Washington State Department of HEALTH

WASHINGTON STATE BOARD OF HEALTH

# Newborn Screening Technical Advisory Committee (TAC)

## NOTICE OF PUBLIC MEETING

Tuesday, June 17, 2025
10:00 a.m. – 4:00 p.m.

**Note:** This is a virtual meeting held via Zoom with in-person meeting space at the Interurban Hotel, 223 Andover Park E, Tukwila, WA 98188. Room: Mount Si II. Meeting access and instructions are provided below. Language interpretation available.

**Newborn Screening Technical Advisory Committee (TAC) Agenda**

**Review of the Condition Wilson Disease**

| Time | Agenda Item | Speaker |
|---|---|---|
| 10:00 a.m. | 1. Welcome and Agenda | Kelly Oshiro, TAC Co-Chair, State Board of Health<br>Nirupama Nini Shridhar, TAC Co-Chair, Department of Health<br>Kelly Kramer, State Board of Health<br>Allegra Calder, BERK Consulting |
| 10:20 a.m. | 2. March cCMV TAC Meeting Recap | Kelly Kramer, State Board of Health |
| 10:35 a.m. | 3. April Board Meeting Review | Kelly Kramer, State Board of Health<br>Kelly Oshiro, TAC Co-Chair, State Board of Health<br>Nirupama Nini Shridhar, TAC Co-Chair, Department of Health |
| 10:55 a.m. | 4. Overview Wilson Disease | Kelly Kramer, State Board of Health |
| 11:10 a.m. | 5. Family Perspective | Taodun Li |
| 11:30 a.m. | 6. Wilson Disease: Natural History, Diagnostic Testing, and Treatment | Dr. Sihoun Hahn, Biochemical Geneticist, Seattle Children's Hospital, Key Proteo, Inc.<br>Dr. Pamela Valentino, Pediatric Hepatologist, Seattle Children's Hospital |

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# Newborn Screening Technical Advisory Committee (TAC)

| Time | Agenda Item | Speaker |
|---|---|---|
| 12:30 | Lunch | |
| 1:15 p.m. | 7. Treatment Continued: Nutrition Considerations | Beth Ogata, University of Washington Genetic Medicine |
| 1:30 p.m. | 8. Available Screening Technology | Megan McCrillis, Department of Health |
| 1:40 p.m. | 9. Cost-Benefit Analysis | Megan McCrillis, Department of Health |
| 2:10 p.m. | 10. Public Health Infrastructure Readiness | Megan McCrillis, Department of Health |
| 2:30 p.m. | 11. Washington Criteria Review for Wilson Disease and Discussion | Kelly Kramer, State Board of Health<br>Kelly Oshiro, TAC Co-Chair, State Board of Health<br>Nirupama Nini Shridhar, TAC Co-Chair, Department of Health<br>Allegra Calder, BERK Consulting |
| 2:50 p.m. | 12. Vote | Kelly Oshiro, TAC Co-Chair, State Board of Health<br>Nirupama Nini Shridhar, TAC Co-Chair, Department of Health<br>Allegra Calder, BERK Consulting |
| 3:00 p.m. | Break | |
| 3:15 p.m. | 13. Discussion and Next Steps | Kelly Oshiro, TAC Co-Chair, State Board of Health<br>Nirupama Nini Shridhar, TAC Co-Chair, Department of Health<br>Kelly Kramer, State Board of Health<br>Allegra Calder, BERK Consulting |
| 3:45 pm | Adjourn | Kelly Oshiro, TAC Co-Chair, State Board of Health<br>Nirupama Nini Shridhar, TAC Co-Chair, Department of Health<br>Allegra Calder, BERK Consulting |

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# Newborn Screening Technical Advisory Committee (TAC)

**Zoom Meeting Information:**
**Please click the link below to join the webinar:**
https://us02web.zoom.us/j/82455128738?pwd=daqYIpbMiOdugDrpWGu56ZSjzRRLQo.1
**You can also dial-in using your phone for listen-only mode:**
**Call in:** +1 (253) 205 0468 (not toll-free)
**International numbers available:**
**Webinar ID:** 824 5512 8738
**Passcode:** 726507

**Important Meeting Information to Know:**

- This meeting is open to the public. The public can observe the meeting online or in person at Town Center 2, 111 Israel Rd. S.E. Tumwater, WA 98501. Room: 153.
- The Technical Advisory Committee will not take formal action or receive public comment. If you have comments or materials you would like to share with the full Board, please send them to wsboh@sboh.wa.gov.
- Times are estimates only. We reserve the right to alter the order of the agenda.
- Every effort will be made to provide Spanish interpretation, and American Sign Language (ASL). Should you need confirmation of these services, please email wsboh@sboh.wa.gov in advance of the meeting date.
- If you would like meeting materials in an alternate format or a different language, or if you are a person living with a disability and need reasonable modification, please contact the State Board of Health at (360) 236-4110 or by email wsboh@sboh.wa.gov. Please make your request as soon as possible to help us meet your needs. Some requests may take longer than two weeks to fulfill. TTY users can dial 711.

# TAC de la **evaluación del recién nacido**

## AVISO DE REUNIÓN PÚBLICA

Martes, 17 de junio de 2025
de 10:00 a. m. a 4:00 p. m.

**Nota:** Esta es una reunión virtual mediante Zoom con sala de reunión presencial en el Interurban Hotel, 223 Andover Park E, Tukwila, WA 98188. Salón: Mount Si II. A continuación, le proporcionamos el acceso a la reunión y las instrucciones. Hay servicios de interpretación a otros idiomas disponibles.

**TAC (por su sigla en inglés, Comité de Asesoramiento Técnico) de la evaluación del recién nacido**

**Revisión de la enfermedad de Wilson**

| Hora | Punto del orden del día | Orador |
|---|---|---|
| 10:00 a.m. | 1. Bienvenida y orden del día | Kelly Oshiro, copresidenta del TAC, Mesa Directiva de Salud del Estado<br>Nirupama Nini Shridhar, copresidenta del TAC, Departamento de Salud<br>Kelly Kramer, Mesa Directiva de Salud del Estado<br>Allegra Calder, BERK Consulting |
| 10:20 a.m. | 2. Resumen de la reunión del TAC sobre cCMV de marzo | Kelly Kramer, Mesa Directiva de Salud del Estado |
| 10:35 a.m. | 3. Revisión de la reunión de la Mesa Directiva de abril | Kelly Kramer, Mesa Directiva de Salud del Estado<br>Kelly Oshiro, copresidenta del TAC, Mesa Directiva de Salud del Estado<br>Nirupama Nini Shridhar, copresidenta del TAC, Departamento de Salud |
| 10:55 a.m. | 4. Descripción general de la enfermedad de Wilson | Kelly Kramer, Mesa Directiva de Salud del Estado |
| 11:10 a.m. | 5. Perspectiva familiar | Taodun Li |
| 11:30 a.m. | 6. Enfermedad de Wilson: historia natural, pruebas de diagnóstico y tratamiento | Dr. Sihoun Hahn, genetista bioquímico, Hospital de Niños de Seattle, Key Proteo, Inc.<br>Dr. Pamela Valentino, hepatóloga pediátrica, Hospital de Niños de Seattle |

# TAC de la **evaluación del recién nacido**

| Hora | Punto del orden del día | Orador |
|---|---|---|
| 12:30 | Almuerzo | |
| 1:15 p.m. | 7. Tratamiento (continuación): consideraciones nutricionales | Beth Ogata, Universidad de Washington, Medicina Genética |
| 1:30 p.m. | 8. Tecnología de detección disponible | Megan McCrillis, Departamento de Salud |
| 1:40 p.m. | 9. Análisis del costo-beneficio | Megan McCrillis, Departamento de Salud |
| 2:10 p.m. | 10. Preparación de la infraestructura de salud pública | Megan McCrillis, Departamento de Salud |
| 2:30 p.m. | 11. Revisión y debate de los criterios de Washington para la enfermedad de Wilson | Kelly Kramer, Mesa Directiva de Salud del Estado<br>Kelly Oshiro, copresidenta del TAC, Mesa Directiva de Salud del Estado<br>Nirupama Nini Shridhar, copresidenta del TAC, Departamento de Salud<br>Allegra Calder, BERK Consulting |
| 2:50 p.m. | 12. Voto | Kelly Oshiro, copresidenta del TAC, Mesa Directiva de Salud del Estado<br>Nirupama Nini Shridhar, copresidenta del TAC, Departamento de Salud<br>Allegra Calder, BERK Consulting |
| 3:00 p.m. | Receso | |
| 3:15 p.m. | 13. Debate y próximos pasos | Kelly Oshiro, copresidenta del TAC, Mesa Directiva de Salud del Estado<br>Nirupama Nini Shridhar, copresidenta del TAC, Departamento de Salud<br>Kelly Kramer, Mesa Directiva de Salud del Estado<br>Allegra Calder, BERK Consulting |
| 3:45 p.m. | Cierre de la sesión | Kelly Oshiro, copresidenta del TAC, Mesa Directiva de Salud del Estado<br>Nirupama Nini Shridhar, copresidenta del TAC, Departamento de Salud<br>Allegra Calder, BERK Consulting |

# TAC de la **evaluación del recién nacido**

**Información sobre la reunión de Zoom:**
**Para unirse al seminario web, haga clic en el siguiente enlace:**
https://us02web.zoom.us/j/82455128738?pwd=daqYIpbMiOdugDrpWGu56ZSjzRRLQo.1
**También puede participar por teléfono, mediante la modalidad de solo escucha:**
**Llamada:** +1 (253) 205 0468 (no es un número gratuito)
**Números internacionales disponibles:**
**Id. del seminario web:** 824 5512 8738
**Contraseña:** 726507

**Información importante de la reunión que debe saber:**

- Esta reunión es pública. El público puede observar la reunión en línea o en persona en Town Center 2, 111 Israel Rd. S.E. Tumwater, WA 98501. Salón: 153.
- El Comité de Asesoramiento Técnico no tomará medidas formales ni recibirá comentarios del público. Si tiene algún comentario o material que desee compartir con toda la Mesa Directiva, envíelos a wsboh@sboh.wa.gov.
- Los horarios son estimativos. Nos reservamos el derecho de modificar el orden de los puntos que se tratarán en la reunión.
- Se hará todo lo posible para proporcionar interpretación en español y ASL (por su sigla en inglés, lenguaje de señas americano). Si necesita la confirmación de estos servicios, envíe un correo electrónico a wsboh@sboh.wa.gov antes de la fecha de la reunión.
- Si desea acceder a los materiales de la reunión en un formato alternativo o en otro idioma, o si tiene una discapacidad y necesita una modificación razonable, comuníquese con la Mesa Directiva de Salud llamando al (360) 236-4110 o enviando un correo electrónico a wsboh@sboh.wa.gov. Le pedimos que presente su solicitud lo antes posible para ayudarnos a satisfacer sus necesidades. Es posible que algunas solicitudes tarden más de dos semanas en atenderse. Los usuarios de TTY pueden marcar 711.

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Newborn Screening Technical Advisory Committee (TAC)

## TAC Membership June 2025 TAC

| MEMBER | ALTERNATE | REPRESENTING |
|---|---|---|
| **Kelly Oshiro, JD**<br>Board Co-Chair<br>Assistant Attorney General | | Washington State Board of Health (Board) |
| **Nirupama (Nini) Shridhar, MPH, PhD**<br>Department Co-Chair<br>State Genetics Coordinator | | Department of Health (Department) |
| **Joan Chappel, RN, MSN**<br>Nursing Consultant Advisor/Supervisor | **Sunpreet Bhangoo, RN**<br>Occupational Nurse Consultant | Washington Health Care Authority (HCA) |
| **Byron Raynz**<br>Parent Advocate | | Parent/Child Advocacy |
| **Emily Shelkowitz, MD**<br>Pediatrics, Medical Genetics | **Christina Lam, MD**<br>Medical Director, Biochemical Genetics | Pediatric Specialty Care, Seattle Children's Hospital Biochemical Genetics |
| **Eric Leung, MD**<br>Neonatologist | | Neonatology and Washington Chapter of the American Academy of Pediatrics (WCAAP) |
| **Heather Hinton, MS**<br>Certified Genetic Counselor | | Genetic Counseling, MultiCare Yakima Memorial |
| **Joon-Ho Yu, MPH, PhD**<br>Pediatrics/Public Health Bioethicist | | Bioethics, Department of Epidemiology, University of Washington<br><br>Bioethics, Treuman Katz Center for Pediatric Bioethics and Palliative Care |

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Newborn Screening Technical Advisory Committee (TAC)

| | | |
|---|---|---|
| **Kristine Alexander, PhD, MCR**<br>Senior Medical Policy Research Analyst | | Private Insurers, Regence Health Plans |
| **Krystal Plonski, ND, LAc, EAMP, FABNP**<br>Naturopathic Pediatrics and Acupuncturist | | Naturopaths, Seattle Children's Hospital, and Washington Association of Naturopathic Physicians (WANP) |
| **Lisa McGill Vargas, MD**<br>Neonatologist | **Rucha Shukla, MD**<br>Neonatologist | Pediatrics, Neonatal-Perinatal Medicine, Sacred Heart Medical Center Neonatology Intensive Care Unit (NICU) |
| **Peggy Harris**<br>Public Health and Children's Health Advocate | | Parent/Child Advocacy, Save Babies Through Screening Foundation |
| **Priyanka Raut, DNP, MHS, RN**<br>Senior Director of Nursing | | Pediatrics, Yakima Valley Farmworkers Clinic |
| **Roberta (Bobbie) Salveson, ARNP, PhD**<br>Pediatric Nurse Practitioner, Medical Genetics | | Pediatric Specialty Care, Mary Bridge Children's Hospital Biochemical Genetics |
| **Molly Parker, MD, MPH**<br>Family Medicine Physician | | Provider, Population Health, Jefferson Healthcare |
| **María Sigüenza**<br>Executive Director | | State Commissions, Commission on Hispanic Affairs |
| **Steve Kutz, BSN, MPH**<br>Chair, Washington State American Indian Health Commission | | State Commissions, American Indian Health Commission |
| **Leslie Gesner, LM, CPM** | | Community Care Midwifery |

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# Newborn Screening Technical Advisory Committee (TAC)

**Newborn Screening TAC Staff Support**

**Kelly Kramer**
Board Newborn Screening Policy Advisor

**John Thompson**
Department Director of Newborn Screening

**Megan McCrillis**
Department Newborn Screening Policy Advisor

**Molly Dinardo**
Board Policy Advisor

**Melanie Hisaw**
Board Executive Assistant

**Crystal Ogle**
Board Administrative Assistant

**Michelle Larson**
Board Communications Manager

**Anna Burns**
Board Communications Consultant

**Marcus DeHart**
Board Communications Consultant

# Newborn Screening Technical Advisory Committee (TAC)

## Newborn Screening Technical Advisory Committee (TAC) Charter

**Start Date:** October 28, 2024 **End Date:** June 30, 2025 (tentative)
**Members:** See TAC Membership Addendum A

### OBJECTIVE

Serve as an expert advisory committee on newborn screening for the Washington State Board of Health (Board). Review and recommend possible updates to the Board's current newborn screening process and criteria. Additionally, evaluate several candidate conditions for potential inclusion in the Washington State mandatory newborn screening panel and provide recommendations to the Board.

### BACKGROUND

The Board establishes the rules for newborn screening in Washington, including deciding which conditions all newborns must be tested for at birth. To make these decisions, the Board assembles a multidisciplinary Technical Advisory Committee (TAC) comprised of family representatives and representatives from healthcare, social services, advocacy organizations, public health, and more. Using available evidence, the TAC then assesses candidate conditions using guiding principles and five newborn screening criteria to determine which conditions should be added to the panel.

### KEY ACTIVITIES

This TAC is being convened to complete the following key activities:

- Review the Board's current newborn screening candidate condition review process and criteria and identify opportunities for improvement.
- Determine whether branched-chain ketoacid dehydrogenase kinase (BCKDK) deficiency meets the Board's criteria for newborn screening panel inclusion and provide a recommendation to the Board. This is a requirement of Senate Bill 6234 (Chapter 105, Laws of 2024).
- Determine whether congenital cytomegalovirus (cCMV) meets the Board's criteria for newborn screening and provide a recommendation to the Board. This is a requirement of Senate Bill 5829 (Chapter 96, Laws of 2024).
- Review other possible candidate conditions recently brought in front of the Board between 2024 and 2025.

### TAC TIMELINES (Tentative)

- Meeting 1, Process and Criteria Review – Monday, October 28, 2024
- Meeting 2, BCKDK Deficiency Review – January 2025
- Meeting 3, Criteria Intro to cCMV – February 2025
- Meeting 4, Cost-Benefit Analysis of cCMV – March 2025
- Meeting 5, Wilson Disease Review – June 2025

### COMMITTEE NORMS AND EXPECTATIONS

- Be here now and stay purpose-oriented
- Listen for understanding; seek clarification and resist assumptions
- Appreciate the strength of diverse cultures and perspectives
- Engage respectfully; see with new eyes and hear with new ears
- Move up into a speaking role; move into a listening role
- Stay on topic and mind the time
- Assume positive intent; acknowledge and repair harms
- Try to avoid speaking with someone else is speaking
- Commit to using inclusive language in committee discussions and if possible, try to avoid using idioms or slang terms
- State your name each time you begin talking, and speak at a moderate pace to ensure language interpreters can appropriately translate what is being said
- Use acronyms where possible after introducing technical terms or proper nouns and encourage other committee members to do the same.

Washington State Department of HEALTH

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# **Newborn Screening** Technical Advisory Committee (TAC)

## Newborn Screening Technical Advisory Committee (TAC) Charter

### DECISION MAKING

- Proposed voting methods: This committee will use anonymous voting via Microsoft Forms and open discussion of results to inform committee decisions and recommendations.
- Proposed Primary or Alternative Member voting: Both primary and alternative TAC Members may attend these meetings, however, if both are in attendance the primary TAC member will be responsible for speaking and voting during the meeting. The alternative member only speaks and votes when the primary is not in attendance.

### INFORMATION SHARING

The Newborn Screening TAC planning team will:

- Email and post meeting materials at least 48 hours before the scheduled meeting.
- Email updates and notices to TAC members and designated alternatives.
- Post information on the Newborn Screening Criteria Review Project webpage.

### RESOURCES/REFERENCE MATERIALS

- Chapter 246-650 WAC – Newborn Screening.
- Washington State Board of Health Process to Evaluate Conditions for Inclusion in the Required Newborn Screening Panel.
- Washington Department of Health Newborn Screening Webpage

# GUIDANCE FOR SPEAKING WITH LANGUAGE INTERPRETATION

The Washington State Board of Health (Board) offers American Sign Language and Spanish interpretation during our regular public meetings. We do this as a part of our work towards increasing language access.

**We ask all speakers at Board meetings to follow this guidance to create an accessible meeting environment.** If you have any questions or need guidance for presenting, please contact Board staff for support.

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**WHAT TO EXPECT DURING A BOARD MEETING**

- You will receive a simplified version of this document at your seat on the day of the Board meeting.
- Board staff or interpreters may give you cues to slow down your pace. The cues may include:
  - Raising a paddle sign to signal you to slow down.
  - Making a brief verbal interruption asking you to slow down.

**TIPS FOR SPEAKING AND PRESENTING DURING THE MEETING**

We ask that you help us mitigate the need for interruptions by speaking at a comfortable pace. Our ASL and Spanish interpreters cannot deliver your message accurately if you speak too quickly.

- Take a breath after each sentence to give the interpreter time to deliver your message.
- If you are reading from a script, please be aware that you may read faster than you speak.
- To help the interpreters and audience identify you, state your name each time you begin talking.
- Wait until someone else finishes speaking before you speak. Interpreters can only choose one person to interpret at a time.
- Pause after introducing technical terms, proper nouns, dates, numbers, or figures to allow for interpretation.

**TIPS FOR TECHNICAL TERMS**

- We recommend including a pause after introducing technical terms, proper nouns, dates, numbers, or figures.
  - Example: *"This briefing will discuss rulemaking around newborn screening for Ornithine Transcarbamylase Deficiency (OTCD) [pause for interpretation, wait for cue from interpreter to continue], Chapter 246-650 WAC [pause for interpretation, wait for cue from interpreter to continue]."*
- After you introduce technical terms or proper nouns use their acronyms for the remainder of the introduction.
  - Example: *"For the remainder of this discussion, I will refer to this condition as OTCD."*
- If you are using visual materials (e.g., tables), incorporate descriptive language of the visual material.
  - Example: *"This is a table showing XXXX. And now, we'll look at this part of the table…"*

# Wilson Disease Review

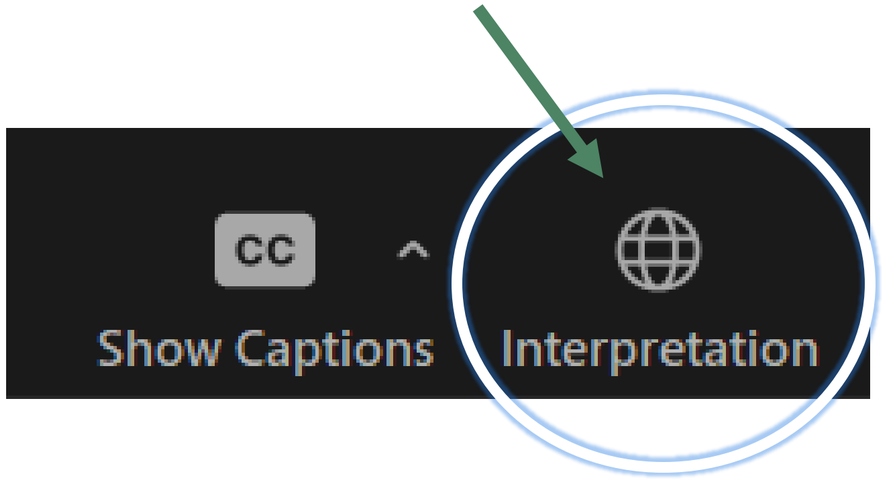
## Newborn Screening Technical Advisory Committee (TAC)

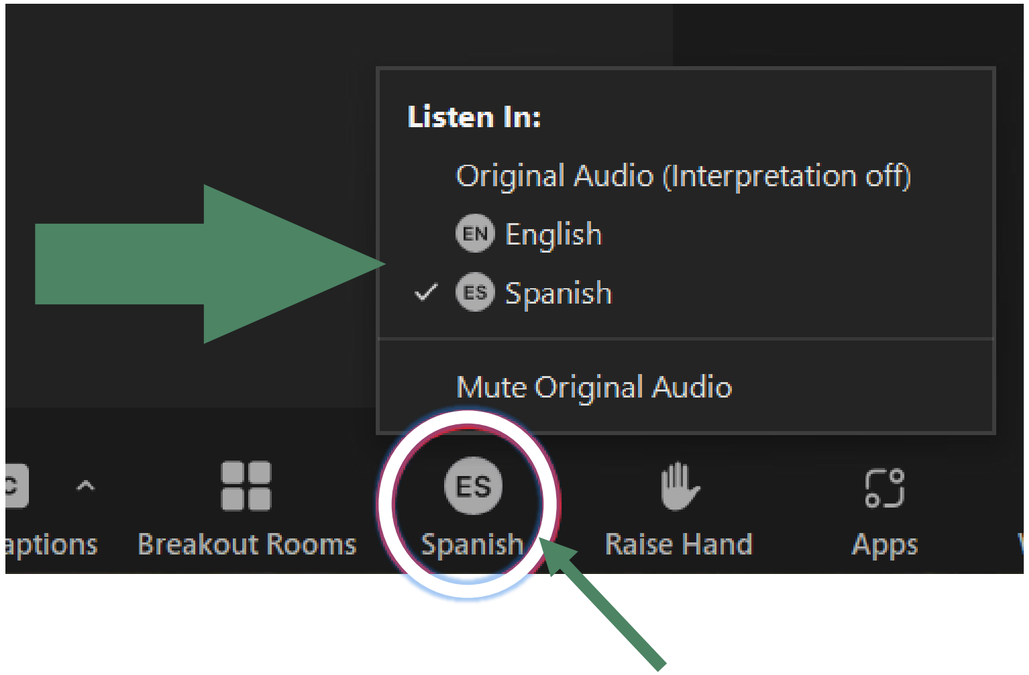
Kelly Kramer, Policy Advisor
June 17, 2025

WASHINGTON STATE BOARD OF HEALTH

# Canales de Idioma de Zoom
## Zoom Language Channels

**Canales de idioma**
Language channels



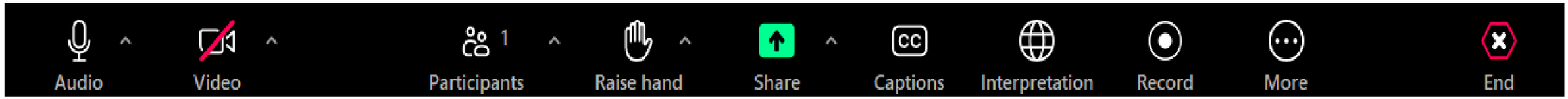

**Elige un idioma**
Choose a language

# Zoom Webinar Functions

Mute/ unmute mic

View participants, change your name

Closed Captioning/Live Transcription




Turn webcam on/off

Raise hand feature

Leave meeting

Note: Depending on your role, you may not have access to all functions identified on this slide.

# Agenda

- Meeting Introduction and Overview
- Recaps:
  - cCMV TAC
  - April Board Meeting
- Wilson Disease Overview
- Family Perspective
- Wilson Disease Natural History, Diagnostic Testing, Treatment
- Lunch

# Agenda Continued

- Nutrition Considerations
- Available Screening Technology
- Cost Benefit Analysis
- Public Health Infrastructure Readiness
- Discussion
- Vote
- Next Steps

# Introductions



# TAC Meeting

## Overview and Purpose

# cCMV TAC Recap

- Senate Bill 5829 (2024 legislative session)
- Viral infection passed from a pregnant person to their unborn child
- cCMV DNA detected via real-time PCR
  - Three options for specimen type: blood, salvia, urine
  - Urine has the highest sensitivity and specificity
- Universal urine screening benefit/cost ratio= 0.72

# April 2025 Board Meeting

- Congenital Cytomegalovirus
  - Board reviewed TAC recommendations
    - Will not add cCMV to our mandatory newborn screening panel
  - RCW 70.83 specifies testing of dried blood spot specimens.
  - Infrastructural and budgetary concerns for non-DBS
  - Focus of prevention efforts

- Other Updates:
  - Federal landscape
    - ACHDNC terminated
    - No updates on the status of the RUSP
    - The Board will still review 4 RUSP conditions for Washington NBS by November 2026

# Three Guiding Principles

Three guiding principles govern all aspects of the evaluation of a candidate condition for possible inclusion in the NBS 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/condition should outweigh harm to families, children and society.

# Overview Wilson Disease

- August 2024 Key Proteo submitted petition to the Board requesting Wilson Disease to be considered for the newborn screening panel

- Wilson Disease is a rare, inherited metabolic disorder
  - Prevents body from eliminating excess copper
    - Copper builds up in tissues
    - Too much copper is toxic to body

- Seattle Children’s Hospital hosts the Wilson Disease Center of Excellence
  - Care team includes biochemical geneticists, hepatologists, psychiatrists, neurologists, nutritionists, social workers.



