WASHINGTON STATE BOARD OF HEALTH

HEALTH PROMOTION COMMITTEE
SPECIAL MEETING SUMMARY NOTES

What: Newborn Screening Technical Advisory Committee - Ornithine Transcarbamylase Deficiency

When: July 7, 2021

Participating by Zoom: Technical Advisory Committee (TAC) Members: Dr. Tom Pendergrass, Dr. Scott Lindquist, Joan Chappell, Trish Anderson, Dr. Krystal Plonski, Maria Siguenza, Shari Maier, Kristine Alexander, Byron Raynz, Victoria Raynz, Dr. Ben Wilfond, Dr. Sihoun Hahn, and Peggy Harris; Presenters Dr. Angela Sun, Dr. Anna Scott, Dr. John Thompson, Michael Katsuyama; Board of Health and Department of Health Staff and three members of the public.

Summary Notes:
Co-chair Dr. Scott Lindquist welcomed TAC members, staff, and members of the public and provided a brief introduction of the members and purpose of today's meeting. Sam Pskowski, Board Staff, provided an overview of the virtual meeting functions and expectations. Co-chair Dr. Tom Pendergrass reviewed the purpose of the meeting and directed TAC members to the meeting one summary notes for approval. There were no edits to the summary notes. Co-chair Pendergrass then introduced Michael Katsuyama, Department of Health Staff, to present on criterion five, the cost-benefit analysis.

Mr. Katsuyama presented on the cost-benefit analysis, noting that the analysis is not able to quantitatively account for the associated emotional costs and that the analysis focused on the severe neonatal form of Ornithine Transcarbamylase Deficiency (OTCD). He walked through the decision tree model and discussed the no-screening model and screening model. He noted the model utilized Washington's assumed annual birth rate of 74,000, a prevalence of OTCD of 1:157,833 taken from the California experience, and the assumption of all surviving patients having the goal of receiving a liver transplant. The model used data from California to identify that screening would find 27% of cases before symptoms arose and 73% would be post-symptomatically. The model shows a benefit/cost ratio of 0.59, for every $1 spent, screening would save $0.59 for a net benefit of ($261,206.95) [note: during the presentation, an error was detected in the formula for total benefits. The benefit/cost ratio was updated to 0.69]. Mr. Katsuyama also discussed the sensitivity analysis conducted to identify which parameters have the most impact on the benefit/cost ratio and mentioned that the prevalence is most influential.

TAC member Trish Anderson asked if the model considered the impact of the decreasing birth rate in the analysis. Dr. John Thompson, Department of Health clarified that the model used the predicted birth rate for 2021 and is similar to that of several years ago. Co-chair Pendergrass asked if there are more births does the sensitivity of the screening increase. Dr. Thompson clarified that it does not change significantly.

Co-chair Pendergrass reminded members about the importance of timeliness between when a blood spot is taken and when the result is available.

Dr. Thompson presented on the remaining sub-points of the fifth criterion and identified a discrepancy in the previously provided benefit cost ratio. He shared an updated ratio of 0.69 with the members. Dr. Thompson then shared additional information on the variability of clinical presentation of OTCD, the ambiguous results when screening for low citrulline, and possible unintended consequences of screening, including the impacts of the system failing and risk for litigation.

TAC member Byron Raynz asked if there are low citrulline levels that identify other urea cycle disorders considered part of the false positive rate in the analysis. Dr. Thompson clarified that the analysis was targeted for OTCD. Co-chair Pendergrass noted that low citrulline are not a direct indicator of OTCD.

TAC Member Ben Wilfond asked about the extent to which other newborn screening labs use courier services, commenting that there is certain to be an impact on detection rate with more timeliness. Dr. Thompson indicated there are several states using courier services that are paid for as part of the newborn screening fee. He indicated that staff inquired with those programs to understand their costs. Co-chair Pendergrass noted that the courier service is just one piece of this slowing down the process and shouldn't assume a courier service will allow us to identify all cases. TAC Member Wilfond noted there would be a partial improvement over the current state.

