Long-Term Follow-Up
National Projects

Heartland Genetics and Newborn Screening Collaborative Annual Conference

August 25, 2011

Amy Brower, PhD

Presentation Overview

- Long-Term Follow-Up
- Introduction of Data Set Development
- Data Capture Tool Development
- Emerging Efforts
  - SACHDNC Statements
  - Workgroups Focused on LTFU
  - Research Projects
# Screening Across the Life Course

## Newborn Screening

<table>
<thead>
<tr>
<th>Category</th>
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<td>Newborn Screening</td>
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<tr>
<td>Diagnostic</td>
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<td>Preconceptual</td>
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<td>Presymptomatic</td>
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<td>Predispositional</td>
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### Newborn Screening

- Comprehensive System
  - Screening
  - Diagnosis
  - Long-Term Follow-Up
- All of the conditions are chronic and require medical care and other related services throughout the affected individual’s lifetime
Newborn screening is one of the nation’s most successful public health programs.

Newborn screening programs test babies for disorders that are often not apparent at birth.

What to Screen For?

- Principles of population screening
  - Incidence of condition
  - Screening test
  - Treatment
  - Cost

- Newborn screening
  - Incidence
  - Screening test in newborn period
  - Treatment and/or benefit
From 1960 to 2005 the number of conditions screened varied from state to state

The American College of Medical Genetics (ACMG) recommended a uniform panel of 29 core conditions and 28 secondary conditions

Federal Advisory Committee created nomination and evidence review process to add new conditions to the panel

Currently 30 core conditions and 29 secondary conditions

Nomination and Review Process

Evidence Based Expansion

“Woe to the child which kissed on the forehead tastes salty. He is bewitched and will soon die.”

Northern European Folklore
Long-Term Follow-Up of Newborn Screening Patients

- Selected Milestones
  - HRSA Regional Collaboratives and NCC (2004)
  - Recommended Uniform Screening Panel (2005)
  - SACHDNC Statement on LTFU (2008)
  - NICHD NBSTRN (2008)
  - NICHD Hunter Kelly Newborn Screening Research Program (2009)
  - HRSA NCC Long-Term Follow-Up Data Collection Workgroup (2008)
  - CDC Surveillance Project (2008 – 2011)
  - Joint Workgroup – HRSA NCC LTFU and NICHD NBSTRN Clinical Centers Workgroup (2009)
  - SACHDNC Statement on LTFU (2011)

SACHDNC Statements on LTFU

- Key Features
  - Assurance and provision of quality chronic disease management
  - Condition-specific treatment
  - Age-appropriate preventive care throughout the lifespan of affected individuals

- Components
  - Care coordination through a medical home
  - Evidence-based treatment
  - Continuous quality improvement
  - New Knowledge discovery
Identifying, developing, and testing the most promising new screening technologies, in order to improve already existing screening tests, increase the specificity of newborn screening, and expand the number of conditions for which screening tests are available.

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

Public Law 110-204
Newborn Screening Saves Lives Act of 2007

Work in consultation with the appropriate State departments of health, and focus research on screening technology not currently performed in the States and conditions on the uniform screening panel.

Other activities that would improve newborn screening, as identified by the Director.

Health Outcomes

• Demographics
• SES
• Family History
• Prenatal History
• Neonatal History
• Birth Measurements
• Newborn Screening
• Hearing Screening
• Diagnostic Testing

Childhood

• Monitoring Labs
• Diet
• Therapies
• Emergency Management
• Developmental Screening
• Imaging Studies
• Intercurrent Complications

Adult

• Monitoring Labs
• Diet
• Therapies
• Emergency Management
• Imaging Studies
• Intercurrent Complications

• Create a uniform dataset for all conditions “80%”
• Create condition-specific datasets
NBS Stakeholders

- Pediatricians
- Family Physicians
- Metabolic Dieticians
- Pediatricians
- Family Physicians
- Metabolic Dieticians
- Screening Laboratories
- Follow-Up Programs
- IT Teams
- EDHI Teams
- State Public Health Departments
- Medical Providers
- Consumers
- Researchers
- Academic Centers
- Clinical Centers
- Federal Agencies
- Professional Societies
- Rare Disorders Network
- Patient
- Family
- Caregivers
- Community
- Advocacy Organizations
- Patient
- Family
- Caregivers
- Community
- Advocacy Organizations

