



Washington State Board of Health

Overview of BCKDK Deficiency and Criteria Review

Kelly Kramer, Policy Advisor – March 12, 2025

WASHINGTON STATE 
BOARD OF HEALTH

Overview

- Branch Chain Keto Acid Dehydrogenase Kinase Deficiency Review
- Voting Results
- Review of Criteria to Evaluate Conditions for the Newborn Screening Panel
- Voting Results



Background: Branch-Chain Ketoacid Dehydrogenase Kinase (BCKDK) Deficiency

- Senate Bill 6234 (2024 legislative session)
 - Directed the Board of Health to conduct a review of BCKDK Deficiency to determine if this condition should be added to our mandatory newborn screening panel
- No state program screens for BCKDK
- Federal Recommended Uniform Screening Panel has not reviewed



Overview of BCKDKD

- Branch-chain ketoacid dehydrogenase kinase deficiency (BCKDKD)
 - Rare, genetic amino acid disorder
 - 21 cases identified worldwide
 - Characterized by epilepsy, autism and intellectual disability
 - Reduced levels of branched chain amino acids
 - Prevents protein production, inhibits development and growth
- Screening method
 - Tandem mass spectrometry using dried bloodspot
 - Low amino acid levels
- Diagnostic Test
 - Plasma amino acid test
 - DNA testing
- Treatment for BCKDKD:
 - High protein diet
 - Supplement branch-chain amino acids



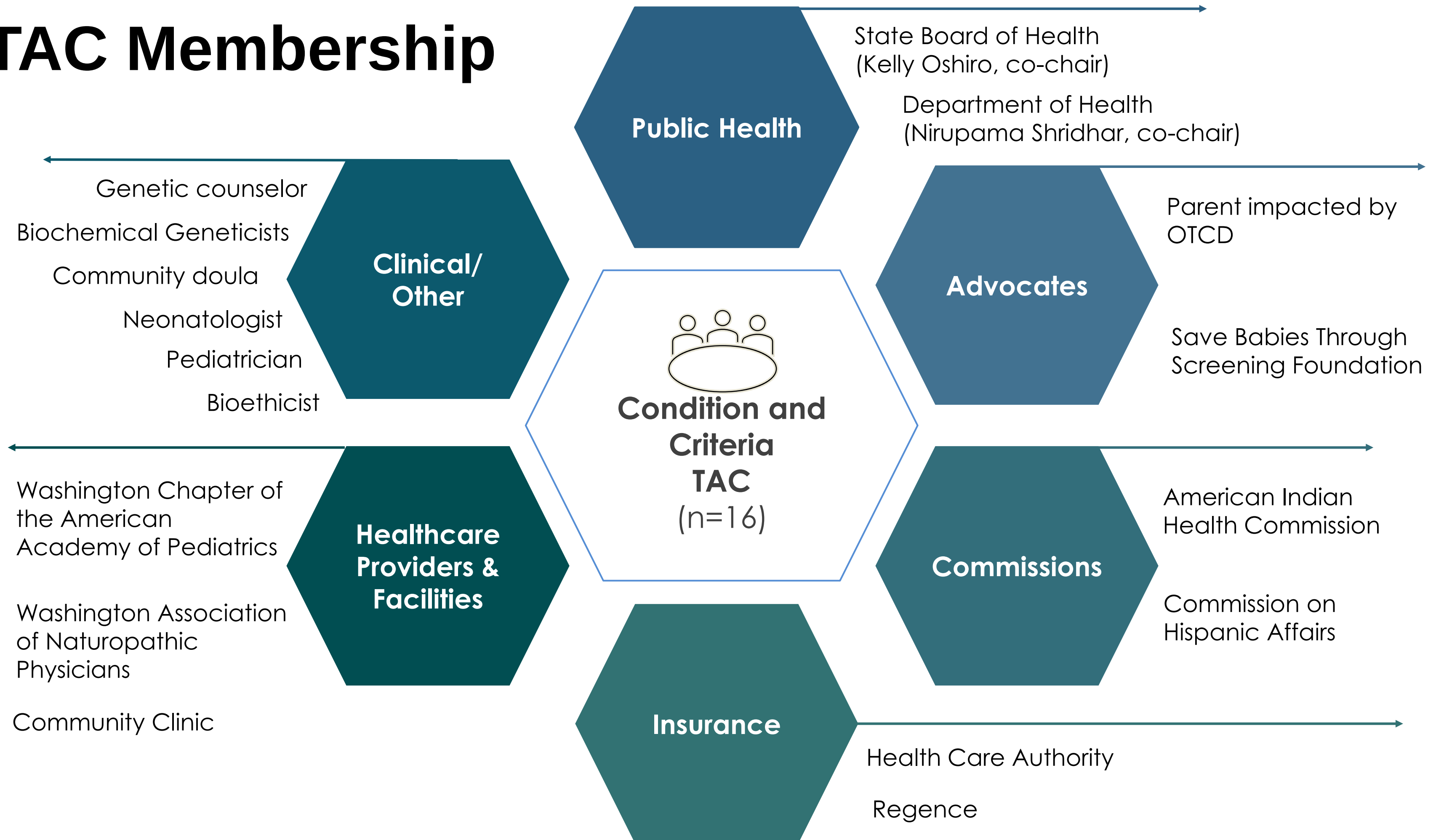
- Novarino G, et al. Mutations in BCKD-kinase lead to a potentially treatable form of autism with epilepsy. *Science*. 2012 Oct 19;338(6105):394-7. doi: 10.1126/science.1224631. Epub 2012 Sep 6. PMID: 22956686; PMCID: PMC3704165.
- Trine Tangeraas, et al BCKDK deficiency: a treatable neurodevelopmental disease amenable to newborn screening, *Brain*, Volume 146, Issue 7, July 2023, Pages 3003–3013, <https://doi.org/10.1093/brain/awad010>

