Long-Term Follow-Up Elements of Pompe Disease

Marci Sontag, PhD

Amy Brower, PhD

June 22, 2017

Presentation Outline

- Long-Term Follow-Up and Newborn Screening
- Key Efforts and Guidance
- Resources and Tools

Presentation Outline

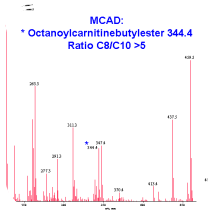
- Long-Term Follow-Up and Newborn Screening
- Key Efforts and Guidance
- Resources and Tools

Long-Term Follow-Up in Newborn Screening

- Early detection, diagnosis, and intervention can prevent death or disability and enable children to reach their full potential
- Lifelong treatment in most cases
- Long term care occurs in specialty clinics
- State based newborn screening programs have interest in outcomes and service utilization to improve their programs

Prenatal Education

Screening



Diagnosis and Short-Term Follow-Up

Clinical Care and Long-Term Follow-Up

Presentation Outline

- Long-Term Follow-Up and Newborn Screening
- Key Efforts and Guidance
- Resources and Tools

Key Efforts and Guidance

Newborn screening conditions: What we know, what we do not know, and how we will know it

Harvey L. Levy, MD

Abstract: Expanding newborn screening beyond that for phenylketonuria was always the goal of Guthrie once phenylketonuria screening was on solid ground. He succeeded in this effort to an extent, adding screening for galactosemia, maple syrup urine disease, and homocystinuria. Screening for congenital hypothyroidism, congenital adrenal hyperplasia, biotinidase deficiency, and a few additional disorders was added by others over the years. However, a very large expansion of covered metabolic disorders eluded Guthrie despite his best efforts. This required a new screening technology, tandem mass spectrometry, which was not available until recently. Now, almost all developed newborn screening program use

This story was repeated as disorders were added—congenital hypothyroidism, congenital adrenal hyperplasia, and biotinidase deficiency. Perhaps, the single exception was sickle cell disease, which was almost as well understood when added to NBS as now.[6] Nevertheless, screening for sickle cell was really screening for hemoglobinopathies, and identification of so many of the latter has opened up a new window into the myriad of hemoglobin variants.

The recent very major expansion of NBS, made possible by tandem mass spectrometry, is a continuation of this story but

Long-term follow-up in newborn screening: A systems approach for improving health outcomes

Michele A. Lloyd-Puryear, MD, PhD[1], and Amy Brower, PhD[2]

Background: Newborn screening is a complex system of interrelated multidimensional components singly focused on safeguarding the health of our nation's newborns. The long-term health outcome and well-being of individuals identified by newborn screening represents a meaningful measurement of the performance of the newborn screening system. This assessment of long-term follow-up requires a systems approach that connects stakeholders, processes, and outcomes through the collection, integration, evaluation, and sharing of key data and metrics. **Methods:** A review of the principles of a systems approach and its application to newborn screening long-term follow-up was performed. Past and current efforts by HRSA/MCHB that address individual components of newborn screening were assessed and utilized to

Newborn screening programs are a multifaceted system of education, screening, diagnosis and referral (short-term follow-up [STFU]), treatment and care management (long-term follow-up [LTFU]), and ongoing evaluation of the effectiveness of all components. Education about newborn screening optimally begins prenatally, and information is provided to prospective parents by their obstetrician. The screening process for the infant begins in the hospital or birthing facility. Currently, there are two types of screening performed: one requires blood (dried blood spot screening) and the other is physiologic (hearing screening). For dried blood spot screening, blood is obtained from the newborn infant (usually by a heel stick) and applied to special standardized filter paper. The filter paper has an attached

The context and approach for the California newborn screening short- and long-term follow-up data system: Preliminary findings

Lisa Feuchtbaum, DrPH, MPH[1], Sunaina Dowray, MPH[2], and Fred Lorey, PhD[1]

