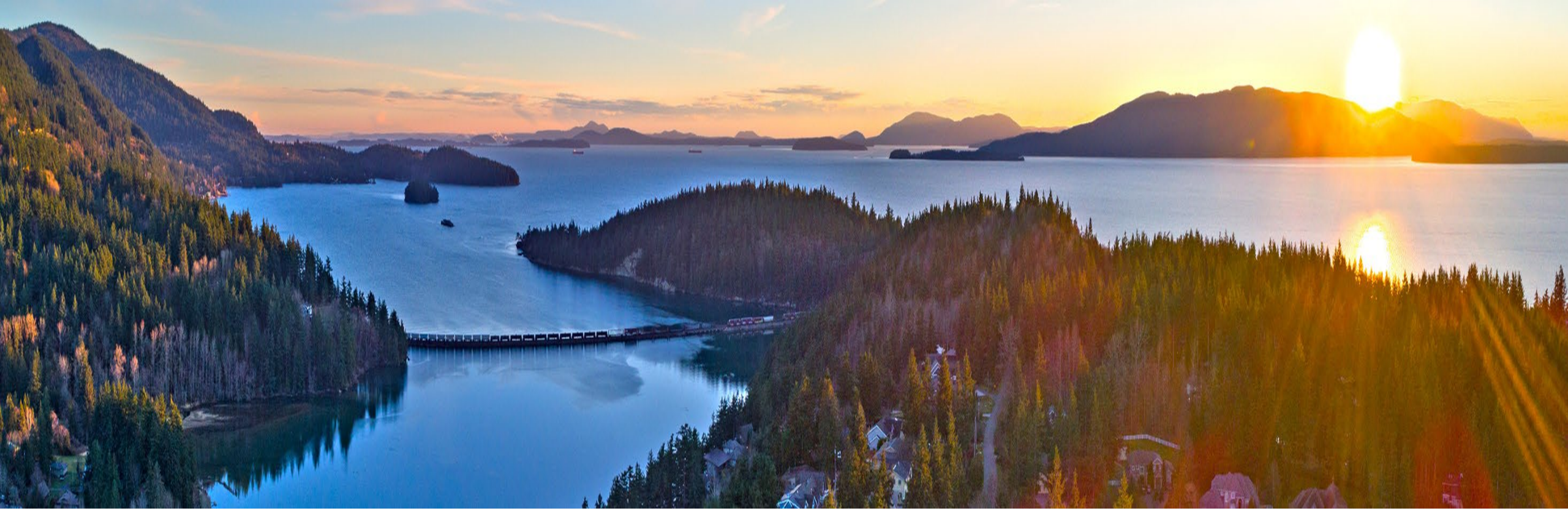

Washington State Board of Health

Qualifying Assumption Analysis Findings – Mucopolysaccharidosis type II (MPS II)

March 8, 2023

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Board Policy for Newborn Screening Criteria

Three guiding principles govern all aspects of the evaluation of a candidate condition for possible inclusion in Washington's Newborn Screening panel:

- Decision to add a screening test should be driven by evidence. For example, test reliability and available treatment have been scientifically evaluated, and those treatments can improve health outcomes for affected children.
- All children who screen positive should have reasonable access to diagnostic and treatment services.
- Benefits of screening for the disease or condition should outweigh harm to families, children, and society

Newborn Screening Criteria

- Available screening technology
- Diagnostic testing and treatment available
- Prevention potential and medical rationale
- Public health rationale
- Cost-benefit/cost-effectiveness

MPS II Qualifying Assumption

- Petition - Mucopolysaccharidosis type II (MPS II)
    - Submitted October 26, 2022, requesting an amendment to chapter 246-650 WAC to add MPS II as a condition for newborn screening
    - MPS II added to the federal Recommended Uniform Screening Panel (RUSP) in 2022
    - At the Board's November 2022 meeting, Members adopted the motion to deny the petition and direct Board staff and the Department to perform a qualifying assumption analysis of MPS II
- Preliminary review of five criteria
    - John Thompson – DOH
    - Molly Dinardo – SBOH