Introduction of Long-Term Follow-Up Data Sets

- Joint effort
  - NCC/RC Long-Term Follow-Up Workgroup
    - Heartland - Julie Miller and Stephen Kaler
  - NBSTRN Clinical Centers Workgroup
- Objective
  - Develop minimum data set with accompanying informatics tools to
    - Enhance health services delivery
    - Empower research
    - Facilitate surveillance
- Scope
  - Conditions in current recommended newborn screening panel
Methodology

- Literature and Key Effort Review
- Stakeholder Engagement
- Expert workgroups
  - Hemoglobinopathies
  - Endocrinopathies
  - Metabolic Disorders
  - CF
  - Hearing Loss
  - SCID
  - LSD
- Standardization and Coding

Defining a Uniform Data Set

Intake
- Demographics
  - SES
  - Family History
  - Prenatal History
  - Neonatal History
  - Birth Measurements
  - Newborn Screening
  - Hearing Screening
  - Diagnostic Testing

Childhood
- Monitoring Labs
  - Diet
  - Therapies
  - Emergency Management
  - Developmental Screening
  - Imaging Studies
  - Intercurrent Complications

Adulthood
- Monitoring Labs
  - Diet
  - Therapies
  - Emergency Management
  - Imaging Studies
  - Intercurrent Complications
Locations of Information Exchange

Prenatal and Birth
- Prenatal Care
- Birthing Facility

Screening
- Public Health Laboratory
- Birthing Facility (Hearing)

Short-Term Follow-up
- Public Health Laboratory
- Reference Laboratory

Long-Term Follow-up
- Public Health Follow-up
- Medical Home
- Specialist
- Primary Care Provider

Basic, Translational and Clinical Research

Data Sets

- Clinical Data Set
- Research Data Set
- Public Health/Surveillance Data Set
Data Sets

- Demographics
- SES Measurements
- Genotype
- Imaging Studies
- Laboratory Studies
- Diagnosis
- Treatment
- Development

Next Steps

- Finish data sets
- Review with Effective Follow-Up Workgroup
- Transfer to National Library of Medicine (NLM)
- Stakeholder buy-in
- Data dictionary & standardized language
- Develop data collection tool
- Summarize, communicate and disseminate
- Pilot
Emerging Efforts

- PIDTC Data Set
- HRSA Categorical Models
- NYMAC Diagnosis Guide
- Industry Registries
- Disease Group Registries
- NORD Patient Registry

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<th>Information Source</th>
<th>LTFU Data Set Question/HRSA Topic Area/NYMAC Clinical Note</th>
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<td>Two disease-causing mutations</td>
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Public Health Focus - Data Categories Identified

- Subjective Summary – Well or Not
- Continuity of Care
- Patient Tracking
- Physical/Growth Parameters
- Access/Barriers to Care
- Services
- Health Status
- Review of Systems
- Disorder Related Interventions
- Developmental Assessment
- Subjective Summary – Well or Not
- Data Quality
Identified Questions

- Are we preventing or reducing morbidity/mortality without additional harm?
- Is there universal access to the program?
- Are we doing this in the most effective way?
- Are we doing this in the most cost effective way?
- Is the disorder on newborn panel?
- What percent of children with disorders remain in care between the ages of one and five years old?
- What percent become lost to follow-up?
- What percent of parents refuse treatment?

Questions

- What percent died due to problems associated with the disorder?
- What percent were determined not to need ongoing treatment?
- What percent of children (combined or by specific type of disease) had age appropriate developmental status with respect to speech, physical development, mental/cognitive development, gross motor and fine motor development?
- What percent of children were severely delayed with respect to any of the developmental measures and what year of life did the delays become apparent?
Questions

- What percent of patients experienced symptoms associated with their disorder and at what age did the symptoms become apparent?
- In any given year, what percent of children experienced the loss of skills they had previously acquired?
- What percent of children had no hospitalizations or emergency room visits in the previous year of life?
- What disorders are associated with the greatest number of hospitalizations and emergency room visits due to disorder-related complications?
- What disorders are associated with the highest utilization of metabolic center visits?
- What percent of children are receiving a multidisciplinary team of services, including nutritional counseling, health education and social services counseling?