Cost Benefit, Cost Effectiveness Analysis

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Policy Analyst for the Department of Health's
Newborn Screening Program



TAC Membership

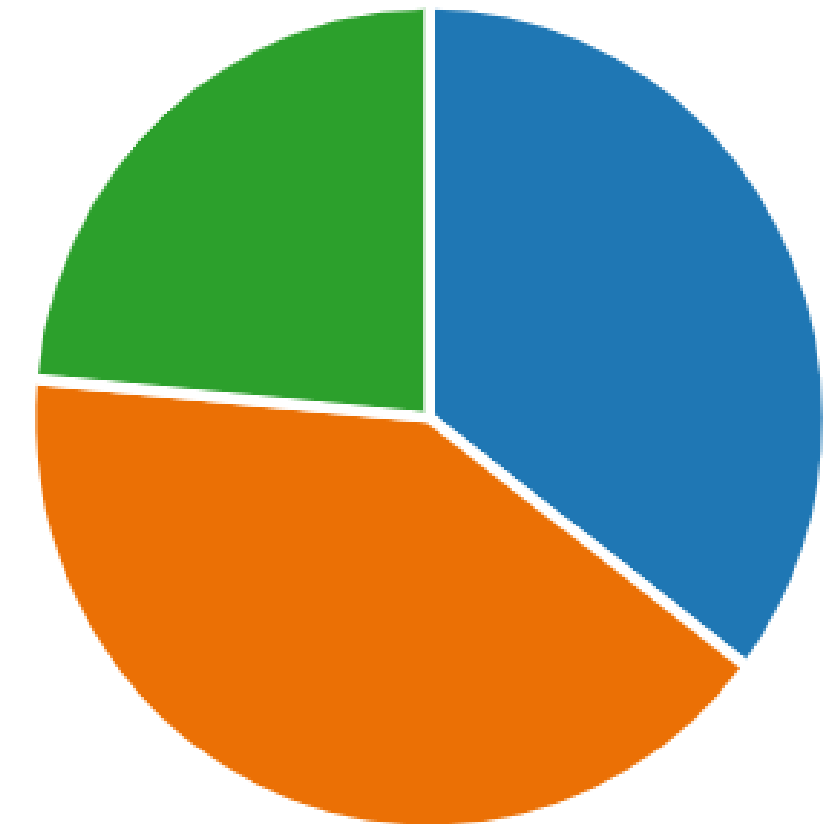
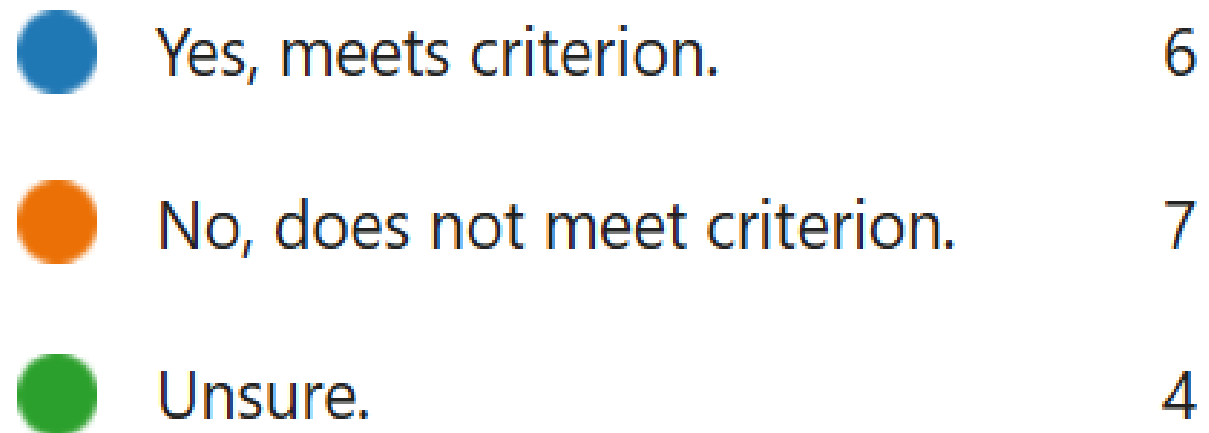


