DRAFT 3-24-25

Oregon Health Authority
Northwest Regional Newborn Bloodspot Screening Advisory Board

Meeting Summary — March 4, 2025

Location
Videoconference

Quorum
Board attendees constituted a quorum for the meeting.

Board Members Attending
Marilyn Hartzell, M.Ed., Board Chair, Family Representative
Angela Douglas, MD Representative of a statewide association of pediatricians
Cheryl Grabham, Representative of advocacy association regarding newborns with medical or rare disorders
Rusha Grinstead, Representative of Medicaid or insurance industry
Andrea Keating, LDM, CPM, Representative of a statewide association of midwives
Jill Levy-Fisch, Representative of advocacy association regarding newborns with medical or rare disorders
Mort Murry, MD, Representative of advocacy association regarding newborns with medical or rare disorders
Sherly Paul, Representative of a statewide association of nurses
Elizabeth Powers, MD, FAAFP, Representative of birthing center or hospital
Kara Stirling, MD, Representative of a birthing center or hospital
Amy Yang, MD, Contracted medical consultant

NBS Program Staff
Patrice Held, Newborn Screening Program Manager
Amber Gamel Miller, Public Health Nurse
Kasfian Khan, Legislative and Community Engagement Coordinator
Sarah King, Client Service Coordinator
Akiko Saito, Business Director

Guests
Jessica Scott Schwoerer, MD

Members of the Public
Lesa Brackbill
Alyssa Carr
Keri Esser, DPT
Rachel Finch
Kathy Fraiser

Anna Grantham, Hunters Hope
Lisa Hamilton
Miles Johnson
Randy and Lisa Johnson
Pat Kruis
Carolyn Lee, State Rep. Susan McClain's Office
Cindy Mohr
Joe Monaco
Nikki Monaco
Susan Monaco
Stacy Pike, Krabbe Connect
Kassie Schnell
Afra Syed
Jawad Syed
Tammy Wilson

Jensen Strategies Facilitation Team

Erik Jensen, Facilitator
Emily Rehder, Operations Manager

ACTION ITEMS

The Board recommended Infantile Krabbe Disease to the Northwest Regional Newborn Bloodspot Screening (NWRNBS) Panel.

MEETING AGENDA ITEMS

1. **Welcome**

   Chair Marilyn Hartzell opened the meeting welcoming all the participants. A welcome was extended to the new Board members Cheryl Grabham and Rusha Grinstead.

2. **Meeting Overview**

   Advisory Board Facilitator, Erik Jensen, reviewed the meeting agenda, disorder review protocol steps, and opportunity and procedure for public comment. The Board would follow its disorder review protocol, which includes a scientific report of Infantile Krabbe Disease (IKD), discussion of the Step 2 criteria, public testimony on the potential inclusion of IKD to the panel (Step 3), and the Board's deliberations and recommendations based on the Step 4 criteria and the public input.

3. **Krabbe Scientific Review Presentation**

   Dr. Jessica Scott Schwoerer, presented the scientific review of IKD with the following summary points:

   - Krabbe is a lysosomal storage disorder caused by galactocerebrosidase (GALC) deficiency. The deficiency leads to accumulation of psychosine causing injury to neurologic cells and abnormal brain myelination.
   - There are four categories of Krabbe Disease: (1) Infantile Krabbe Disease (IKD); (2)

late infantile Krabbe Disease (LIKD); (3) juvenile Krabbe Disease; and (4) adult onset Krabbe Disease. This disorder presents in 1 in 100,000 to 250,000 births (all categories) although there is concern these numbers are underestimated due to under diagnosis.

- Infantile Krabbe Disease was added to the national Recommended Uniform Screening Panel (RUSP) in 2024.
- Testing:
    - At least 10 states are currently screening for Krabbe Disease. The estimated number of Oregon newborns to test positive (low GALC activity), based upon the data from other states, is 25 each year. From this cohort, the number of newborns who test positive with psychosine greater than 10 is less than 1 per year. It is estimated that there will be 1 positive IKD screen every 5 years.
- Treatment:
    - The treatment options for Krabbe Disease are either symptomatic care if diagnosed post-symptomatically or a hematopoietic stem cell transplant (HSCT) typically taken from umbilical cord blood, if diagnosed pre-symptomatically.
- Feasibility:
    - Estimated cost of screening for Infantile Krabbe Disease is $8.44 per infant screened, with the inclusion of additional personnel for the laboratory and follow-up teams.