MPS II 101

- Inherited X-linked metabolic disorder
- Result of abnormalities in the iduronate-2-sulfatase (I2S) enzyme, caused by IDS gene mutations
- Two primary classifications of MPS II
    - Severe – onset in early childhood with neurological deterioration, rapid disease progression (symptom onset ~2.7 years)
    - Attenuated – onset later in childhood, slower progression (symptom onset ~4.3 years)
- Signs and symptoms vary, and can include:
    - Hearing loss, enlarged facial features (e.g., swollen lips, large/rounded cheeks, broad nose, swollen tongue), enlarged liver or spleen, joint stiffness, hernias, poor vision, impaired developmental and motor skills, behavioral issues

MPS II and Newborn Screening Programs

- States that currently screen for MPS II
  - Illinois (since 2017)
  - Missouri (since 2018)
- States that have pilot testing programs
  - New York
  - Taiwan

MPS II Available Screening Technology

- Two methods (~732,000 screened)
  - Tandem mass spectrometry – Illinois
  - Fluorometry – Missouri
  - Neither method could be multiplexed with current testing in WA
- Prevalence: 1:62,500 births
- Test performance
  - Sensitivity: 100% (no known false negatives)
  - Specificity: 99.99%
  - Positive Predictive Value: 9.5%

MPS II Diagnostic Testing and Treatment Available

- Diagnostic tests
  - Urinary glycosaminoglycans (GAGs)
    - dermatan sulfate, heparan sulfate
  - Molecular testing can be helpful
  - Testing available at Seattle Children's or other reference labs
- Treatment
  - Weekly enzyme replacement therapy (ERT): Elaprase (Idursulfase)
  - Management requires support from multidisciplinary biochemical genetics team
  - Infrastructure and treatment available at Seattle Children's hospital
    - Current staffing levels are low with recruitments in progress

MPS II Prevention Potential and Medical Rationale

- Early treatment may prevent or delay some MPS II symptoms and improve quality of life
- ERT treatment associated with
  - Improvements in mobility outcomes, cardiac and respiratory symptoms
  - Decreased mortality in adulthood (in UK study with ERT, median age of death increased 3.5 years)
- Limitations of current treatment
  - Lack of targeted treatment for neurological symptoms
  - Data is lacking regarding benefit of early vs. symptomatic treatment
- Due to the rareness of the condition, peer reviewed evidence base is limited
  - Current evidence relies on expert and patient reported benefits

MPS II Public Health Rationale

- According to findings in the federal report, screening for MPS II in newborn screening programs would identify more cases of MPS II compared with clinical identification
- MPS II X-linked recessive pattern warrants universal screening
    - MPS II primarily affects babies assigned male at birth, and babies assigned female at birth can be carriers of the gene
    - If the birthing parent is a carrier of the MPS II gene:
        - 50% risk that babies born as male will have the disease
        - 50% risk that babies born as female will be a carrier of the disease

MPS II Cost-Benefit/Cost-Effectiveness

- Federal Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC)
  - Limitations from evidence review report (2/20/2022):
    - "Limited data were available for many parameter inputs. Insufficient data were available to project long-term outcomes for MPS II, either through newborn screening or clinical identification."
    - "Given the rare nature of newborn screened conditions, data are typically scarce for conditions being considered for addition to the RUSP. Compared with other conditions that have been nominated and considered for addition to the panel, data for the consideration of MPS II were considerably sparser."
  - Without additional published data, any formal cost-benefit analysis would rely solely on expert opinion
  - Other, non-quantifiable considerations could be reviewed and discussed
    - Psychosocial benefits/harms including impact of ambiguous results
    - Adverse effects/unintended consequences of screening

THANK YOU

WASHINGTON STATE BOARD OF HEALTH

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Resources from Federal Review of MPS II for the RUSP:

- Evidence-Based Review of Newborn Screening for Mucopolysaccharidosis Type II: Final Report. Prepared for the Maternal and Child Health Bureau. February 20, 2022.
  - Final Report
  - Available under Recommendations to HHS Secretary
- Recommendations to the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) for Newborn Screening of MPS II. February 10, 2022.
  - PowerPoint Presentation for the ACHDNC Meeting
  - Available under ACHDNC's February 2022 Meeting Materials