Evaluation of newborn screening for Spinal Muscular Atrophy: A policy analysis prepared for the Washington State Board of Health

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- Genetics
  - 1/10,000 births (8-9/year in WA)
  - 1/75 people carry one copy of the defective gene (SMN1)

- SMN1 gene protects nerve cells needed for movement
  - Functional nerves die off due to lack of protection
  - Extra copies of a separate gene (SMN2) provide some protection
  - 94% have same mutation in SMN1
- **Clinical Symptoms**
  - 50-60% Develop symptoms before 6 months
    - Many appear normal at time of birth
    - Develop weak cry, poor suck and swallow
  - 40-50% develop symptoms after 6 months
    - Lose ability to sit or walk
    - Develop difficulty coughing and breathing
  - 5% develop symptoms in adolescence
- Diagnosis confirmed with genetic testing
- SMA added to Recommended Uniform Screening Panel (RUSP) in July
Evaluation of a candidate condition for the Washington newborn screen

Five criteria must be met in order for a condition to be added to the NBS:

- Screening test(s) are available
- Diagnostic testing and treatment are available
- Newborn detection of the condition allows early diagnosis and intervention
- Nature of the condition justifies population-based screening
- Benefits of treatment outweigh costs of screening
Adding a new condition to the newborn screen (NBS)

Request to State Board of Health (Board) to add condition to NBS

TAC reviews condition against 3 guiding principles and 5 inclusion criteria

The Board adds condition to the list of required conditions

The Board convenes Technical Advisory Committee (TAC)

TAC makes a recommendation to the Board to add the condition

Legislature approves funding to screen new condition
Sensitive, specific, and timely tests available and can be adapted to mass screening

- Centers for Disease Control and Prevention (CDC) developed assay
  - Essentially no false positives, 94% sensitive
  - Does not identify carriers or rare mutations of SMN1 gene
  - Technical assistance available

- CDC assay can be multiplexed with existing Severe Combined Immunodeficiency (SCID) screening test

- Second tier screen to detect SMN2 copy number
Diagnostic testing and treatment available

- Diagnostic testing:
  - No confirmatory diagnostic test needed for positive screen
  - Further testing available for children with symptoms who had negative screens (~1 every 2 years)

- Treatment:
  - 3 children’s hospitals in Washington offer coordinated care
    - PT/OT/Pulmonary/Rehabilitation
  - Nusinersen (Spiranza) approved for use in 2016
    - Only available at Seattle Children’s Hospital
    - 6 doses in first year, 3 doses/year in following years
Findings: Criteria 2

Sites for treatment and therapy

*Seattle is the only site which offers nusinersen
Prevention potential and medical rationale

● Neuron destruction is progressive and starts from birth
  ○ Without screening, diagnosis occurs once symptoms have appeared

● Treatment with nusinersen has been shown to improve symptoms in 50% of symptomatic children who start treatment before 7 months

● Unclear how to counsel parents of children with 0 SMN2 copies (likely not candidates for nusinersen therapy) or higher number of SMN2 copies (may never develop disability)
Public health rationale

- Most cases have no family history to suggest carrier screening or prenatal testing

- Pan-ethnic disorder, males and females affected equally

- Carrier frequency is high and similar to other autosomal recessive disorders included in the screening panel, e.g., cystic fibrosis

- Initiating treatment early will likely decrease care needs and increase potential productivity
Cost-benefit/Cost-effectiveness

● Cost
  ○ Screening: NY estimated SMA screen to add $0.10 to cost of NBS (currently ~$100) when multiplex with SCID. Some estimates up to $1
    ■ 90,000 births/year in WA—$10-90,000/year in additional cost
  ○ Cost to care for child with SMA ranges from $100,000-200,000/year
  ○ Treatment: Nusinersen costs $750,000 in the first year, $375,000/year thereafter
    ■ Long term studies required to understand cost savings of early diagnosis/treatment

● Cost/benefit considerations:
  ○ Prevalence in Washington state:
    ● ~9 affected babies born annually
    ● 1/20 would not have developed symptoms until adolescence or adulthood
      ○ Positive screening test could increase distress/medical costs compared to no-screening
Recommended stakeholders for Technical Advisory Committee

- Medical providers
  - Pulmonary, Rehabilitation medicine
  - Seattle Children’s Hospital, University of Washington Medical Center
- Bioethicists
- Families and friends
- Advocacy organizations
  - Cure SMA
  - Muscular Dystrophy Association
  - Saving Babies Through Screening Foundation
- Health plans
  - Washington State Healthcare Authority (Medicaid, public employees)
  - Regence, Premera, Kaiser Permanente
- Tribal health organizations
- Other state public health agencies
  - Washington State Board of Health
  - Washington State Department of Health
Summary

SMA is a progressive neurologic condition affecting ~ 9 newborns/year in WA

SMA can be identified easily using available genetic screening tests

Early treatment with nusinersen can slow or stop progression of the disease

SMA meets criteria to move forward with convening a Technical Advisory Committee
Thank you!!
# Background: SMA types

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<th>Type</th>
<th>Age of Onset</th>
<th>Respiratory Support at Birth</th>
<th>Sit</th>
<th>Stand</th>
<th>Walk</th>
<th>Life Expectancy</th>
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