WEBVTT

1
00:00:00.040 --> 00:00:03.850
Mikaela Miller: So, I'm… Oh, thanks, Stephanie.

2
00:00:04.470 --> 00:00:06.629
Mikaela Miller: I'm going to…

3
00:00:06.660 --> 00:00:25.410
Mikaela Miller: go ahead and move into the roll call and introduction. So, this is how we've always done it in the past. We just ask that everyone, gives their name, organization, role in a physical description. We do this physical description just to help give yourself

4
00:00:25.950 --> 00:00:28.390
Mikaela Miller: A little bit more of a…

5
00:00:28.710 --> 00:00:47.700
Mikaela Miller: idea for those of us who are, or anyone who's joining who may be visually impaired, you can share whatever you're comfortable sharing, and I'm going to pass it off to Shelly here to just give a quick introduction to you all, and then we'll let Jen popcorn it around.

6
00:00:48.430 --> 00:01:05.539
Shelly Eagen: Great. Well, thanks everybody for joining. My name is Shelly Egan. I am a pediatric nurse practitioner, and I'm the chair of the committee. I am a Caucasian female with brown hair, I have a blurred background, and I have a gray top on today.

7
00:01:06.980 --> 00:01:09.180
Jennifer Banna: Good morning, everyone. I'm Jen Biana.

8
00:01:09.290 --> 00:01:14.779
Jennifer Banna: I am the Director for Montana's Family to Family Health Information Center.

9
00:01:14.900 --> 00:01:26.840
Jennifer Banna: And I'm the co-chair. I have brownish-blonde hair with some blue in it, and I'm wearing a blue sweater today, because blue is

my favorite color.

10
00:01:26.930 --> 00:01:34.929
Jennifer Banna: I'm gonna go ahead and… let's see, are we just introducing voting members, or are we doing all voting and non-voting?

11
00:01:34.930 --> 00:01:39.919
Mikaela Miller: We do just the voting and non-voting, no one from the public.

12
00:01:39.920 --> 00:01:45.399
Jennifer Banna: Perfect, just wanted to make sure before I got started. I'm gonna go ahead and send it over to Abe, then.

13
00:01:46.950 --> 00:02:01.829
Abe Elias: Thanks, Jen. Thanks, Jen. Yeah, I'm A.B. Lias, I'm at Shodel Children's Hospital, I'm the Chief Medical Officer. I'm a middle-aged white male with black-gray hair, and I'm wearing a white shirt and a gray sweater today.

14
00:02:03.280 --> 00:02:08.360
Abe Elias: Thanks, Ava. Yeah, thank you. I'm gonna hand it over to Jeannie.

15
00:02:08.820 --> 00:02:10.349
Abe Elias: How are you doing?

16
00:02:11.770 --> 00:02:24.519
Jeanne Lee: Hi, I'm Jeannie Lee. I supervise newborn screening and serology at the Montana Public Health Laboratory. I'm a non-voting member on this committee.

17
00:02:24.620 --> 00:02:42.409
Jeanne Lee: Representing the Public Health Lab. I'm a middle-aged woman. I have, collarbone-length brown hair, and today I'm wearing a light pink top with a light gray cardigan.

18
00:02:48.200 --> 00:02:50.380
Jennifer Banna: Okay, we can send it over to Shaanalia.

19

00:02:54.200 --> 00:03:03.549
Shawnalea Chief Goes Out, DPHHS: Hello, Shawna Lee at Chiefs goes out. I am the Perinatal Health Program Officer within the Health Resources Division. I am here representing Medicaid.

20
00:03:04.940 --> 00:03:18.079
Shawnalea Chief Goes Out, DPHHS: Again, this will be my last meeting as I am transitioning out of my role. My physical description is I'm Native American, so brown, black hair, I currently have a headset on, a jean jacket, and a black shirt.

21
00:03:19.870 --> 00:03:21.180
Jennifer Banna: Okay, Steven?

22
00:03:22.310 --> 00:03:31.090
Steven Shapero: Yes, my name is Steven Shapiro. I'm a member of the committee, and my role is to represent families, parents.

23
00:03:31.420 --> 00:03:35.050
Steven Shapero: Who are affected by, newborn screening.

24
00:03:35.410 --> 00:03:41.540
Steven Shapero: I am a white male, I'm 71 years old, I'm wearing a hat and a gray flannel shirt.

25
00:03:43.400 --> 00:03:45.280
Jennifer Banna: Okay, Lynn?

26
00:03:49.390 --> 00:04:07.799
Lynne Wood: Hi, I'm Lynn Wood. I am a pediatric neurologist in Billings. I'm here to serve as a physician on the committee. I am a middle-aged Caucasian woman with long, dark brown hair. I'm wearing a blue floral blouse and a baggy tan sweater.

27
00:04:07.800 --> 00:04:14.409
Lynne Wood: And I had my camera off at the beginning, because I was eating my breakfast, and I care about you guys, and didn't want to make you watch me scarf my food, but all done now.

28
00:04:15.930 --> 00:04:17.829
Jennifer Banna: Thanks, Lynn. Miranda?

29
00:04:19.970 --> 00:04:39.559
Miranda Reddig: Yeah, hi everybody, my name is Miranda Reddick. I'm the Newborn Hearing Screening Coordinator with the State of Montana. I'm a non-voting member, of this committee. Let's see, I am a 31-year-old female, I have brownish blonde hair, it's very long, and I am wearing a gray shirt today.

30
00:04:40.840 --> 00:04:42.070
Jennifer Banna: Thank you, Nikki.

31
00:04:44.530 --> 00:04:54.900
Nikki Goosen: Hi, my name is Nikki Gosin. I am with the Montana Public Health Laboratory. I do the short-term follow-up for the blood spot screening.

32
00:04:55.070 --> 00:05:04.869
Nikki Goosen: Today, I… well, I'm a Caucasian female, I'm wearing a black long-sleeve shirt, and I've got my brown hair pulled up into a bum.

33
00:05:07.120 --> 00:05:09.100
Jennifer Banna: Thank you, Jacqueline.

34
00:05:13.540 --> 00:05:28.969
Jacqueline Isaly: I am Jacqueline Isley, I'm the Family and Community Health Bureau Chief at DPHHS. I am a Caucasian female, blonde hair, and blue eyes, and I'm wearing a sort of burgundy top.

