ACHDGDNC
Work Group on (Infant, Childhood and Adolescent Genetics and Newborn Screening) Research

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Range of Newborn Screening Questions [1]

- Systems
  - Outcomes in those identified by screening
  - Quality improvement
  - Health disparities across all parts of program
  - How to develop long-term follow-up program data
  - Capacity of system for expansion
  - Role of in-nursery point-of-care technology
  - **Natural/clinical histories of candidate diseases**
- Screening
  - New technologies for NBS
  - When to screen NICU infants after transfusions or hyperalimentation

Range of NBS Questions 2

- Short-term follow-up
  - True significance of false-positive or transiently abnormal screens
  - Outcomes in infants with markers of unclear significance
- Diagnosis
  - Preferred methods of diagnosis and confirmation
  - New technologies in NBS
- Management
  - Best treatments for many conditions
    - Carnitine in MCAD?
    - Managing non-classical CAH?
  - Expected outcomes after extended chronic disease management
  - Benefits of collaborative management
    - Medical home partnerships
  - Managing next group of maternal conditions impacting infants

Range of NBS Questions 3

- Education
  - How best to educate public as screening expands
- Pre-NBS Program Issues
  - What to include in screening?
    - Developing evidence base around all criteria on nomination form

Questions Beyond Newborn Screening

- Which conditions are amenable to screening at later times in life?
- Why do we screen?
- What is needed to adapt public health systems to life-long screening?
- How do we maximize the quality of and access to genetic services?

Developing the Evidence Base for Genetic Diseases

- Can use same infrastructure developed to track long term follow-up of NBS patients
- Requires level of detail beyond NBS LTFU
- Minimize impact of ascertainment bias on some criteria

Major Gaps in the System

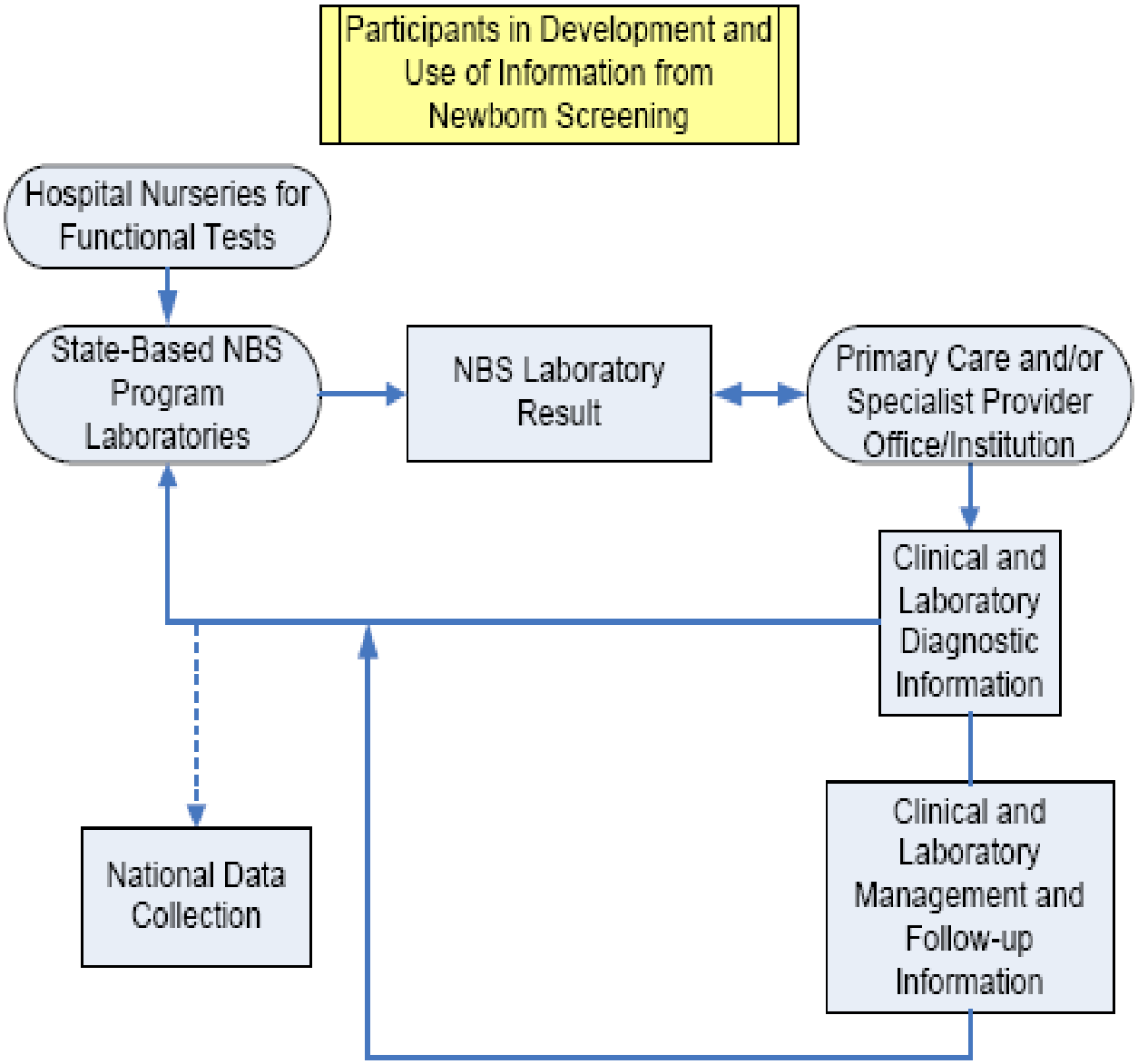
- Long-term outcomes of individuals identified in NBS
- Evidence base on genetic diseases to inform decision-making
- Data on validity of tests
- Capacity of States to absorb increasing numbers of conditions
- Best approaches to quality improvement (QI)
- Data Collection