# Wilson Disease

## Family Perspective



# **Wilson Disease:**
# Natural History, Diagnostic Testing, and Treatment

# Lunch



# **Treatment Continued:**
# Nutrition Considerations

# Available Screening Technology



# Cost-Benefit Analysis

# Public Health Infrastructure Readiness



# Discussion:

## Washington Criteria Review for Wilson Disease

# Newborn Screening Criteria

1) Available Screening Technology

2) Diagnostic Testing and Treatment Available

3) Prevention Potential and Medical Rationale

4) Public Health Rationale

5) Cost-Benefit and Cost Effectiveness

6) Public Health Readiness

# 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 ≥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 healthcare system, newborn screening program, and families.
- 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 availability and proximity to treatment for anyone diagnosed with the condition is considered acceptable based on the frequency of treatment needed.
- 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 infantile-onset forms of the condition (within one year of life) balance the impact of detecting later onset forms of the condition.
- 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. 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

# 6. Public Health Infrastructure 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.

# **Newborn Screening** Technical Advisory Committee (TAC)

## Wilson Disease TAC Voting Ballot- Condition Evaluation with NBS Criteria- June 2025

# Newborn Screening Technical Advisory Committee (TAC)

## Wilson Disease TAC Ballot - Overall Recommendation- June 2025

# Break

# Results and Discussion

# Updates and Next Steps

- Board staff to present TAC's recommendations at the August 20, 2025 Board of Health meeting

- Implement screening for GAMT, OTCD, ARG1-D by January 2026

- Upcoming TAC meetings:
  Four RUSP conditions by November 2026
  - 3MCC
  - Congenital hearing loss
  - Infantile Krabbe disease
  - MPS-II

- Criteria Feedback Survey

WASHINGTON STATE BOARD OF HEALTH

# THANK YOU

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**Minutes for the Newborn Screening Technical Advisory Committee (TAC)**
March 26, 2025
Hybrid Meeting
ASL (or CART) and Spanish interpretation available
Department of Health Town Center 2,
111 Israel Rd. S.E. Tumwater, WA 98501. Room: 153.
Virtual meeting: ZOOM Webinar

## Technical Advisory Committee Members present:

### Online Participants:

Kelly Oshiro, JD, Board Vice Chair and TAC Co-Chair
Nirupama (Nini) Shridhar, MPH, PhD, TAC Co-Chair
Eric Leung, Washington Chapter of the American Academy of Pediatrics (WCAAP)
Byron Raynz, Parent Advocate
Heather Hinton, MultiCare Yakima Memorial
Joon-Ho Yu, Department of Epidemiology, University of Washington Bioethics, Treuman Katz Center for Pediatric Bioethics and Palliative Care
Priyanka Raut, Yakima Valley Farmworkers Clinic
Krystal Plonski, Naturopaths, Seattle Children's Hospital, and Washington Association of Naturopathic Physicians (WANP)
Peggy Harris, Parent/Child Advocate, Save Babies Through Screening Foundation
Kristine Alexander, Regence Health Plans
Lisa McGill Vargas, Sacred Heart Medical Center Neonatology Intensive Care Unit (NICU)
Taylor Kaminski, Global Perinatal Services
Emily Shelkowitz, Seattle Children's Hospital Biochemical Genetics
Cathleen Ackley, Parent Advocate

## Technical Advisory Committee Members Absent:

Roberta (Bobbie) Salveson, Mary Bridge Children's Hospital Biochemical Genetics
Joan Chappel, Washington Healthcare Authority (HCA)
Christina Lam, Seattle Children's Hospital Biochemical Genetics
María Sigüenza, Commission on Hispanic Affairs
Steve Kutz, American Indian Health Association
Tawny Hooley, Parent Advocate

## State Board of Health (Board) staff present:

Michelle Davis, Executive Director
Kelly Kramer, Newborn Screening Project Policy Advisor
Molly Dinardo, Policy Advisor
Melanie Hisaw, Executive Assistant
Crystal Ogle, Administrative Assistant
Michelle Larson, Communications Manager
Anna Burns, Communications Consultant

## Guests and Participants:

Allegra Calder, Facilitator
Ann Melvin, Seattle Children's Hospital
John Thompson, Department of Health
Julie Walker, Department of Health
Michele Greenwood, Spokane Ear Nose & Throat
Samantha Fuller, Department of Health
Megan McCrillis, Department of Health

1. **Welcome and Introductions**

Kelly Kramer, Board staff, welcomed attendees and noted that the purpose of today's meeting is to complete the review of congenital cytomegalovirus (cCMV).

Kelly K. reviewed the agenda for the meeting and shared that Dr. Ann Melvin and Michelle Greenwood would join to support the discussion.

Allegra Calder, Facilitator, welcomed everyone to the meeting. Facilitator Calder asked TAC members to introduce themselves.

Kelly Oshiro, TAC Co-Chair, described the Board's authority and how conditions are reviewed. TAC Co-Chair Oshiro stated that today's meeting is to review cCMV for inclusion on the Washington Newborn Screening Panel, as directed by Senate Bill 5829.

Nini Shridhar, TAC Co-Chair, shared that the meeting would wrap up the cCMV review with Department of Health presentations, followed by a TAC discussion and vote.

2. **March Board Meeting Recap**

Kelly Kramer, Board staff, shared a brief update from the March 12 Board meeting. The Board reviewed the TAC's discussion on Branched-Chain Ketoacid Dehydrogenase Kinase (BCKDK) Deficiency and decided not to move forward with adding the condition to Washington's Newborn Screening (NBS) panel due to limited data. The Board also approved the NBS criteria, with one small change to rename criterion six to "public health infrastructure readiness" to better reflect its intent.

Kelly Oshiro, TAC Co-Chair, said the Board appreciates the TAC's time and commitment to review the criteria and BCKDK Deficiency. TAC Co-Chair Oshiro said the Board was impressed by the level of work and will also share feedback on how the new criteria worked during the congenital cytomegalovirus (cCMV) review.

Eric Leung, Committee Member, noted that some documents still refer to "Five Criteria" and suggested updating them to avoid mentioning a specific number going forward.

Kelly K. responded to Member Leung that they will update all materials and thanked them for bringing that up.

Kelly K. shared an update on House Bill 1697. The bill was related to the Recommended Uniform Screening Panel (RUSP) alignment, and it would have required the Board to adopt all RUSP conditions and shorten the timeframe to review. The bill is not moving forward at this time.

3. **February cCMV TAC Review**

Kelly Kramer, Board staff, summarized the February 11, 2025, Newborn Screening TAC meeting and expressed appreciation to Dr. Ann J Melvin, MD, MPH, Emeritus Professor, Children's Hospital, for the thorough review of the natural history, diagnostic testing, and treatment for congenital cytomegalovirus (cCMV). The minutes for the meeting are in today's packets.

Kelly K. reviewed the discussion today; Parent perspectives; Natural history, diagnostic testing, and treatment; Available screening technology; Early Hearing Detection, Diagnosis, Intervention Program; and Available resources – audiology.

Kelly K. focused on the condition, symptoms, diagnosis and treatment of cCMV (see materials on file). cCMV is an infection passed from a pregnant person to their baby. It affects about 1 in 200 newborns in the U.S. cCMV is a leading cause of nonhereditary hearing loss and can also cause developmental delays, vision problems, seizures, and organ issues. Diagnosis requires testing urine or saliva within 21 days of birth. Antiviral treatments may reduce hearing loss and improve development. Children with cCMV should have regular hearing and vision check-ups.

4. **Update on cCMV Parent Education Materials (Mel)**

Julie Walker, Department of Health (Department), Early Hearing Detection, Diagnosis & Intervention Program (EHDDI), shared updates on Senate Bill 5829 and congenital cytomegalovirus (cCMV) educational materials. The Department has created an informational flyer that discusses preventing cCMV while pregnant and will be translated into 12 languages. Julie discussed upcoming projects, including the Watch Me Grow Washington (WMG) and sending flyers to families in May and June 2025. The Department will do a social media campaign in June for CMV awareness month. Julie highlighted partnerships with the Department of Children, Youth, and Families, the Office of Superintendent of Public Instruction, county resources, and additional external partners for material distribution (see presentation on file).

Peggy Harris, Committee Member, noted that outreach and education in schools of cCMV is wonderful.

Kelly Kramer, Board staff, thanked Julie for this education project and all the work.

5. **Cost-Benefit Analysis- cCMV**

Megan McCrillis, Department staff, reviewed the cost-benefit analysis (CBA) for congenital cytomegalovirus (cCMV). The analysis focused on two screening models for cCMV: ‘no screening’ and ‘urine filter paper.’ The dried blood spot model didn’t meet sensitivity benchmarks, and saliva screening had implementation challenges.

Unlike most screenings aimed at reducing mortality, cCMV screening focuses on the early detection of hearing loss, which can develop later in some infants. Washington sees about 80,000 births annually, with roughly 1 in 244 affected by cCMV. The urine filter paper model shows high sensitivity (99.4%) and is more practical, though some false positives and negatives are expected. (see presentation on file).

Eric Leung, Committee Member, asked what threshold is used to determine a positive result.

Megan was not sure of a specific threshold but noted the feasibility study measured viral loads in dried urine samples. Megan noted that they will have to look at additional research for method development for universal newborn screening (NBS).

Megan explained that babies who screen positive for cCMV and are symptomatic at birth follow the same path as the no-screening model, which also applies to false negatives who are detected later. Start-up costs for screening aren't included in the cost-benefit ratio, which currently shows a benefit of 72 cents per dollar spent and a net cost to the system. The dried blood spot model performs worse, with lower sensitivity and higher costs. Sensitivity analysis suggests that if cCMV prevalence is higher or if late-onset hearing loss affects 20% of symptomatic babies, costs could break even. Intangible factors like emotional impact and infections prevented were also noted. Follow-up for positives would last six years, with frequent hearing checks. Year one would monitor about 309 infants, growing to around 1,800 by year six. Data from other programs, like Minnesota and Ontario, show challenges with false positives and mild abnormalities, indicating further evaluation is needed.

Cathleen Ackley, Committee Member, appreciated the CBA but noted a different vision was shared in a prior TAC meeting. The question was raised about why the analysis focused on hearing loss instead of other neurodevelopmental conditions.

Megan explained that hearing loss was the focus because more data is available for the CBA, while evidence on other neurodevelopment outcomes is limited. Other benefits might emerge over time if the screening is implemented, but this analysis reflects what can be reasonably measured right now. Megan noted these models probably represent a slim snapshot.

Member Ackley referenced a CBA of cCMV by the Infectious Diseases Society of America (IDSA) that included multiple neurodevelopmental issues in its analysis. The CBA did not include our geographic region. Overall, the CBA was worth it because of the additional things they looked at. Member Ackley said they would be happy to consider looking at other outcomes.

Megan said that for our primary purposes, we must look at changes based on screening. Antiviral treatment helps symptomatic infants detected early, but the model assumes these cases are already identified without screening. While other CBAs exist, they may not apply to Washington's situation, though additional resources are welcome.

John Thompson, Department staff, thanked Member Ackley and expressed interest in reviewing the additional information. John agreed with Megan that the model compares the status quo with the introduction of screening. In the literature that they have found, there is no difference in cost or benefit if they were to model the development outcomes. John emphasized that 15% of babies with cCMV develop late-onset hearing loss and benefit from early intervention. John highlighted that the biggest impact is preventing CMV spread in pregnancy to reduce death and disability. John praised Julie's prevention efforts.

Member Ackley agreed and offered to discuss the ISDA studies further. Member Ackley asked if Minnesota and Ontario were only considering hearing loss and related costs. Were they also considered early intervention and impacts? Particularly in Minnesota, were impacts on the costs of Medicaid and the state budget considered?

Megan stated that they do not have CBAs for Minnesota or Ontario and are unsure if they conducted these.

Member Ackley noted the Chimes study might provide more detailed data beyond hearing loss and include other neurodevelopmental issues that can appear outside the expected timeframes. Member Ackley agreed on the importance of prevention and noted that many people think CMV is like a common cold. Member Ackley emphasized the need for screening options for pregnant people alongside prevention efforts, since CMV is mostly benign until pregnancy occurs.

Megan explained that six years is an example. Subject matter experts are still unsure how long to follow those with cCMV. The CBA focus is on hearing, but neurodevelopmental outcomes can be determined later over time.

John explained that the CBA is a living document and can be updated as new research or treatments emerge. Such as if a new medication shows it saves lives, the model would be revised to reflect that.

Member Leung expressed gratitude to Member Ackley. Member Leung pointed out that Minnesota is the only state that has universal screening. It is challenging to adopt a CBA with targeted hearing screens as an initial method, then proceed to tests for urine or CMV through other methods. Member Leung inquired about the benefits of a two-tier system, such as urine and targeted hearing. Member Leung also asked whether Washington's CBA is specific to oral anti-retroviral or intravenous antiretroviral (ARV). Additionally, was the proposed treatment model for six weeks or six months?

Megan said the model used oral ARV, which is the current best practice. The treatment length was based on the latest Redbook guidance, which is six months for kids with symptoms and hearing loss.

Member Leung stated that the cost of NBS ranges from $25 to $13 to create a ratio equal to 1. But is that assuming that we don't change the cost of screening? Member Leung noted bringing this up, as the Board can recommend the cost of expanding and accommodating the program.

Megan explained that the current NBS fee estimates, based on staffing and test kit costs, range around $3 per baby. To achieve a cost-benefit ratio of 1, the fee would need to be $13 per baby. However, this $13 fee isn't considered realistic now unless new, more efficient technology lowers testing costs.

Member Leung said in the CBA, the cost was higher than the benefit. Member Leung asked what would need to be charged in addition so that the ratio improves?

Megan said the model is looking at the public health system's costs. The increasing fee is to cover the additional costs that are going into the system. If CMV is more common than we thought, then more kids with late onset hearing will reap additional benefit. That improves the benefit-cost ratio from a societal level, which is where our ratio comes from.

Krystal Plonski, Committee Member, thanked Megan and asked if other states are using urine sample testing for screening for cCMV. Are Minnesota and Ontario using dried bloodspot?

Megan said there are some urine screening programs for other conditions that are not CMV. The two programs we referenced are using universal screening with just a dried bloodspot.

Member Plonski asked how many other states are testing for this.

Megan answered that Minnesota was the first state to launch cCMV screening and mentioned that there are additional states that have begun screening or are considering it. The data shared from Minnesota was from 2023-24. Other states that have implemented screening have not conducted it long enough to establish a large enough data pool.

Member Plonski asked if the Recommended Uniform Screening Panel (RUSP) conditions or other conditions under review utilize urine testing?

Megan noted that some conditions can use urine for detection. The MS/MS in our laboratory is an excellent tool for accurately detecting conditions via dried blood spot.

John stated that there are high false positive rates in some conditions being detected by MS/MS. Per conversations with the follow-up supervisor, urine may be a useful secondary test if the Board were to approve this specimen type in newborn screening.

Nini Shridhar, TAC Co-Chair, thanked Megan for the analysis and asked what the current capacity for pediatric audiology is. TAC Co-Chair Shridhar raised concerns about adding 1,800 patients to the system, especially since only a small number might benefit, and questioned how that could affect diagnosis rates.

Megan noted that this may be addressed during the public health readiness section but asked if Julie Walker can provide input.

Julie Walker, Department staff, said the exact numbers aren't available but that Seattle Children's Hospital currently has a two to three-month wait time. Not all audiology clinics in Washington specialize in pediatrics. There are audiology clinics in Washington but not all specialize in pediatrics. Mary Bridge Hospital and Seattle Children's have 8-9 clinics, the University of Washington has nine pediatric clinics, and there are 21 other pediatric audiology clinics.

Kelly Kramer, Board staff, added that Michele Greenwood will join the meeting in the afternoon and can offer further insights.

Member Ackley shared that the CMV Foundation was created in 2014 and that Minnesota started screening in 2021 due to the Vivian Act. There was a powerful New York Times best seller that shared a personal story of CMV that spurred national attention to this issue. Member Ackley expressed support for targeted screening and offered to share additional data to help inform Washington's CBA.

John explained that targeted screening shows no measurable benefit, making it impossible to calculate a cost-benefit ratio. For infants who are asymptomatic at birth but develop hearing loss later, intervention services would still be accessed, so no added benefit could be attributed to targeted screening.

Emily Shelkowitz, Committee Member, asked if there are any studies about siblings at risk and if any program has looked at that data. Is there a reason that Minnesota settled on six years of follow-up?

Megan shared that families could request dried blood spot testing for cCMV if symptoms appear later. But this type of follow-up is uncommon in other programs. The six-year follow-up timeline aligns with when most hearing loss typically emerges. It is unclear when Minnesota plans to conclude follow-up.

Julie shared that at an Early Hearing Detection and Intervention conference, they learned that a six-year timeline is recommended for audiological monitoring. The CMV program is looking at the best timeline to conduct active follow-up by determining if families attend appointments and the types of hearing tests being conducted.

Rucha Shukla, Committee Member, asked what criteria were used for targeted screening. Was it just failed hearing screenings that led to ordering CMV screening? The majority of infected kids can be asymptomatic.

John stated that yes, the model was if the baby failed their hearing screen.

Member Shukla would like to hear the numbers Member Ackley cited for targeted screening.

Member Ackley said the information came from a national infectious disease report that included over seven criteria, including neurodevelopmental concerns.

**BREAK**

6. **Public Health Infrastructure Readiness**

Megan McCrillis, Department staff, introduced “public health infrastructure readiness” as the newest criterion for discussion. This criterion had previously been considered informally as part of cost-benefit analyses but was largely addressed behind the scenes rather than explicitly outlined. Megan provided an estimate of the resources required to begin congenital cytomegalovirus (cCMV) testing for the laboratory (see presentation on file).

John Thompson, Department staff, explained that the screening fee would need to be increased to cover these additional resources. Typically, implementation of a new screening begins two to three years after the Board's approval.

Eric Leung, Committee Member, asked whether the model included costs for data analysis over time.

John responded that it did not. While the lab has historically engaged with the community through presentations at the annual newborn screening (NBS) symposium and has occasionally published papers, such activities are not part of their standard duties and thus were not included in the cost model.

Priyanka Raut, Committee Member, raised a related concern regarding data transparency. In clinical settings, information is received for abnormal results but not for normal screenings, which creates ambiguity.

John explained that the follow-up team positions would address this gap. The first Health Services Consultant 2 would contact primary care providers (PCPs) to coordinate diagnostic testing following positive results. The second would manage confirmed cases, ensuring follow-up hearing screenings every three months, at least for the first year, mirroring the Minnesota model. The exact duration of follow-up has yet to be determined.

Member Raut asked how educational materials would be developed to protect siblings following a positive case.

John explained that educational materials, such as referral packets and brochures, would be created in collaboration with experts and distributed to both parents and providers.

Member Leung asked Member Raut to clarify their earlier comment and confirmed that providers should receive both normal and abnormal screening results

Kelly Kramer, Board staff, introduced Michele Greenwood.

Michele Greenwood, Audiology, Spokane Ear, Nose, & Throat, presented on the standard audiological care pathway for infants. This typically begins at six months of age, with screenings every three months until age two. Michelle emphasized the challenges of access for families in rural areas of Washington.

Kelly K. invited Michelle to comment on infrastructure readiness.

Michele raised concerns about limited access to initial Auditory Brainstem Response (ABR) testing and whether providers outside Spokane are ready for ongoing screenings.

Kelly K. asked about current clinic capacity given the rise in patient volume.

Michele said their clinic could likely accommodate the need by establishing a specialized clinical day for cCMV patients. Michele noted uncertainty regarding capacity in other regions.

Rucha Shukla, Committee Member, emphasized the travel burden for families in remote areas and expressed concern over the logistical challenges of requiring multiple long-distance visits for testing.

Member Leung voiced concern about the ability of clinics to handle new diagnoses and suggested that dedicated scheduling might help manage increased demand.

Michele noted that their clinic currently reserves appointment slots for newborns who fail NBS screenings. However, more patient data would be needed to determine the number of additional slots required.

Member Shukla added that estimates should include potential patient numbers from northern Idaho and eastern Oregon. Member Shukla suggested involving clinics in the development of specimen collection training, particularly for urine samples, since many newborns remain hospitalized for 24-48 hours.

John shared insight from a conversation with the director of Quebec's urine NBS program, where families are sent home with a collection kit. The process of collecting and drying urine on filter paper achieves a 99% specimen acceptability rate. John viewed this as a strong indication that a similar model could be adopted successfully.

Heather Hinton, Committee Member, raised concerns about long-term follow-up and access to care for children who may require frequent hearing screenings. Member Hinton asked whether care would remain with PCPs or require ongoing specialist involvement.

Emily Shelkowitz, TAC Member, asked whether any existing programs had factored in the availability of developmental services to support asymptomatic children and prevent progressive hearing loss.

Megan responded that the cost-benefit analysis (CBA) stopped at screening implementation and did not include services such as speech-language pathology (SLP).

Member Leung supported Member Shelkowitz's question, noting that hearing loss often co-occurs with other conditions requiring services like occupational and physical therapy. Member Leung also noted that in many community health systems, pediatricians are considered specialists and refer patients to additional providers as needed.

Member Shukla added that all children diagnosed with cCMV would be eligible for early intervention programs, significantly increasing the load on those services. Member Shukla emphasized the strain this would place on eastern Washington, which already faces substantial shortages in healthcare access.

Cathleen Ackley, Committee Member, shared an informational resource that may address Member Shelkowitz's question regarding developmental services.

### 7. Washington Criteria Review for cCMV and Discussion

Kelly Kramer, Board staff, reviewed criterion one and opened it up for questions.

Rucha Shukla, Committee Member, asked about Dr. Melvin's presentation. Does Washington have a higher prevalence of cytomegalovirus (CMV) than other states?

Dr. Ann Melvin, Seattle Children's Hospital, said no, the papers cited aren't from mass screening data, so hard to say for sure.

Kelly K. reviewed criterion two and three and opened it up for questions.

Eric Leung, Committee Member, said this is a unique condition and doesn't fit well within criterion three.

Kelly K. reviewed criterion four and opened it up for questions.
Member Leung noted that this was a particularly difficult point when this topic was reviewed several years ago. Dr. Melvin's presentation updated the TAC on research and shared several resources that helped address previous concerns.

Dr. Melvin explained that there isn't an effective risk-based screening since simply being born poses a risk, making it challenging because many infants show no symptoms.

Kelly K. reviewed criterion five and opened it up for questions.

Member Leung pointed out that congenital Cytomegalovirus (cCMV) screening appears to lose money, but emphasized the difference between cost-benefit and cost-effectiveness. They weren't sure if the group had discussed cost-effectiveness much.

John Thompson, Department staff, stated the analysis was a cost-benefit analysis, not a cost-effectiveness analysis.

Dr. Melvin asked what a cost-effectiveness analysis is.

John explained that cost-effectiveness analyses include quality of life when measuring benefits. Their current cost-benefit analysis looks only at dollar costs and savings. John noted drawbacks in the current system, especially for babies without symptoms.

Member Shukla asked about data on early versus late onset and diagnosis of hearing loss.

John stated that Megan did include that information in the model. There are benefits for early identification of hearing loss, estimated at 2.4 million worth of benefit per year.

Michele Greenwood, Audiology, Spokane Ear Nose & Throat, shared that there are social and developmental lags from hearing loss, including language skills. Michele discussed the emotional impact on families of false positives. In the past, many providers were not onboard with universal hearing screening due to the fear of causing trauma in families.

Kelly K. reviewed criterion six and opened it up for questions.

Heather Hinton, Committee Member, asked how accessible antiretroviral (ARV) treatment is for families.

Dr. Melvin noted that most families are unfamiliar with cCMV, which can make treatment decisions difficult. In their experience, insurance coverage for treatment has generally not been a barrier. Regarding the cost to families, Dr. Melvin explained that the initial appointment typically occurs with a pediatrician and questioned whether that visit would provide a significant benefit. However, much of the follow-up care can be conducted virtually via telehealth. Given the expected number of affected individuals, Dr. Melvin suggested that capacity concerns may be minimal.

Member Shukla raised similar concerns in the previous meeting. It was noted that some infant care providers offer initial consultations through telemedicine. Broadening access and identifying a wider network of specialists, particularly within hospital systems, could help streamline care pathways. Knowing whom to contact within those systems could improve efficiency for patients and families.

Member Leung asked Dr. Melvin whether treatment could be easily protocolized, especially involving ARVs, in a way like how treatment for HIV in newborns had previously been

handled. Member Leung brought up past efforts in disseminating HIV treatment protocols statewide and inquired whether similar processes could be developed using blood tests, liver function tests (LFTs), and other standard measures.

Dr. Melvin stated that they are considering this suggestion.

Member Shukla asked whether data exists showing long-term benefits of early intervention, particularly over several years. The question focused on whether benefits accumulate over time, possibly leading to cost neutrality or even long-term cost savings following initial stabilization.

Megan responded that the modeling work focused on a one-year birth cohort, tracking children with and without late-onset hearing loss. The model estimated economic benefits based on early identification. Megan offered to provide a publication that explains how the benefit values were calculated. While long-term benefits were considered, further study would be required to explore that dimension more fully.

John added that the model did not assess cumulative effects across years. Each analysis provided a snapshot of a single year's birth cohort, measuring costs and benefits over six years. This process is repeated for each new cohort, resulting in discrete, year-by-year evaluations rather than a continuous, long-term analysis.

Member Leung emphasized that startup costs are typically one-time expenses. Member Leung noted the importance of factoring in longer-term infrastructure implications.

Member Shukla highlighted that early diagnosis can lead to earlier interventions like cochlear implants and speech therapy. These may improve long-term outcomes even if those benefits are hard to quantify.

Cathleen Ackley, Committee Member, affirmed the previous comment and shared that *Listen and Talk*, a school on the east side, supports children born with hearing loss, especially those affected by CMV. The school's robust early education program ends at kindergarten, aligning with key stages of language and cognitive development. The hope is that early intervention allows children to thrive in public education afterward. Member Ackley stressed that while these benefits are hard to measure, they are critical to child development and long-term success.

Allegra Calder, Facilitator, asked for any final questions or comments. It was noted that members could vote "unsure" if needed. Comments submitted during the vote would be discussed and forwarded to the Board to capture areas of consensus and divergence. Input remains valuable and welcomed.

Member Shukla directed a question to John and Megan, requesting a clear summary of the expected financial cost if urine spot screening were implemented. The request focused on understanding annual cost implications and emphasized the importance of hearing this clearly before voting.

John explained that, from the Department's perspective, the benefit-cost ratio from the urine screening model was approximately 0.72. Shared that in Minnesota, 75% of children

were not receiving proper diagnostic follow-up 75% of children were not receiving proper diagnostic follow-up and that ratio dropped to around 0.58. In other words, for every $1 spent, the estimated return could range between 58 and 72 cents. John acknowledged that the model does not include intangible benefits which are difficult to measure but still impactful. Committee members were encouraged to consider these nuances when making decisions on behalf of families and the broader community.

Peggy Harris, Committee Member, reflected on the emotional difficulty of remaining unbiased and shared a personal experience involving the diagnosis of a child.

8. **Vote**

Allegra Calder, Facilitator, introduced the voting section of today's meeting.

Peggy Harris, Committee Member, discussed how it's hard not to be biased through this and thinking about those who are affected more than those who are not.

Facilitator Calder appreciated Member Harris' comments and emphasized that it's important to vote for what you think based on what you know.

Member Shukla said it would be nice to compare some of the other conditions that are on the newborn screening (NBS) panel and compare their costs.

John Thompson, Department staff, shared a table that provided additional information of the current conditions on the NBS panel and their benefit-cost ratio.

Kelly Kramer, Board staff, provided additional information to TAC members on how to vote. The first vote is for the cCMV condition evaluation with the Newborn Screening Criteria. Once the first vote is completed, the TAC will move to a second vote to determine overall if they think cCMV should be added to the NBS panel.

Kelly K. reviewed the initial vote from the TAC members. For criterion one, most TAC members agreed that cCMV meets the criteria. For criterion two, half of the TAC members felt it met the criteria, while the other half were either unsure or disagreed. For criterion three, most TAC members believed it met the criteria. Similarly, for criterion four, the majority felt it met the criteria. For criterion five, half of the TAC members agreed it met the criteria, while the other half were either unsure or disagreed. Finally, for criterion six, half of the TAC members believed it met the criteria, while the other half were either unsure or disagreed.

Facilitator Calder reminded TAC members that we do not need consensus for these votes.

Kelly K. introduced the second voting ballot. This vote is to ask TAC members for their overall recommendation of cCMV to the NBS panel. While TAC members voted, the TAC went into a break.

**LUNCH**

**9. Discussion and Next Steps**

Eric Leung, Committee Member, said this has been one of the most difficult discussions in the last five years and reminded everyone that it is okay to be unsure.

Kely Kramer, Board staff, reviewed the second vote and the anonymous comments submitted.

Member Leung expressed uncertainty about whether generating demand would lead to the necessary infrastructure being developed. They cautioned that this approach might be overly optimistic.

Rucha Shukla, Committee Member, shared a similar concern. While supportive of including congenital cytomegalovirus (cCMV), they worried that the system may not be able to meet the demand, even if it exists, and could become overwhelmed.

Member Leung added that funding pediatric systems across the state has long been a challenge, noting that children have consistently been a vulnerable population. The high costs involved contribute to skepticism, yet do not deter them from advocating. They voted yes, emphasizing that despite consistent failures in securing adequate funding for children's care, persistent advocacy remains essential.

Peggy Harris, Committee Member, agreed and thanked Member Leung for their comments.

Emily Shelkowitz, Committee Member, shared feeling somewhat uninformed but noted that the rationale for adding cCMV, though different, sparked reflection. They found it valuable to consider infrastructure and capacity, which in the case of cCMV, seemed more robust compared to other conditions. They speculated whether this was influenced by current global or societal conditions and invited other members to share thoughts on that comparison.

Member Leung appreciated the perspective and remarked on the difficulty of comparing this condition to others already on the panel, noting that those conditions differ.

Member Harris added that when considering previous additions to the panel, there had been fewer concerns about infrastructure and more comprehensive information available on the respective conditions. This situation felt different.

Member Shelkowitz said their second observation regarding the discussion on hearing loss therapeutics. They noted the absence of a TAC member from the Deaf or Hard of Hearing community and suggested that this is a perspective that should be included on the panel.

Cathleen Ackley, Committee Member, said part of their advocacy here is to represent that community.

Priyanka Raut, Committee Member, acknowledged the diversity of perspectives on the committee and echoed Member Shelkowitz's earlier point, expressing optimism that the group would continue to become more inclusive.

Member Harris said community groups are important. Just need to keep building on those groups.