35
00:05:29.890 --> 00:05:33.490
Jennifer Banna: Thank you. Rosala, who's our newest member.

36
00:05:41.880 --> 00:05:44.120
Jennifer Banna: Rosella, can you hear us okay?

37
00:05:49.820 --> 00:05:52.110
Jennifer Banna: Okay, we'll come back to her. Cody?

38
00:05:58.630 --> 00:06:00.320
Jennifer Banna: I think you're muted, Cody.

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39
00:06:00.560 --> 00:06:09.390
Dunmire, Kotie C.: Oh, hi. Sorry, I'm Cody, I am 40 years old, I'm
Caucasian, I have blonde hair, and I'm wearing a white t-shirt today.

40
00:06:10.980 --> 00:06:12.430
Dunmire, Kotie C.: Thank you. Thank you.

41
00:06:12.430 --> 00:06:15.579
Jennifer Banna: Did we miss any… one besides…

42
00:06:16.300 --> 00:06:19.199
Jennifer Banna: Rosala, who's a voting… non-voting member… oh, Debbie!

43
00:06:19.450 --> 00:06:20.300
Debbie Gibson: Yeah, go ahead.

44
00:06:20.300 --> 00:06:23.409
Jennifer Banna: There you go, and I see pictures, it makes it… I'm
like, I know!

45
00:06:23.760 --> 00:06:41.289
Debbie Gibson: I joined a little late, sorry about that. I'm Debbie
Gibson, I'm the Laboratory Services Bureau Chief, so with the Montana
Public Health Lab. I've got, dark blonde hair and blue eyes, Caucasian
female, and wearing a flowered blue shirt.

46
00:06:42.900 --> 00:06:43.880
Jennifer Banna: Thank you.

47
00:06:44.170 --> 00:06:45.999
Jennifer Banna: Rosella, are you there now?

48
00:06:49.310 --> 00:06:57.959
Mikaela Miller: I will send her an email just to make sure she's not
having any technical difficulties. Okay. And I think… did…