1. Available Screening Technology

Sensitive, specific, and timely tests are available for the condition that can be adapted to mass screening.

Screening test: tandem mass spectrometry

Analyte: low branch chain amino acids



Themes:

Screening technology is available, but performance, i.e., sensitivity and specificity, are unknown.

2. Diagnostic Testing and Available Treatment

Accurate diagnostic tests, medical expertise, and effective treatment are available for the evaluation and care of all infants identified with the condition.

Diagnostic tests: plasma amino acids, genetic testing
Treatment: high protein diet, supplementation

● Yes, meets criterion.	6
● No, does not meet criterion.	6
● Unsure.	5

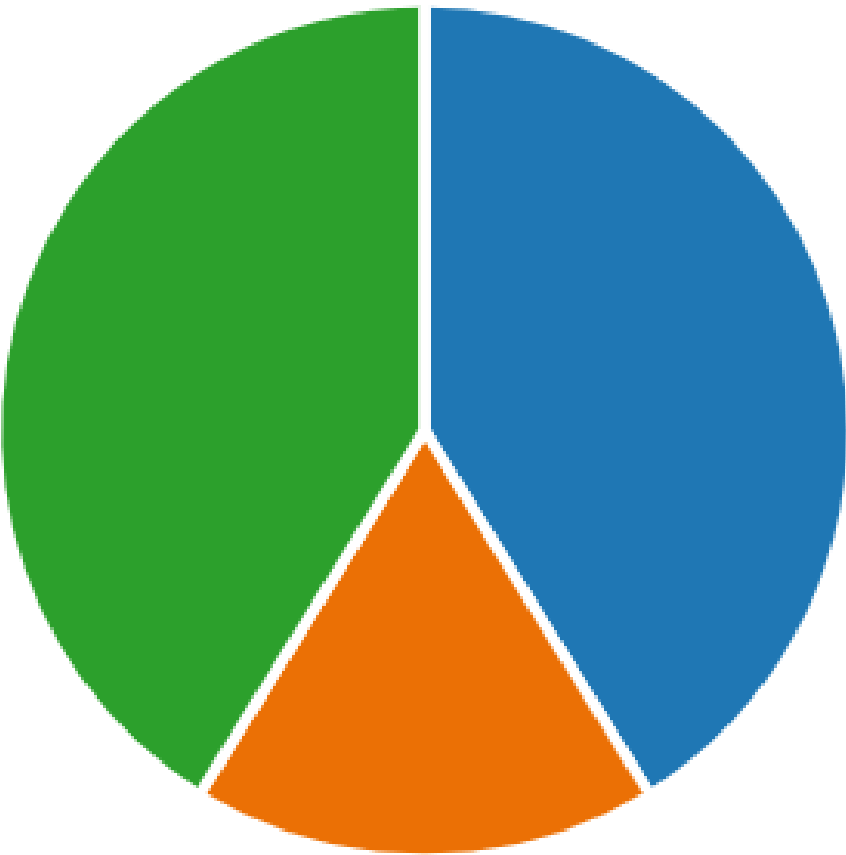
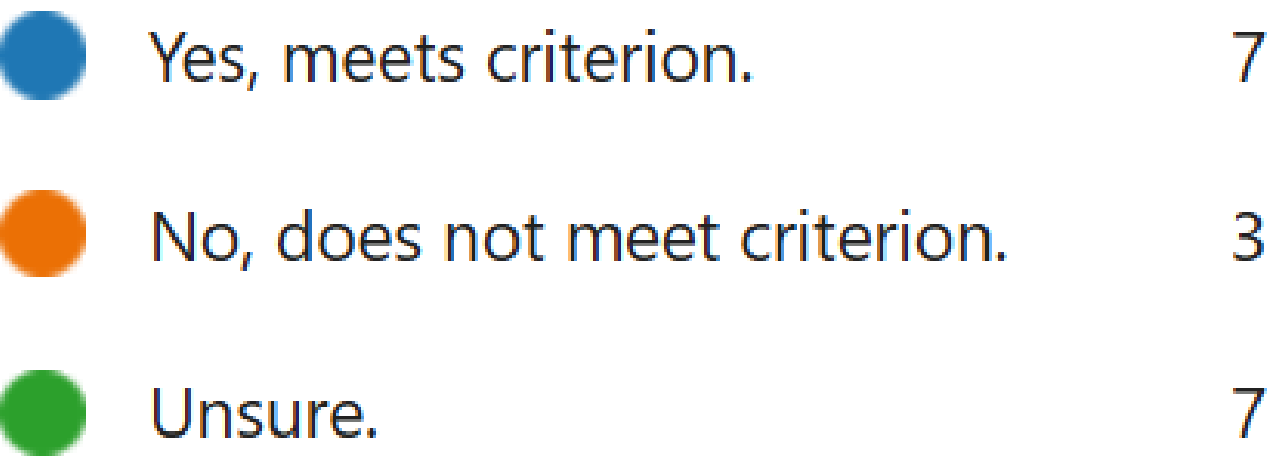


Themes:

Limited data on the effectiveness of follow-up care and outcomes for early diagnosis of BCKDK deficiency.

3. Prevention Potential and Medical Rationale

The newborn identification of the condition allows early diagnosis and intervention.



Themes:
Limited data in literature.

4. Public Health Rationale

The nature of the condition justifies population-based screening rather than risk-based screening or other approaches.