Member Leung asked Member Raut whether the Farmworkers Clinic has access to community health workers who help connect them to services.

Member Raut confirmed that such programs exist, including partnerships with Seattle Children's Hospital. They emphasized the importance of those initiatives.

Kelly K. will present the TAC's recommendations of cCMV at the April 9 Board meeting.

Kelly Oshiro, TAC Co-Chair, explained that urine screening can't move forward without legislative approval. Rulemaking likely wouldn't begin until July 2026, and the Board may not revisit the condition until urine collection is formally added.

Member Leung asked whether the Board must go through the full process of drafting new RCWs to make these changes.

TAC Co-Chair Oshiro confirmed that review of RCWs would be necessary.

Member Leung shared that they had reviewed the RCWs themselves and were unsure about the level of legislative involvement required for the Board to carry out its responsibilities. They questioned whether modifying the wording of an RCW constitutes a lengthy legislative process.

TAC Co-Chair Oshiro asked whether other Recommended Uniform Screening Panel (RUSP) conditions utilize urine samples, noting that it is a consideration.

Member Leung explained that these legislative challenges were part of why they previously testified in opposition to House Bill 1697. Member Leung wanted to clarify the extent of the process involved, based on how transparent the requirements currently appear.

Molly Dinardo, Board staff, confirmed that the issue will need to be discussed at a Board meeting.

Kelly K. said that the TAC will review the condition of Wilson Disease in either late May or early June.

Member Leung noted that the TAC has historically met as an ad hoc committee; this is the first time we have done a standing committee.

Kelly K. said we will assess this at the Wilson Disease committee. At the next TAC meeting, we can discuss if this group would like to move forward working together through the biennium.

John Thompson, Department staff, thanked TAC members for their time and perspective.

**ADJOURNMENT**

Kelly Oshiro and Nini Shridhar, TAC Co-Chairs, adjourned the meeting at 2:30 p.m.

WASHINGTON STATE BOARD OF HEALTH

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Kelly Oshiro, TAC Co-Chair and Nini Shridhar, TAC Co-Chair

Washington State Department of HEALTH

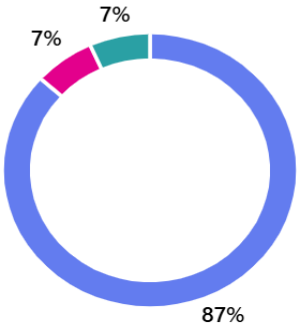
WASHINGTON STATE BOARD OF HEALTH

# Newborn Screening Technical Advisory Committee (TAC)

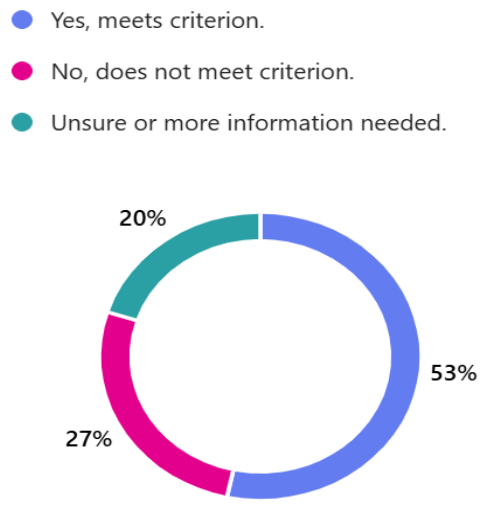
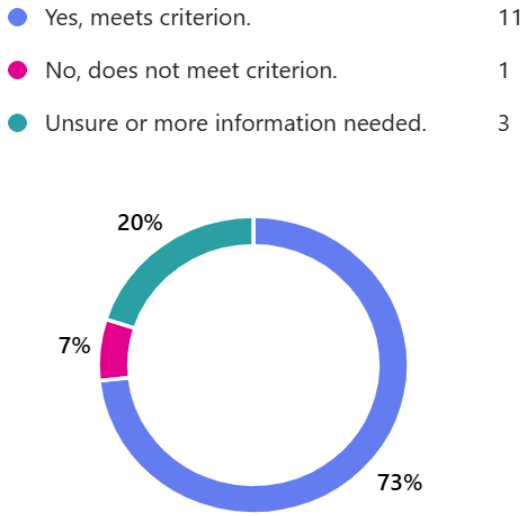
## Meeting to Review Congenital Cytomegalovirus (cCMV) for the Newborn Screening Panel

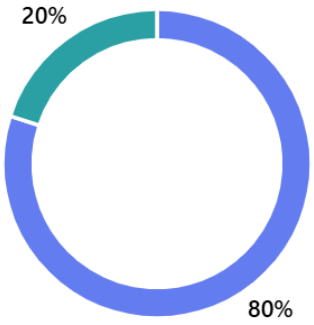
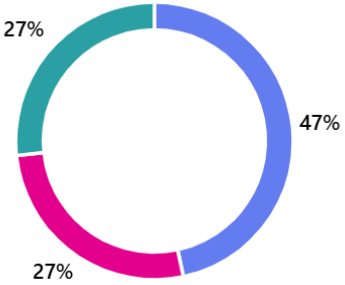
### TAC Member Voting Summaries and Comments

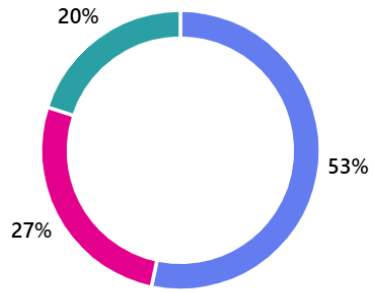
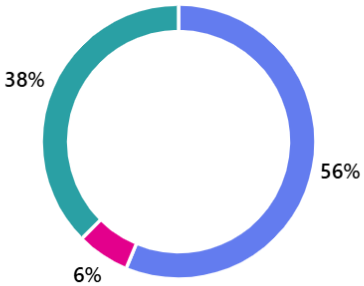
The following is a compilation of comments from TAC members provided when voting on each individual criteria, and an overall recommendation. Comments have been summarized and are organized by each criterion and then overall comments provided.

| Criteria | Major themes |
|---|---|
| 1. Available Screening Technology<br>Yes, meets criterion. 13<br>No, does not meet criterion. 1<br>Unsure or more information needed. 1<br>  | • Urine PCR is the gold standard screening test for cCMV due to sensitivity and specificity.<br>• Universal screening may not prevent irreversible harm, but allows for prevention of progression of hearing loss and developmental delays . |

(continued on the next page)

| | |
|---|---|
| 2. Diagnostic Testing and Treatment Available<br>  | • Concern that medical expertise is not reasonably available to all newborns screened and for the capacity of treatment centers. |
| 3. Prevention Potential and Medical Rationale<br>  | • Screening for cCMV will not eliminate harm but can ameliorate consequences of infection. |

| | |
|---|---|
| 4. Public Health Rationale<br>Yes, meets criterion. 12<br>No, does not meet criterion. 0<br>Unsure or more information needed. 3<br>  | • Risk-based screening not an option as most babies with cCMV are asymptomatic at birth.<br>• Targeted hearing screening misses a majority of cases. |
| 5. Cost Benefit / Cost Effectiveness<br>Yes, meets criterion. 7<br>No, does not meet criterion. 4<br>Unsure or more information needed. 4<br>  | • Intangible benefits may be received from cCMV screening such as limiting family turmoil from a late diagnosis and connection to early intervention.<br>• Cost benefit is negative. |

| | |
|---|---|
| 6. Public Health Infrastructure Readiness<br>Yes, meets criterion. 8<br>No, does not meet criterion. 4<br>Unsure or more information needed. 3<br>  | • Lack of infrastructure in Washington, especially in rural areas.<br>• Demand for infrastructure will be stronger if universal screening is implemented.<br>• State and community partners to re-evaluate needs after cCMV screening is implemented. |
| Overall Recommendation to add cCMV to the mandatory newborn screening panel<br>I recommend the Board add universal screening of cCMV to the list of conditions for which all... 9<br>I do not recommend the Board add cCMV to the list of conditions for which all Washington-born... 1<br>At this time, I do not recommend the Board add cCMV to the list of conditions for which all... 6<br>  | • cCMV prevention and education should be prioritized for people who are pregnant.<br>• Concerns for lack of infrastructure, especially for audiological follow-up.<br>• Rural Washington populations have limited accessibility to healthcare services.<br>• More data on long-term health outcomes for asymptomatic infants is needed and may lead to an improvement in the cost-benefit of cCMV screening over time. |

Washington State Department of HEALTH

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Newborn Screening Technical Advisory Committee (TAC)

# Wilson Disease (WD) Overview

Newborn Screening Technical Advisory Committee
June 17, 2025

## ABOUT THE CONDITION

- Wilson Disease (WD) is a rare inherited disorder of copper metabolism.
- WD is caused by changes in the *ATP7B* gene, that reduce or eliminate the protein responsible for removing excess copper.
- Copper then accumulates in the body, especially in the liver and brain.
- WD may be detected via tandem mass spectrometry. The technology application will be reviewed at the TAC meeting.
- About 1 out of 30,000 individuals is affected by WD.

## SYMPTOMS

- Most individuals with WD first develop symptoms between the ages of 5 and 35.
- WD symptoms vary between individuals, but can include:
    - Hepatic symptoms such as inflammation, cirrhosis, or liver failure.
    - Neurological dysfunction such as movement disorders, tight muscles, or difficulty swallowing.
    - Psychiatric disorders such as depression or anxiety.
- In about half of those with WD, the liver is the only major organ system affected. Other patients with WD may have neurological or psychiatric symptoms only, or a combination of these systems affected.
- Many individuals with WD exhibit Kayser-Fleischer (KF) rings, which are copper deposits in the cornea of the eye.

## DIAGNOSIS

- WD is often diagnosed years after symptoms begin, due to their non-specific nature. Diagnosis usually involves a physical exam and tests like ceruloplasmin levels, 24-hour urinary copper excretion, liver function tests, or a liver biopsy.
- Genetic testing for changes in the *ATP7B* gene is the gold standard for confirming a diagnosis.

## TREATMENT

- Treatment for WD can include:
    - Preventing excess copper accumulation by limiting dietary intake of copper.
    - Removing excess copper from the body through chelation therapy drugs.
    - Blocking the absorption of copper in the intestinal tract through zinc acetate medication.
- Lifelong treatment is necessary to manage WD. Nonadherence may result in severe health complications, including liver failure or death.
- Liver transplantation may be necessary for those with severe liver damage or failure.

Mulligan, C., & Bronstein, J. M. (2020). Wilson disease: An overview and approach to management. *Neurologic Clinics*, *38*(2), 417–432. https://doi.org/10.1016/j.ncl.2020.01.005

Schilsky, M. L., et al. (2022). A multidisciplinary approach to the diagnosis and management of Wilson disease: 2022 practice guidance on Wilson disease from the American Association for the Study of Liver Diseases. *Hepatology*, *77*(4), 1428–1455. https://doi.org/10.1002/hep.32801

Wilson Disease Association. (2021, August 30). *Living with Wilson disease*. https://wilsondisease.org/living-with-wilson-disease/

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Washington State Department of HEALTH

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**Newborn Screening** Technical Advisory Committee (TAC)

# Placeholder for Materials

*Materials for Agenda Item 5 - Family Perspective will be added up to three business days after the meeting.*

Washington State Department of HEALTH

WASHINGTON STATE BOARD OF HEALTH

**Newborn Screening** Technical Advisory Committee (TAC)

*Agenda Item 6*
*Wilson Disease: Natural History, Diagnostic Testing, Treatment will be added up to three business days after the meeting.*

# Newborn Screening for Wilson Disease

Sihoun Hahn, MD, PhD
Professor of Pediatrics
University of Washington School of Medicine
Seattle Children's Hospital
Director, Center of Excellence for Wilson Disease

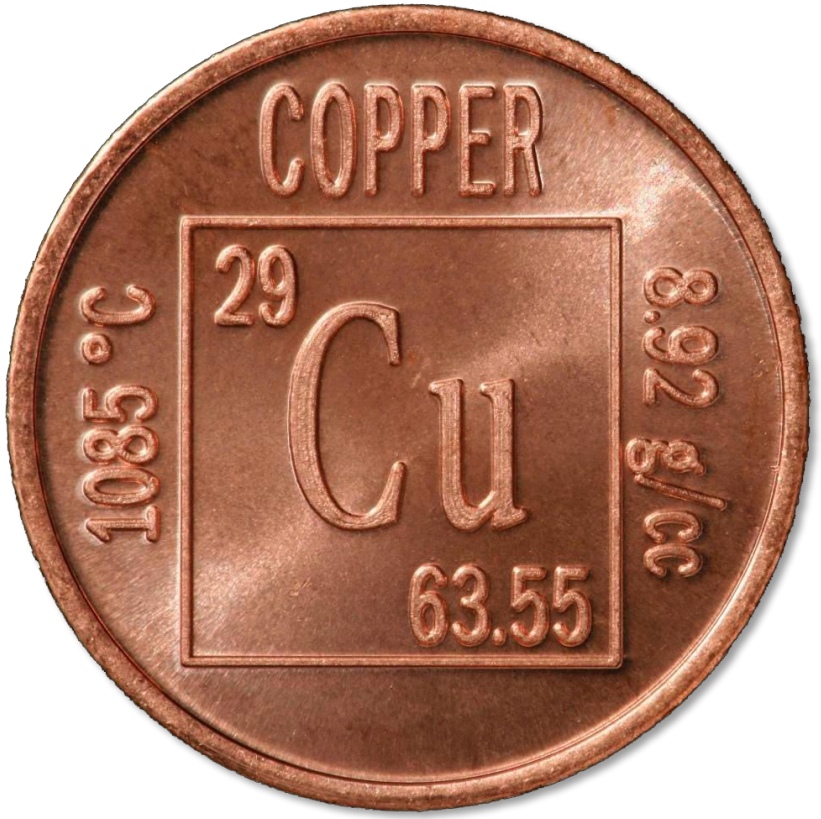
Founder and CMO, Key Proteo, Inc

# FCOI

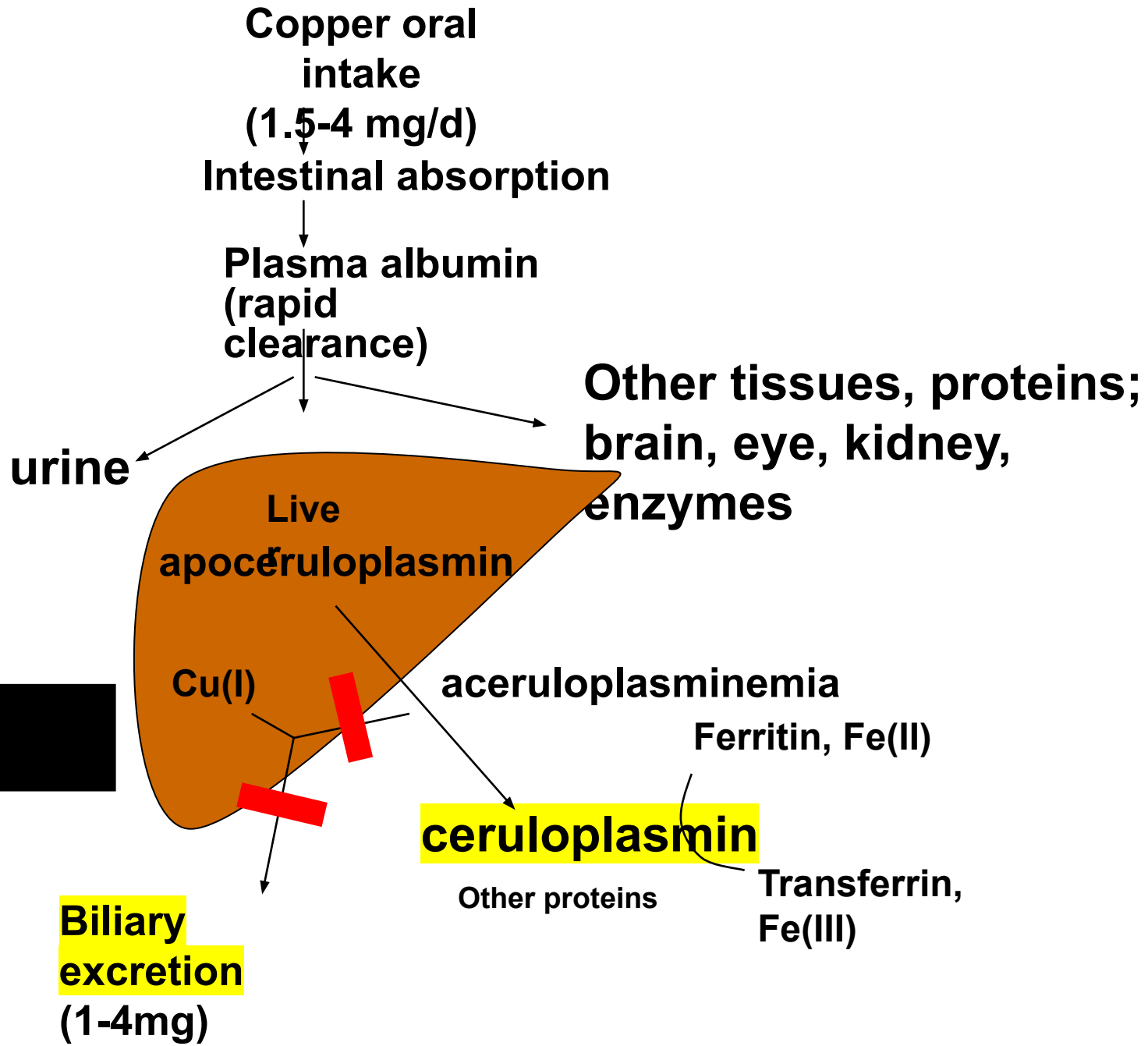
- Sihoun Hahn, MD, PhD, is a member of the Seattle Children's Hospital workforce and is serving as Chief Medical Officer of Key Proteo, Inc. He is an inventor of intellectual property that has been licensed to Key Proteo, Inc. Dr. Hahn is the founder of Key Proteo, Inc. and has ownership equity interests in the company.

# Copper is an Essential Heavy Metal

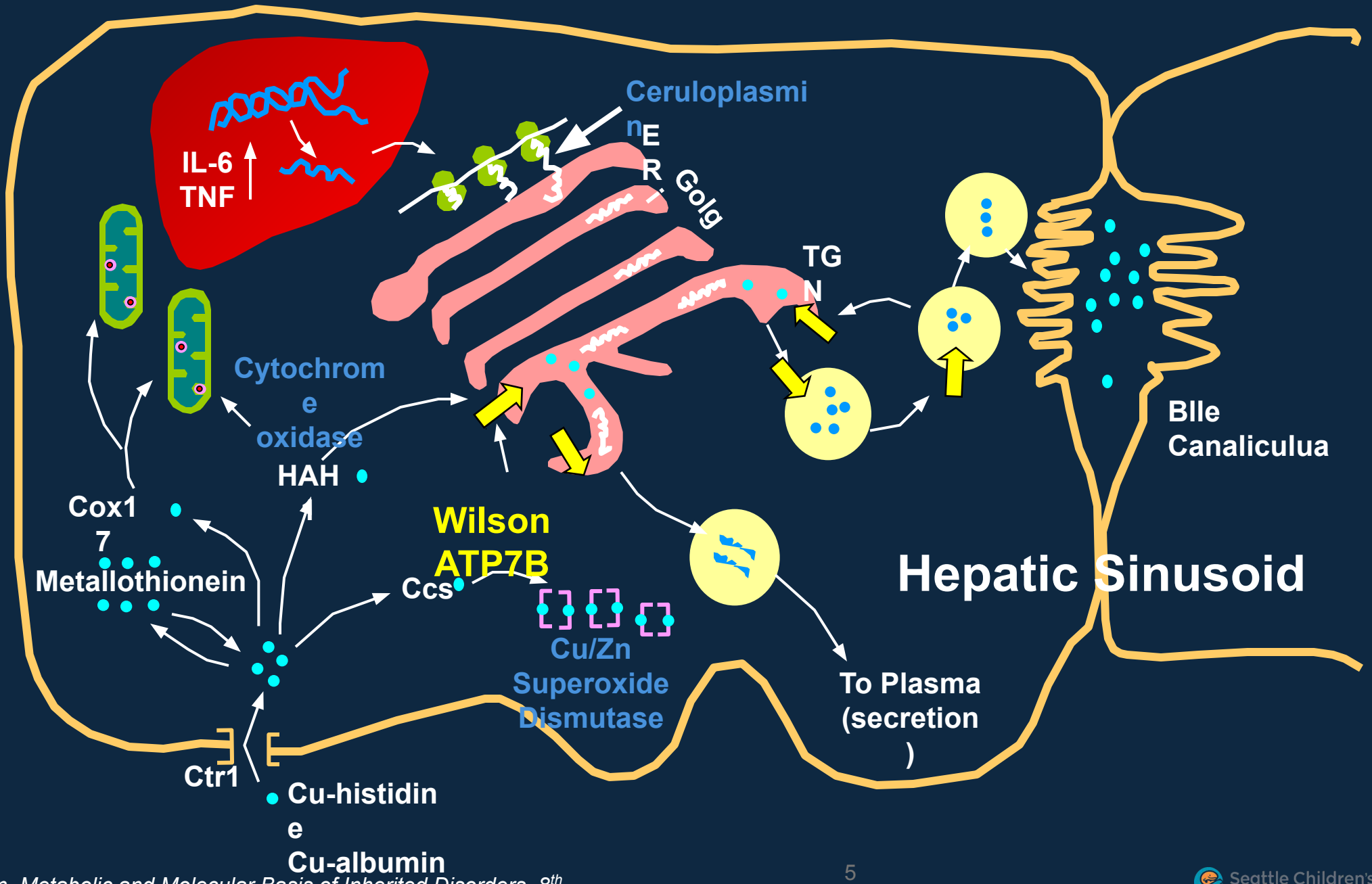
1. Energy Production: Cytochrome c oxidase
2. Connective Tissue Formation: Lysyl oxidase
3. Iron Metabolism: Ceruloplasmin for iron absorption and transport
4. Antioxidant: Superoxide dismutase
5. Neurological Function: Myelin formation
6. Immune System: Neutrophil activity
7. Others: melanin production, cholesterol



# Wilson




*Cox DW, J Gastroenterol Hepatol , 1997*




*Culotta and Gitlin, Metabolic and Molecular Basis of Inherited Disorders, 8th Ed*

# Wilson Disease is a Copper Transport Disorder

- **Genetics** [1]**:**
  - Autosomal Recessive condition caused by pathogenic variations in the *ATP7B* gene, which encodes a P-type Cu-transporting ATPase
  - Majority of mutations results in markedly decreased level of ATP7B protein due to enhanced degradation, absence or decay of mRNA *
- **Epidemiology:**
  - Incidence: approximately 1 in 30,000 [2-6]
  - Carrier frequency of 1:90 [3,7]
  - High-prevalence regions [7,8]
    - ~ 1:2,707 in Sardinia; ~ 1:2,600 in Canary Island; ~ 1:15 in Crete
- **Diagnosis**: Combination: Biochemical tests (copper, ceruloplasmin), Liver Biopsy, Genetic Testing
- **Treatment:** Zinc conjugates, Penicillamine, Trientine, Liver Transplant, Gene therapy (in clinical trials)

**Hepatology, 2009; Proc Natl Acad Sci U S A, 1998; Gastroenterology, 2007; Curr Issues Mol Biol, 2001; Proteins, 2008; Genetics, 1998; Blood, 2005; Mol Genet Metab, 2005; BMC Gastroenterol, 2010; Nat Genet, 2004; Annu Rev Biochem, 2007*

1. Chang IR, Hahn S. Handb Clin Neurol 2017;142:18-34; 2. Roberts EA, Schilsky ML. Hepatology 2008;47:2089-2111; 3. EASL. J Hepatol 2012;56:671-685; 4. Socha P et al. J Pediatr Gastroenterol Nutr 2018;66:334-344; 5. Poujois A et al. Clin Res Hepatol Gastroenterol 2018;42:57-63; 6. Cheung KS et al. World J Gastroenterol 2017;23:7716-7726; 7. Camarata M, Hahn S. Academic Press, 2019; 105-114; 8. Gao J et al. Genet Med 2019;21:1155-1163

# Diagnostic Guideline for Wilson Disease

*"No single test is alone enough"*

## 1. Clinical Suspicion

Children or young adults with unexplained liver disease

- Neuropsychiatric symptoms (movement disorders, tremor, psychiatric changes)
- Hemolytic anemia with Coombs-negative findings
- Low alkaline phosphatase to bilirubin ratio in acute liver failure
- Family history of WD

## 2. Lab Tests:

Serum transaminases : elevation
Serum ceruloplasmin : < 20 mg/dl (NCC >15 ug/dL)
Serum copper : <0.75 ug/ml
Urinary copper excretion : > 100 ug/day
Liver copper : > 250 ug/g dry tissue
Slit Lamp exam: Kayser Fleischer ring in the cornea/ Brain MRI
DNA test (sibling should undergo genetic testing)

3. Leipzig scoring system

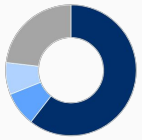
# Management of Wilson Disease

**Goals of Treatment**

- Remove accumulated copper
- Prevent further copper buildup
- Reverse or stabilize symptoms
- Prevent progression to liver failure or neurologic disability

1. **Initial evaluation:**
   - Extent of liver damage, neuro and psychiatric issues
   - Baseline image: MRI, ultrasound
2. **Medications:**
   - Zinc: blocks the copper absorption
   - Chelators: Trientine, Penicillamine, TTM
   - Symptomatic treatment for neurological symptoms
3. **Diet:**
   - Low copper diet (avoid shellfish, liver chocolate, nuts, mushrooms)
4. **Liver Transplant**
   - Acute liver failure, decompensated liver failure
   - Not curative for neurological symptoms
5. **Monitoring and Follow-Up** (adherence to therapy)
   - 24 hour urine copper, LFTs, CBC, INR
   - Image study
6. **Clinical trial**: Gene therapy (promising results)

# Frequency of ATP7B variants varies by geographic regio

**Sardinia**

- c.-441_-427del
- p.Met822fs
- p.Val1146Met
- Others

**Spain**

- p.Met645Arg
- Others

**Greece**

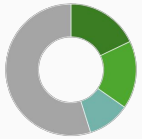
- p.His1069Gln
- p.Arg969Gln
- Others

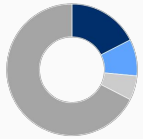
**Poland**

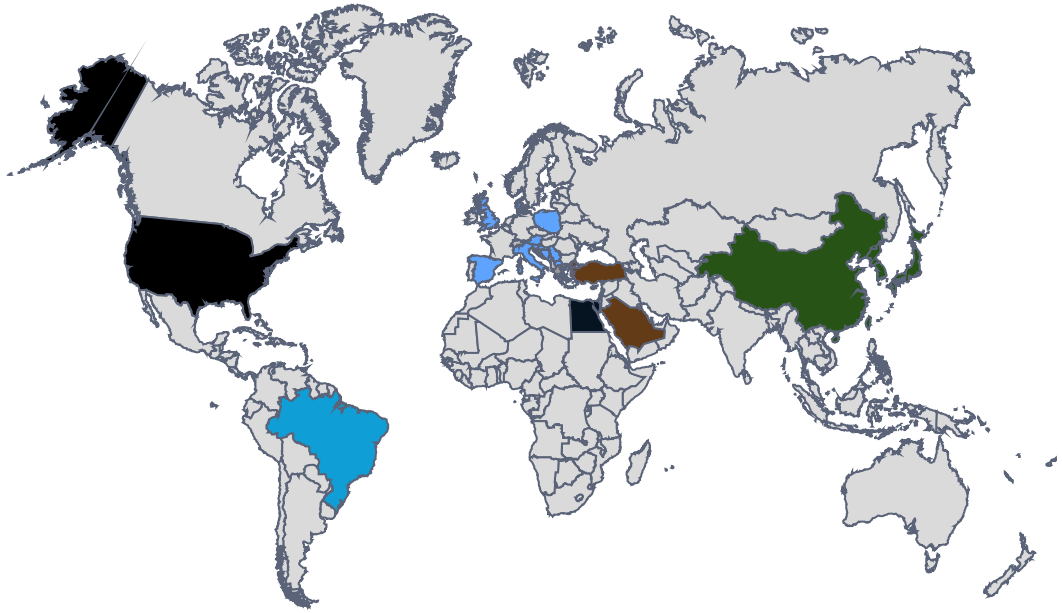
- p.His1069Gln
- p.Ala1135fs
- p.Gln1351*
- Others

