Population Screening: Lessons Learned from the Advisory Committee on Heritable Disorders in Newborns and Children

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The beginning of newborn screening

- **PKU**
  - 1961 – pilot studies
  - 1963 – Massachusetts mandated screening
  - 1975 – 43 states had passed laws requiring screening
Newborn Screening

- State based public health program
- Advantages
  - Equity
  - Laboratory standards
  - Uniform approach (efficiency)
  - Responsibility
    - Ensures optimal quality for all newborns
    - Urgency
    - Organization – diagnosis and follow-up systems in place
Population based newborn screening: some important/unique issues

- Conditions are rare
- Newborn is asymptomatic
- Mandated
  - Does not arise from a parent’s request
  - Opt-out
Population based newborn screening: some important/unique issues

- Screening must be seamlessly followed by
  - Diagnostic testing
  - Short term follow-up
  - Long term follow-up
- Potential harms of false positive results, diagnostic procedures, treatment
- Opportunity costs
Pressures on NBS System

- Advances in technology
- Advances in diagnosis
- Advances in treatment
- Interest groups and advocates
- Changing environment
- Competing needs for public health funds
Newborn screening evolution

- Advancing technology
  - Tandem mass spectrometry
  - 2003 - Individual state newborn screening panels varied from 3 to 45 conditions

- AAP, ACMG, Health Resources Services Administration (HRSA) recommended the establishment of a standardized evidence based approach to newborn screening and conditions included on the screening panel
Advisory Committee on Heritable Disorders in Newborns and Children

- Federal Advisory Committee
  - Established by Congress in 2000
  - Reauthorized in 2015 (ACHDNC)
  - 15 members
    - NIH, FDA, CDC
    - HRSA, AHRQ
  - Organizations
    - AAP, AAFP, ACMG, APHL, ASTHO, MOD, SIMD
Routine Uniform Screening Panel (RUSP)

- 2005 – American College of Medical Genetics expert panel recommended screening for 29 core conditions with reporting of 25 additional secondary conditions

- 2005 - SACHDNC recommended the panel to the Secretary of Health and Human Services
CDC: Ten Great Public Health Achievements — United States, 2001–2010

- **Maternal and Infant Health**
  - Reduction in neural tube defects
    - Folic acid
  - Expansion of screening of newborns for metabolic and other heritable disorders

*MMWR 2011;60(19):619-23*
States screening for the core bloodspot conditions in the RUSP

- **Results:**
  - >98% of infants born in the US screened
  - ~12,500 diagnosed with one of the 29 core conditions
  - Overall cost: $30/infant

*MMWR 2012;61(21):390-393*
Conditions Nominated for the RUSP since initial panel approved

- **Recommended by ACHDNC and approved by the Secretary**
  - SCID (2010)
  - Critical Congenital Heart Disease (2011)
  - Pompe (2015)
  - MPS 1 (2016)
  - ALD (2016)

- **Not Approved by ACHDNC**
  - Pompe (2008)
  - Fabry Disease (2008)
  - Niemann-Pick Disease (2008)
  - Spinal Muscle Atrophy (2008)
  - Krabbe Disease (2009, 2010)
  - ALD (2010)
  - Hemoglobin H Disease (2010)
  - 22q11.2 Deletion Syndrome (2012)
  - Neonatal Hyperbilirubinemia (2012)
Universal Screening Status of the 34 Core Disorders (April 2017)
ACHDNC: Choosing conditions recommended for the RUSP

- Define and develop a standardized and transparent approach to
  - condition nomination
  - evidence review
  - decision-making process
- Involve all stakeholders
ACHDNC: Condition Review Process

Nomination Package Submitted → HRSA Review → N&P Workgroup Review → Full Committee Vote

- If sufficient evidence - Condition Review Workgroup
  → Full Committee Vote
  → Recommend to the Secretary to add the condition to the RUSP
  → Secretarial Action: Add or not add the condition to the RUSP

- Not sufficient evidence to move the condition forward to the CRWG.
- The condition is not ready for inclusion to the RUSP.
- Secretary may send recommendation to the ICC for further review.