● Yes, meets criterion.	2
● No, does not meet criterion.	12
● Unsure.	3

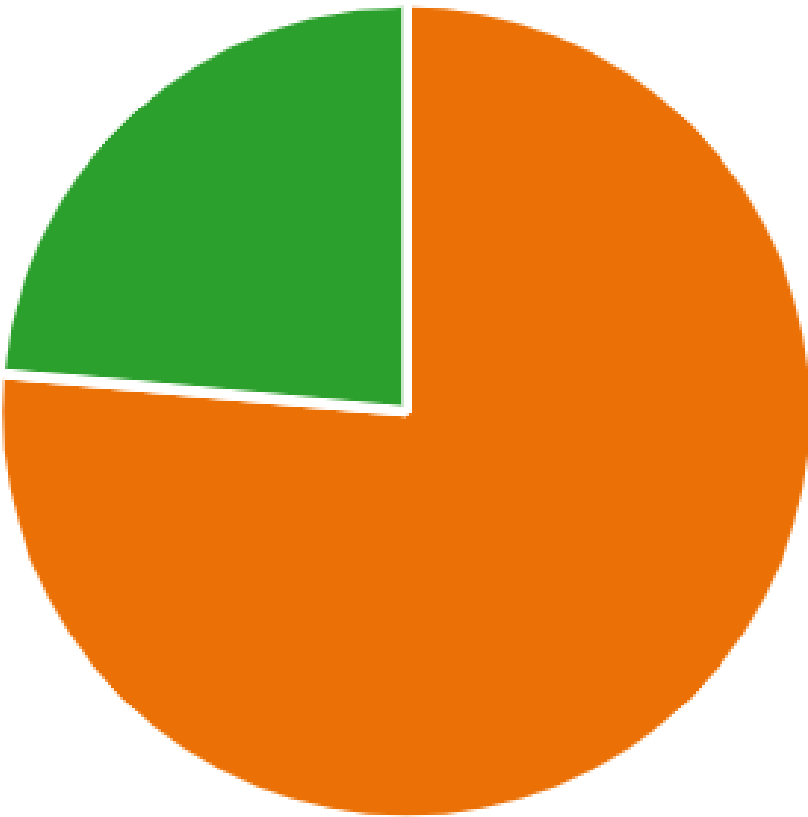


Themes:
Limited data in literature.

5. Cost-benefit and Cost- effectiveness

The outcomes outweigh the costs of screening. All outcomes, both positive and negative, need to be considered in the analysis.

● Yes, meets criterion.	0
● No, does not meet criterion.	13
● Unsure.	4

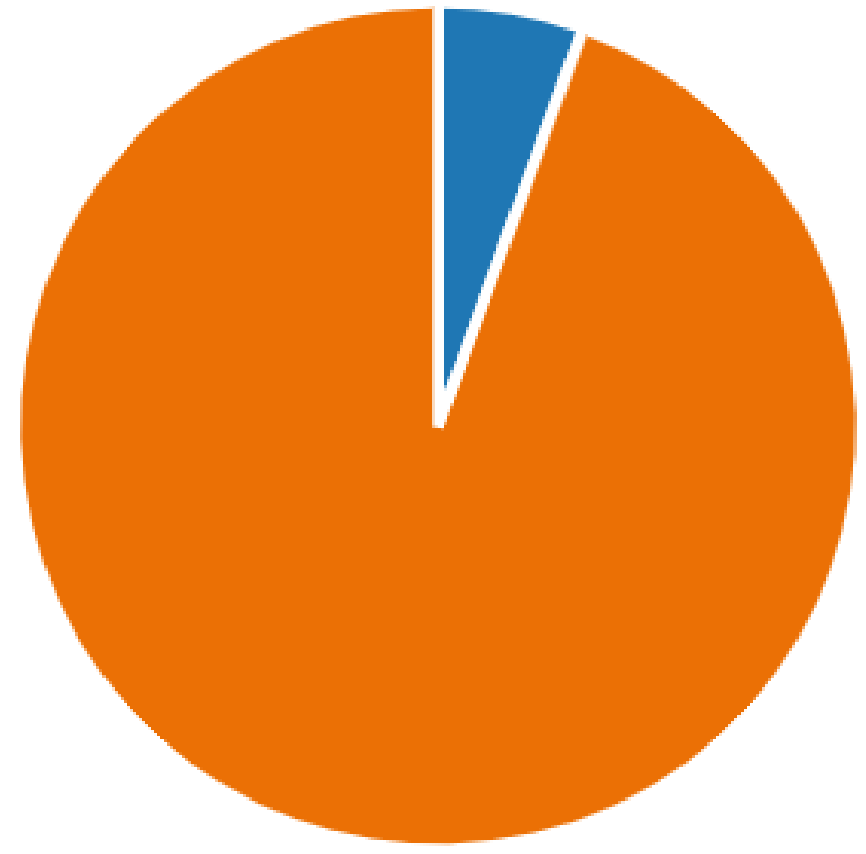


Themes:
Unable to determine cost/benefit ratio due to limited data.

Overall Recommendation for BCKDK Deficiency

Each TAC member voted as to whether they recommend BCKDK deficiency to Washington’s mandatory newborn screening panel.