TAC Member Raynz noted that prevalence is key in the analysis and using the California data versus that from the literature is a large range and asked if we know how many babies born in Washington have had OTCD. Dr. Anna Scott noted that in her three and a half years at Seattle Children's she is aware of two neonates who presented and had lab testing done for OTCD and one adult with very late presentation. TAC Member Sihoun Hahn added he is aware of maybe five to six cases over ten years. TAC Member Peggy Harris asked if the only cure is liver transplant. Co-chair Pendergrass clarified that yes, liver transplant that is successful can cure the absence of the OTCD enzyme and that there are other therapies to moderate rises in ammonia.

Co-chair Pendergrass commented that at the prior meeting, it was noted that one case per week would be a huge increase in workload for the diagnostic lab and asked TAC Member Hahn if he still felt that were true. TAC Member Hahn responded that this is a burden on both the clinical team and the lab due to the urgent nature of the condition. Dr. Scott provided baseline information, noting that the last few years there have been 200 referrals from the newborn screening program and an additional fifty per year would be a twenty-five percent increase. She noted that receiving the samples on weekends presents additional challenges; it can be done as they run twenty-four hours a day but would take approximately four hours to complete. TAC Member Hahn indicated that it could be done, and that communication would be key. Co-chair Pendergrass commented that these changes would affect the cost and delivery of care and may justify a need for more staff.

TAC Member Wilfond commented that his impression is that in general newborn screening finds lower prevalence than expected. Dr. Thompson clarified that typically when a condition is newly screened for, the prevalence is higher than anticipated noting MCAD as an example. This is not the case for OTCD. TAC Member Anderson asked if the team had evaluated the availability and timeliness of liver transplant. Mr. Katsuyama clarified that it was not built into the model but the outcomes for babies across the spectrum of liver transplant timeliness are captured in the existing mortality rates. Further, the effect of liver transplant availability and timeliness are built into the estimated cost of the transplant. Dr. Thompson added that the understanding was transplant typically occurs within the first year of life. TAC Member Harris asked about the quality of life during the time prior to a transplant. Dr. Angela Sun noted that the baby may be in the neonatal intensive care unit to be stabilized and then discharged with medication and protein-restricted diets and that providers will monitor their weight and growth. TAC Member Hahn asked Dr. Sun how many OTCD patients they have seen. Dr. Sun approximated thirty to fifty which includes newborns, infants, and late onset adult cases. Co-chair Pendergrass commented that families come from all over to seek care at Seattle Children's which presents a challenge in finding true prevalence in Washington State.

Co-chair Pendergrass directed TAC members to now consider OTCD against the fifth criterion. He noted that the committee has discussed the prevalence and positive predictive values of the screening and diagnostic tests, the variability of clinical presentation, impacts of ambiguous results and heard today about the possible unintended consequences of screening. Co-chair Lindquist reviewed the numbers for prevalence and positive predictive values commenting that California's positive predictive value of 2.7% is very low. Dr. Thompson agreed that California's numbers are low, but provided that Massachusetts has a 15% positive predictive value and that Washington would likely follow their testing model. TAC Member Harris asked to clarify if 0.69 is the correct benefit cost ratio. Dr. Thompson confirmed. TAC Member Shari Maier asked if the costs presented include all of the Massachusetts screening tests. Dr. Thompson clarified that the costs presented include the test for low citrulline and secondary markers.

Co-chair Pendergrass directed the committee to their inbox to find a ballot for voting on the fifth criterion and final recommendation to the full Board. The meeting broke until 11:45 a.m. for voting.

Co-chair Pendergrass commented on the importance of the task the committee was asked to undertake and expressed his appreciation for the engagement and involvement of members while noting the challenges of conducting such a conversation virtually. Co-chair Lindquist then provided the results of the voting and summarized some comments on the limitation of data. He noted that despite the low prevalence and cost-effectiveness, it did not appear to affect some member's decision to recommend including this condition on the newborn screening panel.

Criteria	Yes	No	Unsure
Cost-benefit / Cost-effectiveness	7	4	2
Overall Recommendation	9	3	1

Co-chair Pendergrass commented that the comments and results of these meetings will come together in a report that will be brought to the full Board. Co-chair Lindquist noted that with around fifty percent of committee members voted yes for cost-effectiveness and seventy percent voted to recommend it is not a slam dunk. He clarified that the final decision sits with the Board. Co-chair Pendergrass and Dr. Thompson shared a possible timeline if the Board proceeds, of beginning screening in July 2023. Ms. Pskowski closed by asking committee members to share any feedback about the meeting process.

The meeting adjourned at 11:51 a.m.

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