Building a Data Collection Infrastructure

- Regional Collaboratives
- States
- Private sector providers
- Database needs
  - Federated and unfederated data to allow research and improved practice
    - HIPAA compliance and identifiable data
- Balancing the protection from harms against working towards the greater good

Opportunities

- Development of electronic health systems


Participants in Development and Use of Information from Newborn Screening
Hospital Nurseries for Functional Tests
State-Based NBS Program Laboratories
NBS Laboratory Result
Primary Care and/or Specialist Provider Office/Institution
Clinical and Laboratory Diagnostic Information
National Data Collection
Clinical and Laboratory Management and Follow-up Information

Organizations Involved

- HRSA
  - Regional Genetics and Newborn Screening Collaborative groups
    - Bridges between public health, primary care and specialists
  - National Newborn Screening and Genetics Resource Center (NNSGRC)
    - Mainly works with State labs and programs
      - Ongoing deidentified aggregate data collection from State programs
- NICHD
  - Newborn Screening Translational Research Network
    - Data collection
- CDC
  - Surveillance
  - Epidemiology
- States

Sources of Information

- After Diagnosis is Established Data is Needed From?
  - Families
  - Providers
  - Public health labs

The Minimal Information That Must Flow Among Participants

- Newborn Screening Program Reporting to Providers
  - Screening test results
    - analytes and analyte levels
    - laboratory reference ranges due to significant variability in methods and ‘case’ definitions
    - result interpretation
  - May include providers accessing NBS results prior to having received notification from program
- Diagnosis Providers Reporting to NBS Program/Primary Care
  - Laboratory diagnostic information
    - Enzymology
    - Mutations
    - Analytes, analyte levels and reference ranges
  - Clinical Information
    - Disease specific phenotype information

Communication and Information Needs of Participants

- Interoperable electronic communication systems between primary care providers, specialist providers in private or institutional environments and State programs
- Standardized laboratory and clinical languages to allow data compatibility
- Protocols to drive data compatilibility

Additional Information Related to Diagnosed Patients and Use of Data

- Long-term outcomes to inform program
- Long-term follow-up and management details to inform evidence base
  - Natural history of treated disease
  - 2nd generation treatment clinical trials

Issues to Address to Realize Goals

- State sovereignty vs. realistic scientific needs for as many cases as possible to be gathered
- Databases
  - Standardizing laboratory and clinical languages for EMR compatibility
    - HHS to use NBS as a model
  - EHRs to support patient needs
- Systems
  - Role of NCC/RC system will be critical
  - Development of system (s)
  - Data collection
  - National dried blood spot repositories

Meetings and Programs Planned to Inform Research Agenda

- Policy issues for States in developing national dried blood spot repositories and shared data (HRSA)
- National Collaborative Study in Rare Genetic Diseases (NICHD)
- Newborn Screening Translational Research Network (NICHD)
- Newborn Screening Translational research Initiative (CDC)
- Meetings with EMR AND CDS Developers (HRSA)

Organizing the Research Work Group

- Define participants
- Capturing research needs identified by ACHDGDNC subcommittees
- Identifying knowledge gaps as identified by evidenced-based reviews

Thank you

Addendum

National Collaborative Research in Rare Genetic Disease

National Data Collection: Principles and Recommendations

- Establish a clinical research enterprise built on open communication strategies and on trust

- Employ multifaceted approach to clinical research, including natural history studies, population studies, epidemiology, genotype-phenotype correlations, and clinical trials

- Use a wide range of research approaches to address the distinct issues raised by different disorders

National Data Collection: Principles and Recommendations

- Establish partnerships that include communities, patient advocacy groups, local, state, national and international authorities, industry, and a diverse array of medical and public health professionals, to address long-term translational research needs.
- Assemble an open source toolkit for translational research on genetic disorders to enable the establishment of:
  - Accessible repositories of well-curated biological materials
  - Registries of affected individuals who may be recruited as participants for clinical studies
  - Systematic phenotypic assessment and analysis of environmental influences using standardized vocabularies and ontologies that underlie electronic health info systems
  - Flexible and appropriate data collection (historical and prospective), retrieval and communication, among different investigators/studies

National Data Collection: Principles and Recommendations (2)

- Develop models that permit the creation of widely dispersed but tightly integrated translational research networks.
- Professionals and lay communities will require training to enable active participation in translational research and clinical trials.
- Advocate for modification of the system of ethical review that will facilitate multi-center translational studies and clinical trials.

National Data Collection: Principles and Recommendations (3)

- Establish models for the handling of intellectual property; provide incentives for innovation and access to discoveries for clinical application
- Establish mechanisms to ensure that clinical research leads not only with the cutting-edge science, but with the high touch of human interactions that value and empower patients as active, informed and respected partners
  - As part of the research process, participants are informed of relevant outcomes and progress of research studies in which they take part in a timely manner, and prior to any publication.