Purpose: State newborn screening programs are designed to prevent morbidity and mortality from hereditary disorders through early detection and ongoing disease management. These programs have traditionally focused on short-term follow-up. However, capturing data on the long-term follow-up process is emerging as a new priority. Long-term follow-up data can be used to assess the accessibility, continuity, and quality of care provided to these children. The California Newborn Screening Program uses a Web-based data collection system for short-

tity and quality of services these children receive and monitoring their health outcomes over time.[6–9]

Several nationwide surveys conducted in the last 4 years have evaluated the percent of state NBS programs engaged in LTFU. In addition, these surveys assessed the programs' follow-up processes and evaluated program staff views on their roles and responsibilities related to follow-up. Results indicate that many NBS program staff has not seen their role as extending beyond the STFU pe-

MEETING REPORT

Long-term follow-up of newborn screening patients

Susan A. Berry, MD[1], Michele A. Lloyd-Puryear, MD, PhD[2], and Michael S. Watson, PhD[3]

Abstract: New technology in newborn screening permits clinicians to approach strategies for defining optimal treatments for newborn-screened conditions. The Health Resources and Services Administration Maternal and Child Health Bureau, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the Centers for Disease Control and Prevention have all established initia-

collaborative efforts in improving management for individuals with conditions such as inborn errors of metabolism. At the same time, substantial interest in research endeavors to improve this care has also emerged. The Eunice Kennedy Shriver National Institute of Child Health and Human Development has established translation research in the arena of NBS as a national priority for research activity. Finally, the Centers for

What questions should newborn screening long-term follow-up be able to answer? A statement of the US Secretary for Health and Human Services' Advisory Committee on Heritable Disorders in Newborns and Children

Cynthia F. Hinton, PhD, MPH[1], Lisa Feuchtbaum, DrPH, MPH[2], Christopher A. Kus, MD, MPH[3], Alex R. Kemper, MD, MPH[4], Susan A. Berry, MD[5], Jill Levy-Fisch, BA[6], Julie Luedtke, BS[7], Celia Kaye, MD, PhD[8], and Coleen A. Boyle, PhD, MS[1]

SACHDNC Statement on LTFU

Assure the best possible outcome for individuals with disorders identified through newborn screening

Key Features

- Quality chronic disease management
- Condition-specific treatment
- Age-appropriate preventive care throughout the lifespan

Central Components

- Care coordination through a medical home
- Evidence-based treatment
- Continuous quality improvement
- New knowledge discovery

Long-Term Follow-Up in the Public Health Context

PEAS

- Long-Term Program Evaluation
- Nine Assessments

ACHDNC Statement

- Overarching Questions
- Families
- Medical Home
- State/Nation

National Quality Forum

- Newborn Screening Outcome Measure
- Hearing Screening Outcome Measures

Presentation Outline

- Long-Term Follow-Up and Newborn Screening
- Key Efforts and Guidance
- Resources and Tools

Resources and Tools

NewSTEPs	• Case Definitions • Short-Term Follow-Up • State Profiles • Implementation Efforts
NBSTRN	• Informatics Infrastructure – Pilot and Grantees • Disease Specific and Candidate Conditions CDEs • LSD Workgroup and Clinical Integration Group
NCC	• Public Health Focus • Leveraging the Regional Genetics Network Activities • NCC/RC LTFU Data Workgroup - Minimum CDE Set
Joint Committee	• RUSP Conditions • Subject Matter Experts Across Newborn Screening Stakeholder Groups • Applicable for Research and Public Health

SURVEILLANCE CASE DEFINITIONS

- Surveillance case definitions are intended to establish uniform criteria for *disease reporting*

- NOT intended for use as
  - criteria for establishing clinical diagnoses
  - determining the standard of care necessary for a particular patient
  - setting guidelines for quality assurance
  - providing standards for reimbursement
  - initiating public health actions