49
00:06:58.140 --> 00:07:02.759
Mikaela Miller: We have a few more Miranda, Amber, or Kayla to go yet.
```

50
00:07:02.760 --> 00:07:04.989
Jennifer Banna: Oh, Amber didn't go, I saw her, and then she disappeared.

51
00:07:04.990 --> 00:07:05.790
Mikaela Miller: Perfect.

52
00:07:05.790 --> 00:07:06.720
Jennifer Banna: Hey, Amber?

53
00:07:06.940 --> 00:07:20.450
Amber Bell: Hi, I am Amber Bell. I am a non-voting member. I am the Children's Special Health Services Section Supervisor, and I am a middle-aged woman,

54
00:07:21.270 --> 00:07:26.520
Amber Bell: With long, dark, straight brown hair, and…

55
00:07:26.730 --> 00:07:29.660
Amber Bell: A blue sweater on today.

56
00:07:31.010 --> 00:07:31.839
Jennifer Banna: Thank you.

57
00:07:34.080 --> 00:07:35.609
Jennifer Banna: And if we missed anybody else.

58
00:07:35.880 --> 00:07:37.419
Jennifer Banna: You'll have to help me out with that one.

59
00:07:41.090 --> 00:07:43.150
Jennifer Banna: As I can see, we have professionals.

60
00:07:43.150 --> 00:07:44.280
Amber Bell: Did you go, Kayla?

61
00:07:44.630 --> 00:07:59.930

Kayla Cummins: So, I'm Kayla Cummins, I am the Admin 3 Assistant at the Early Childhood and Family Support Division. I am 38, I am multi-race, so I have tan skin, and I am wearing a yellow shirt, and I have curly brown hair.

62
00:08:07.750 --> 00:08:08.840
Mikaela Miller: Okay.

63
00:08:09.210 --> 00:08:14.580
Mikaela Miller: Trying to think, Kathy, I'm not sure if you had a chance to go.

64
00:08:14.790 --> 00:08:25.160
Mikaela Miller: We're just doing introductions, roll call, so on the screen you can just do name, organization, role, and then brief physical description, whatever you're comfortable sharing.

65
00:08:25.160 --> 00:08:25.760
kathy Crowley: Okay.

66
00:08:26.130 --> 00:08:45.000
kathy Crowley: I'm Kathy Crowley. I'm the birth center representative for the team. I work out of Roots Midwifery and Origin Health in Missoula. I have… wear glasses, I have dirty blonde hair that's up in a bun today.

67
00:08:45.110 --> 00:08:49.610
kathy Crowley: I am, I guess middle-aged.

68
00:08:49.860 --> 00:08:54.779
kathy Crowley: white female, and I'm wearing a print shirt.

69
00:08:58.930 --> 00:09:03.089
Mikaela Miller: Perfect. Okay. I think maybe now we have everyone.

70
00:09:03.580 --> 00:09:09.630
Mikaela Miller: Other than Stephanie and I, so I'll go really quick. My name's Michaela, I work for

71
00:09:09.630 --> 00:09:28.719

Mikaela Miller: Yarrow, a public health contractor, and I'm here to facilitate the meeting today. Physical description, I'm wearing a burgundy sweater, I have white skin. Behind me, there is some bright sunlight today, and so, my camera's a little bit blurry. And then with me here today is Stephanie.

72
00:09:29.030 --> 00:09:38.499
Mikaela Miller: She also works for Yarrow, and she's going to be doing some of the Zoom, running the Zoom and taking notes for us, and I'll let you give a description, Stephanie.

73
00:09:38.780 --> 00:09:47.419
Stephanie Burkholder: Yeah, thanks. Hi, everybody. I'm Stephanie Burkholder. I am a Caucasian female with brown and gray hair.

74
00:09:47.530 --> 00:09:58.110
Stephanie Burkholder: And I have a blue shirt on, and I did put my email address in the chat. If you're having any technical difficulties, go ahead and just email me directly, and we'll help you get sorted.

75
00:10:02.290 --> 00:10:03.410
Mikaela Miller: Alright.

76
00:10:07.140 --> 00:10:10.509
Mikaela Miller: Jen, if you want to go ahead and read our acknowledgement…

77
00:10:12.360 --> 00:10:19.900
Jennifer Banna: So we want to thank the families, caregivers, and committee members and advocates for their contributions to the Montana Newborn Screening Program.

78
00:10:19.900 --> 00:10:38.719
Jennifer Banna: We recognize that each condition reviewed affects children and families in Montana, and we strive to balance the emotions and vulnerabilities shared with the need for careful, sometimes difficult discussions on logistics and finances. Our goal to ensure that… our goal is to ensure the process is publicly accessible, transparent, and carefully examined.

79
00:10:38.720 --> 00:10:39.550

Jennifer Banna: Thank you.

80
00:10:43.020 --> 00:10:44.119
Mikaela Miller: Thanks, Jen.

81
00:10:46.390 --> 00:11:03.499
Mikaela Miller: And I'm just gonna start off today with just a quick acronym, so you're going to be seeing this a lot today. Normally, we do try to avoid acronyms, but this is one that I think we'll be seeing quite a bit. So, metachromatic Leukodystrophy, MLD,

82
00:11:05.790 --> 00:11:28.370
Mikaela Miller: And the agenda for today, so, as you've seen, we've done kind of the welcome and roll call. We just have a few brief updates for everyone. We're going to review the MLD nomination packet. We'll have just, like, a short 15 minutes or so to review, or to have, to give our committee a chance to discuss that packet, if there's anything that stood out to them in any of the responses.

83
00:11:28.690 --> 00:11:31.919
Mikaela Miller: Then we're going to have the family presentation.

84
00:11:32.310 --> 00:11:40.399
Mikaela Miller: Then we'll take a short 10-minute break, kind of right in the middle of the meeting there, and then we'll have our SME present for us.

85
00:11:40.460 --> 00:11:43.080
Mikaela Miller: The state lab is going to present.

86
00:11:43.080 --> 00:12:01.239
Mikaela Miller: And then we'll have a longer chunk of discussion time there for you to… the committee members to go over anything that came up during those presentations. They're also welcome to ask, I believe, our SME, and then we'll have, of course, Jeannie and Nikki on as well, if you would like to ask them any questions.

87
00:12:01.420 --> 00:12:15.920
Mikaela Miller: And then we're gonna roll into a 10-minute public comment period. I'll kind of go over how that works here in just a moment, and then we're going to wrap it up and go over, what our next meeting's going to look like.

88
00:12:16.380 --> 00:12:20.510
Mikaela Miller: And hopefully we'll be able to close it off around noon.

89
00:12:23.930 --> 00:12:26.690
Mikaela Miller: Alright, so public comment period.

90
00:12:29.790 --> 00:12:47.470
Mikaela Miller: Just so that you can prepare any comments you have, this is how we're going to run that. It is reserved just for members of the public, not our committee members. As I showed earlier, committee members can make any comments or ask any questions during that discussion period.

91
00:12:47.470 --> 00:13:01.389
Mikaela Miller: When we reach the public comment period, if anyone from the public would like to make any statements, please use your raise hand feature in your Zoom pop-up bar, or, if you're calling in, that's star 9.

92
00:13:01.580 --> 00:13:06.429
Mikaela Miller: And I will call your name, you can unmute yourself and share your comment.

93
00:13:06.660 --> 00:13:28.109
Mikaela Miller: Just so that we can give everyone a chance to comment, since this is only a 10-minute period, everyone will have 2 minutes maximum, for their comments, so we'll have Stephanie with a little timer running, and she'll put in the chat a little warning once you hit that minute, 45-second mark, and then at 2 minutes, I'll start