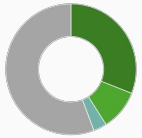
**Former Yugoslavia**

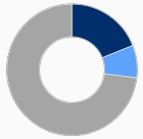
- p.His1069Gln
- p.Met769fs
- Others

**Japan**

- p.Asn958fs
- p.Arg778Leu
- c.1708-5T>G
- Others

**Italy**

- p.His1069Gln
- p.Val845fs
- p.Met769fs
- Others

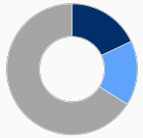


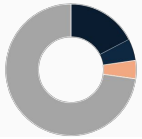
**China**

- p.Arg778Leu
- p.Pro992Leu
- p.Thr935Met
- Others

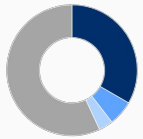
**UK**

- p.His1069Gln
- p.Met769Val
- Others

**Korea**

- p.Arg778Leu
- p.Asn1270Ser
- p.Ala874Val
- Others

**Denmark**

- p.His1069Gln
- p.Trp779*
- Other

**Turkey**

- p.His1069Gln
- p.Gly710Ser
- p.Gln457*
- Others

**Austria**

- p.His1069Gln
- p.Gly710Ser
- p.Met769fs
- Others

**USA**

- p.His1069Gln
- p.Asn1270Ser
- Others

**Brazil**

- p.Ala1135fs
- p.Leu708Pro
- Other

**Egypt**

- IVS18+6 T>C
- p.Ala11140Val
- p.Lys832Arg
- Others

**Saudi Arabia**

- p.Gln1399Arg
- p.Ser774Arg
- Others

*, termination codon; fs, type of change is a frame shift; IVS, intron



1. Chang IR, Hahn S. Handb Clin Neurol 2017;142:18-34; 2. Gomes A, GV Dedoussis, Ann Hum Biol 2016; 43(1): 1–8

# ATP7B

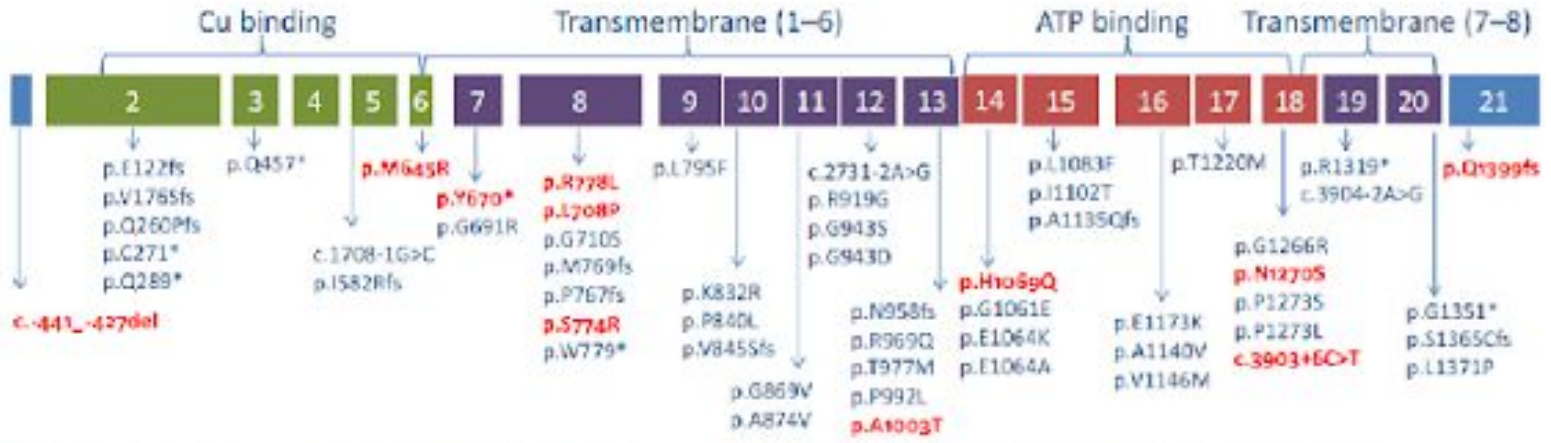
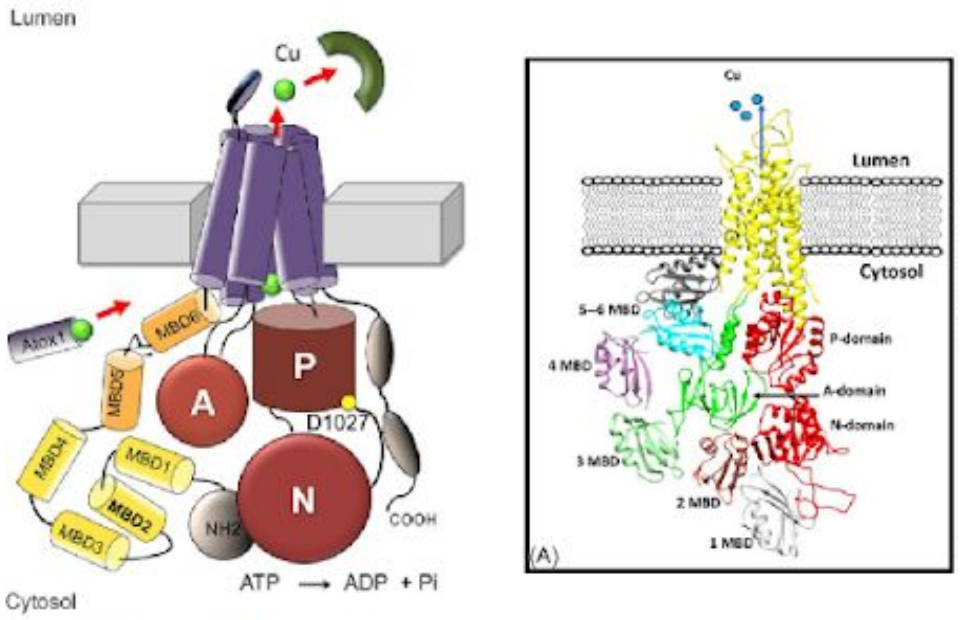
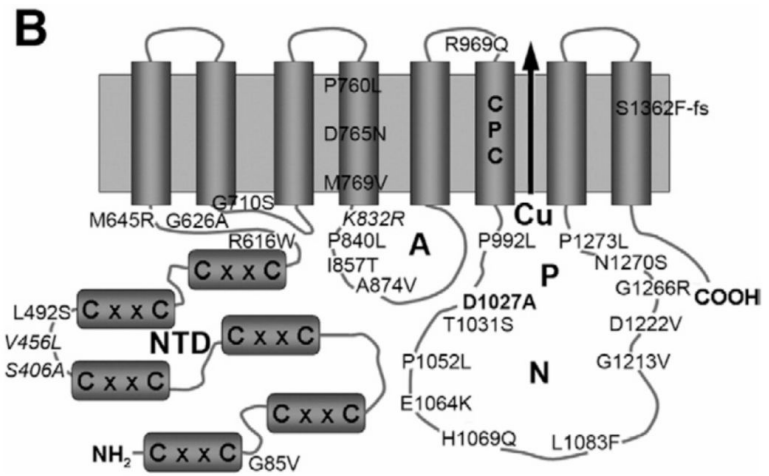



FIG. 1 A schematic representation of the ATP7B gene with common mutation sites including p.H1069Q, pR778L, and p.E1064K.












Wilson disease: pathogenesis, molecular mechanisms, diagnosis, treatment and monitoring, edited by Weiss and Schilsky, 2019

# ATP7B gene variants from ClinVar
## https://www.ncbi.nlm.nih.gov/clinvar/

- ~1,200 submissions related to ATP7B.

- Common classifications:
  - Pathogenic/Likely pathogenic: >400 variants
  - Uncertain significance (VUS): ~600 variants
  - Conflicting interpretations: ~100 variants

**Genetic test alone cannot reach to the diagnosis**

# Natural History Stages of Wilson Disease

## (1) Silent Accumulation Phase (Infancy to Early Childhood)

- **Copper accumulation begins at birth**, particularly in the liver**.** Liver copper levels rise gradually and silently.
- Typically **asymptomatic for years**, though damage is ongoing.

## (2) Hepatic Presentation (Childhood to Adolescence)

- First symptoms often appear between ages **4–15**.
- Can range from **mild transaminase elevation** to: Hepatomegaly, Chronic hepatitis, **Acute liver failure** (often in children/teens), **Decompensated cirrhosis**

## (3) Neurological/Psychiatric Manifestations (Adolescence to Adulthood)

- Begin when hepatic copper spills into systemic circulation and deposits in the CNS.
- Symptoms include: Depression, personality changes, school failure or behavioral problems in adolescents, progress to tremors, dysarthria, dystonia, parkinsonism, cognitive decline,

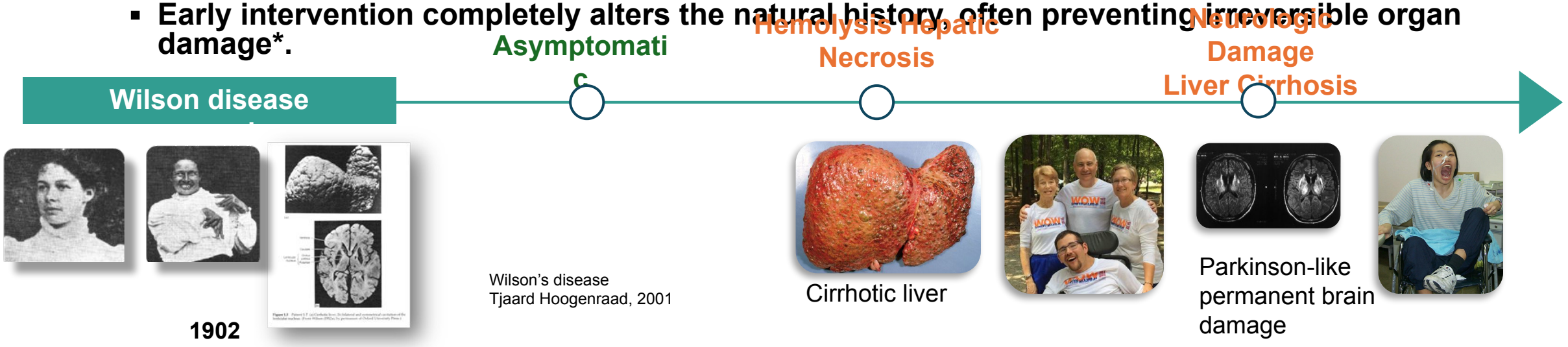
## (4) Multiorgan Involvement and Irreversible Damage

- Ocular: **Kayser-Fleischer rings** in Descemet's membrane Renal tubular dysfunction (Fanconi-like syndrome) Cardiomyopathy, osteopenia, and endocrinopathies may appear
- Without treatment, **death typically occurs between 10–40 years** due to liver failure or neurodegeneration

# Wilson disease (WD) is a slowly progressive and lethal disease if untreated,

*If diagnosed early, WD is one of the most treatable genetic diseases*

- **Recognition, screening, and differential diagnosis of WD still challenge physician today**
  - As many as 75% of all patients with WD may be undiagnosed or misdiagnosed [1,2].
  - Diagnosis is usually delayed on an average by months or several years, and in some cases for decade(s) [3,4,5]
  - Many cases are misdiagnosed as autoimmune hepatitis, psychiatric illness, or movement disorders
  - At least half of patients with WD are never diagnosed and die of untreated disease (globally) [6]
- **Early intervention completely alters the natural history, often preventing irreversible organ damage*.**






1. Brain 2013;136:147687, 2.Lancet 1982;i:1469 3.Gut 2000;46:41519, 4.Mov Disord 2009;24:50918 5. Clinical and Translational Perspectives on Wilson Disease edited by Nanda Kerkar and Eve Roberts
6. Wilson disease: A clinician's guide to recognition, diagnosis and management Dr. George Brewer, 2001

# Early intervention completely alters the natural history, preventing irreversible organ damage*

- **European Wilson Disease Registry (EUROWILSON)**
  - Patients diagnosed before symptom onset or early in disease course had **significantly better survival** without liver transplant and fewer neurological complications.
  - *Ferenci et al., Gut, 2007;56(8):1155-1162.*

- **US NIH Natural History Cohort**
  - Pre-symptomatic siblings identified through family screening had **normal outcomes** with zinc or chelator therapy and no progression to cirrhosis or neurological disease over years.
  - *Roberts EA & Schilsky ML. Hepatology, 2008;47(6):2089-2111.*
- **Pediatric Case Series**
  - In children diagnosed early (especially through screening of siblings or incidental labs), therapy **prevented disease progression and normalized labs**.
  - *Weiss KH et al., Liver International, 2013;33(4):512–520.*

# A Letter from Father of Child (1/2)

Our son was 17 years old and preparing to go serve an LDS mission for two years somewhere in the world. He went in for his routine physical with our family doctor. Two days after that physical I received an urgent phone call from our family doctor indicating that I needed to get him to the hospital lab to do additional work to figure out what was going on and that it was a mystery, urgently…

Platelet blood count was approximately 38 instead of the normal 200. Over the course of the next six months with two different oncology specialist doctors we chased every leukemia, bone cancer, and blood cancer that are known. He underwent two separate bone marrow biopsies.

….We made our appointment and began yet another journey of unknowns, additional tests and more doctor visits. When results came back, there were many red flags of concern as to the balance and health of my son's liver.

Additional tests were ordered again and more visits to doctors and hospitals. Ultrasounds, MRIs and CAT scans were ordered…

Our son, now 18-years-old has stage 4 cirrhosis of the liver that will never heal…. The required medication for an individual at this stage of Wilson's Disease is literally $40,000 a month without insurance….

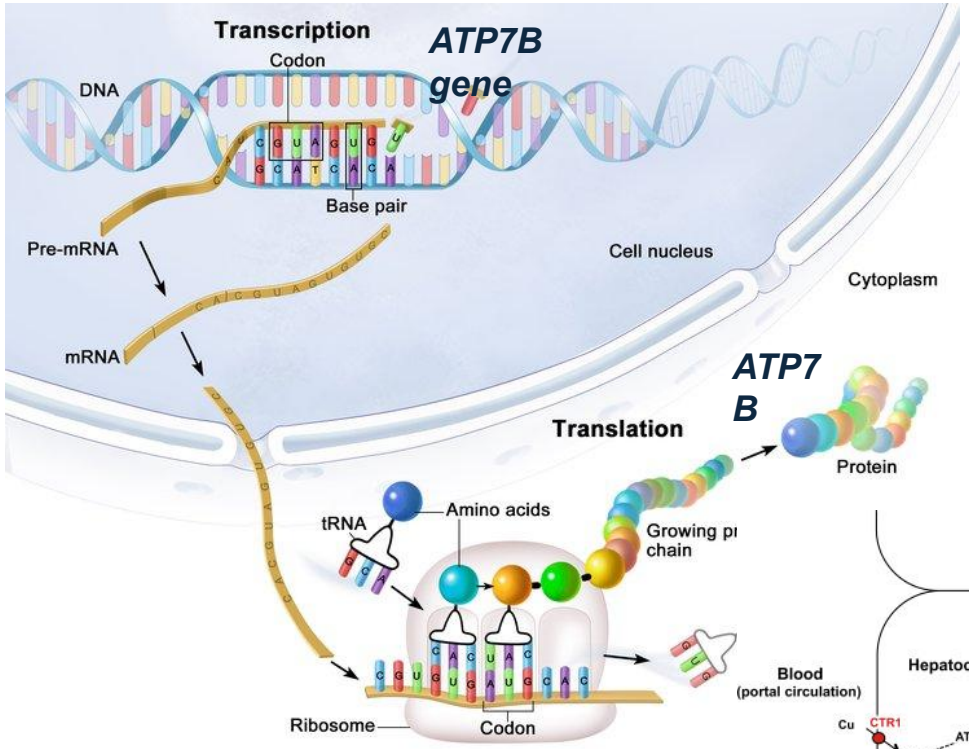
# A Letter from Father of Child (2/2)

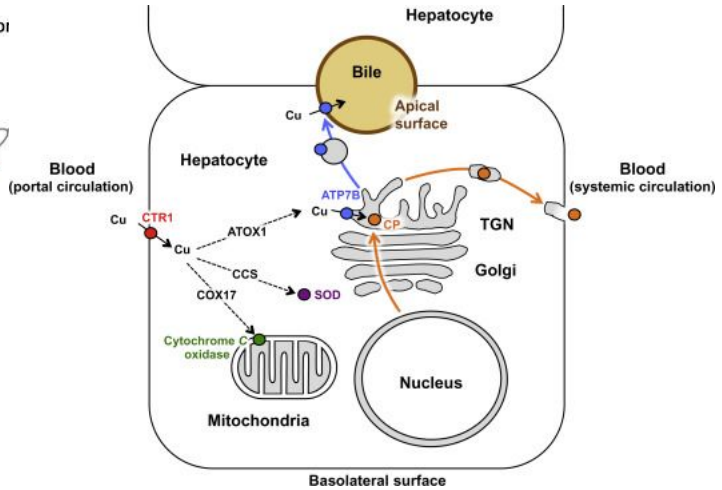
My son is 15 , diagnosed the disease early  from 5 years but unfortunately because Wilson disease and its medicine  are very rare in my country, also laboratory tests are not accurate , so doctors couldn't determine the right dose.

He started to complain from only one year from muscle strain and increasing in saliva . Since a year ago, he started to complain from his handwriting, was getting smaller and he couldn't improve it, also the other hand is closed all time with pain , laboratory test showed high amount of copper in urine and blood and again abdominal ascites , MRI showed copper in brain and Keyser Fleisher ring.  Also, there is involuntary movements in his right arm specially during speaking and also involuntary movements in his foot  fingers… also increasing in saliva and problems in speech….. now he takes 3 capsule of 250 mg penicillamine and medicine contains (carbidopa  25mg  and levodopa 250 mg ) also 3 capsules of zinc  everyday but no improvement in  neurological situations or in speaking…..

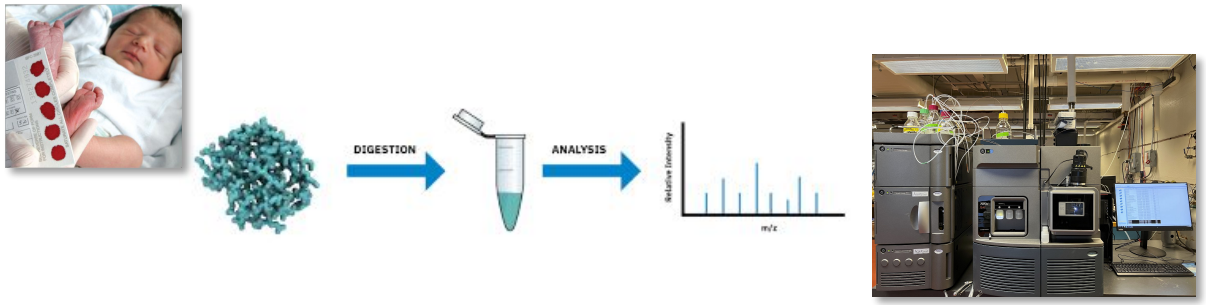
Please I need to know if his neurological symptoms will be permanent or it could be improved by time , and if there is any meds can remove copper from his brain and improve his involuntary movements , please help…..

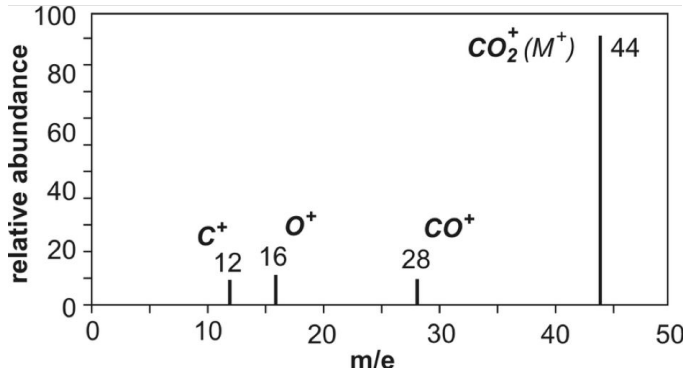
# ATP7B protein itself is an excellent biomarker for NBS of Wilson disease

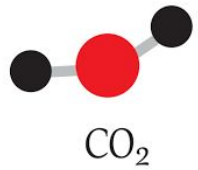



**Majority of mutations results in markedly decreased level of ATP7B protein due to enhanced degradation, absence or decay of mRNA**

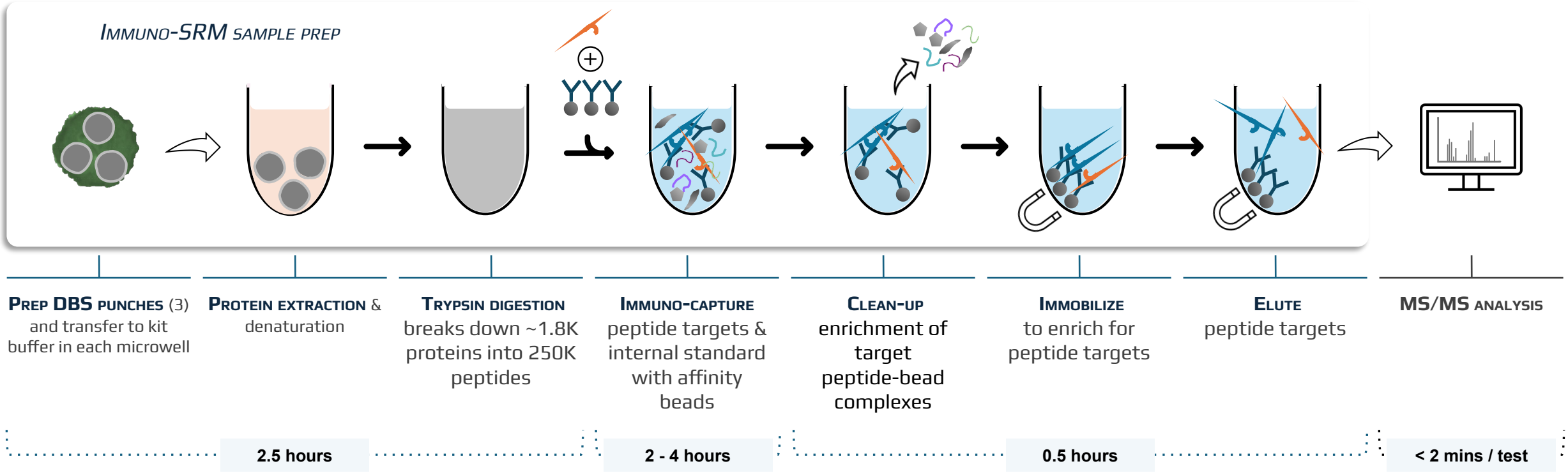


# Multiplex immuno-enrichment for selected monitoring reaction mass spectrometry

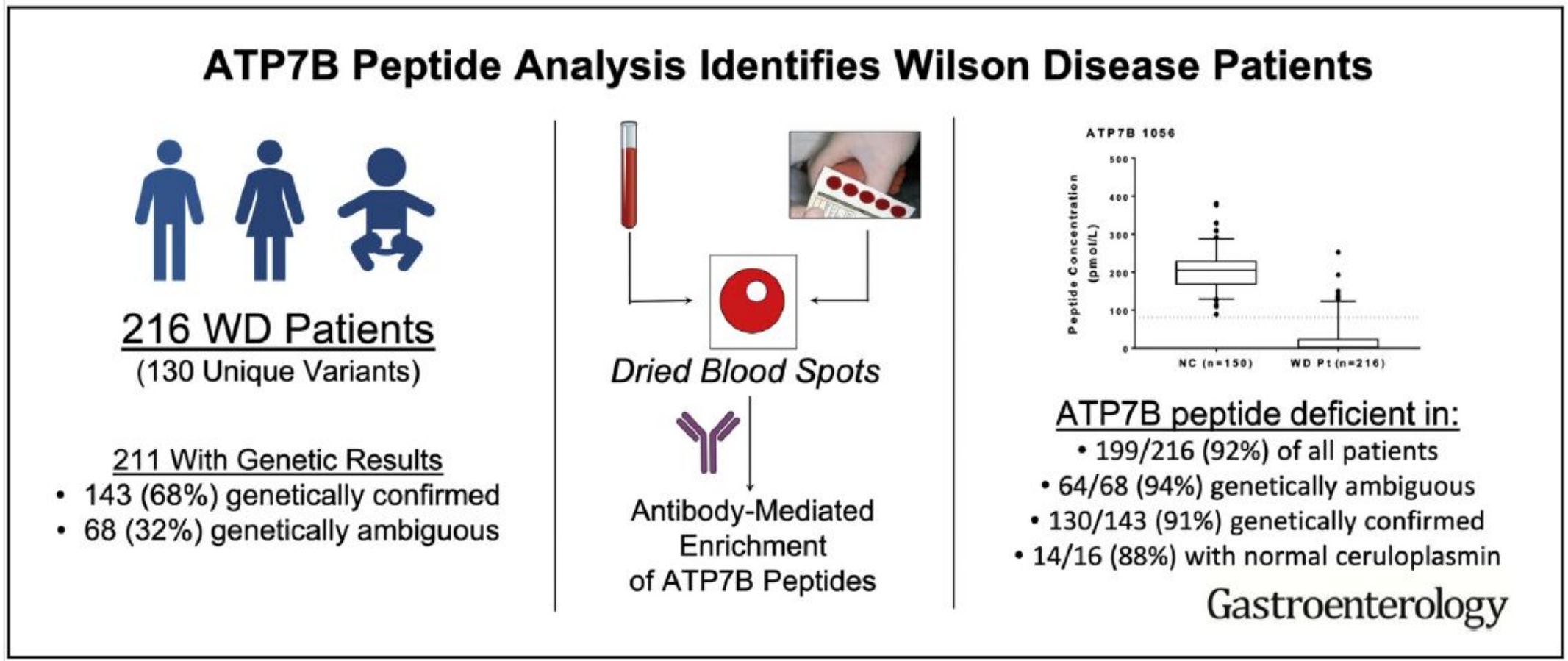
- Enables precise quantification of previously undetectable rare disease biomarkers
  from dried blood spot specimens - *using existing mass spec workflows*



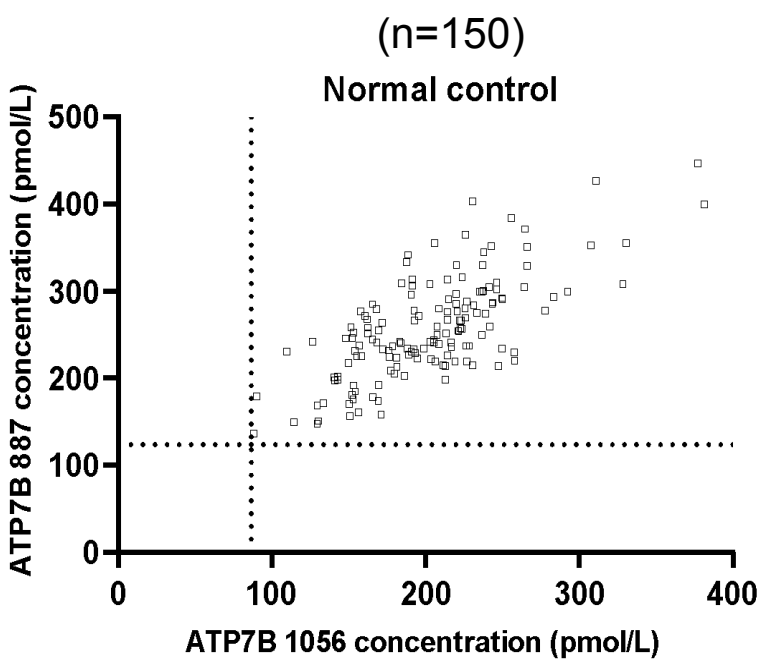
Gastroenterology 2021;160:2367–2382

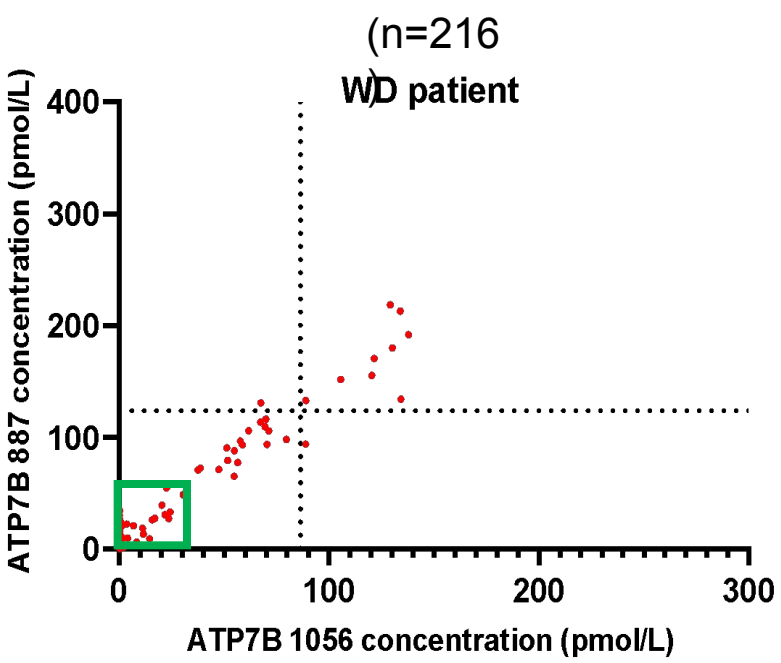
# CLINICAL—LIVER

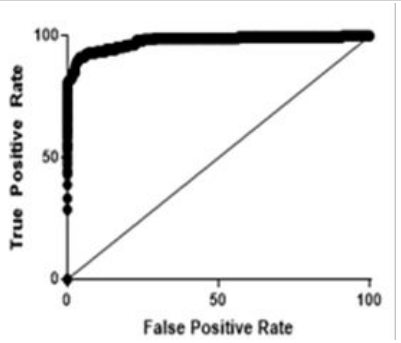
## Direct Measurement of ATP7B Peptides Is Highly Effective in the Diagnosis of Wilson Disease

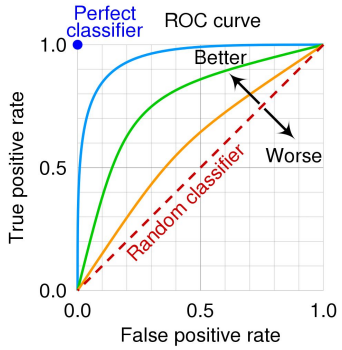


# Wilson Disease: Majority of patients are deficient in ATP7B peptides



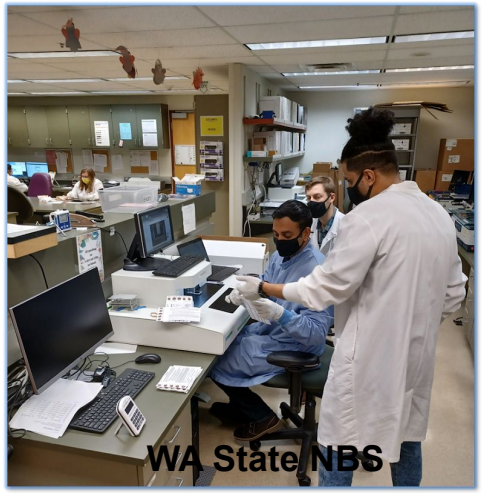

- Large Retrospective Study
  - 216 WD patients, 48 carriers,150 healthy controls
- 199 / 216 patients (92.1%) had at least 1 ATP7B peptide below diagnostic cutoff.
  - ~80% of patients had ATP7B < 32 pmol/L and <56 pmol/L for ATP7B 1056 and ATP7B 887 respectively
- ROC curve shows AUC 0.98, sensitivity 91.2%, specificity 98.1%, PPV 98.0% and NPV 91.5%



*Collins CJ et al.. Gastroenterology. 2021, 160(7):2367-2382*

# We successfully developed a first-of-its-kind proteomic-based IVD kit manufactured from CMO to identify 4 conditions and began a pilot study with WA State as of 2022

- ❑ Assay validation studies were designed following guidelines from relevant CLSI documents
- ❑ A total of 3,294 newborns and 32 WD cases were blindly tested at three sites (SCH, APL, KP).
  - No presumptive positive cases were detected
  - **All confirmed 32 positive disease cases were screened positive,** and repeats were concordant with initial results








The project titled "Pilot Study for Newborn Screening of **Wilson Disease and IEI (XLA, WAS, and ADAD)"** (2021-085-Department of Health) was approved by the Washington State Institutional Review Board.