CASE DEFINITIONS FOR NEWBORN SCREENING PUBLIC HEALTH SURVEILLANCE: POMPE DISEASE

Pompe Disease
(aka Acid Alpha-Glucosidase Deficiency)

Category	Mutation Status	GAA Enzyme Activity	Cardiac Involvement	Clinical Symptoms/Lab Findings	CRIM Status
Definite, early-onset Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	Yes	Present	Negative
Definite, early-onset Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	Yes	Present	Positive
Definite, early-onset Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	Yes	Not present	Negative
Definite, early-onset Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	Yes	Not present	Positive
Definite, early-onset Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	No	Present	Negative
Definite, early-onset Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	No	Present	Positive
Definite, Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	No	Not present	Negative
Definite, Pompe disease	2 disease-causing mutations or positive skin or muscle bx	Low	No	Not present	Positive
Definite, early-onset Pompe disease	1 disease-causing mutation*	Low	Yes	Present	Negative
Definite, early-onset Pompe disease	1 disease-causing mutation*	Low	Yes	Present	Positive

NewSTEPs
A Program of the Association of Public Health Laboratories™

1209 CDE's

Choose a Case Report Form and/or Section

Case Report Form 

Select a Case Report Form

Section 

Select a Section

Choose a Condition Category and/or Conditions

Condition Category 

Select a Condition Category

Condition 

Pompe disease (GAA) ×

Choose Other Categories

Keyword 

Match whole word

Project 

Select a Project

1,209 CDEs from search criteria

Show CDE's

Click the search button to see the CDE's

Clear

Provide Feedback to NBSTRN about CDEs

(lpdr_nbstrn@acmg.net)

Public Health Minimum Data Set

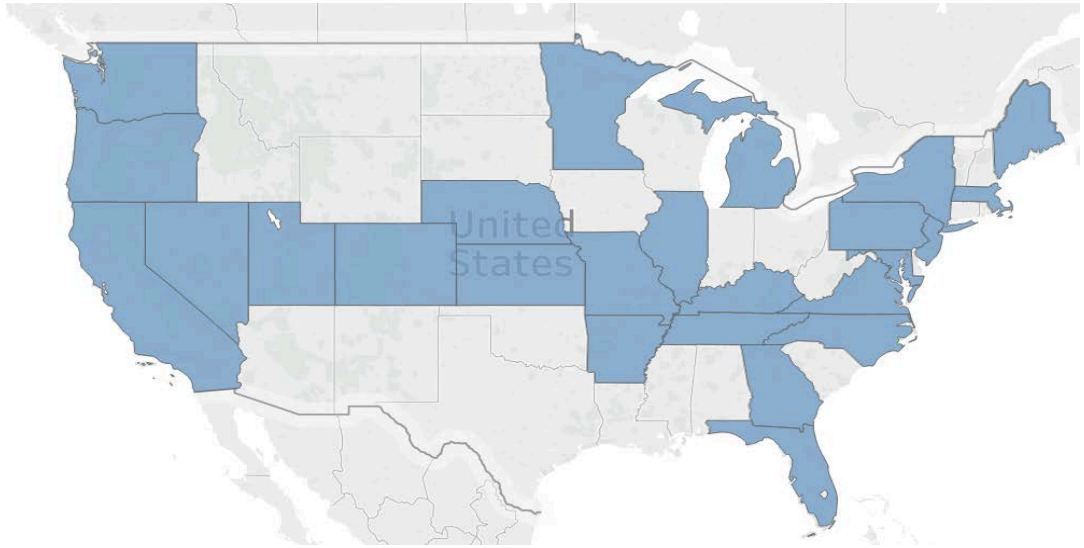
- Diagnosis
- Condition Specific Care within the Past 12 Months
- Date or Age of Appropriate Intervention
- Alive or Deceased