Next Steps

- Survey meeting attendees to match public health data categories with LTFU data set elements
- Generate public health data set
- Disseminate public health data set
- Finalize public health data set
- Pilot
- Develop assessment measures
Data Capture Tool Development

Establish stakeholder relationships
- NBSTRN NCC (Brower)
- IBEMC (Berry, Hiner, Bentley, Cameron)
- Colorado (Thomas, Turtle)
- NLM (Zuckerman, Goodwin)
- HRSA (Therrell)

Gather requirements (IBEMC, Colorado)
Mock disease eCRF (MCAD)
Common data element (CDE) standards (Brower, NLM)
* Establish standards
* Validate standards
Create/obtain CDE data dictionary definitions
Implement dictionary viewer (see following)
CDE eCRFs (see following)
## Uniform Dataset

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**Newborn Screening Translational Research Network**

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## REDCap Modules

```
REDCap

Uniform Dataset
  - Informed Consent
  - Demographics
  - Initial Testing

Disease 1
  - Interval Assessment

Disease 2
  - Initial Testing
  - Interval Assessment
```

**Newborn Screening Translational Research Network**
REDCap Data Entry

- All common data elements have been entered
- Validation discussions happening now
- First disease specific set in progress

Data Dictionary

- Data dictionary will track definitions and accepted values for common data elements and each disease specific set of elements
In progress/upcoming

- Select pilot disease (FAO)
- FAO eCRF
  - Create eCRF
  - Add disease-specific definitions
  - Validation 1 (IBEMC)
  - Validation 2 (Colorado)
- Technical requirements
- Compliance/security requirements

Security Considerations

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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| With PHI | • Identity confirmation after search results  
  • Identity confirmation during data entry  
  • Downstream ability to link to VRDBS/DBS/Other  
  • No additional knowledge needed by providers, better enabling point-of-service data entry by any approved provider | • Substantially more development and maintenance effort/cost  
  • Likely will delay timelines for production system launches  
  • Other privacy issues |
| Without PHI | • Less development and maintenance effort/cost | • Ability to initially and persistently confirm identity is lost to the provider  
  • Reduced ability to update patient record based on knowledge at time of service |
FISMA Low Risks:
Record Finding

- "FISMA low" solution introduces substantial risk to data integrity in some situations
- No mechanism for confirming patient identity during lookup transaction
- No mechanism for constant confirmation of patient identity on data entry screens (next slide)
- Risk is slightly mitigated by using highly variable codes for patients

Newborn Screening Translational Research Network
SACHDNC Statements

Long-term follow-up after diagnosis resulting from newborn screening: Statement of the US Secretary of Health and Human Services’ Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children

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

- Need for expansion of vocabulary and coding guidance to include confirmatory testing

- Need for a standard messaging and coding approach to capturing common and condition specific follow-up datasets

- Need for education of primary care physicians about the value of HL7 NBS messages and including NBS in a lifetime medical record
HRSA NCC LTFU Data Workgroup

Newborn screening conditions: What we know, what we do not know, and how we will know it
Harvey L. Levy, MD

The context and approach for the California newborn screening short- and long-term follow-up data system: Preliminary findings
Lea Touchstone, PhD; MPH; Jasmine Hornway, MPH; and Fred Levy, PhD

Long-term follow-up of newborn screening patients
Susan A. Berry, MD; Michele A. Lloyd-Puryear, MD, PhD, and Michael S. Watson, PhD

Long-term follow-up in newborn screening: A systems approach for improving health outcomes
Michele A. Lloyd-Puryear, MD, PhD, and Amy Brown, PhD

Research Projects

- Pilot Newborn Screening Project for Identification and Prospective Follow-up of Infants with Spinal Muscular Atrophy
  - Kathy Swoboda – University of Utah

- Inborn Errors of Metabolism Collaborative: Defining the Natural History of Inborn Errors of Metabolism
  - Cynthia Cameron – Michigan Public Health Institute
Summer 2011 Apologies!

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