Int. J. Neonatal Screen. **2025**, 11, 6

# WA Pilot Study of Newborn Screening

***Demographic information for the 30,024 de-identified newborn samples received from the Washington State Department of Health Newborn Screening Lab***

| Category | Number | % |
|---|---|---|
| Male | 14,518 | 48.5 |
| Female | 15,476 | 51.5 |
| < 1500 g BW | 311 | 1.0 |
| 1500 - 2500 g BW | 1,796 | 6.0 |
| > 2500 g BW | 27,917 | 93 |

| DOC | Number | % |
|---|---|---|
| 0 day (< 24 h) | 4,845 | 16.3 |
| 1 day | 12,361 | 41.2 |
| 2 day | 6,617 | 22.0 |
| 3 day | 3,836 | 12.8 |
| 4 day | 1,352 | 4.5 |
| 5 day | 567 | 1.9 |
| 6 - 14 days | 446 | 1.5 |

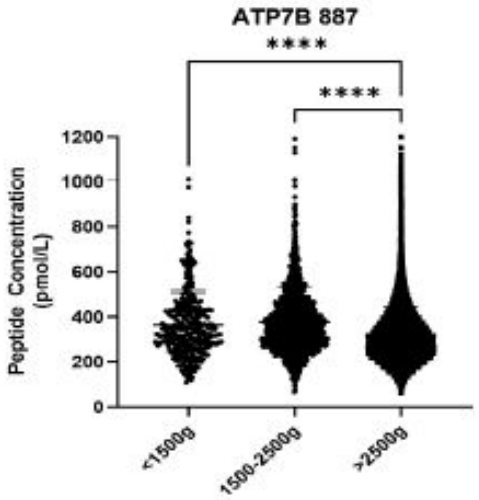
| Ethnicity | Number | % |
|---|---|---|
| White | 16,104 | 58.6 |
| Hispanic | 5,109 | 18.6 |
| Asian | 2,879 | 10.5 |
| Black | 1,906 | 6.9 |
| Native American | 560 | 2.0 |
| Other | 916 | 3.3 |

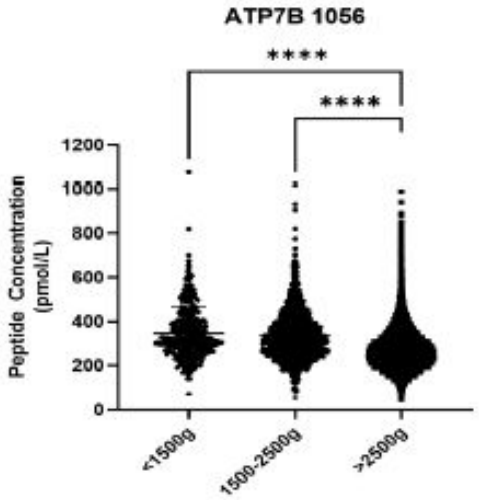


Int. J. Neonatal Screen. **2025**, 11, 6

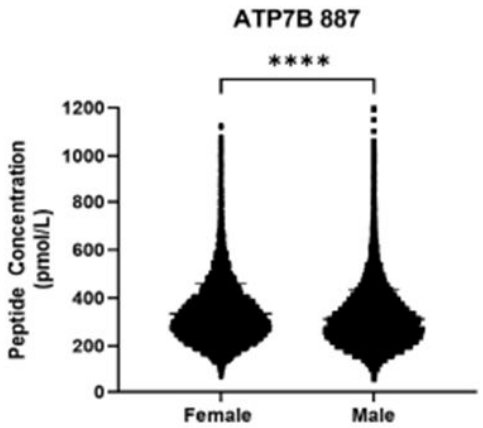
# WA Pilot Study of Newborn Screening

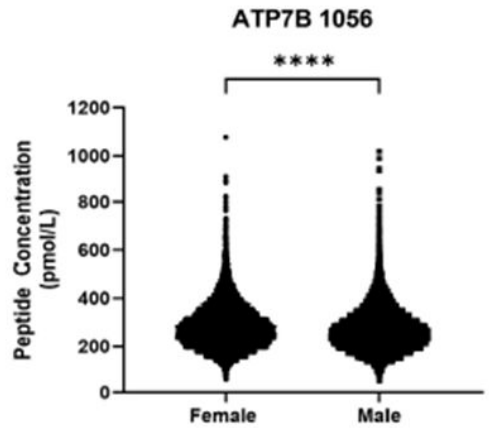
***BW or Gender did not impact the overall cutoff range***




| Peptide | <1500g mean (n = 311) | 1500-2500g mean (n = 1796) | >2500g mean (n = 27,917) | p-value <1500g vs >2500g | p-value 1500-2500g vs. >2500g |
|---|---|---|---|---|---|
| ATP7B 887 | 364.3 | 378.9 | 319.2 | < 0.0001 | < 0.0001 |
| ATP7B 1056 | 346.9 | 335.3 | 272.7 | < 0.0001 | < 0.0001 |



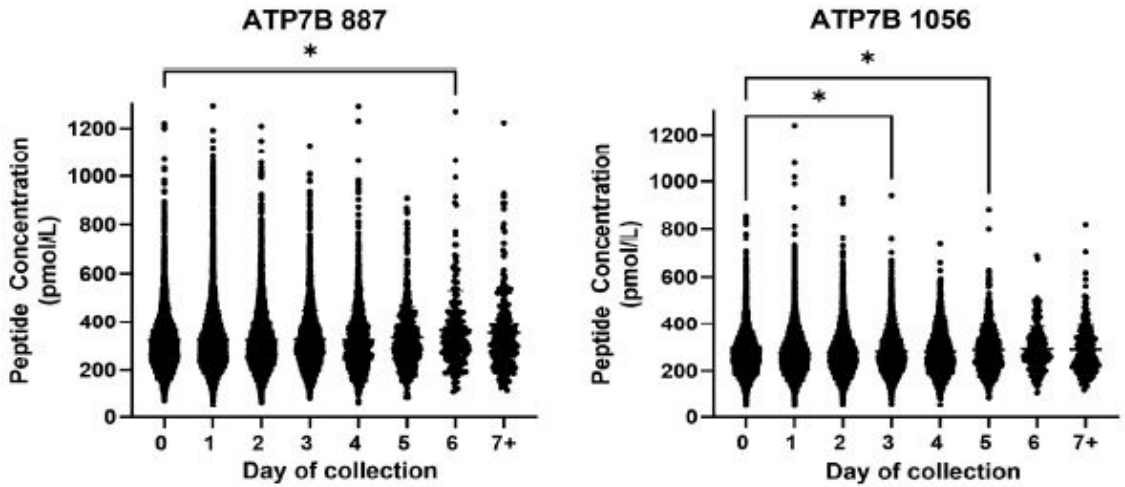

| Peptide | Female mean | Male mean | Difference between means | p-value |
|---|---|---|---|---|
| ATP7B 887 | 333.4 | 313.6 | 19.8 | < 0.0001 |
| ATP7B 1056 | 284.7 | 270.3 | 14.5 | < 0.0001 |

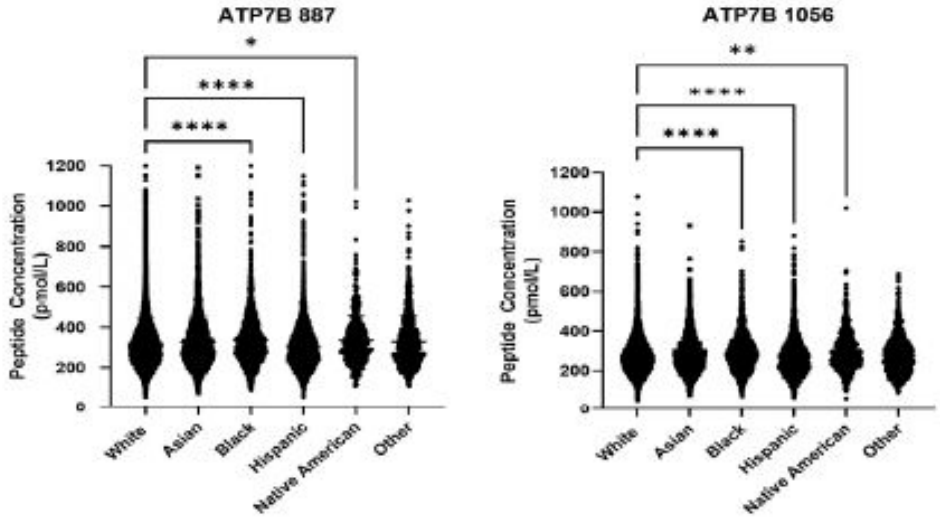


Int. J. Neonatal Screen. **2025**, 11, 6

# WA Pilot Study of Newborn Screening

***Age of collection or ethnicity did not impact the cut off***




| Peptide | Day 0 mean | Day 1 mean | Day 2 mean | Day 3 mean | Day 4 mean | Day 5 mean | Day 6 mean | Day 7+ mean |
|---|---|---|---|---|---|---|---|---|
| ATP7B 887 | 322 | 324 | 321 | 323 | 321 | 332 | 363 | 353 |
| ATP7B 1056 | 274 | 276 | 278 | 280 | 280 | 289 | 292 | 289 |

| Peptide | White mean | Asian mean | Black mean | Hispanic mean | Native American mean | Other mean |
|---|---|---|---|---|---|---|
| ATP7B 887 | 321 | 328 | 338 | 309 | 336 | 330 |
| ATP7B 1056 | 278 | 281 | 293 | 269 | 294 | 281 |



Int. J. Neonatal Screen. **2025**, 11, 6

# Four presumptive positive cases detected for WD

- One likely true positive with two VUS
- Three False Positive (3/25,000 = 0.012%)
- PPV 25%
- Please note that current cut-off was tentatively set (moving target)

**True Positive**

| Sample | Specimen Age (Days) | BW (g) | Sex | Diagnosis | MS System | ATP7B 887 | ATP 1056 | WASP 274 | ADA 93 | BTK 545 | BTK 407 | GENOTYPE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1 | 4105 | M | WD | ESI Low Flow | **71.0** | **96.5** | 1782.7 | 5169.5 | 1467.8 | 1677.9 | p.Pro610Leu/ p.Arg1224Leu |

**False Positive**

| Sample | Specimen Age (Days) | BW (g) | Sex | Diagnosis | MS System | ATP7B887 | ATP1056 | WASP274 | ADA93 | BTK 545 | BTK 407 | GENOTYPE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 3690 | M | WD | ionKey | **67.6** | **134.5** | 2569.4 | 3452.7 | 823.3 | 895.5 | c.3402del |
| 2 | 2 | 3870 | M | WD | ESI Low Flow | **66.4** | **70.0** | 2193.3 | 7598.3 | 2030.5 | 1293.1 | NO VARIANTS |
| 3 | 2 | 3840 | F | WD | ESI Low Flow | **64.3** | **59.2** | 1307.1 | 2414.2 | 594.8 | 470.3 | p.Met33Thr |



Int. J. Neonatal Screen. **2025**, 11, 6

# A probable positive case detected for WD

| True Positive | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sample | Specimen Age (Days) | BW (g) | Sex | Diagnosis | MS System | ATP7B 887 | ATP 1056 | WASP 274 | ADA 93 | BTK 545 | BTK 407 | GENOTYPE |
| 1 | 1 | 4105 | M | WD | ESI Low Flow | **71.0** | **96.5** | 1782.7 | 5169.5 | 1467.8 | 1677.9 | p.Pro610Leu/ p.Arg1224Leu |

Ethnicity: Checked as "others"

p.Arg1224Leu

MAF=0.0001262

p.Pro610Leu

MAF=0.0001374

No clinical reports

**TABLE 2** Variants of unknown significance according to the ACMG Standards and Guidelines[2] detected in 135 children without previous positive genetic findings which correspond to the phenotype or are untypical but compatible with the phenotype

| Disease | Fa No [sub No] | Age[a] | Clinical data | Gene[b] | Variant |
|---|---|---|---|---|---|
| ALGS | 22 [LP77] | 2 mo | Neonatal cholestasis with GGT↑, no other ALGS symptoms | *NOTCH2* | c.4999G>A, p.(Val1667Ile) het |
| | 23 [LP82] | 12 d | Neonatal cholestasis with GGT↑, no other ALGS symptoms | *NOTCH2* | c.3995G>A, p.(Arg1332His) het |
| | 24 [LP112] | 1.5 mo | Only few clinical symptoms (neonatal cholestasis, failure to thrive) | *NOTCH2* | c.6094C>A, p.(His2032Asn) het |
| | 25 [LP132] | 3.5 mo | Clin. syndromal biliary atresia (Heterotaxy syndrome) | *NOTCH2* | c.6094C>A, p.(His2032Asn) het |
| | 26 [LP89] | 15 y | Characteristic phenotype (face, heart, cholestasis, cirrhosis, vertebral anomalies) | *JAG1* | c.-100C>T het, 5′-UTR, (novel) |
| | 27 [LP101] | 8 y | Characteristic phenotype face, heart, failure to thrive, cirrhosis) | *JAG1* | c.2917-10A>G het, intronic, (novel) |
| WD | 28 [LP91] | 16 y | Steatosis hepatitis, elevated liver enzymes, normal CP, urinary copper, cMRI | *ATP7B* | c.3671G>T, p.(Arg1224Leu) het c.*16G>A het, 3′-UTR |

*Clinical Genetics:*

# Summary

- Demonstrated the feasibility of LC-MS/MS proteomics for NBS of Wilson disease
- WD met the criteria in WA State to be qualified for NBS
    1. Available Screening Technology
    2. Diagnostic Testing and Treatment Available
    3. Prevention Potential and Medical Rationale
    4. Public Health Rationale
    5. Cost-benefit/Cost-effectiveness
    6. Public Health Infrastructure Readiness
- Cost effectiveness
    - kit cost per sample ~$10
    - Treatment with zinc pennies/day
    - Economically feasible for broad implementation
- If we do not do NBS for WD, “heroic” effort would be required to substantially change the current paradigm --- another 120 years?


27

# Acknowledgements


## Key Proteo, Inc

Claire Klippel, BS
Jiwoon Park, PhD
Sean Sandin

## Seattle Children's Research Institute

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Tim Grotzer, BS
Kayla Croney, MS

## Wilson Disease Association

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Alice Williams

## Washington State NBS Laboratory

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Aranjeet Singh
Jonathan Hill
Brandon Officer
Tareq Shahbal
Emily Hamacher

## Alberta Precision Laboratories

Dennis Orton, PhD
Tara Winstone, PhD
Xue Chen, PhD

All family members and patients who entrusted us with their stories.

## Proof of Evidence Study: Gastroenterology 2021

*Christopher J Collins, Fan Yi, Remwilyn Dayuha, Phi Duong, Simon Horslen, Michelle Camarata, Ayse K Coskun , Roderick H J Houwen, Tudor L Pop, Heinz Zoller, Han-Wook Yoo, Sung Won Jung,* ***Karl H Weiss****,* ***Michael L Schilsky****,* ***Peter Ferenci****, Si Houn Hahn*

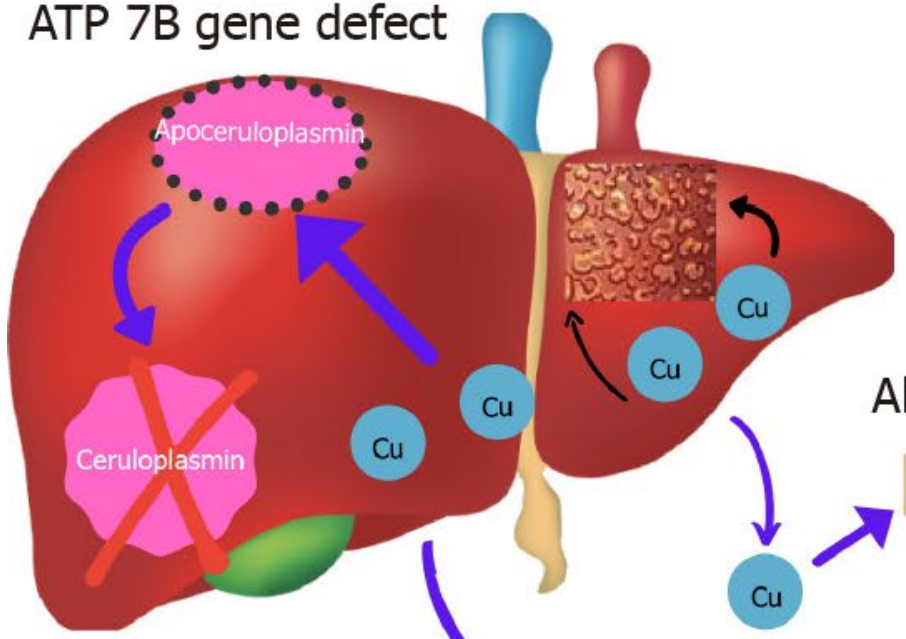
NIH Grants

# Wilson Disease and Liver Disease in Children

**Pamela L. Valentino MD, MSc**
Associate Professor of Pediatrics, UW
Medical Director, SCH Liver Transplantation Program
SCH Liver & Intestinal Failure Clinical Center Director

# Outline

- Diagnosis and Management of Wilson disease
- Management of Infantile Wilson disease
- Access to Pediatric Hepatology




Albumin

Cu

Transcuprein

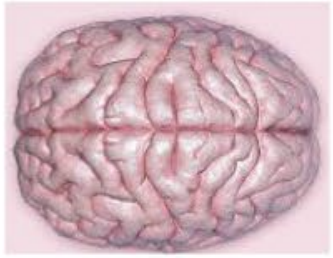
Cu

Cu

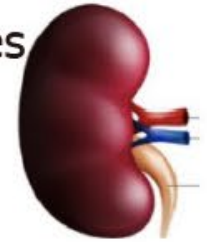
Cu

Cu

Free copper



Behavioral changes
Deterioration in school performance
Dystonia
Dysarthria
Tremors
Masl like facies
Psychiatric diturbances



Proximal renal
tubular acidosis

Kayser- Fleischer ring

Hemolysis

Seattle Children's
HOSPITAL · RESEARCH · FOUNDATION

Seetharaman, J. and M. S. Sarma (2021). World J Hepatol 13(11): 1552-1567

# How do children with Wilson Disease currently present to medical attention?

- Acute Liver Failure
- Abnormal liver tests on blood tests or imaging
- Family screening

# Children with Wilson Disease at presentation

## Fulminant Liver Failure

- Children develop jaundice (yellow eyes or skin) or are sleepy
- Require admission to intensive care unit
  - *High health care costs and resource utilization*
- Medicines to treat Wilson disease are typically unsuccessful
- *Almost always requires **liver transplantation*** to avoid mortality
  - *High health care costs and resource utilization*

# Children with Wilson Disease at presentation

## Abnormal liver tests

- Liver biochemistry (ALT, AST) are typically abnormal at 3 years of age and higher in WD
- Imaging of the liver can be abnormal (bright liver on ultrasound or nodular (bumpy) on CT)
- Children do not undergo routine blood tests per AAP
  - Serendipitous detection of abnormal tests occur with other illnesses
- Patients can already have advanced liver disease or cirrhosis by the time they are detected
- Treatment aimed at de-coppering the body to prevent need for liver transplantation

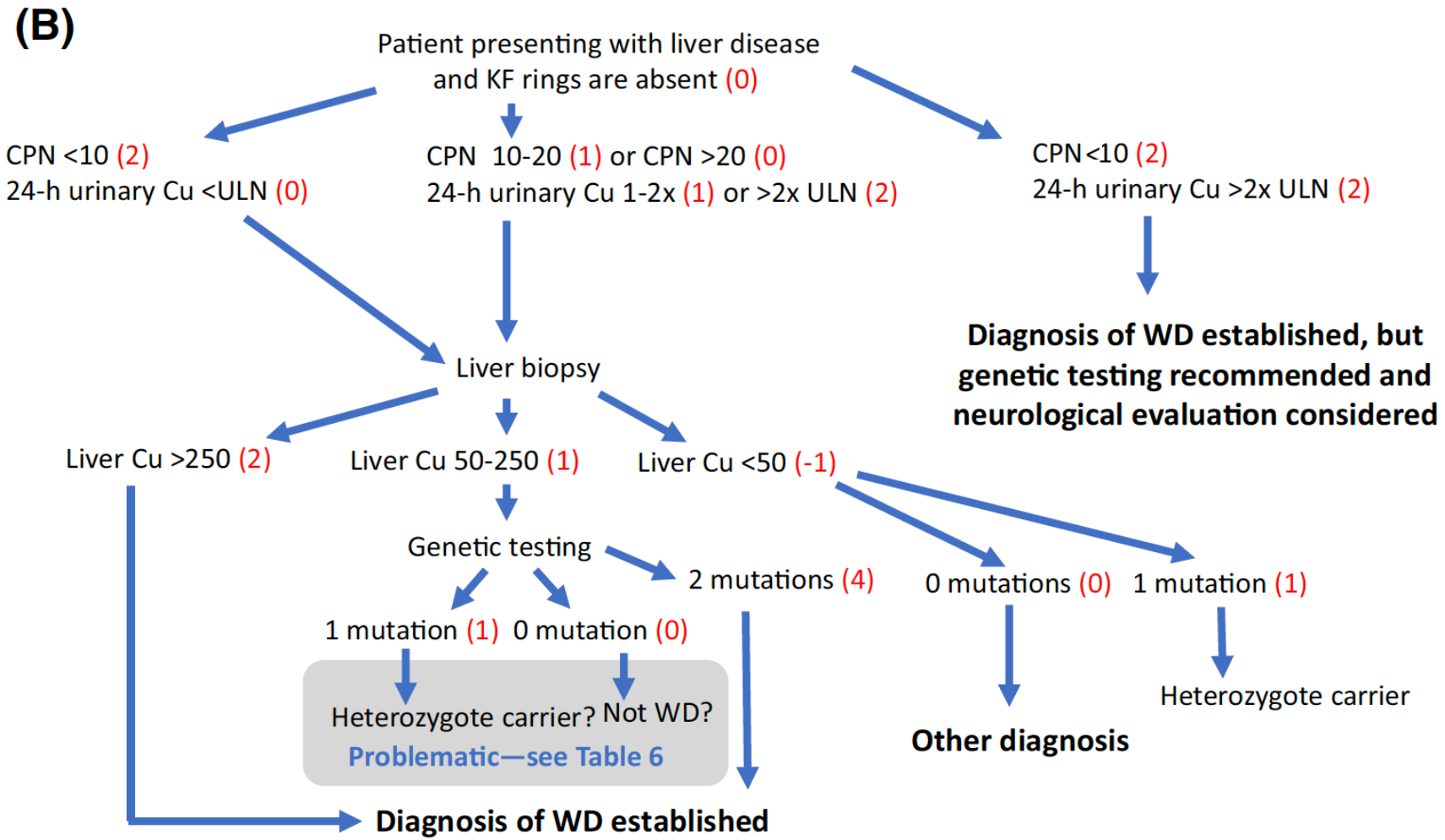
# Children with Wilson Disease at presentation

## Family screening

- Testing of first-degree relatives for known ***ATP7B* mutations**
  - Prenatal molecular genetic testing can identify parents who are carriers

- This is the only current opportunity to catch WD early in the disease course
- Infants and younger siblings have been diagnosed with mild or NO liver disease

# Approach to testing




## Leipzig score

**KF rings**

present =2, absent= 0;

**Ceruloplasmin** (mg/dl)

normal >20 =0, 10–20 =1, <10 =2;

**24-h urinary Cu** (µg/24 h)

<ULN = 0; 1–2× ULN = 1;
>2× ULN = 2;

**Liver Cu** (µg/g dry weight liver)

>5× ULN = 2, 50–250 = 1, <50 = −1;

**Genetic testing**

two disease-associated mutations = 4,

one disease-associated mutation = 1.

