Implementation and One Year of Screening for Spinal Muscular Atrophy: The Minnesota Experience

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SMA Panel Addition Timeline

**National/Federal**

- **2016**: CDC asked us to partner with them to develop a screening method
- **2017**: Dec 2016: Spinraza approved by FDA
- **2018**: May 2017: Federal committee recommends SMA go to evidence review
- **2019**: July 2018: Secretary of HHS approves recommendation; SMA added to the RUSP

**Minnesota**

- **2016**: Jul 2016: We meet with SMA specialists in MN; SMA slotted for discussion at next advisory committee meeting
- **2017**: Aug 2016: Parent advocate engages with us
- **2018**: Apr 2017: Advisors hear presentations from specialists, screening lab, and parent advocate
- **2019**: Oct 2016: Advisors hear first presentation from SMA specialists in MN and provided parent testimony

- **Feb 2017**: SMA submitted to the HRSA for the 2nd time requesting addition to the RUSP
- **Feb 2018**: Federal committee recommends adding SMA to the RUSP
- **Mar 2018**: Screening for SMA begins in MN
- **Dec 2017**: Commissioner of Health approves committee recommendation
Prior to Implementation

• Stakeholder Engagement
  • SMA workgroup created
    • Clinicians
    • Newborn Screening Staff (Lab, Short Term Follow-up, & Operations)
    • Child and Family Health-Long Term Follow-up
    • Families
  • Workgroup discussion/advice for diagnostic form and data collection
    • Confirmatory results and diagnosis (not categorizing into SMA types)
    • Treatment information and symptoms
    • Condition specific data for long term follow-up
    • Developing condition specific information/fact sheets for families/providers

• Implementation Meetings- Internal Only
  • Weekly meetings and after implementation debriefing
SMA Screening Test
Normal vs Positive Result

Normal – *SMN1* Present

Positive – *SMN1* Absent
SMA Cut-off Criteria

SMA Screen (qPCR)

- **Positive**
  - SMN1 Cq ≥ 30.00 or UND
  - and RNaseP Cq < 28.00
  - Refer to diagnostic

- **Inconclusive**
  - SMN1 Cq ≥ 30.00 or UND
  - and RNaseP Cq ≥ 28.00 or UND
  - Request a repeat dried blood spot

- **Within Normal Limits**
  - SMN1 Cq < 30.00
  - and RNaseP Cq < 28.00
Population Median

**SMN1 Population Median**

SMA Runs 3/1/2018 to 3/1/2019
• All positive specimens had zero amplification
  • Clear cut results

• Multiplexing with SCID is very helpful
  • Poor quality samples tend to have late amplification for TREC, RNaseP, and SMN1
    • No inconclusive results were reported

• Does not detect/identifies carriers
Limitations of Screening Assay

• Does not find point mutations (i.e., compound heterozygotes)
  • Result output will look within normal limits and there will be false negatives (approximately 5%)

• Does not find SMN2 copy numbers
  • SMN2 copy number is determined clinically during confirmation of SMN1 results
Follow-up Experiences
Outcomes

- 8 positive results 3/1/2018 to 3/1/2019
- 66,062 infants screened → Incidence of 1:8,258
- Previously reported incidence of 1:6,000 to 1:10,000
- All positive results have confirmed
- $SMN2$ copy numbers have ranged from 2 to 4
- Symptomatic but not yet diagnosed family member has also been identified because of positive screening result
Timeliness (from date of birth)

- Time to evaluation:
  - Median = 12 days
  - Range = 8 days to 15 days

- Time to treatment/first injection:
  - Median = 16 days
  - Range = 11 days to 66 days
Lessons Learned

• **Early Collaboration with the CDC**
  - Collaboration started in 2016 and allowed the lab to be prepared for the addition of SMA

• **Communication, Communication, Communication**
  - Internal communication always has room for improvement
  - Project manager for implementation would be helpful

• **Gene Therapy Availability**
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