Proposed: ACHDNC Nomination Package Revision

January 29, 2024

ACHDNC
Secretary's Advisory Committee on Heritable Disorders in Newborns and Children

Current Nomination Process Challenges

- Burden on nominators to put together the nomination package
  - In some cases, weeks/months of work for a condition not ready for evidence review
- Unclear terminology in the nomination package
- No area on nomination form to share additional information
- ACHDNC N&P workgroup oftentimes do not have sufficient information to recommend the package to full-evidence based review

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Step 1: Preliminary Nomination

1. Is there a screening test available for use at a population level in the newborn period?

2. Is there an agreed upon way for a clinical specialist to confirm the diagnosis after a positive screen?

3. Is there a prospective, population-based newborn screening project that has identified at least one infant with the condition?

4. Does early identification through newborn screening lead to better health outcomes compared to usual clinical identification?

   If there is not information about health outcomes from newborn screening, does early identification based on family history, such as resulting from having an older sibling with the condition, lead to better health outcomes compared to usual clinical identification?

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Step 1: Preliminary Nomination

- If “yes” to all 4 questions, nominators submit 1-3 peer-reviewed publications for each question to HRSA website
- HRSA staff meet with nominators to gather information
- HRSA staff present information to the ACHDNC Chair and selected committee members
- After hearing information and reviewing the publications, the Chair/committee members provide feedback to the nominators on the readiness for Step 2
- Glossary of terms to help nominators (e.g. “population level”)

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Step 2: Complete Nomination Package

- Section I: The Condition
- Section II: Newborn Screening
- Section III: Net Benefit of Newborn Screening
- Section IV: Other Considerations
- Section V: References
- Section VI: Glossary of Terms
- Section VII: Potential Benefits/Harms of Newborn Screening

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Step 2: Complete Nomination Package - Instructions

- Please answer each of the questions below as clearly and succinctly as possible.
- The ACHDNC does not expect nominators to be able to provide comprehensive answers to all questions, particularly those regarding potential harms and public health impact. The ACHDNC will use the information you provide to decide whether there is enough peer-reviewed evidence of net benefit to proceed to a full evidence review.
- For each key point you make, please identify the one or more most relevant peer-reviewed references.
- A glossary of terms can be found in Section VI.
- We encourage nominators to keep in touch with HRSA staff as they complete this second stage, as you will likely have questions about how to answer some of these questions. Please contact us at ACHDNC@hrsa.gov.

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Section 1: The Condition

1. What is the specific condition to be screened for (“target condition”) and how is it defined after screening?
2. How is the condition typically diagnosed now without newborn screening?
3. What is the birth prevalence of the condition in the United States or comparable population? Is the condition more common in certain groups in the United States?
4. What is the typical progression of the condition when diagnosed without newborn screening?

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Section II: Newborn Screening

1. What approach is recommended for newborn screening? Please be specific regarding the type of sample and screening algorithm leading to diagnostic referral?

2. How is the condition diagnosed after a positive newborn screen? Describe the steps that a clinical specialist would need to take to establish the condition

3. What other conditions could be identified through screening for the target condition as nominated? This includes phenotypes of the target condition that are not being nominated for newborn screening (e.g. late-onset, mild variants). Will screening for the target condition identify carriers?

4. Please describe the approach and outcomes from population-level screening for the condition. Outcomes of interest include estimation of the birth prevalence, and the frequency of identification of other phenotypes or conditions, screening test characteristics (e.g., sensitivity, specificity, positive predictive value, negative predictive value).

Section III: Net Benefit of Newborn Screening

1. What is the expected benefit to infants and families for detection of the condition through newborn screening compared to usual clinical identification?

2. If known, are there potentials harms to infants and families for detection of the condition through newborn screening compared to usual clinical identification?

3. If known, are there other benefits (or harms) that may result from implementing a state newborn screening program for the targeted conditoin (e.g. infants identified with other conditions, or opportunity costs to a state public health system)?

4. What treatment and management protocols are available for newborns identified with the condition through newborn screening?

5. Is there a plan for longitudinal follow-up of newborns identified through newborn screening? For example, will there be a patient registry? For how many years would infants with the condition be followed?

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Other Sections

- Section IV: Other Considerations
  - Additional information for ACHDNC
- Section V: References
- Section VI: Glossary of Terms
- Section VII: Potential Benefits/Harms of Newborn Screening
  - This table is designed to help nominators consider the full range of benefits and harms that may occur with state newborn screening programs.

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ELSI Research Questions

Table 1 Sample ELSI research questions

Key ELSI questions	Potential data sources	Sample ELSI research questions
Issues related to NBS results		
What are the potential ELSI of positive screening results related to a new condition?	•Families •Clinicians •Administrative databases	•Do caregivers treat an infant differently when a presymptomatic diagnosis is made? •What are the potential harmful or beneficial effects of an NBS diagnosis on maternal–infant bonding or other family dynamics? •Are there potential harms from subsequent diagnostic testing (which may be invasive) and treatment and how do these harms impact the net benefits of screening? •What are the financial costs of diagnosis and follow-up? What is the system-wide cost?
What are the potential ELSI implications of false positive screening results related to a new condition?	•Families •Clinicians •Administrative databases	•Do caregivers treat an infant differently as a result of receiving a false positive screen result? ◦Are there long-lasting psychological consequences for a positive screening test in infants who do not have a condition? What is the effect of a false positive on maternal–infant bonding?

*Goldenberg, et al. "Including ELSI Research Questions in Newborn Screening Pilot Studies" Genetics in Medicine, 2018

Discussion