- **I recommend** the Board add BC... 1
- **I do not recommend** the Board... 17



Themes:

Inadequate information to recommend to the Board to add BCKDK deficiency to the newborn screening panel.

Board Member Next Steps

Possible action: The Board may consider the following-

- The Board **accepts** the Newborn Screening TAC's recommendation for the Board to **not** add BCKDK deficiency to the NBS panel

OR

- The Board **declines** the Newborn Screening TAC's recommendation for the Board and directs staff to initiate rulemaking to include BCKDK deficiency on the NBS panel.



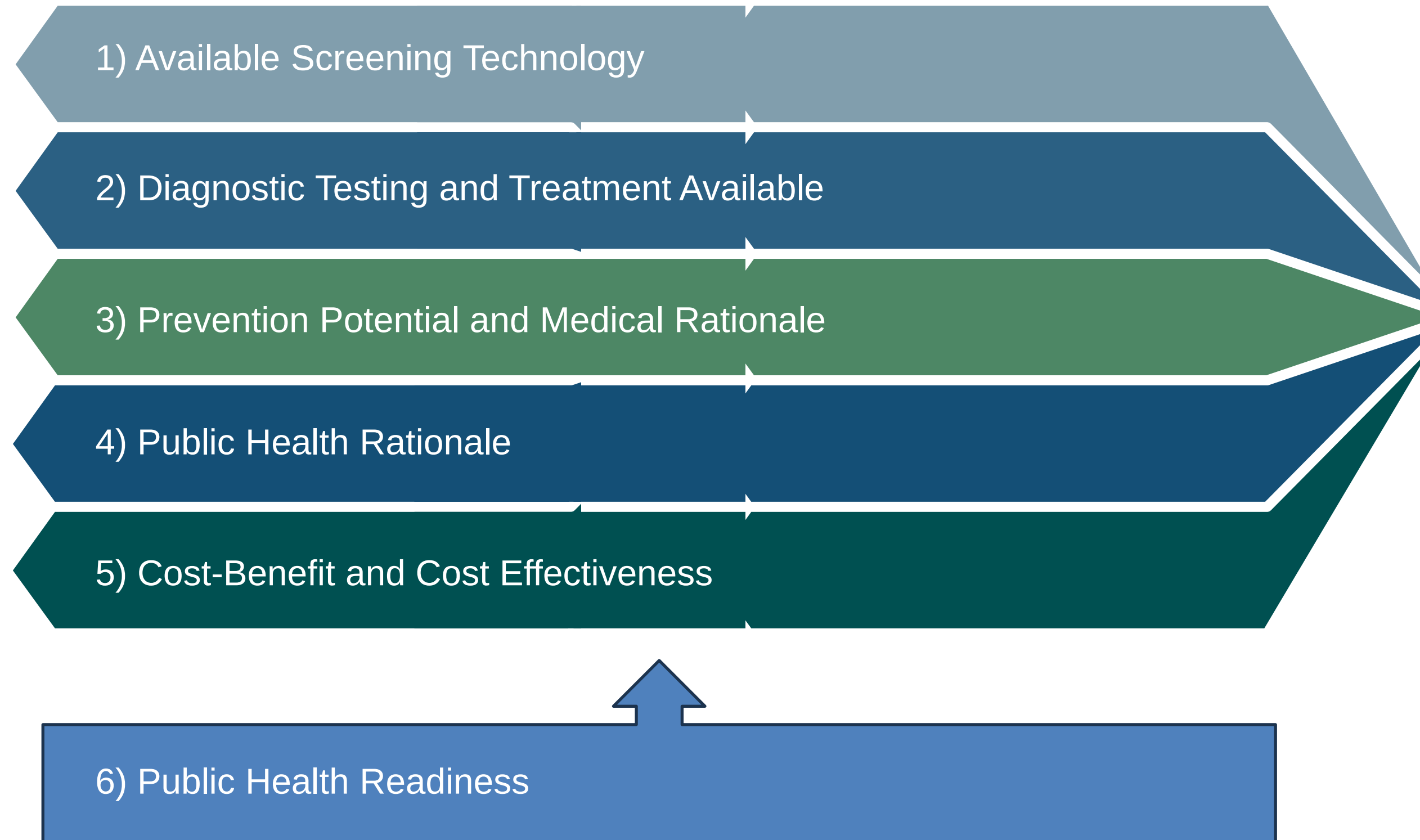


Washington State Board of Health

Overview of Criteria Review

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Newborn Screening Criteria



1. Available Screening Technology

Sensitive, specific, and timely tests are available for the condition that can be adapted to mass screening.