94
00:13:28.110 --> 00:13:34.180
Mikaela Miller: Asking you to kind of wrap it up, so that we can go on to the next public comment.

95
00:13:34.550 --> 00:13:47.589
Mikaela Miller: So, if you have any questions or additional comments as well, if you did not get a chance to share those during the public comment period, we do take those to our email up to 1 hour after the meeting ends.

96
00:13:50.890 --> 00:14:08.129
Jennifer Banna: Michaela, this is Jen. Now that we've talked about the subject matter expert and the family being here, I know that they're not all going to go at once, but because we can see their faces, would it be okay to have them introduce themselves, just so we can kind of see who else is in the room that's going to be presenting to us today? Just a quick introduction?

97
00:14:08.390 --> 00:14:14.429
Mikaela Miller: Yeah, and I actually don't think I see the SME or the family presenters on here quite yet.

98
00:14:14.430 --> 00:14:23.990
Jennifer Banna: Okay, that's fine then. I was just thinking… I was just thinking that we… I wanted to welcome them, and let them know that we're glad that they're here, and… but I wasn't sure who they were, so okay, thank you.

99
00:14:23.990 --> 00:14:36.500
Mikaela Miller: Yeah, no, thank you for that. I will, point that out once we see them hop on. We… they're a little crunched for time, so we did give them more of that specific window they'll be presenting in, but I'll keep an eye out for that.

100
00:14:38.050 --> 00:14:39.270
Mikaela Miller: All right.

101
00:14:39.900 --> 00:14:56.759
Mikaela Miller: Just some quick ground rules here. We've just set these up so we can facilitate, you know, the most effective and respectful meeting that we can. So when you're not talking, just please mute your microphone. These are all pretty straightforward, just…

102
00:14:56.760 --> 00:15:06.089
Mikaela Miller: Have your video on if you can, unless there's distractions in your background. There will be the chat active during the meeting for the committee members.

103
00:15:06.090 --> 00:15:24.670
Mikaela Miller: Ask clarifying questions if you don't understand something. Of course, we just try to avoid talking over each other or

interrupting other speakers. Try to avoid acronyms when you're speaking if you can. Just remember to focus on our collective interests and goals here today.

104
00:15:24.720 --> 00:15:43.569
Mikaela Miller: Any next steps or action items, we will try to assign those to a specific individual, just to help ensure accountability and keep things rolling with the committee. And then just to ensure equity and voice of engagement, we may call on specific attendees for some more input.

105
00:15:44.160 --> 00:15:48.169
Mikaela Miller: And I just want to highlight that this meeting is a safe space.

106
00:15:48.190 --> 00:16:06.690
Mikaela Miller: And, we're just here to guide the determination of screening for newborn conditions in the state of Montana. If you don't feel comfortable sharing in this meeting space, please let me or Stephanie know, and we can communicate with you in another way. So if it's private chat or email, we're happy to do that as well.

107
00:16:14.860 --> 00:16:26.880
Mikaela Miller: Okay, just some short updates here. We wanted to update everyone on Pompeii, so we are currently screening now for Pompeii in the state of Montana.

108
00:16:26.880 --> 00:16:34.899
Mikaela Miller: Thank you to our voting members and internal committee who are a part of that. Screening for that condition began on January 15th.

109
00:16:34.900 --> 00:16:48.000
Mikaela Miller: This caused the panel to go up $11, and so we are up to now $161.80, and I believe that's the current price if… I know some committee members like to know that as we go into these conversations.

110
00:16:48.200 --> 00:17:01.359
Mikaela Miller: A brief ASMD update. So, this is… this condition is in the rulemaking process currently. The state is working with Wisconsin to determine when screening may begin in Montana.

111

00:17:02.260 --> 00:17:20.060
Mikaela Miller: And then I just wanted to point out briefly, we do have a new committee member, Rose Lapine. She's a family nurse practitioner, and she worked in the Blackfeet Tribal Public Health, and she will be holding position on the committee as the representative of a tribal healthcare system.

112
00:17:20.109 --> 00:17:26.959
Mikaela Miller: And I know… Rose, hi! If you want to introduce yourself, I know you didn't have a chance to earlier.

113
00:17:30.020 --> 00:17:41.289
Rosaula Nympha La PINE: Okay, good, good morning to everybody. I'm Rosa Pine. I'm American, Filipino, by, citizenship.

114
00:17:41.440 --> 00:17:50.860
Rosaula Nympha La PINE: Actually, currently, I am here in the Philippines. It is now… 11… In the evening,

115
00:17:51.850 --> 00:18:07.560
Rosaula Nympha La PINE: all of you are probably wearing some kind of warm clothing. I'm wearing something warm. It's really very hot in here, very humid. But overall, I'm happy to be a part of the committee, and thank you for welcoming me.

116
00:18:10.130 --> 00:18:17.019
Mikaela Miller: Thanks, Rose. We're happy to have you here, even though, you know, time zones were a little bit tricky, so thank you for being here.

117
00:18:20.140 --> 00:18:21.850
Mikaela Miller: Alright.

118
00:18:23.390 --> 00:18:30.640
Mikaela Miller: So here's just a super brief introduction to the MLD nomination packet that we received.

119
00:18:30.640 --> 00:18:44.969
Mikaela Miller: Please note, this is just a really quick, broad overview of some of the items from the packet, but later in the meeting, we'll be hearing a lot more from our subject matter expert and the lab presentations, and then, of course, the family

presentation as well.

120
00:18:49.980 --> 00:18:57.150
Mikaela Miller: So, MLD is typically grouped into 3 different types, and those depend on the age of onset.

121
00:18:57.150 --> 00:19:12.980
Mikaela Miller: So there's the late infantile form appearing between about 6 months and 2 years. It's the most common and most severe, with early signs including loss of motor skills, muscle weakness, difficulty walking, followed by neurological decline.

122
00:19:12.980 --> 00:19:18.460
Mikaela Miller: There's the juvenile form, begins roughly ages 3 and 16.

123
00:19:18.500 --> 00:19:27.439
Mikaela Miller: And often starts with behavioral or learning difficulties, along with clumsiness, then progresses to motor impairment.

124
00:19:30.290 --> 00:19:49.139
Mikaela Miller: Then there's the adult form, which is the rarest and slowest form. It can emerge in the late teens or even later, and it's often first marked by psychiatric symptoms such as depression, personality changes, cognitive or cognitive decline before physical symptoms begin to develop.

125
00:19:49.260 --> 00:19:54.089
Mikaela Miller: And then, across all types, symptoms generally worsen over time.

126
00:19:58.680 --> 00:20:08.449
Mikaela Miller: So, how is this disorder currently identified? It's identified between a combination of clinical evaluation, lab testing, and imaging.