**Score ≥4**: WD highly likely

**Score 2–3**: WD probable

**Score 0–1**: WD unlikely


Schilsky, M. L., et al. (**2022**). Hepatology. PMID: 36151586

Ferenci, P., et al. (2019). Hepatology 69(4): 1464-1476

# All patients with Wilson disease require treatment

- **Liver transplantation** for fulminant liver failure
  - **High health care costs and resource utilization**
  - *Lifelong immunosuppression and risk of complications*
- **Copper chelation** (Trientine and penicillamine)
  - Removes copper from the body and liver via renal excretion (in urine)
  - **High health care costs* & many adverse effects*
- **Zinc therapy**
  - Reduce absorption of copper
  - Few adverse effects
  - ***Initiated in infants and family screening***
  - ***Inexpensive***

***Organized from higher to fewer complications or adverse reactions***

# Nutrition

- High-copper food avoidance
- Water safety – well water testing, use of water purifiers
- Surveillance with a Dietician
- Avoid copper dishware / pots

- **Diet can be more liberal if:**
  - The total body copper is not high
  - The liver disease is not severe






REVIEW ARTICLE

# Management of Wilson Disease Diagnosed in Infancy: An Appraisal of Available Experience to Generate Discussion

*Pamela L. Valentino, †Eve A. Roberts, ‡Stacey Beer, ‡Tamir Miloh, §Ronen Arnon, ||Jennifer M. Vittorio, and ¶Michael L. Schilsky

*JPGN* • Volume 70, Number 5, May 2020

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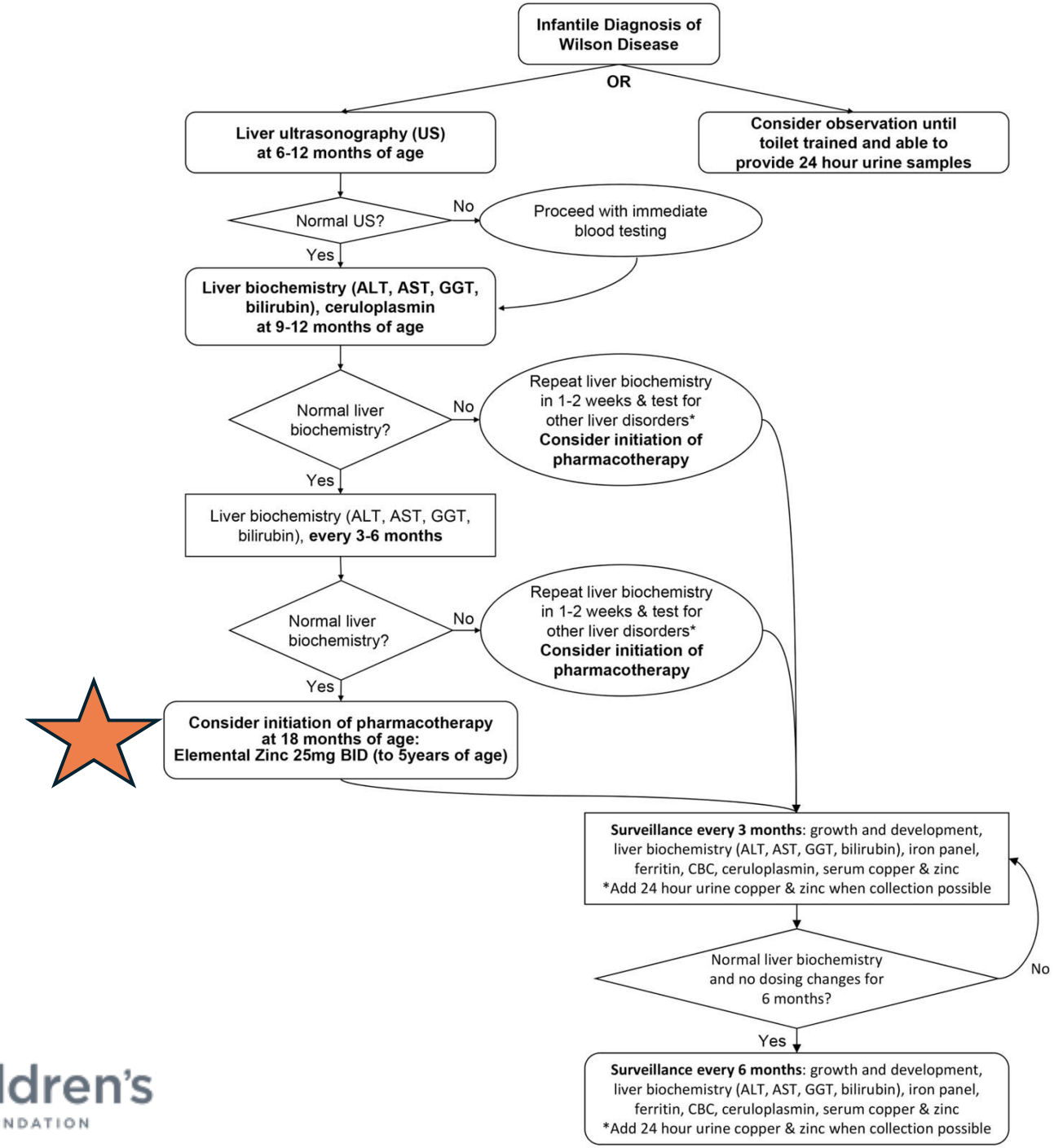
Valentino PL, et. Al.J Pediatr Gastroenterol Nutr 2020;70:547-554

https://pubmed.ncbi.nlm.nih.gov/31899725/

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Valentino PL, et. Al.J Pediatr Gastroenterol Nutr 2020;70:547-554

https://pubmed.ncbi.nlm.nih.gov/31899725/

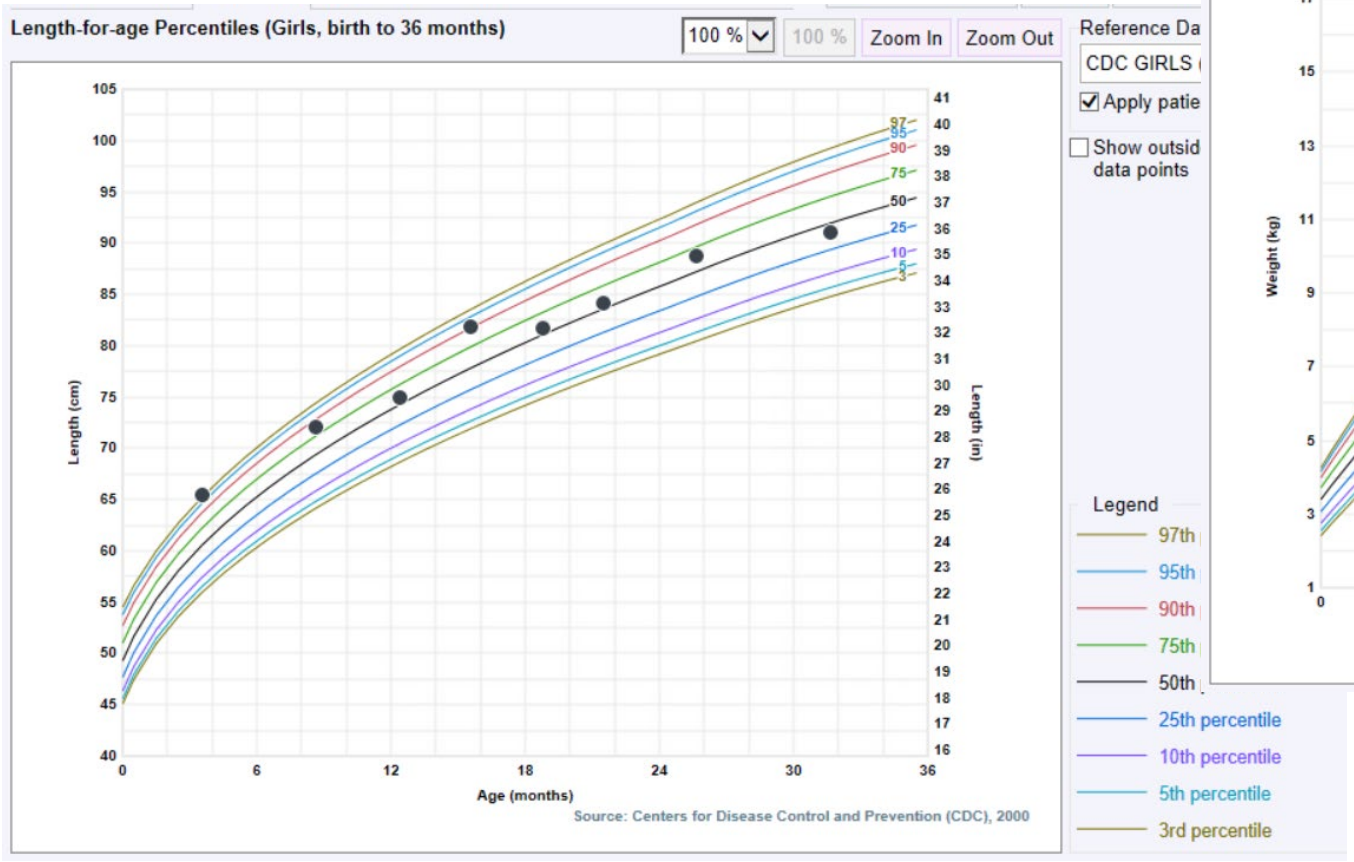
# Case of Infantile WD

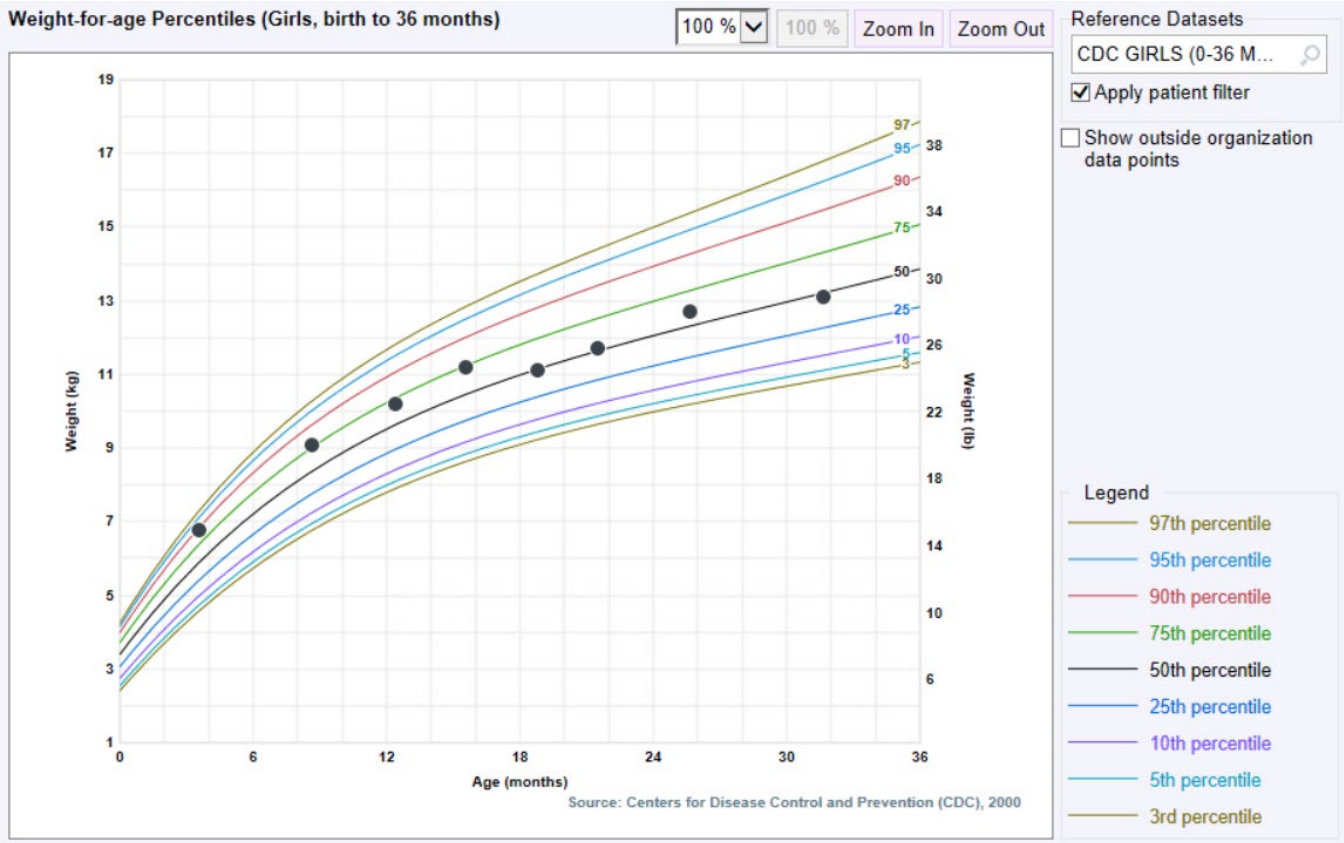
- Mother was a healthy woman who had difficulty with conception.
  - On fertility testing a DNA panel was sent
  - One mutation of *ATP7B was* identified
  - c.3207C>A (p.His1069Gln) – leads to rapid degradation of *ATP7B* protein
- Father was also tested: one mutation of *ATP7B* identified
  - c.845delT (p.Leu282Profs*2) – producing a truncated ATP7B protein

- Eventually the patient was conceived and was a healthy term baby at birth.
- Genetic testing for *ATP7B* was obtained in the infant at 42 days-old.
  - Both mutations identified
  - **WD diagnosed at 2 months of life.**

Valentino PL, et. Al.J Pediatr Gastroenterol Nutr 2020;70:547-554

# Normal growth on regular infant formula



# Case of Infantile WD

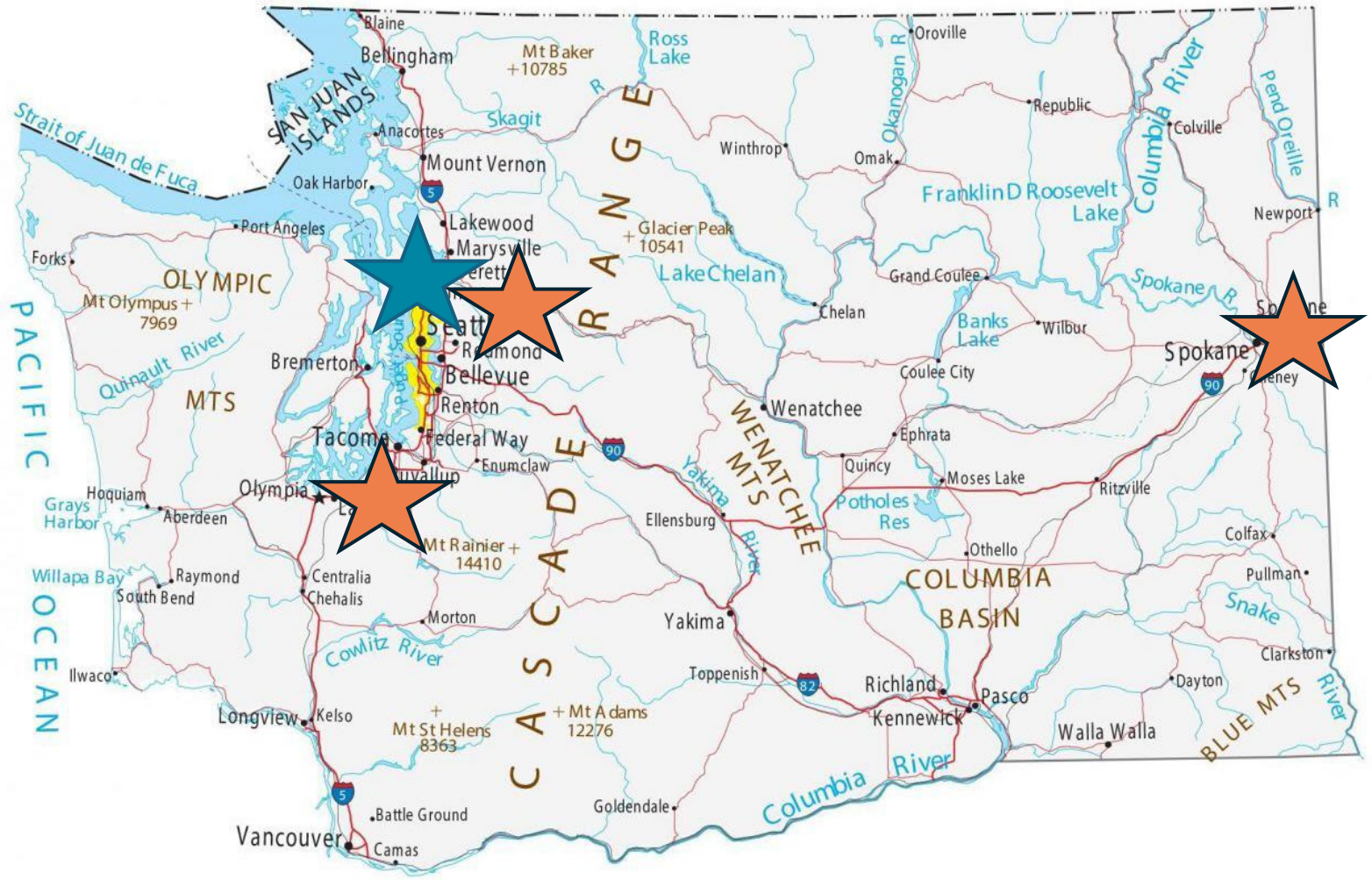
- At 18 months-old:
  - Clinically well
  - Eating 4-food groups
    - “High” copper foods excluded
  - No hepatosplenomegaly
    (liver and spleen not enlarged)
  - Normal US

| Age at testing: | 8 months | 12 months | 15 months | 18 months |
|---|---|---|---|---|
| ALT (U/L) (normal < 33) | 21 | 25 | 15 | 20 |
| AST (U/L) (normal < 32) | 54 | 40 | 42 | 39 |
| GGT (U/L) (normal < 42) | 18 | 14 | 12 | 14 |
| Direct Bilirubin (mg/dL) (normal < 0.4) | 0.2 | 0.1 | <0.2 | <0.2 |
| Ceruloplasmin (mg/dL) (normal > 20) | 8 | 11 | 11 | 7 |
| Serum Copper (mcg/dL) (normal 20 – 70) | 25 | 27 | 28 | 25 |

- **Zinc initiated at 18 months of age**
- Liver biochemistry remained normal

Valentino PL, et. Al.J Pediatr Gastroenterol Nutr 2020;70:547-554

# Seattle Children's Hepatology Clinic Sites




**SCH Hepatology Clinics**

- **Seattle Children's Hospital**
- **Tacoma**
- **Spokane**

**Seattle Children's Hospital Is a Wilson Disease Center of Excellence**

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# Thank you!

# Questions?

**Pamela L. Valentino MD, MSc**
Associate Professor of Pediatrics, UW
Medical Director, SCH Liver Transplantation Program
SCH Liver & Intestinal Failure Clinical Center Director

Washington State Department of HEALTH

WASHINGTON STATE BOARD OF HEALTH

**Newborn Screening** Technical Advisory Committee (TAC)

# *Agenda Item 7*
# *Treatment Continued: Nutrition Considerations*

# Wilson’s Disease: Nutrition Considerations

Washington State Board of Health

NBS Technical Advisory Committee

June 17, 2025

# Nutrition Considerations for Wilson's Disease

- Restrict dietary copper (+/-)
- Ensure adequate nutrient intake
- Maintain well-balanced diet and healthy body weight
- Address symptoms with nutrition-related issues
  - Dysphagia
  - Renal-related
- Individualized diet approach
  - Allay fears about foods, prevent overly restricted diet
  - Address specific concerns (e.g., vegetarian/vegan, food allergies, GI disorders)
  - Lifespan: breastfeeding

# Nutrition Considerations for Wilson's Disease

- **Restrict dietary copper (+/-)**
- Ensure adequate nutrient intake
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  - Dysphagia
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- Individualized diet approach
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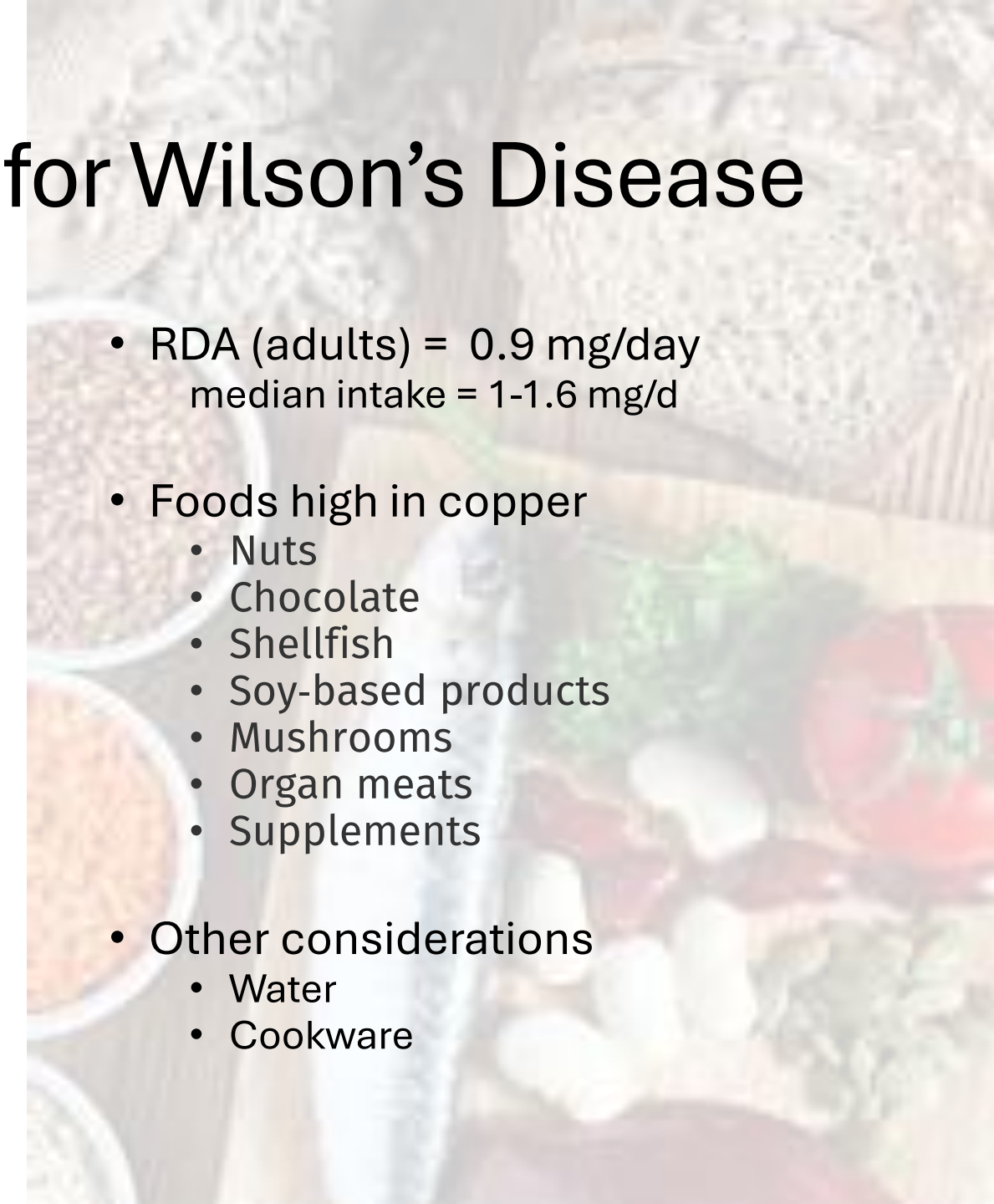
  - Address specific concerns (e.g., vegetarian/vegan, food allergies, GI disorders)
  - Lifespan: breastfeeding



- RDA (adults) = 0.9 mg/day
  median intake = 1-1.6 mg/d
- Foods high in copper
  - Nuts
  - Chocolate
  - Shellfish
  - Soy-based products
  - Mushrooms
  - Organ meats
  - Supplements
- Other considerations
  - Water
  - Cookware

# Nutrition Considerations for Wilson's Disease

- Restrict dietary copper (+/-)
- **Ensure adequate nutrient intake**
- **Maintain well-balanced diet and healthy body weight**
- Address symptoms with nutrition-related issues
  - Dysphagia
  - Renal-related
- Individualized diet approach
  - Allay fears about foods, prevent overly restricted diet
  - Address specific concerns (e.g., vegetarian/vegan, food allergies, GI disorders)
  - Lifespan: breastfeeding

# Nutrition Considerations for Wilson's Disease

- Restrict dietary copper (+/-)
- Ensure adequate nutrient intake
- Maintain well-balanced diet and healthy body weight
- **Address symptoms with nutrition-related issues**
  - **Dysphagia**
  - **Renal-related**
- Individualized diet approach
  - Allay fears about foods, prevent overly restricted diet
  - Address specific concerns (e.g., vegetarian/vegan, food allergies, GI disorders)
  - Lifespan: breastfeeding

# Nutrition Considerations for Wilson's Disease

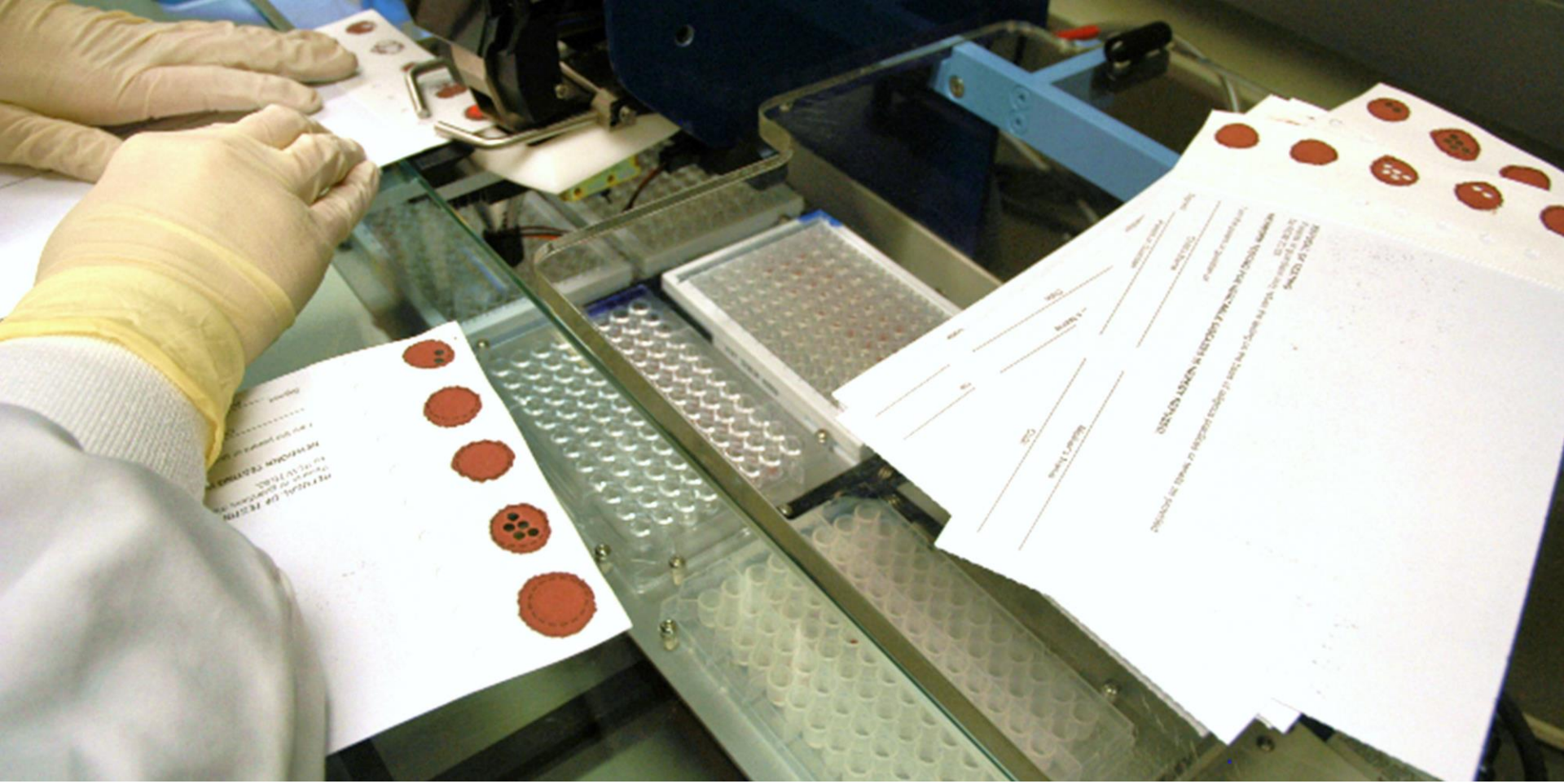
- Restrict dietary copper (+/-)
- Ensure adequate nutrient intake
- Maintain well-balanced diet and healthy body weight
- Address symptoms with nutrition-related issues
  - Dysphagia
  - Renal-related
- **Individualized diet approach**
  - **Allay fears about foods, prevent overly restricted diet**
  - **Address specific concerns (e.g., vegetarian/vegan, food allergies, GI disorders)**
  - **Lifespan: breastfeeding**

Washington State Department of HEALTH

WASHINGTON STATE BOARD OF HEALTH

**Newborn Screening** Technical Advisory Committee (TAC)

# *Agenda Item 8*
# *Available Screening Technology*



# AVAILABLE SCREENING TECHNOLOGY FOR WILSON DISEASE

Megan McCrillis, MPH

Policy Analyst, WA State Newborn Screening Program

Washington State Department of HEALTH

# Does Wilson disease meet the "Available Screening Technology" criterion for inclusion on the WA State Newborn Screening Panel?