- The sensitivity of the screening test is estimated to be $\geq 95\%$.
- The specificity of the screening test is considered acceptable based on the estimated number of false positive results and their potential impact on the families, healthcare system, and newborn screening program.
- A timely test is one that enables intervention before irreversible harm develops, within the current standard timeframes for specimen collection, receipt, testing, and reporting.
- There is adequate peer reviewed evidence to evaluate this criterion.



2. Diagnostic Testing and Available Treatment

Accurate diagnostic tests, medical expertise, and effective treatment are available for evaluation and care of all infants identified with the condition.

- A diagnostic test accurately identifies who needs treatment and is readily available to all newborns screened.
- The available treatment is effective in reducing morbidity or mortality and outweighs any risks or harms of the treatment.
- The medical expertise needed to diagnose and care for those with a positive newborn screen is reasonably available to all newborns screened.
- The appropriate consultants and treatment centers have been identified and have capacity for the expected increase in diagnostic testing and/or referrals.



3. Prevention Potential and Medical Rationale

The newborn identification of the condition allows early diagnosis and intervention. Important considerations include:

- There is sufficient time between birth and onset of irreversible harm to allow for diagnosis and intervention.
- The condition must have an onset form that occurs in infancy (within the first year of life); newborn screening is not appropriate for conditions that only present after the first year of life.
- The benefits of detecting and treating ~~early-onset~~ infantile-onset forms of the condition (within one year of life) balance the impact of detecting later onset forms of the condition.
- ~~Newborn screening is not appropriate for conditions that only present in adulthood.~~
- There is adequate evidence of acceptable quality to evaluate this criterion.



4. Public Health Rationale

The nature of the condition justifies population-based screening rather than risk-based screening or other approaches.

- All available risk-based screening tools for the condition have been considered and are found to be inferior to universal newborn screening.
- There is adequate evidence of acceptable quality to evaluate this criterion.



5. Cost-benefit and Cost-effectiveness

The outcomes outweigh the costs of screening. All outcomes, both positive and negative, need to be considered in the analysis. ~~Important considerations to be included in the economic analyses include:~~

- The economic analysis considers:
 - The prevalence of the condition among newborns.
 - The positive and negative predictive values of the screening and diagnostic tests.
 - Variability of clinical presentation by those who have the condition.
 - Dollar values for costs and benefits of screening vs. no screening.
- The impact of ambiguous results, adverse effects, or unintended consequences of screening, such as emotional or economic impacts on the family and medical system, must also be considered.
- The results of the economic analysis shows that the outcomes, financial or otherwise, outweigh the costs of screening
- There is adequate evidence of acceptable quality to evaluate this criterion
- ~~The impact of ambiguous results. For example, the emotional and economic impact on the family and medical system.~~
- ~~Adverse effects or unintended consequences of screening.~~



6. Public Health Readiness

The Newborn Screening Program's capacity to implement screening within a reasonable timeframe has been considered.

- The systems and staffing necessary to perform the test and report screening results have been identified.
- Resources needed to implement short/long term follow up protocols by the newborn screening program have been identified.
- The accessibility to treatment for anyone diagnosed with the condition is considered acceptable based on the frequency of treatment needed.



Board Member Next Steps

Possible action: The Board may consider the following-

- The Board accepts the Newborn Screening Technical Advisory Committee's (TAC's) recommendation for the Board to adopt the updated criteria used to evaluate conditions for the newborn screening panel.

OR

- The Board declines the Newborn Screening Technical Advisory Committee's (TAC's) recommendation for the Board to adopt the updated criteria used to evaluate conditions for the newborn screening panel. The Board directs NBS TACs to continue to use the current established criteria.



THANK YOU

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