Dr. Schwoerer said the scientific report did cite some potential concerns associated with screening for Infantile Krabbe Disease including:

- Cost of screen given low incidence of IKD,
- Potential delays in NBS results due to timing of specimen collection, transport, first-tier testing, send-out for second-tier testing.
- Identification of only IKD and no other later onset forms of Krabbe Disease.
- HSCT is available and improves survival and neurodevelopmental outcomes based on current data but is not curative.
- Limited data on treatment outcomes for IKD, especially within transplant center with limited experience.
- Morbidity and mortality associated with HSCT (10%).
- Concerns about ability to complete HCST in the 4–6-week timeline due to barriers within the medical system including: Diagnostic evaluation, obtaining insurance coverage of HSCT including in the expediated timeline, concerns about parental stress and well-being for urgent decision making.

Questions and comments related to the presentation included:

- Q: Since the study looks at neurodevelopment, those that passed away are excluded, is that correct?
  A: Correct.
- Q: Do you know an estimate of cases in which parents would choose to move forward with the transplant, but a donor would not be available?
  A: No, information provided in the review.
- Q: Do you have an estimate on how accessing treatment through OHSU that isn't a

specialty center, may affect the mortality rate in comparison to those facilities that specialize in this?
A: No information available.

- Q: For the late onset Krabbe category, did the study mention whether it included people with late infantile disease? Or was late infantile grouped with IKD?
  A: The understanding was that the late infantile cases were reported with the other late onset forms.
- Q: Are we determining for Oregon only or including New Mexico?
  A: New Mexico has a contract with Oregon for screening services. They have a screening panel that (at present) matches Oregon. If Oregon Board adds IKD, then the program can offer this screening test to New Mexico.
- Q: Question about current legislation regarding funding, general fund funding for Krabbe?
  A: HB3192: Allocates $4 million of general funds to bring on five conditions: GAMT, MPSII, Krabbe, DMD, and CMV screening. GAMT and MPSII has been approved by the Board. The bill doesn't designate whether the funding is only for the biennium or ongoing. It lists Krabbe Disease, but we are only voting on IKD, in alignment with the RUSP. There is no guarantee that the bill will pass.
- Q: Considering the fiscal analysis and the determination of appropriate population size, does it include New Mexico? What is the estimate based on?
  A: Cost estimate is based on a per baby- whether it be New Mexico or Oregon. The cost includes all of the staffing, supplies, and clinical care costs that the Program occurs.
- Q: If New Mexico disagrees to add Krabbe is there a cost saving?
  A: Their cost will increase if they add IKD, but there is no cost saving for Oregon.
- Comment: The data shows clean difference between IKD and later onset Krabbe Diseases.
- Comment: IKD is the group that has symptoms in the first few months of life. Moving forward with this vote, we would not pick up the late infantile or other late onset forms.

Patrice Held, NWRNBS Program Manager, said based on the scientific review, the criteria for Step 2 has been met. There was general agreement to move forward to Step 3 of the review process and hear public input on the potential inclusion of IKD on the Oregon Newborn Screening panel.

4. Public Comment on Krabbe Review

Verbal and video testimony from members of the public was shared. The following individuals provided input based on their personal experiences and/or knowledge of IKD:

1. Nikki Monaco
2. Joe Monaco
3. Tammy and Michael Wilson

4. Kat Fraiser
5. Keri Esser
6. Randy Johnson
7. Miles Johnson and Stephanie Mohr
8. Afra Syed
9. Susan Monaco
10. Anna Grantham- Hunter's Hope
11. Stacy Pike- Krabbe Connect
12. Rachel Finch
13. Michael Wilson (video)

All verbal testimony was in favor of adding IKD to the Oregon NBS panel.