9 months for CRWG to review and for the AC to vote.
Assessment of impact on public health system

- Stakeholder meeting – April, 2014
- Policy approved by AC – May, 2014
  - Assessment of readiness and feasibility of implementing comprehensive NBS from the state public health department perspective
    - MPS1 – first condition review with public health system impact included
Issues related to systematic review for rare conditions

- Paucity or absence of randomized clinical trials
- Limited outcomes data
- Limited data on effectiveness of intervention prior to onset of symptoms vs after symptoms develop
- Unpublished data
- Ability to characterize potential benefits and harms
- Ability to adequately study the cost to system
- Ability to determine adequacy of work-force
Components of Condition Review

- Systematic evidence review
- Decision analysis - model harms and benefits
  - Estimation of bounds of benefit and harm
- Public health system impact
  - Cost analysis being added
Decision Analysis/Modeling

- A systematic approach to decision making under conditions of uncertainty
- A decision analytic model (or decision tree) is used to define a set of alternatives and short- and long-term outcomes associated with each alternative
  - Projects a range of health outcomes under various screening assumptions
  - Identifies key areas of uncertainty
- Can project estimates of how screening would likely impact public health of the overall population
  - e.g. estimate impact of newborn screening on prevalence (Prosser et al., 2012)
Public Health Impact: Feasibility and Readiness

- Technical and Clinical Feasibility
  - Established screening test
  - Clear approach to diagnostic confirmation
  - Accepted treatment
  - Plan for long-term follow-up

- Readiness
  - Availability of resources for screening, diagnostic confirmation, long-term follow-up and treatment
  - Authorization for screening
Assessment of public health impact: APHL role

- Development of a factsheet related to the nominated condition
- Webinar to educate state programs
- Survey to 53 US states and territories
  - Identify barriers and facilitators
  - Evaluate opportunity costs
- Interviews with NBS programs currently screening or planning to screen
Cost Assessment

- Determine validated screening procedures for high-throughput screening for the target condition
- Identify states which have considered expansion/conducted initial cost estimates
- Complete the NBS Cost Estimation for Expansion Instrument
- Summarize Cost Estimate Information
- Incorporate summaries of cost assessment into Condition Review Report
<table>
<thead>
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<th>NET BENEFIT</th>
<th>READINESS</th>
<th>FEASIBILITY</th>
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<tbody>
<tr>
<td>Significant Benefit</td>
<td>High Certainty</td>
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<tr>
<td>A1</td>
<td>Ready</td>
<td>Screening for the condition has a high certainty of significant net benefits, screening has high or moderate feasibility, and most public health departments are ready to screen.</td>
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<tr>
<td></td>
<td>Developmental</td>
<td>Screening for the condition has a high certainty of significant net benefits and screening has high or moderate feasibility. However, public health departments have developmental readiness.</td>
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<tr>
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<td>Unprepared</td>
<td>Screening for the condition has a high certainty of significant net benefits and screening has high or moderate feasibility. However, public health departments are unprepared for screening.</td>
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<td>Low Certainty</td>
<td></td>
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<tr>
<td>A4</td>
<td></td>
<td>There is high certainty that screening would have a significant benefit; however, most health departments have low feasibility of implementing population screening.</td>
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<td>Moderate Certainty</td>
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<td>B</td>
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<td>There is only moderate certainty that screening would have a significant benefit.</td>
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<td>Small to Zero Benefit</td>
<td>High or Moderate Certainty</td>
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<td>There is high or moderate certainty that adoption of screening for the targeted condition would have a small to zero net benefit.</td>
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<td>Negative Benefit</td>
<td>High or Moderate Certainty</td>
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<td>There is high or moderate certainty that adoption of screening for the targeted condition would have a negative net benefit.</td>
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<td>There is low certainty regarding the potential net benefit from screening.</td>
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Public Health Challenges with Recent AC Decisions

- Point of Care Testing - CCHD
- Addition of disorders with early and later onset variants
- Readiness
  - Legislative authority
  - Finances
  - New technology
  - Infrastructure
Key Points

- Responsibilities of policy makers
  - Understand the limitations of the evidence
  - Be aware of issues facing programs
    - Understand barriers
  - Develop policies which
    - Are based on current evidence
    - Ensure safe and appropriate growth of programs
Key Points

Collaborative efforts between parent advocates, advocacy groups, professional organizations, investigators, federal advisory committees and state public health programs are needed to successfully improve the health of newborns and children through newborn screening.

R. Rodney Howell, MD
Founding Chairman, SACHDNC, 2005-2012
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