# Available Screening Technology Criterion

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

- The sensitivity of the screening test is estimated to be ≥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

# Current Status of Screening

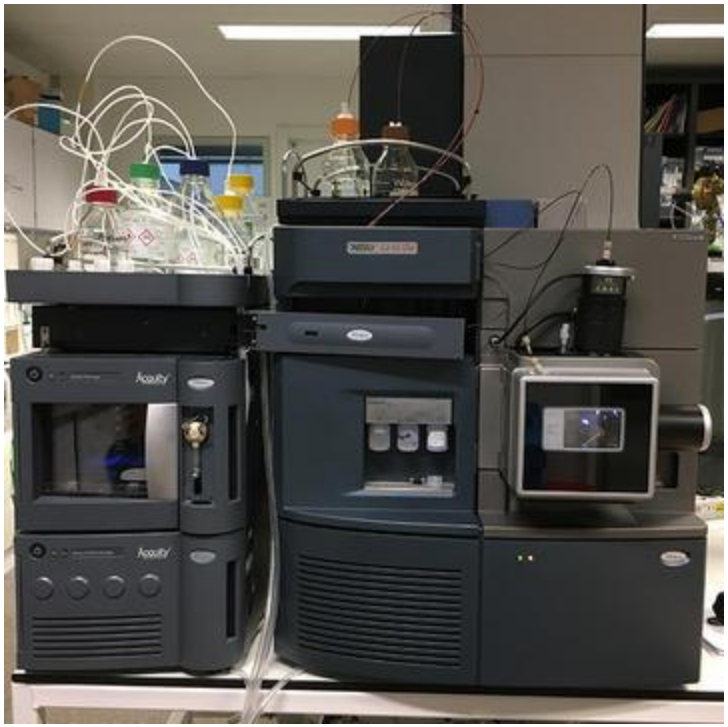
- No U.S. states or other countries are currently screening for Wilson disease
- Wilson disease has not been petitioned to the Recommended Uniform Screening Panel (RUSP)
- Between 2022-2024, a prospective pilot study took place in WA that screened 30,024 newborns

# Screening Test Rationale

- Most individuals with Wilson disease have a DNA variant that results in reduced or absent functional ATP7B protein.
- The measurement of ATP7B peptides in dried blood spots can serve as a surrogate biomarker for the protein, with a low value potentially indicating Wilson disease.

# Screening Test Overview

- Screening test available that looks for abnormally low levels of certain peptides (ATP7B 887, ATP7B 1056) in dried blood spots that act as a surrogate marker for the ATP7B protein, which is reduced in most people with Wilson disease
- Quantification done by liquid chromatography tandem mass spectrometry (LC-MS/MS)
- WA State already uses this equipment to screen for most conditions on our panel
  - However, this would be a new application of the equipment (peptide analysis), so we can't just "piggyback" onto other tests



# Available Screening Technology Criterion

*…The sensitivity of the screening test is estimated to be ≥95%.*

# Sensitivity of Screening Test

- In a blinded clinical validation study including 3,294 WA newborn samples presumably without Wilson disease and 32 samples from genetically confirmed cases of Wilson disease, all 32 were “screen positive” and had at least one peptide result below the cutoff
- To check for potential false negative cases, 34 “borderline” specimens that had peptide concentrations above but near the cutoff were also sent for sequencing
  - 23 had no variants or only a benign variant
  - 6 had one variant of uncertain significance (VUS)
  - 4 were carriers of a pathogenic variant
  - 1 possible true case with one pathogenic variant and one of uncertain significance; both peptide values above cutoff
- Sensitivity approximately: 95.5%

# Sensitivity of Screening Test, Cont.

- The pilot study of 30,024 WA newborn samples identified 1 possible true positive, with 1 of 2 peptides below the cutoff and two DNA variants of uncertain significance
  - Unable to check on clinical status due to blinded nature of pilot study

# Available Screening Technology Criterion

*…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.*

# Specificity of Screening Test

- Of 30,024 newborns screened in the pilot, there were 3 false positive results
- On an annual basis, this rate would equate to approximately 8 false positive results per year
- DNA sequencing would be required to rule out Wilson disease for these infants

# Available Screening Technology Criterion

*…A timely test is one that enables intervention before irreversible harm develops, within the current standard timeframes for specimen collection, receipt, testing, and reporting.*

# Timeliness of Screening Test

- Screening results for Wilson disease would likely be available within one or two days of specimen receipt
- Treatment for asymptomatic infants is initiated at about 18 months of age
- A LC-MS/MS screening test for Wilson disease would be timely enough to intervene before treatment is indicated

# Available Screening Technology Criterion

*…There is adequate peer reviewed evidence to evaluate this criterion*

# Primary Sources

## Establishment of ATP7B peptides as screening marker


- Collins CJ, Yi F, Dayuha R, Duong P, Horslen S, Camarata M, Coskun AK, Houwen RHJ, Pop TL, Zoller H, Yoo HW, Jung SW, Weiss KH, Schilsky ML, Ferenci P, Hahn SH. Direct Measurement of ATP7B Peptides Is Highly Effective in the Diagnosis of Wilson Disease. Gastroenterology. 2021 Jun;160(7):2367-2382.
- Jung S, Whiteaker JR, Zhao L, Yoo HW, Paulovich AG, Hahn SH. Quantification of ATP7B Protein in Dried Blood Spots by Peptide Immuno-SRM as a Potential Screen for Wilson's Disease. J Proteome Res. 2017 Feb 3;16(2):862-871.


## WA pilot and clinical validation study


- Klippel C, Park J, Sandin S, Winstone TML, Chen X, Orton D, Singh A, Hill JD, Shahbal TK, Hamacher E, Officer B, Thompson J, Duong P, Grotzer T, Hahn SH. Advancing Newborn Screening in Washington State: A Novel Multiplexed LC-MS/MS Proteomic Assay for Wilson Disease and Inborn Errors of Immunity. Int J Neonatal Screen. 2025 Jan 10;11(1):6.

# Questions?

Washington State Department of HEALTH

WASHINGTON STATE BOARD OF HEALTH

**Newborn Screening** Technical Advisory Committee (TAC)

# *Agenda Item 9*
# *Cost-Benefit Analysis*

Washington State Department of HEALTH

# COST-BENEFIT ANALYSIS OF NEWBORN SCREENING FOR WILSON DISEASE


Megan McCrillis, MPH
Policy Analyst, WA State Newborn Screening Program
John D. Thompson, PhD, MPA, MPH
Director, Newborn Screening Program

# Does Wilson disease meet the "Cost-benefit/Cost-effectiveness" criterion for inclusion on the WA State Newborn Screening Panel?

# Washington State NBS Criteria

5. **Cost-benefit/Cost-effectiveness**: The outcomes outweigh the costs of screening. All outcomes, both positive and negative, need to be considered in the analysis.

- 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 psycho-social 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.

# Background

- Cost-Benefit model is just one tool, not a definitive answer
- Does not account for every cost and benefit, but focuses on what the major differences would be between no-screening and screening
- Model focuses on costs and benefits from healthcare perspective
  - Does not account for other costs or benefits such as lost wages for caregivers or benefit of avoiding diagnostic odyssey

# Strategy

Decision Tree

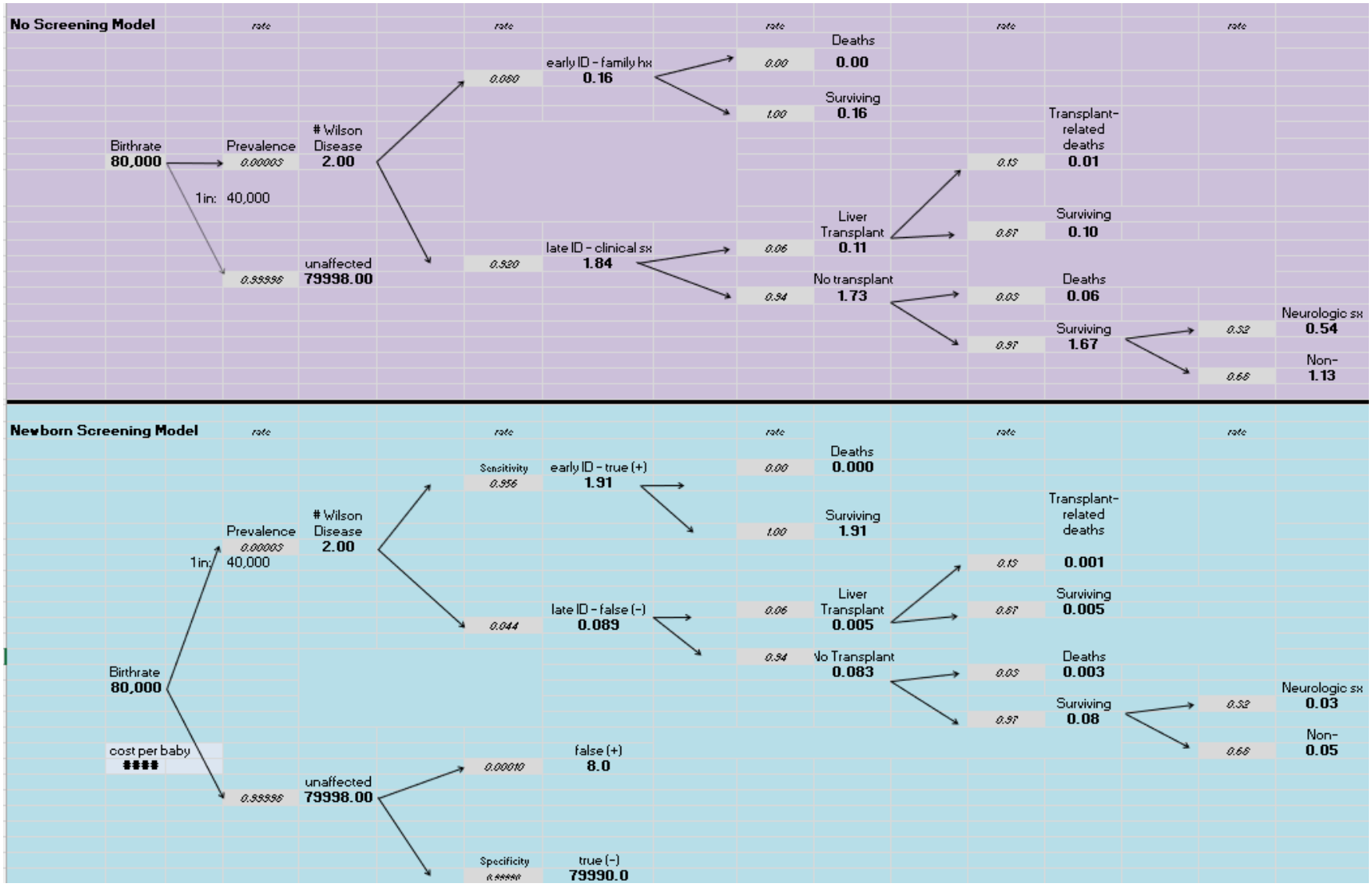
- Compares status quo v. screening model

Data from:

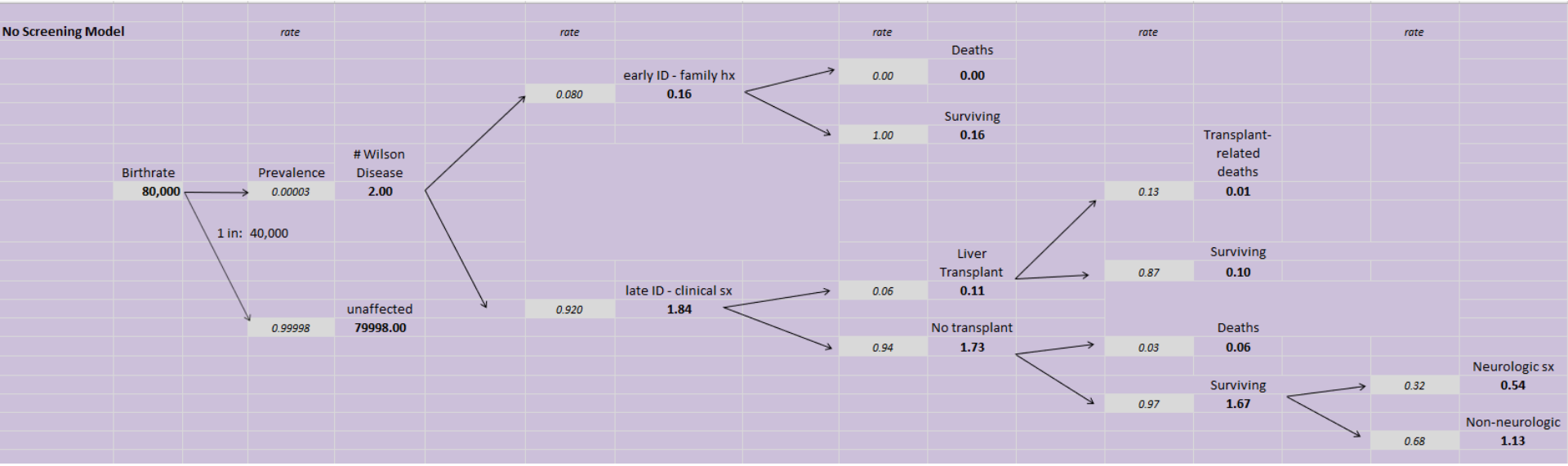
- Primary literature
- States currently screening or pilot studies
- Expert opinion

Sensitivity analysis – vary assumptions

- High and low estimates for parameters


No Screening Model
rate
Birthrate
80,000
Prevalence
0.00005
1 in: 40,000
# Wilson Disease
2.00
unaffected
79998.00
0.99995
0.050
0.950
early ID - family hx
0.16
late ID - clinical sx
1.84
0.00
1.00
0.06
0.94
Deaths
0.00
Surviving
0.16
Liver Transplant
0.11
No transplant
1.73
0.13
0.87
0.03
0.97
Transplant-related deaths
0.01
Surviving
0.10
Deaths
0.06
Surviving
1.67
0.32
0.68
Neurologic sx
0.54
Non-
1.13
Newborn Screening Model
Birthrate
80,000
Prevalence
0.00005
1 in: 40,000
# Wilson Disease
2.00
cost per baby
####
unaffected
79998.00
0.99995
Sensitivity
0.956
0.044
Specificity
0.99990
0.00010
early ID - true (+)
1.91
late ID - false (-)
0.089
false (+)
8.0
true (-)
79990.0
0.00
1.00
0.06
0.94
Deaths
0.000
Surviving
1.91
Liver Transplant
0.005
No Transplant
0.083
0.13
0.87
0.03
0.97
Transplant-related deaths
0.001
Surviving
0.005
Deaths
0.003
Surviving
0.08
0.32
0.68
Neurologic sx
0.03
Non-
0.05

# No Screening Model



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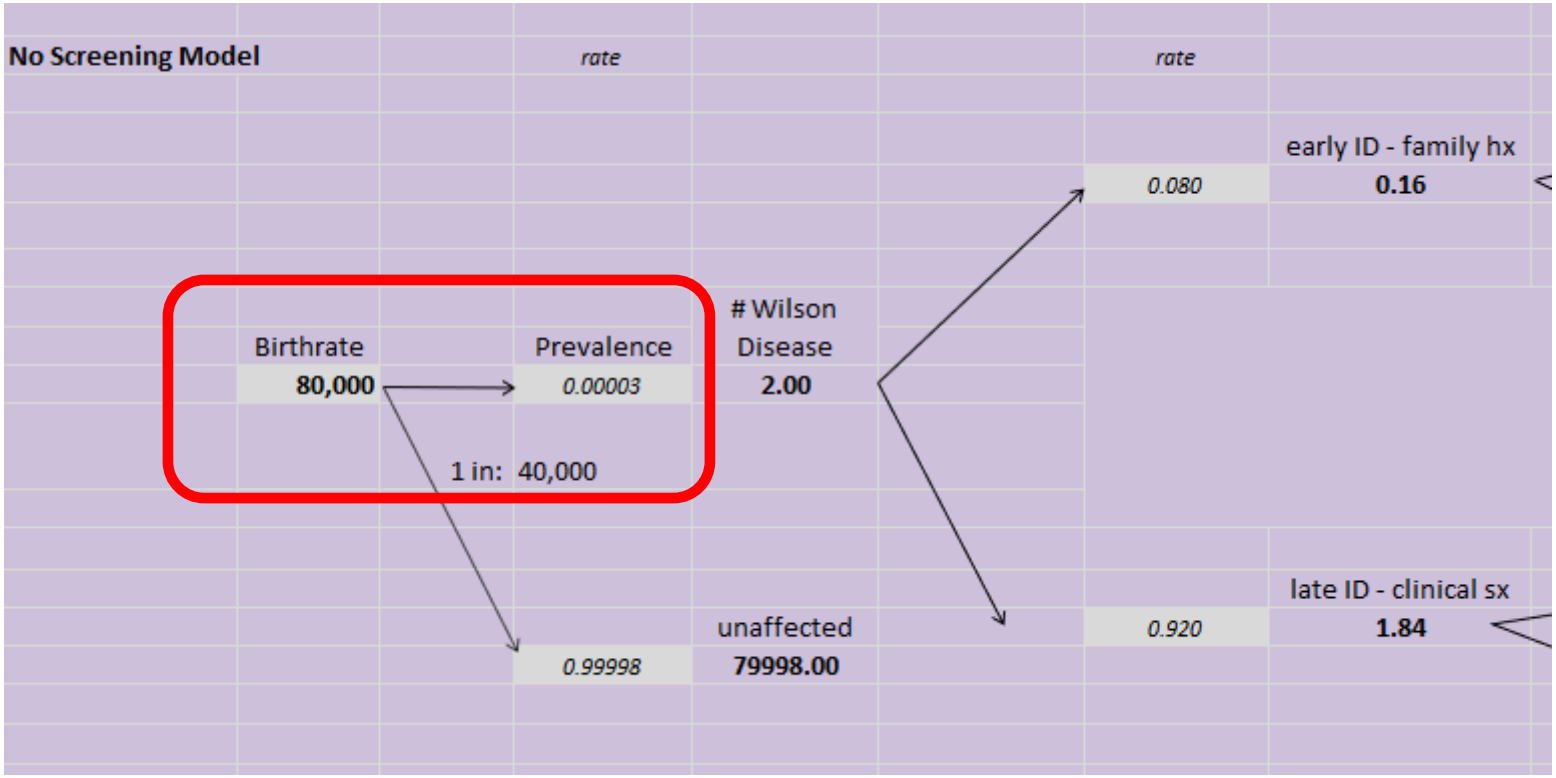
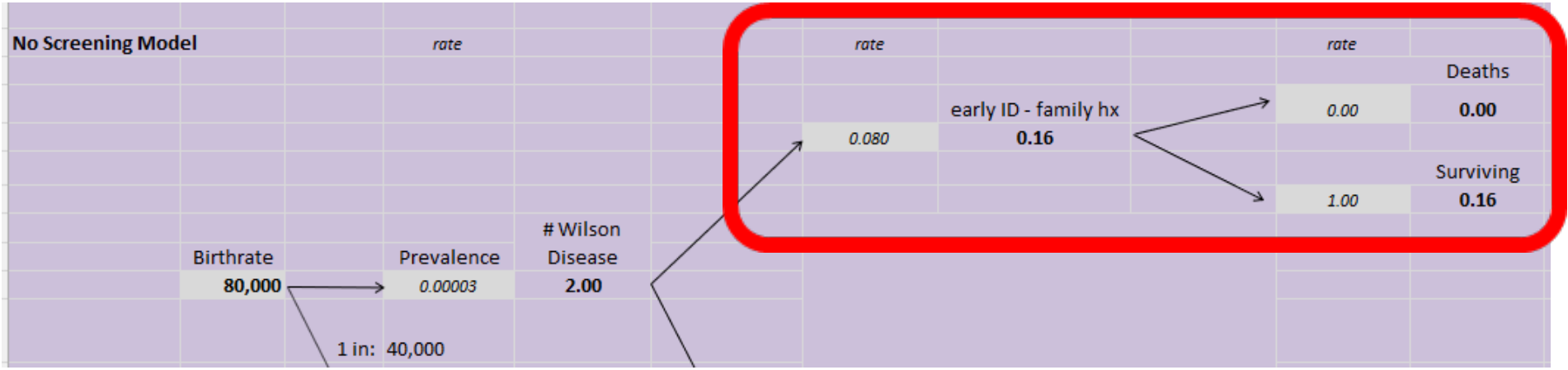
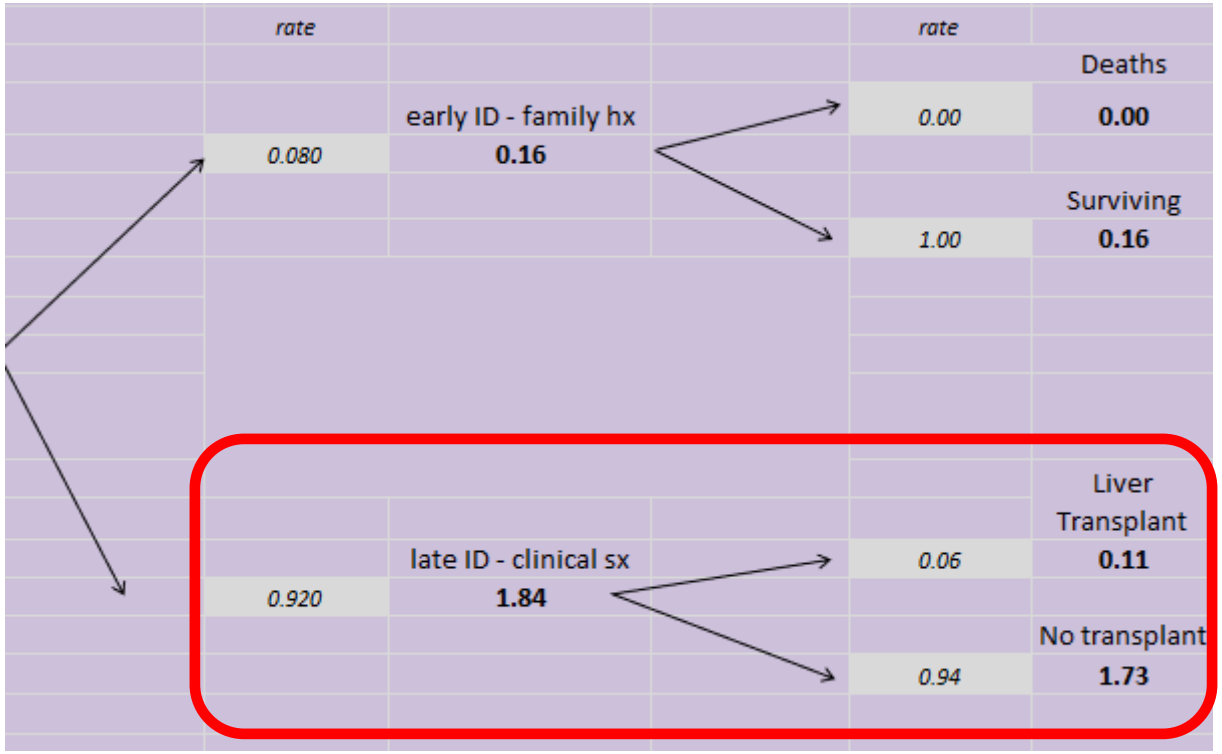


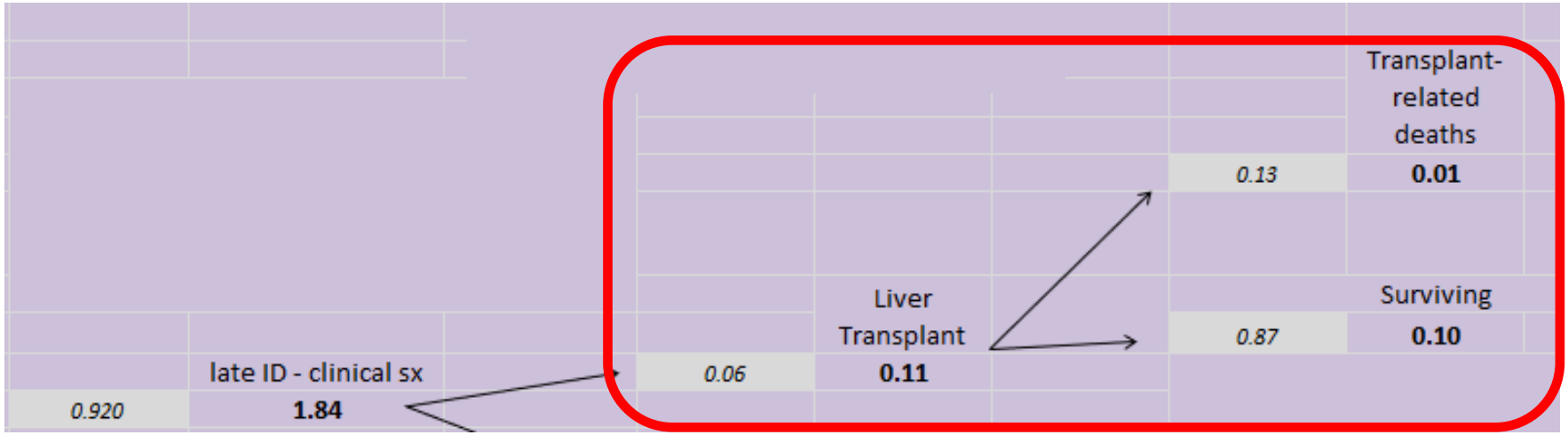
# No Screening Model



# No Screening Model



# No Screening Model



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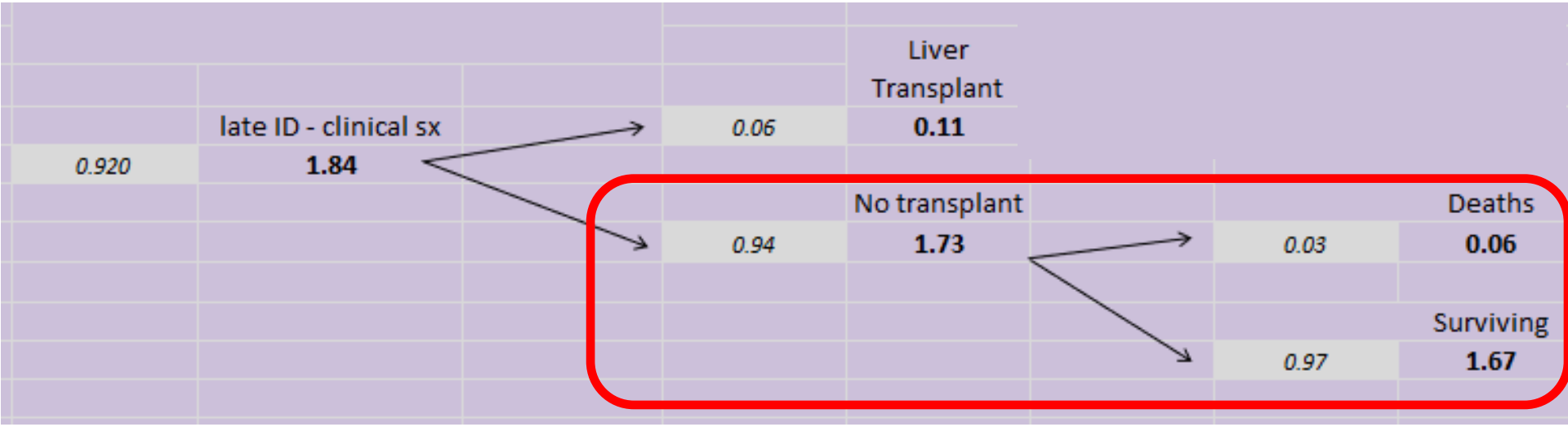