127
00:20:08.840 --> 00:20:20.570
Mikaela Miller: We asked, why should it be screened at birth? And the response was, early detection and management can help mitigate some of the serious health risks and improve quality of life.

128
00:20:20.850 --> 00:20:32.370
Mikaela Miller: How is this disorder treated? So it's hematopoietic stem cell HSC gene therapy. This is an FDA-approved treatment for the early onset form.

129
00:20:32.960 --> 00:20:40.539
Mikaela Miller: Is the treatment in the experimental phase? No. And then the proposed screening test method is the dried blood spot?

130
00:20:46.350 --> 00:21:00.790
Mikaela Miller: And then here, we asked some questions about the states that are currently screening the condition. It looks like there's for sure an active state one, which is in New York. The condition has been reviewed by the RESP.

131
00:21:00.790 --> 00:21:16.150
Mikaela Miller: And then, registries or databases currently established for the condition, at least two. There's a clinician-slash-research-led international registry called MLDI, and there's also a patient-powered registry.

132
00:21:21.060 --> 00:21:26.270
Mikaela Miller: Next, we have some questions regarding the selection criteria.

133
00:21:26.770 --> 00:21:37.989
Mikaela Miller: The first question is, can it be identified at a period of time within 24 to 48 hours after birth, at which it would not ordinarily be clinically detected? That's true.

134
00:21:38.030 --> 00:21:53.070
Mikaela Miller: A test with appropriate sensitivity and specificity is available. That's true. There is a significant risk of illness, disability, or death if babies are not treated promptly, within the recommended time frame for the condition. That's true.

135
00:21:53.110 --> 00:22:06.859
Mikaela Miller: Effective treatment is available, and access to follow-up care and counseling is generally available. True. There are demonstrated benefits of early detection, timely intervention, and efficacious treatment. That's true.

136
00:22:06.960 --> 00:22:08.900
Mikaela Miller: The benefits to babies?

137
00:22:09.330 --> 00:22:15.219
Mikaela Miller: And to society outweigh the risks and burdens of screening and treatment. That's true.

138
00:22:17.890 --> 00:22:37.250
Mikaela Miller: Selection criteria 7, we ask, there are minimal financial impacts on the family. Those responded as true. There is a public health benefit to conducting the test. True. There exist responsible parties who will follow up with families and implement necessary interventions.

139
00:22:37.380 --> 00:22:49.240
Mikaela Miller: Who's responded true. And the last one is the conditions, case definition, and spectrum are well described, which we also received a true response for.

140
00:22:52.140 --> 00:23:11.260
Mikaela Miller: Okay, so I'm happy to leave these slides up for the selection criteria, or if the committee members need me to go back to any other pieces of that overview packet, but we do have, like, 15 minutes or so reserved if anyone has any questions about the packet, or any of those selection criteria.

141
00:23:16.950 --> 00:23:21.390
Shelly Eagen: So we'll go ahead and open it up for discussion with the committee members.

142
00:23:35.110 --> 00:23:39.159
kathy Crowley: What is the incidence in the population of this occurring?

143
00:23:43.510 --> 00:23:56.209
Mikaela Miller: I believe our SME will give that later on in the presentation. I did not see that in the overview packet piece that we had, but we will dive into that a bit later.

144
00:24:03.170 --> 00:24:17.550
Shelly Eagen: I have several questions, but not really related

directly to the packet, and so I think I will hold off on the questions that I have to see if it's answered by the SME or the family, before bringing those up, because I would imagine there'll be

145
00:24:17.630 --> 00:24:23.219
Shelly Eagen: answered at a later time. Does anybody have anything else directly related to the packet?

146
00:24:23.400 --> 00:24:27.119
Jennifer Banna: I have a semi-related to the packet question, but we could also

147
00:24:27.210 --> 00:24:44.660
Jennifer Banna: talk about it later if nobody knows the answer, but we've been talking about the RESP committee and the RESP and all these changes that we've had at the federal level in terms of recommendations, and so the RESP committee, if I understand correctly, doesn't actually… that committee that was reviewing the conditions doesn't actually exist anymore. Is that…

148
00:24:45.060 --> 00:24:45.570
Shelly Eagen: Correct.

149
00:24:45.920 --> 00:24:51.790
Jennifer Banna: But then this… but then this has been added to the RUSP by,

150
00:24:52.430 --> 00:25:03.020
Jennifer Banna: by the Health and Human Services. Okay, I just needed to make sure, because we've been trying to track that, what's going on nationally with the resp and the newborn stuff. So for a minute there, I was like, wait a minute…

151
00:25:03.020 --> 00:25:07.649
Shelly Eagen: Yeah, it was added in December, by the Secretary, so, yeah.

152
00:25:07.650 --> 00:25:10.290
Jennifer Banna: Thank you. That's… that's what I was getting at. Thank you.

153

00:25:19.040 --> 00:25:26.440
Mikaela Miller: Okay. Are there any other questions specific to the packet, or any of those brief pieces I reviewed for right now?

154
00:25:31.020 --> 00:25:32.580
Mikaela Miller: Okay. Yeah.

155
00:25:33.520 --> 00:25:38.620
Shelly Eagen: I saw Kathy's mouth moving. I wasn't sure if she had a question or if she was talking to somebody. Okay.

156
00:25:38.620 --> 00:25:39.220
Mikaela Miller: Okay.

157
00:25:40.150 --> 00:25:47.060
Mikaela Miller: Well, I did see Sarah and Cora, our family presenters, are here, so let me switch…

158
00:25:47.470 --> 00:25:57.739
Mikaela Miller: Presentations. Sarah, I saw your email. I'm happy to share your slides for you, or if you'd like to share those, that's okay too. Do you have a preference for right now?

159
00:25:58.000 --> 00:26:00.349
Sarah Cornell: I think it would be easier if I share them.

160
00:26:00.350 --> 00:26:01.030
Mikaela Miller: Okay.

161
00:26:05.070 --> 00:26:11.900
Mikaela Miller: I think once you go to share them, it will have you ask for permission briefly, and then Stephanie can approve that.

162
00:26:12.620 --> 00:26:15.069
Shelly Eagen: Do you want me to go ahead and start with the introduction?

163
00:26:15.310 --> 00:26:19.590
Mikaela Miller: Yeah, Shelly, if you could go ahead and introduce the two of them before they get started.

164
00:26:19.590 --> 00:26:27.150
Shelly Eagen: Great. So joining us today, thank you for joining us and welcome. We have Sarah Cornell and her daughter Cora Cornell.

165
00:26:27.150 --> 00:26:42.750
Shelly Eagen: They will share their family's experience with metachromatic leukodystrophy. Cora is a 12-year-old survivor of MLD, and together they will offer their perspectives on the diagnosis, treatment, and the impact on children and families.

166
00:26:46.310 --> 00:26:50.459
Sarah Cornell: Before we get started, can you see my screen?

167
00:26:51.750 --> 00:26:54.010
Sarah Cornell: Yes. Yeah. Okay, great.

