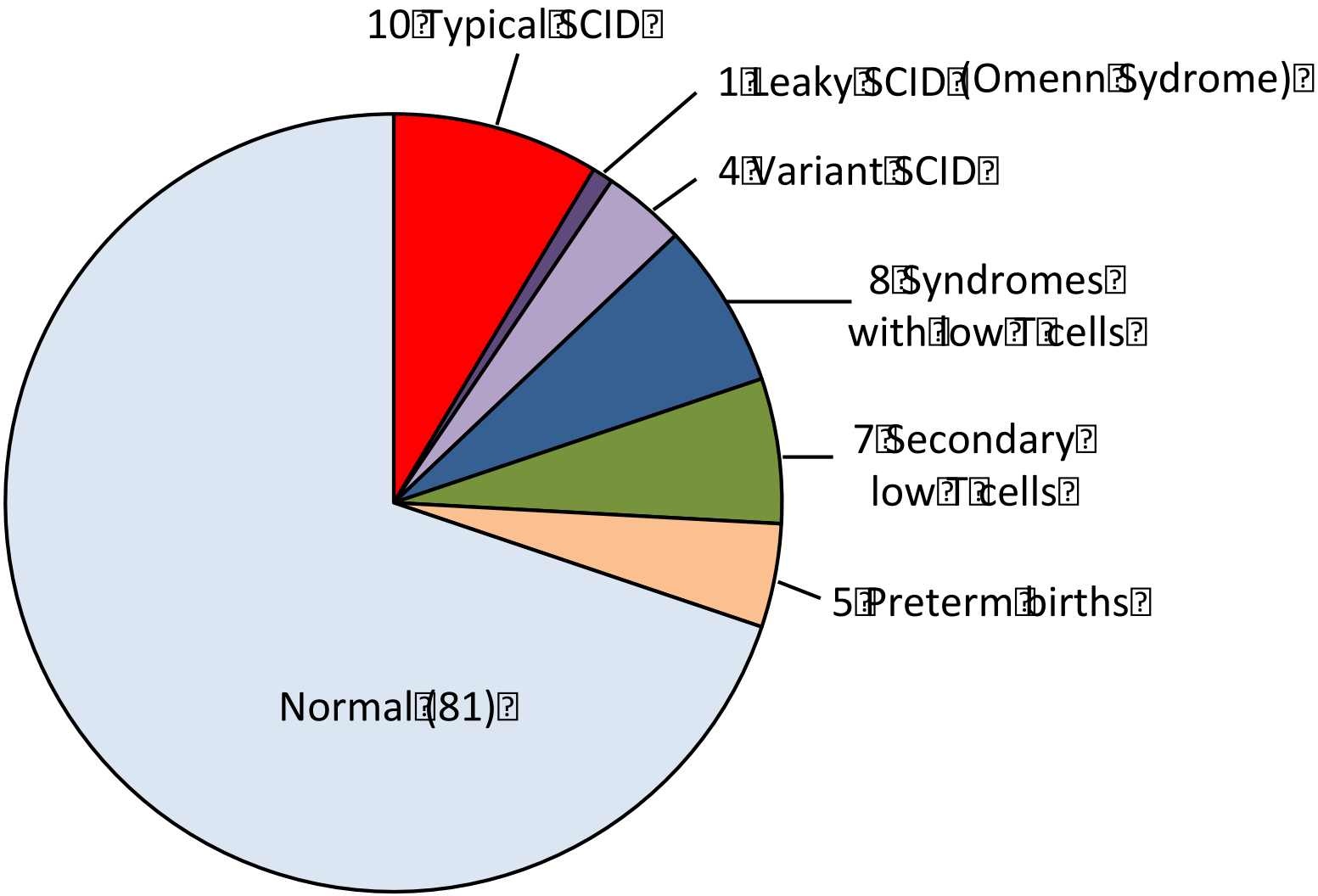
Type of neonatal complications
- ☐ Infection/sepsis
- ☐ Antibiotics
- ☐ Hypoglycemia
- ☐ IV fluids
- ☐ Jaundice
- ☐ Premature (< 37 weeks gestation)
- ☐ Transfused
- ☐ Respiratory distress
- ☐ APGAR < 5
- ☐ Seizures
- ☐ Other

Type of neonatal complications-other, spec _____

Sex ☐ Male ☐ Female

Race
- ☐ Not reported
- ☐ American Indian/Alaskan Native
- ☐ Asian

California Cases to Flow Cytometry in First 18 Months



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California Summary

- 99.91% specificity; missed cases partial ADA, MHC-II.
- Of infants called for confirmatory flow cytometry, 30% had clinically significant T cell lymphopenia.
- Centralized flow cytometry as a 2nd tier test within the screening program permits timely and consistent diagnosis.
- All 11 infants with SCID received definitive treatments, with >90% survival at 6-21 months, superior to outcomes reported for SCID without newborn screening.
- Newborn screening offers the opportunity to study and treat pre-symptomatic immunodeficient infants with a wide spectrum of T lymphopenic disorders.

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Acknowledgment

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Discussion

- **Thank you!**