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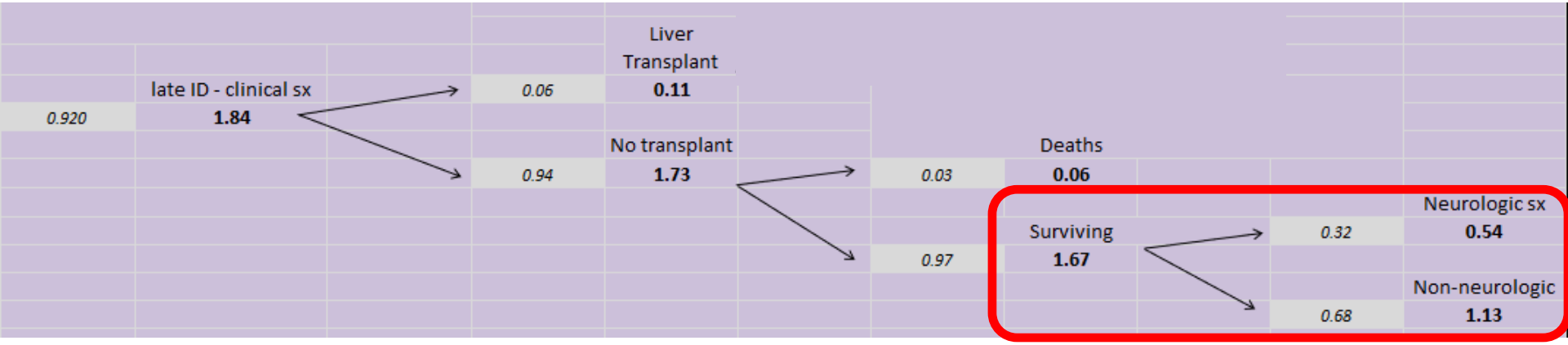
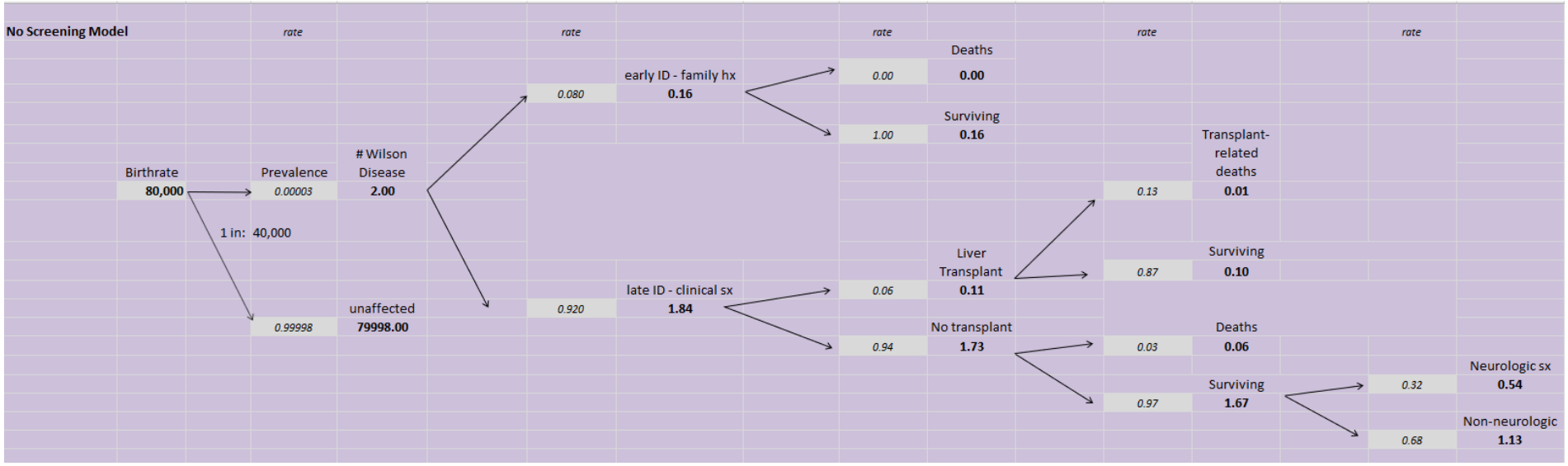
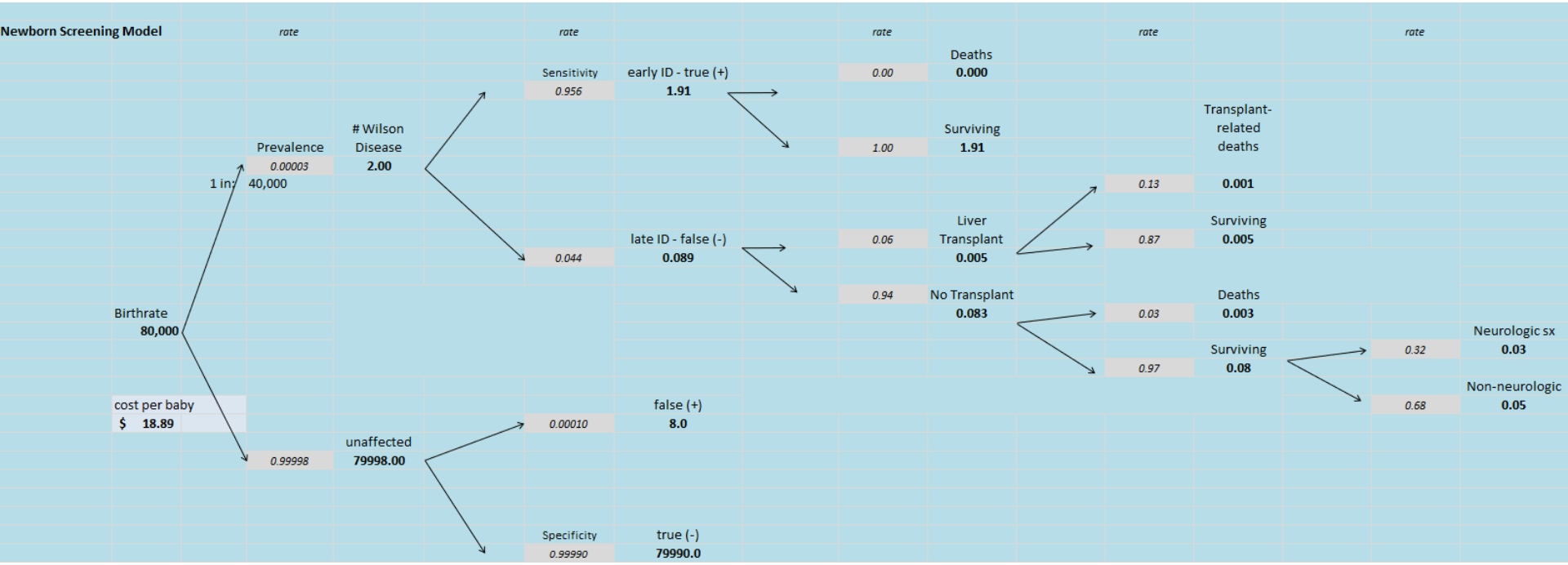


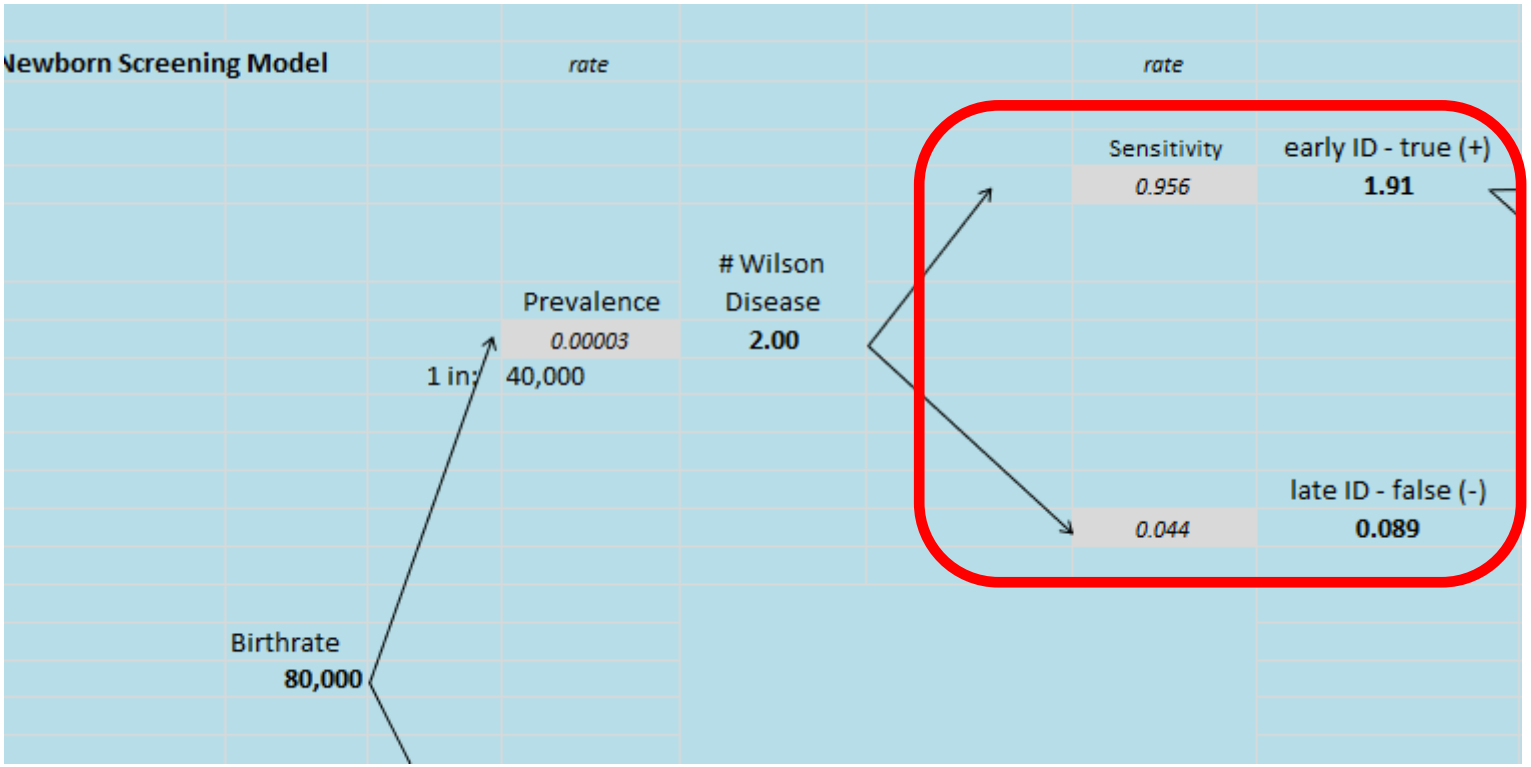
# No Screening Model



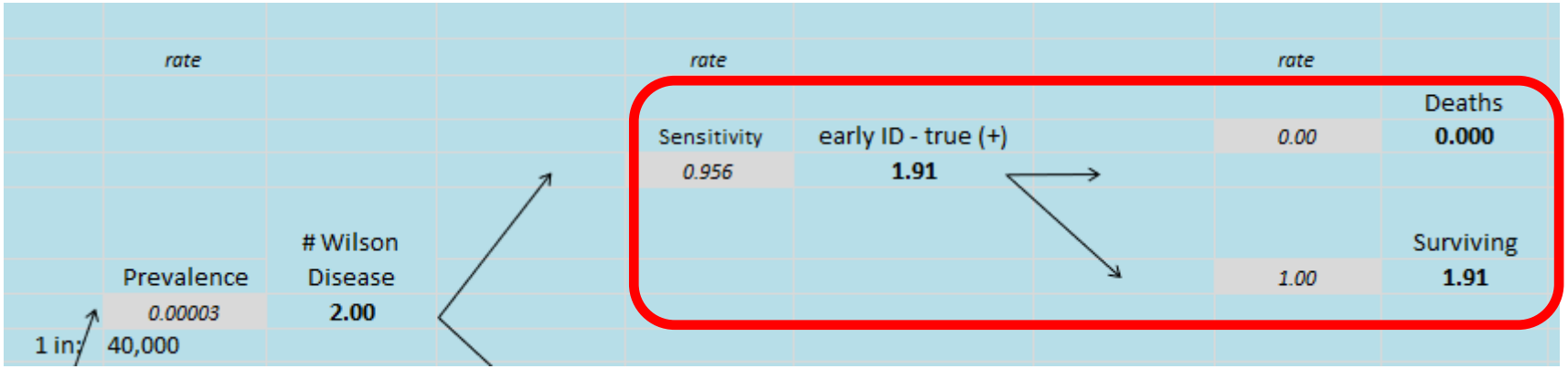
# Universal Screening Model



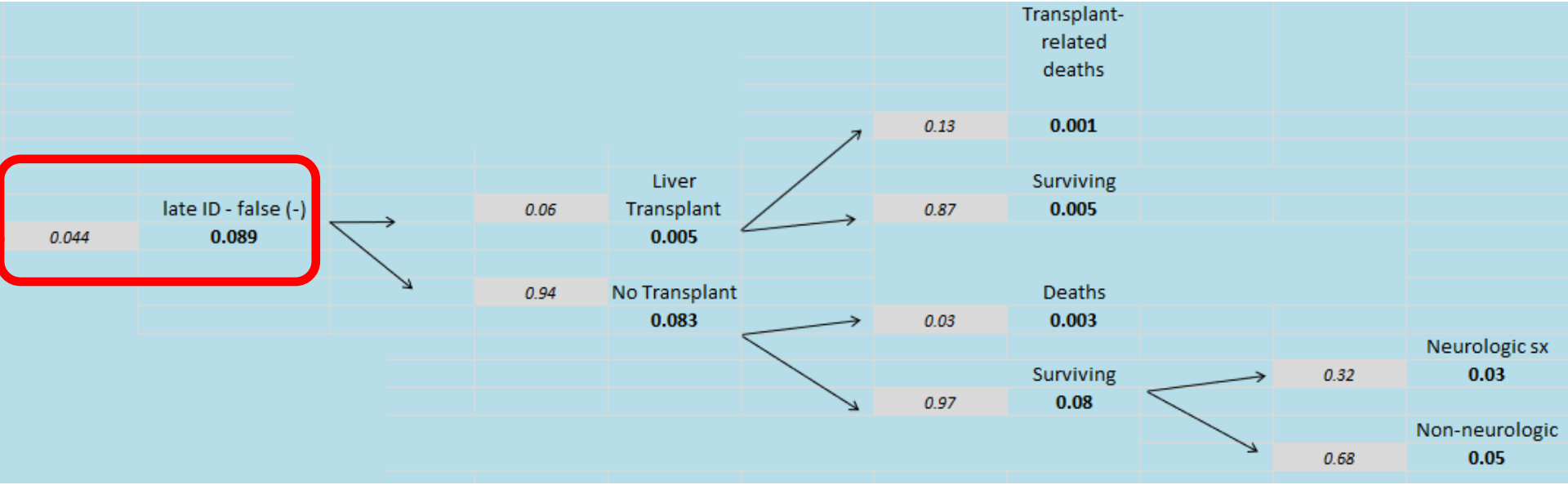
# Universal Screening Model



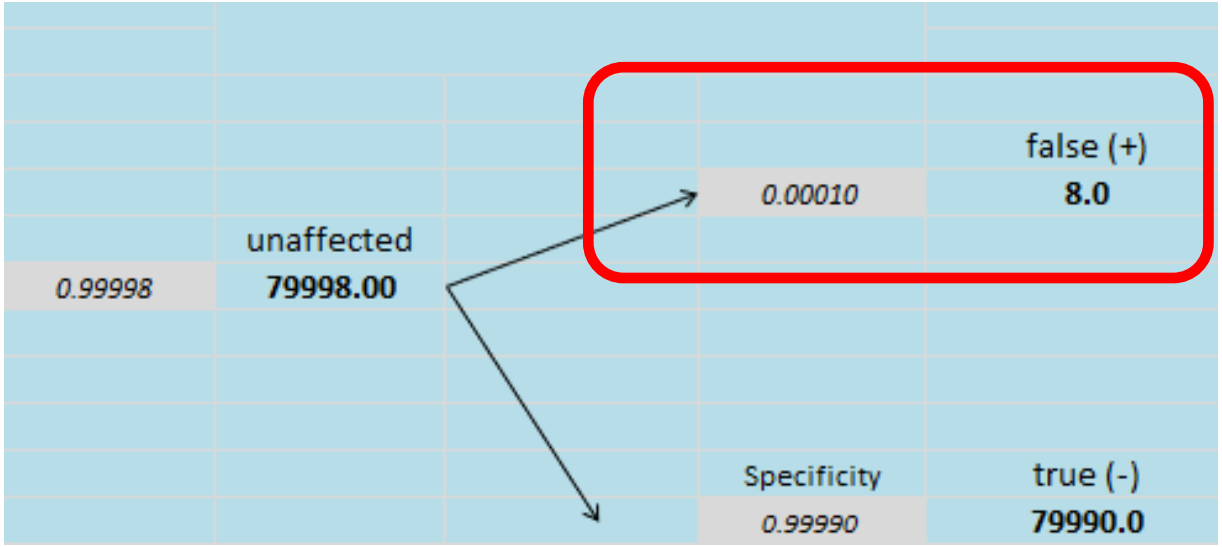
# Universal Screening Model



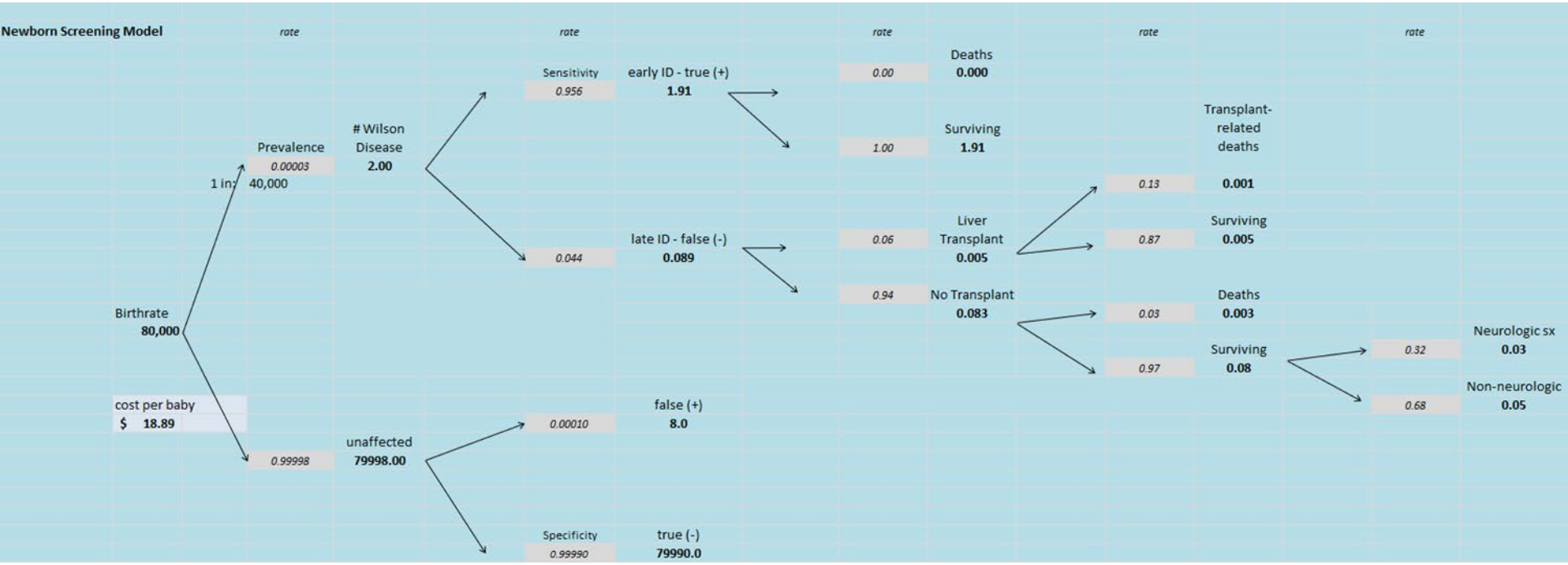
# Universal Screening Model



# Universal Screening Model



# Universal Screening Model



# Benefits

| | |
|---|---|
| **Deaths averted:** | 0.0713 |
| Value of a life | $13,234,472.25 |
| Value of lives saved | $943,106.439 |

# Benefits

| | |
|---|---|
| **Deaths averted:** | 0.0713 |
| Value of a life | $13,234,472.25 |
| Value of lives saved | $943,106.439 |
| **Liver transplants averted:** | 0.1085 |
| Value of liver transplants averted based on unemployment support | $18,711.88 |

# Benefits

| | |
|---|---|
| **Deaths averted:** | 0.0713 |
| Value of a life | $13,234,472.25 |
| Value of lives saved | $943,106.439 |
| **Liver transplants averted:** | 0.1085 |
| Value of liver transplants averted based on unemployment support | $18,711.88 |
| **Severe neurologic cases averted:** | 0.51 |
| Value of severe disability averted based on disability support costs | $1,193,011.19 |

# Benefits

| | |
|---|---|
| **Deaths averted:** | 0.0713 |
| Value of a life | $13,234,472.25 |
| Value of lives saved | $943,106.439 |
| **Liver transplants averted:** | 0.1085 |
| Value of liver transplants averted based on unemployment support | $18,711.88 |
| **Severe neurologic cases averted:** | 0.51 |
| Value of severe disability averted based on disability support costs | $1,193,011.19 |
| **Less treatment costs** | -$51,493.20 |

# Benefits

| | |
|---|---|
| **Deaths averted:** | 0.0713 |
| Value of a life | $13,234,472.25 |
| Value of lives saved | $943,106.439 |
| **Liver transplants averted:** | 0.1085 |
| Value of liver transplants averted based on unemployment support | $18,711.88 |
| **Severe neurologic cases averted:** | 0.51 |
| Value of severe disability averted based on disability support costs | $1,193,011.19 |
| **Less treatment costs** | -$51,493.20 |
| TOTAL Benefits | $2,103,336.31 |

# Costs

| **Cost of screening:** | |
|---|---|
| Per baby | $18.89 |
| Total | $1,511,479.04 |

# Costs

| | |
|---|---|
| **Cost of screening:** | |
| Per baby | $18.89 |
| Total | $1,511,479.04 |
| **Cost of false positives:** | |
| Per baby | $2000.00 |
| Total | $15,986.81 |

# Costs

| | |
|---|---|
| **Cost of screening:** | |
| Per baby | $18.89 |
| Total | $1,511,479.04 |
| **Cost of false positives:** | |
| Per baby | $2000.00 |
| Total | $15,986.81 |
| **Total treatment costs:** | $290,786.32 |

# Costs

| | |
|---|---|
| **Cost of screening:** | |
| Per baby | $18.89 |
| Total | $1,511,479.04 |
| **Cost of false positives:** | |
| Per baby | $2000.00 |
| Total | $15,986.81 |
| **Total treatment costs:** | $290,786.32 |
| TOTAL Costs | $1,818,252.17 |

# Benefits vs. Costs: Universal Screening

| | | | |
|---|---|---|---|
| BENEFITS | | | |
| | TOTAL BENEFITS | | $2,103,336.308 |
| COSTS | | | |
| | TOTAL COSTS | | $1,818,252.17 |
| | ADDITIONAL ONE-TIME START-UP COSTS | | $31,411.62 |

# Benefits vs. Costs: Universal Screening

| | | | |
|---|---|---|---|
| BENEFITS | | | |
| | TOTAL BENEFITS | | $2,103,336.308 |
| COSTS | | | |
| | TOTAL COSTS | | $1,818,252.17 |
| | ADDITIONAL ONE-TIME START-UP COSTS | | $31,411.62 |

**Benefit/Cost ratio = 1.16**

# Benefits vs. Costs: Universal Screening

| | | | |
|---|---|---|---|
| BENEFITS | | | |
| | TOTAL BENEFITS | | $2,103,336.308 |
| COSTS | | | |
| | TOTAL COSTS | | $1,818,252.17 |
| | ADDITIONAL ONE-TIME START-UP COSTS | | $31,411.62 |

**Benefit/Cost ratio = 1.16** **Net benefit = $285,084.14**

# Sensitivity Analysis

# Sensitivity Analysis: Parameters of Note

| Parameter | Base |
| --- | --- |
| specificity | 0.9999 |

# Sensitivity Analysis: Parameters of Note

| Parameter | Base |
|---|---|
| specificity | 0.9999 |
| early ID mortality | 0.00 |

# Sensitivity Analysis: Parameters of Note

| Parameter | Base |
|---|---|
| specificity | 0.9999 |
| early ID mortality | 0.00 |
| Treatment adherence | 100% |

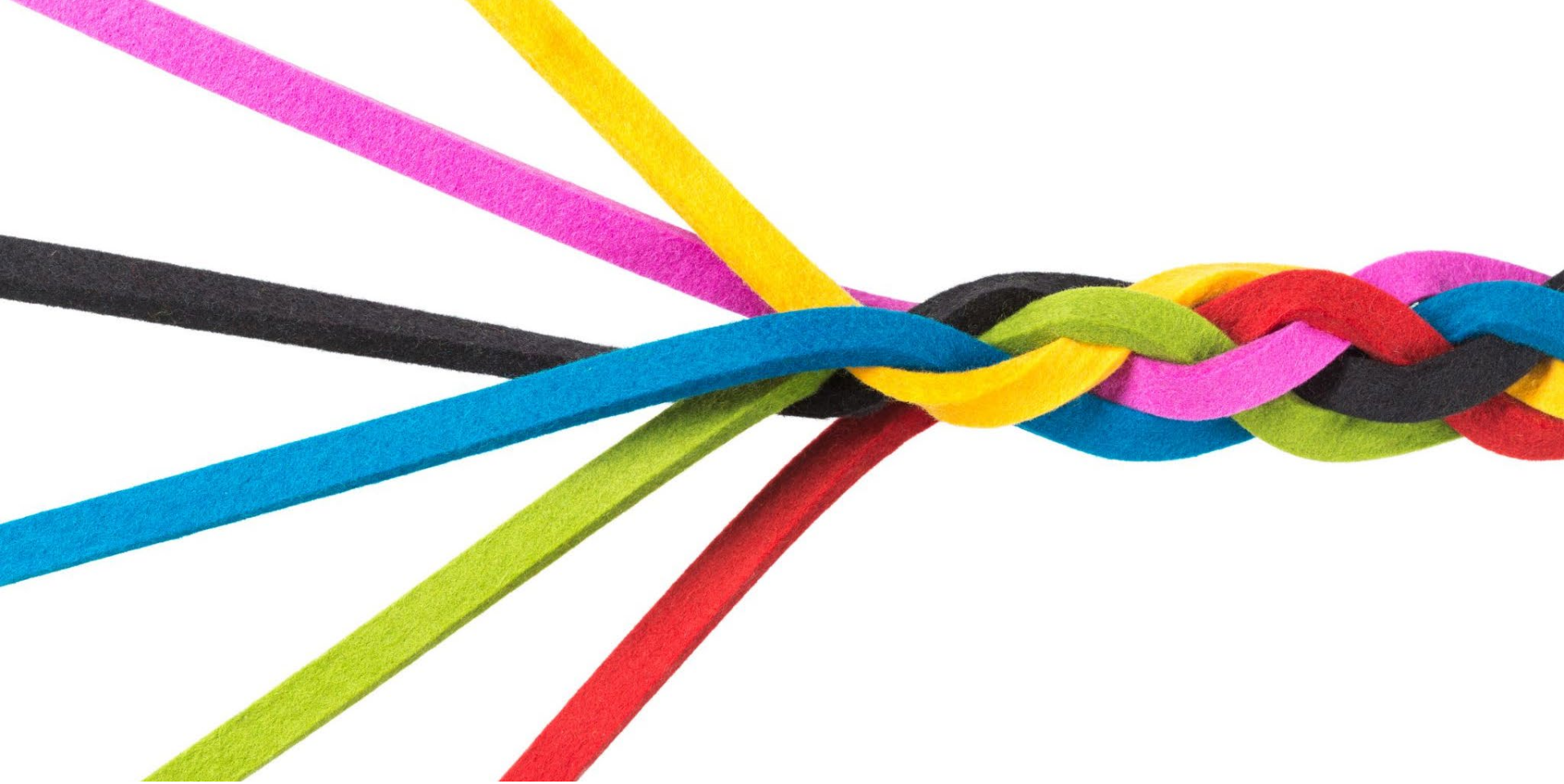
# Questions?

Washington State Department of HEALTH

WASHINGTON STATE BOARD OF HEALTH

**Newborn Screening** Technical Advisory Committee (TAC)

# *Agenda Item 10*
# *Public Health Infrastructure Readiness*



Washington State Department of HEALTH

# PUBLIC HEALTH INFRASTRUCTURE READINESS FOR WILSON DISEASE


Megan McCrillis, MPH
Policy Analyst, WA State Newborn Screening Program
John D. Thompson, PhD, MPA, MPH
Director, Newborn Screening Program

# Does Wilson disease meet the "Public Health Infrastructure Readiness" criterion for inclusion on the WA State Newborn Screening Panel?

# Washington State NBS Criteria

6. **Public Health Infrastructure 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.
- Accessibility to treatment for anyone diagnosed with the condition is considered acceptable based on the frequency of treatment needed.

# Public Health Infrastructure Readiness

**Systems and staffing needed to test and report test results:**

**Systems:**

- Laboratory equipment: (2) Xevo LC-MS/MS

**Ongoing Staffing:**

- 1 Full Time Equivalent, Chemist 2
  - frontline lab staff, to perform the test
- 0.1 Full Time Equivalent, Chemist 3,
  - lab supervisor, to provide testing and reporting oversight

**Start-up Staffing:**

- Approximately 2 months of Chemist 3 work to develop workflow and validate new equipment/methodology

**These needs were included in the cost-benefit analysis**

# Public Health Infrastructure Readiness

**Resources needed to implement short/long term follow up protocols by the newborn screening program have been identified:**

**Ongoing:**

- 0.1 Full Time Equivalent, Health Services Consultant 2

  - this is a member of the follow-up team that provides case management of abnormal results, makes recommendations for diagnostic testing, and ensures true cases are linked into specialty care

**Start-up:**

- Approximately 40 hours of Epidemiologist 2 work, which represents the disorder follow-up supervisor, to develop follow-up procedures, documents, and infrastructure

**These needs were included in the cost-benefit analysis**

# Questions?

Washington State Department of HEALTH

WASHINGTON STATE BOARD OF HEALTH

# **Newborn Screening** Technical Advisory Committee (TAC)

## Newborn Screening (NBS) Technical Advisory Committee (TAC) Voting Instructions

Please use the Microsoft Forms ballot provided by staff during the meeting to vote.

All votes are anonymous. Your votes will be collected and presented by the TAC facilitator and Co-Chairs for further discussion by the group.

Instructions:

- Only TAC members may vote.
- Do not forward or share the form/ballot.
- If you are unsure of not comfortable voting on these options, please indicate so in the form.

If you encounter any technical issues or difficulties accessing the form, please let staff know as soon as possible.