168
00:26:57.230 --> 00:26:58.450
Sarah Cornell: Hey, Cora!

169
00:26:58.670 --> 00:27:01.569
Sarah Cornell: Do you want to kick it off? Do you want to get started, maybe?

170
00:27:01.570 --> 00:27:03.110
Cora Cornell: Okay.

171
00:27:03.650 --> 00:27:17.680
Cora Cornell: Hi, I'm Cora, thank you for letting me speak today. I'm 12 years old, in 6th grade, and I have metachromatic leukodystrophy. I'm lucky, I'm alive.

172
00:27:17.690 --> 00:27:26.130
Cora Cornell: Most families' first child with early onset MLD are diagnosed too late to

173
00:27:26.380 --> 00:27:44.569
Cora Cornell: To be treated. Only younger siblings are saved while the older child dies, so I know I am lucky to be here. And I do enjoy life. I love music, coding and game design, Roblox, YouTube, and

making plans for the future.

174
00:27:44.570 --> 00:27:52.980
Cora Cornell: But luck, you should not have to luck like this. My life has been really hard, because MLD hurt my body and brain.

175
00:27:52.980 --> 00:28:02.730
Cora Cornell: Before diagnosis to delayed, diagnosis also meant I could not get the best treatment at the best time. Instead.

176
00:28:02.820 --> 00:28:07.300
Cora Cornell: Instead, I had to go through a much harder transplant.

177
00:28:07.430 --> 00:28:19.840
Cora Cornell: I'm here today because babies born now have a chance for earlier diagnosis and better treatment. I would give anything for healthier.

178
00:28:19.840 --> 00:28:28.730
Cora Cornell: body in a more narrow childhood. I hope they get that chance. Now, my mom is going to tell you what happened when I was little.

179
00:28:29.910 --> 00:28:35.129
Sarah Cornell: Thanks, Cora, and thank you, everyone, for inviting Cora and I here to speak today.

180
00:28:35.390 --> 00:28:49.129
Sarah Cornell: As Cora noted, unlike most children who survive early-onset MLD, Cora did not have an older sibling who died first and made diagnosis and treatment possible for the next child. She is actually our only child.

181
00:28:49.540 --> 00:29:00.749
Sarah Cornell: So, one of the foremost MLD experts in the world once said about Cora, she is not a rare disease zebra. She is a unicorn. The Unicora.

182
00:29:00.890 --> 00:29:17.950
Sarah Cornell: And that is true. And so, one of the most fundamental points that I would make about our place in the MLD community is that

our journey was rare. We were lucky, even though it's a strange word, to apply for our situation, and quite privileged.

183
00:29:18.710 --> 00:29:26.620
Sarah Cornell: And as Cora argues, though, if what she has suffered is what luck and privilege looks like.

184
00:29:26.780 --> 00:29:35.080
Sarah Cornell: then that underscores how urgently MLD requires newborn screening, which is the only path to a better treatment.

185
00:29:35.460 --> 00:29:45.569
Sarah Cornell: So, there are 3 parts to our story. I think the first is the cost of a delayed diagnosis.

186
00:29:45.990 --> 00:29:56.189
Sarah Cornell: The second is the cost of losing the best treatment window. And the third is how those costs continue years later.

187
00:29:57.000 --> 00:30:12.650
Sarah Cornell: So, I'll start by saying that when, my husband and I moved from New Mexico to Massachusetts, when I was 6 months pregnant, we were just absolutely thrilled to start our family. We had put it off for professional reasons.

188
00:30:12.650 --> 00:30:21.619
Sarah Cornell: And, you know, you couldn't have found happier, expectant parents. And when Cora entered the world, everything felt so perfect.

189
00:30:21.620 --> 00:30:36.490
Sarah Cornell: She developed normally, she hit her early milestones quickly, she slept through the night, she laughed all the time, she barely cried. Other new parents hated me. She was, like, the perfect child. It was heaven.

190
00:30:36.620 --> 00:30:50.380
Sarah Cornell: But in September 2014, when she was 16 months old, everything changed. And this is the last photo I took of Cora before I became convinced that my child was dying.

191

00:30:50.590 --> 00:30:59.939
Sarah Cornell: She had a common childhood virus, with a high fever, and she recovered pretty well, but…

192
00:30:59.940 --> 00:31:13.279
Sarah Cornell: just as she was getting over it, I noticed that she began walking differently. She had sort of a wider gait, she was staggering. I didn't have the technical language for it, so I described it as a drunken sailor walk.

193
00:31:13.530 --> 00:31:26.490
Sarah Cornell: I did go to her pediatrician, and I said, oh, you know, is this, like, regression? Is she losing a motor skill? And her pediatrician told me to stop using alarmist language.

194
00:31:26.540 --> 00:31:39.709
Sarah Cornell: And I had to refuse to leave that office without, referrals, and I was referred to a neurologist in early intervention, which had, like, you know, a 6-month wait to even be evaluated.

195
00:31:39.710 --> 00:31:52.410
Sarah Cornell: We did eventually see a local neurologist, and, I saw the moment where he, like, entered the room and saw Cora trying to step up on a scale, and everything changed.

196
00:31:52.550 --> 00:32:05.369
Sarah Cornell: And so, I thought I was going to get a PT consult at this appointment. But instead, he told me that the symptom that I was watching was something called ataxia.

197
00:32:05.600 --> 00:32:19.130
Sarah Cornell: And he told me that he did not know her exact disease, but that ataxia is typically associated with conditions that were genetic, they were progressive, and they were terminal.

198
00:32:19.250 --> 00:32:33.460
Sarah Cornell: That was not news I expected. My husband wasn't even at the appointment with me. And he, you know, said basically that there was little to be done except to take her home, enjoy our time together, and to spoil her.

199
00:32:33.460 --> 00:32:40.299

Sarah Cornell: He was willing to try to support us as we looked for a diagnosis, but he didn't have a genetics department.

200
00:32:40.380 --> 00:32:51.779
Sarah Cornell: Behind him, and, you know, going sort of disease by disease, with genetic screening would be very costly and, would take a really long time.

201
00:32:51.800 --> 00:33:04.250
Sarah Cornell: So, I decided that I wanted to pursue answers elsewhere, so we turned to major medical centers, like Boston Children's Hospital, Johns Hopkins, and the University of Chicago.

202
00:33:04.420 --> 00:33:19.739
Sarah Cornell: We had hospitalizations, we had testing, we had imaging, we had consultations, but no diagnosis. She had a brain MRI, multiple ones, actually, and they were read as normal, even though they were not.

203
00:33:20.010 --> 00:33:25.779
Sarah Cornell: She had multiple nerve conduction studies. They were also read as normal, even though they were not.

204
00:33:27.330 --> 00:33:36.000
Sarah Cornell: I even requested faster, less expensive lysosomal testing. I actually guessed the right sort of panel to screen my daughter.

205
00:33:36.000 --> 00:33:47.499
Sarah Cornell: It picks up diseases like chorus, but the neurology genetics Clinic refused. They said that was for really sick children, and my child was not sick enough.

206
00:33:47.690 --> 00:34:05.369