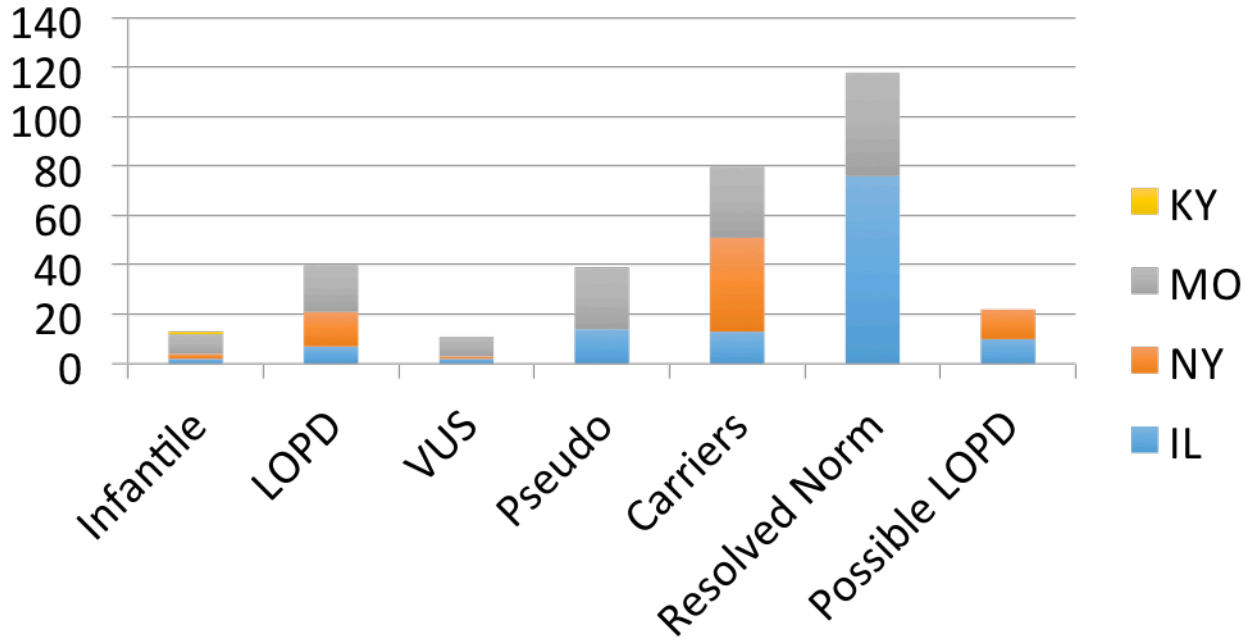
Pompe Newborn Screening Pilots

- Quarterly Clinician Focused Call
- Monthly Webinars – Discussion, Training, Information Sharing
  - 3 NICHD Sponsored Pilot States
  - 4 Screening States
  - 1.3 M Screened (March 2017)

PI	**State NBS**	**Screening Technology**	**Second Tier**	**Diagnostic**
Number Screened to Date	**Results**	**CLIR (Y/N)**	**Algorithm (Y/N)**	LPDR (Y/N)

Participation in Monthly Pilot Call





Sharing Experience and Expertise

- Parent and Clinician Education Materials
- Newborn Screening Workflows
- Screening Algorithms
- Diagnostic Algorithms
- Screening Technologies

Acknowledgements

- NewSTEPs is supported by Cooperative Agreement #U22MC24078 from the Health Resources and Services Administration (HRSA)
- The NBSTRN is funded by #HHSN275201300011C, awarded as a contract between the *Eunice Kennedy Shriver* National Institute of Child Health & Human Development, National Institutes of Health, and the American College of Medical Genetics and Genomics
- NBSTRN LSD Workgroup
  - Co-Chairs - Priya Kishnani, MD and Melissa Wasserstein, MD
  - Lori Wise, Barbara Burton, Michael Msall, Dieter Matern, Deekshea Bali, RonScott, Joe Orsini, Vamsee Pamula