Written statements were submitted in advance and distributed to the Board from the following individuals and organization:

1. Laura Pierson
2. Wayne Scott
3. Alyssa Carr
4. Society for Inherited Metabolic Disorders (SIMD)
5. Cynthia Mohr

Four submitted written testimonials supported adding IKD to the Oregon NBS panel. One written testimony from SIMD did not support adding it to the panel. The Board expressed appreciation to everyone who shared their input with them.

5. Evaluation & Recommendation re: Krabbe Inclusion

Erik facilitated a discussion and decision regarding the recommendation to add IKD to the Oregon Newborn Screening panel. The Board's discussion and evaluation was based on the eight criteria in Step 4 of the disorder review protocol as summarized:

<u>Criterion #1: What is the population level incidence, prevalence, and burden for this disorder for the state/territory?</u>

Patrice shared an incidence of approximately 1 in 100,000 to 1 in 250,000 for Krabbe Disease. It is unknown if Oregon has a higher prevalence. There is no known population with a higher incidence. This information can be located on pages 6,7, and 8 of the evidence report.

- Q: Are the estimates on all categories of the disease or solely the infantile Krabbe? A: Hard to parse out the subtypes. The range estimate is the best guess for the disease spectrum. With such a rare disease, it is challenging in finding incidents of any one subtype.

Criterion #2: Does diagnostic and specialty testing provide a definitive diagnosis for the intended screened disorder?

Patrice offered that psychosine testing provides a definitive diagnosis.

- Comment: With a psychosine cut off of 10nM, a diagnosis can be made.
- Q: Is 10nM the cutoff, since there was talk of 2nM?
  A: A psychosine cutoff of 10nM limits identification to only infantile Krabbe.
- Q: To confirm the boarding is sticking to the criteria of 10nM (infantile Krabbe disease)?
  A: Yes, the first criteria is that the condition needs to be on the RUSP. The RUSP only lists Infantile Krabbe Disease. The advisory board is deliberating only on IKD.
- Q: What is the psychosine level for late onset?
  A: We know that kids with late onset have a psychosine values between 2 and 10nM.
- Q: Will there be any reporting to the doctor of any values under 10nM or is it considered screen negative?
  A: The screening lab will measure GALC enzyme activity in the dried blood spots. If the activity is low, then the program will send the sample to a reference lab for psychosine testing. Mayo currently offers psychosine testing. Mayo agreed to a psychosine cutoff of 10nM to only identify cases of IKD.

Criterion #3: What is the risk for the family with a false positive newborn screen?

Patrice said because of the two-tiered testing, it is anticipated to have very few, if any, false positives.

- Q: Will the low GALC activity be reported or only the second-tier testing psychosine results.
  A: The report will be held until both first- and second-tier test results are received.
- Q: If newborns screen with a low enzyme and the sample is sent for additional testing, are the families notified?
  A: No. It will not be reported until first- and second-tier test results are available. If the enzyme is low and psychosine is less than 10nM, the baby will be reported as “low risk” for Infantile Krabbe Disease.
- Comment: Families appreciate that the testing is happening, and the risk of a false positive is less likely to harm than the risk of a misdiagnosis.

Criterion #4: What is the risk for the family with an unintended diagnosis, such as late-onset disease?

Patrice shared that given the testing structure, it is not anticipated that late onset disease would be identified.

Criterion #5: Is an effective treatment for those with a diagnosis, proven to result in clinically significant benefits, available to families in Oregon?

Patrice noted the treatment for Infantile Krabbe Disease is a bone marrow transplant and there is significant risk of 10% mortality rate. However, if the transplant is successful, the child will live. The transplant, however, is not curative and children may still have gross motor abnormalities.

OHSU does have a transplant team. They are willing to work with families that have a child with Krabbe, but it is not currently a recognized transplant center for newborns with rare conditions., The closest recognized transplant center is in Northern California.