Sarah Cornell: So, my concerns were minimalized. I was, encouraged to consider antidepressants, for me, and her formal medical notes labeled me as a, quote, hypervigilant first-time mother, end quote, and called Cora, quote, clumsy.

207
00:34:05.690 --> 00:34:17.670
Sarah Cornell: And, you know, it's interesting. They asked me to take videos of what I was seeing, and so while other parents were filming,

you know, first words and joyful moments.

208
00:34:17.870 --> 00:34:27.210
Sarah Cornell: I was filming my daughter slipping away, hoping that if I captured the right moment, someone would finally help her, would help us.

209
00:34:27.219 --> 00:34:44.269
Sarah Cornell: And that period lasted nearly a year and a half. It was 17 months. And, you know, life went on, and some of my… my photo role looks like, you know, other kids. There's Cora in the middle with her cousins, there's Cora at a carousel.

210
00:34:44.400 --> 00:34:50.810
Sarah Cornell: Cora for Halloween, and Christmas, shortly before our diagnosis.

211
00:34:50.860 --> 00:35:06.380
Sarah Cornell: And you know, when the diagnosis is MLD, 17 months is not neutral time. It is disease progression time. It costs brain, right? It brings about white matter loss. And so, during that period.

212
00:35:06.380 --> 00:35:16.929
Sarah Cornell: Cora, kept worsening. She was losing muscle tone, she had learned the alphabet, and she had forgotten it. She could recognize letters, and then she lost that skill.

213
00:35:16.940 --> 00:35:35.439
Sarah Cornell: Her speech was changing, she was drooling a bit more, she was overreaching objects, she developed an intention tremor, and all of that was really visible when she was sick or otherwise stressed. That's when I could really see those symptoms much more clearly.

214
00:35:35.440 --> 00:35:40.180
Sarah Cornell: So, in 2016, I went on clinicaltrials.gov.

215
00:35:40.180 --> 00:35:53.419
Sarah Cornell: And I found a University of Michigan research study into the genetic causes of unknown ataxias. And, they accepted CORA after my first email. I couldn't believe it. It was a dream come true.

216
00:35:53.420 --> 00:36:05.870
Sarah Cornell: And she was diagnosed really quickly, actually, because her cause was not unknown. Once they sequenced her, she had two known pathogenic ARSA mutations.

217
00:36:05.870 --> 00:36:24.789
Sarah Cornell: So, I received a call that my child had metachromatic leukodystrophy. The team actually wasn't prepared for what do you do, if there is a treatment. How do we get the news to, the parents? So, you know, once I heard metachromatic leukodystrophy.

218
00:36:24.830 --> 00:36:36.470
Sarah Cornell: There was still no coordinated pathway to confirm that diagnosis. I actually had to independently locate and contact the appropriate lab testing myself.

219
00:36:37.030 --> 00:36:44.879
Sarah Cornell: And I do want to make the point here that, you know, my focus is, of course, how this impacted Cora and my family.

220
00:36:44.900 --> 00:36:58.079
Sarah Cornell: But I do want to emphasize something very important for public health, which is my family had unusual advantages. Education, persistence, the ability to travel, access,

221
00:36:58.400 --> 00:37:10.270
Sarah Cornell: to some of the best pediatric hospitals in the country. And even with all of that, it took nearly a year and a half for Cora to receive a diagnosis.

222
00:37:10.400 --> 00:37:23.860
Sarah Cornell: And so, if that diagnosis depended on luck for us, me seeing that study, right? Imagine what that diagnostic journey is like for families with fewer resources, with less

223
00:37:23.860 --> 00:37:33.370
Sarah Cornell: flexibility or greater geographic barriers. And, you know, that is, of course, part of the reason newborn screening matters. It removes luck from the equation and privilege.

224
00:37:33.600 --> 00:37:48.209

Sarah Cornell: So after we finally confirmed Cora's diagnosis of metachronic leukodystrophy and, you know, passed on that information to these centers, no one actually suggested treatment for CORA for us.

225
00:37:48.340 --> 00:37:56.460
Sarah Cornell: It really would have been extraordinarily unusual for a child who had early onset, symptomatic

226
00:37:56.460 --> 00:38:11.949
Sarah Cornell: MLD to be eligible for treatment after a 17-month delay. And, you know, it took 2 weeks for it to dawn on me that we should at least investigate, because if she was so unusual, maybe she would be unusual in this, this manner too.

227
00:38:11.950 --> 00:38:30.709
Sarah Cornell: So, there was a short delay, and then we reached out and contacted multiple transplant centers with expertise in MLD, and that included the Italian gene therapy team, who was then conducting clinical trials for the now FDA-approved treatment.

228
00:38:30.970 --> 00:38:48.230
Sarah Cornell: And every single center said, yes, go. It is miraculous that your daughter is still eligible. We would not, you know, recommend treating her if she wasn't, and typically she wouldn't be, but we don't know how, but your child, is eligible.

229
00:38:48.870 --> 00:38:49.820
Sarah Cornell: But…

230
00:38:50.090 --> 00:39:06.890
Sarah Cornell: She wasn't on the schedule for gene therapy in Italy, and they couldn't treat her right away. They said maybe, maybe 6 to 12 months, they could get her in. And her disease was progressing in real time. We did not have 6 to 12 months.

231
00:39:07.090 --> 00:39:15.019
Sarah Cornell: So we made the absolutely wrenching decision to take Cora to Duke University for a cord blood transplant.

232
00:39:15.260 --> 00:39:25.140
Sarah Cornell: And, you know, we knew the risks, but we also knew exactly how she would die if we did nothing. So, we chose that

transplant.

233
00:39:25.360 --> 00:39:35.509
Sarah Cornell: And, you know, I know that today you will hear more science after us, but I do want to explain one simple point that's important to understand, CORA's trajectory.

234
00:39:35.550 --> 00:39:51.370
Sarah Cornell: Modern gene therapy uses a child's own corrected cells rather than donor cells, and that greatly reduces the risk of graft versus host disease, and usually requires much less prolonged immunosuppression.

235
00:39:51.420 --> 00:39:59.379
Sarah Cornell: In other words, earlier diagnosis Means not only earlier treatment, but safer treatment.

236
00:39:59.810 --> 00:40:04.709
Sarah Cornell: For Quora, Treatment was a race against time.

237
00:40:04.850 --> 00:40:17.009
Sarah Cornell: for babies identified by screening, it's a timely, planned intervention. But because CORA was diagnosed too late, we lost that window, and we lost gene therapy.

238
00:40:17.420 --> 00:40:31.900
Sarah Cornell: So, Cora underwent a cord blood transplant at Duke University, which has an amazing team. Here she is getting ready, for her transplant. We were proactively shaving her head.

239
00:40:31.900 --> 00:40:41.359
Sarah Cornell: And here she is on transplant day. She's checking out those beautiful, blood cells that she's about to get.

240
00:40:41.410 --> 00:40:53.959