- Comment: Criteria 5,6,7 are intricately tied. A bone marrow transplant is the way to go in terms of effective treatment, however it is not a cure. With timely treatment, children will still have significant development disabilities, mainly in motor function. The quality of life is significantly different than the natural progression of disease. The problem is how equitable this would be for Oregonians. We need to figure out ways on how we can deliver bone marrow transplants by 30-40 days of life. The recommended timeframe for treatment is 30 days of life. We struggle to get results back in a timely fashion and we have unsatisfactory testing to deal with as well. The real time frame for the transplant is 30 days after diagnosis. The only way to be equitable and to deliver the fast turnaround, is to admit the child into the hospital. It is logistically impossible to do all the needed confirmatory testing and prep for transplant as an outpatient.
- Q: Do we have information about other states that have dealt with these issues?
  A: We can't compare to states that are doing psychosine testing in house but will need to look at experience of states that send out their testing. The timeframes would be more in line with them potentially.
- Comment: Facilitating the care would require hospitalizations and rural communities would struggle to get access to care. I don't think it is a logistical impossibility but that it is an indication for admission into the hospital.
- Q: What is the turnaround time from the first screen?
  A: Metrics on the time from birth to report is: 95% of screening samples are reported within 7 days of life. Mayo runs psychosine testing every day and would have a 24-hour turnaround time. We would be looking at roughly 10 days of life for reporting an abnormal result.
- Comment: Would not be able to meet the metrics delivered in the report since Oregon does not do in house testing but would be about half a week behind.

Criterion #6 What are the significant risks associated with treatment, if any?

(See discussion summary under Criteria 5 above)

Criterion #7: Is equitable long-term follow-up and management of the disorder available to families in Oregon?

(See discussion summary under Criteria 5 above)

Criterion #8: Do the population level public health benefits of screening outweigh the risks and harms?

- Q: Should we consider the costs, or the funding availability for screening?
  A: The question at hand is whether to add IKD to the panel. You have received information regarding potential for general funds. At this point, the discussion of funding is separate from the question of whether to add IKD to the panel.
  A: If you choose to recommend IKD, the program needs to find funds.
- Comment: Understand that there are concerns about timeline and access, it feels irresponsible to make a decision on fears rather than based on possibilities.
- Comment: In previous cases we have used this time to identify barriers to make it more equitable to all Oregonians; creating changes and opportunities and changing the status quo. We do consider everything because Oregonians have specific challenges. Not to say it isn't the right thing to do, but how do we get it right every single time for every person diagnosed with this condition. We want to make sure we have all the ducks in place and smooth out the rough edges as best as we can.
- Comment: Want to make sure that equitable access to diagnosis is an important consideration.

While multiple Board members suggested additional discussion would be helpful regarding IKD testing implementation, they indicated they were prepared to make a decision regarding adding IKD to the Oregon Newborn Screening panel. The Board voted on the following question: Considering the results of the scientific review, testimony received, and the disorder evaluation criteria, do you agree with a recommendation to add the Infantile Krabbe Disease to the Northwest Regional Newborn Bloodspot Screening (NWRNBS) Testing Panel?

Decision: The Advisory Board, by consensus, **recommended** the inclusion of Infantile Krabbe Disease to the NWRNBS testing panel. The decision was made using the 1-5 consensus tool with 1 for full agreement and 5 for no agreement:

Dr. Angela Douglas	1
Rusha Grinstead	3
Cheryl Grabham	2
Marilynn Hartzell	1

Jill Levy-Fisch	1
Andrea Keating	2
Dr. Mort Murry	1
Sherly Paul	2
Dr. Elizabeth Powers	1
Dr. Kara Stirling	3
Dr. Amy Yang	2

Erik thanked the members of the public for sharing their stories with appreciation for their time. He noted the Board will discuss the IKD testing implementation at a future meeting.

6. Approval of Meeting Summary

Approval of the September 4, 2024, and December 4, 2024, meeting summaries was postponed to the next meeting on May 28, 2025, due to lack of time.

7. Wrap-up

With gratitude for an informative session Chair Hartzell adjourned the meeting.