Sarah Cornell: And you know, at first, things seemed really hopeful, seemed like they were going really well. She was one of those children who barely reacted to chemo. You couldn't even tell she was getting it.

241
00:40:53.960 --> 00:41:05.370

Sarah Cornell: And she engrafted quickly, she enjoyed things like in-hospital bingo, there she is out in the hallway playing basketball.

242
00:41:05.400 --> 00:41:11.010
Sarah Cornell: But our projected 6 weeks inpatient at Duke

243
00:41:11.080 --> 00:41:18.050
Sarah Cornell: Soon turned into 9 months inpatient, because Cora suffered complication after complication.

244
00:41:18.360 --> 00:41:28.679
Sarah Cornell: She had 3 serious viral reactivations while her immune system was too weak to fight them. One of those viruses reached her brain.

245
00:41:28.910 --> 00:41:35.860
Sarah Cornell: Another caused hemorrhagic cystitis so severe that she nearly bled to death multiple times.

246
00:41:36.160 --> 00:41:45.780
Sarah Cornell: She developed Unexplained lung crises, She stopped eating, and eventually they had to put in a feeding tube.

247
00:41:45.970 --> 00:41:55.800
Sarah Cornell: And the medical team had to balance fighting infection while suppressing what they feared was graft versus host disease.

248
00:41:56.110 --> 00:42:02.230
Sarah Cornell: So, she received massive doses of steroids, and they helped save her life.

249
00:42:02.420 --> 00:42:08.380
Sarah Cornell: But they also damaged her bones. One day, her pelvis fractured while she was napping.

250
00:42:08.580 --> 00:42:17.399
Sarah Cornell: She suffered multiple spinal fractures, the first while she was reaching for a doll. And she spent much of her childhood in

251
00:42:17.520 --> 00:42:24.180

Sarah Cornell: Isolated in an 8x8 small room with everybody gowned up, with, gloves and masks on.

252
00:42:24.490 --> 00:42:44.259
Sarah Cornell: Eventually, we made the decision to transfer her back to Boston, to go to Boston Children's, and it wasn't actually because we thought Cora was improving, but rather because, if the worst happened, we wanted to be closer to our friends and family, our support system.

253
00:42:44.470 --> 00:42:51.629
Sarah Cornell: So here we are, at Boston Children's in time for Christmas in 2016.

254
00:42:51.830 --> 00:43:10.039
Sarah Cornell: But instead, something extraordinary happened. Boston Children's transplant team saved her. You know, she spent nearly 5 more months inpatient at Boston Children's. All of her old problems persisted, and we had some new ones.

255
00:43:10.040 --> 00:43:23.309
Sarah Cornell: Like, hemolytic anemia and, lung problems, sort of got worse, and she had blood clots in her brain, so there are new forms of monitoring going on.

256
00:43:23.310 --> 00:43:32.389
Sarah Cornell: And, you know, her team was really honest with us. They said they fully didn't… they did not fully understand the root causes of what was happening to Cora.

257
00:43:32.390 --> 00:43:49.039
Sarah Cornell: But they kept her alive under their care, and slowly, she recovered. And eventually, we were discharged from the hospital after more than a year inpatient, well more than a year, and it was amazing.

258
00:43:49.040 --> 00:43:57.680
Sarah Cornell: You know, this is sort of what our outpatient life looked like. This is her, afternoon tray of meds.

259
00:43:57.680 --> 00:44:11.779
Sarah Cornell: And I know that because it fit on one tray. But, you

know, for us, this was a miracle, and I think this is the part of the story that most people think is the ending, but it wasn't.

260
00:44:12.020 --> 00:44:29.160
Sarah Cornell: You know, I do want to fully acknowledge that after years of, now, hospitalization and isolation, Cora was able to re-enter the world, and she did so with joy. You know, we sort of were able to go outside.

261
00:44:29.160 --> 00:44:38.089
Sarah Cornell: She was reunited with her family, she got to see other children, we went to the beach, we went to playgrounds.

262
00:44:38.090 --> 00:44:48.349
Sarah Cornell: She learned to ride a bike, she started kindergarten, it was, just amazing. She went trick-or-treating for Halloween.

263
00:44:48.350 --> 00:45:05.349
Sarah Cornell: And eventually, she walked a 5K to raise awareness and funds for MLD. You know, I was there with, like, a stroller, being like, Cora, get in the stroller, and she goes, no, I am walking across that finish line, and she walked the whole thing.

264
00:45:05.450 --> 00:45:13.330
Sarah Cornell: And, you know, we thought that the hardest part was behind us, that our lives, you know, were going to…

265
00:45:13.630 --> 00:45:26.540
Sarah Cornell: move forward along an expected path now. But, the consequences of the delayed diagnosis and the harder treatment path actually continued past 2019.

266
00:45:26.850 --> 00:45:38.459
Sarah Cornell: Cora was, in late 2019, diagnosed with a permanent immunodeficiency, that they believe stems from her transplant.

267
00:45:38.460 --> 00:45:54.529
Sarah Cornell: She cannot make antibodies normally, so her immune protection comes from weekly, infusions of immunoglobulins. But of course, this is 2019, and what happens is 2020. Then comes COVID.

268

00:45:54.630 --> 00:46:04.369
Sarah Cornell: And Cora can't mount a normal immune response, and replacement antibodies always lag circulating strains.

269
00:46:04.370 --> 00:46:18.960
Sarah Cornell: So she is medically vulnerable to COVID even now. She is not eligible for COVID protections, like monoclonal antibodies that adult immunocompromised people have access to.

270
00:46:19.140 --> 00:46:34.819
Sarah Cornell: And 2020 brought other problems for us as well. Healthcare systems, of course, were strained. Many of Cora's physicians left Boston Children's, Dana-Farber, Mass General, and she needed follow-up care, and it did not happen in time.

271
00:46:34.820 --> 00:46:51.260
Sarah Cornell: And I repeatedly sought, follow-up specialty care for her, even though there wasn't a crisis, but, like, I knew that she needed it. So that included things like endocrine care and, bone care. And I kept seeking these appointments

272
00:46:51.720 --> 00:47:03.679
Sarah Cornell: And, you know, we weren't able to get in, and those delays had enormous consequences for my family. Post-transplant osteoporosis.

273
00:47:03.780 --> 00:47:16.120
Sarah Cornell: and primary ovarian insufficiency, which worsens osteoporosis, are known risks, and they can be treated proactively, but that's not what happened for Cora.

274
00:47:16.200 --> 00:47:23.940
Sarah Cornell: In 2024, Cora's life dramatically changed. In the morning, she went to an academic summer camp.

275
00:47:24.250 --> 00:47:41.909
Sarah Cornell: She had friends over to swim at our house in the afternoon, and then she went horseback riding in the evening. So she was really exhausted when she got out of bed that night for a drink of water, and she fell. It was so unusual for her. She almost never fell. But she did, and her hip broke.

276

00:47:42.070 --> 00:47:53.220
Sarah Cornell: And then began… then began a cascade. She had to be off her feet for 6 months while that fracture healed. That worsened her bone density further.

277
00:47:53.290 --> 00:48:07.419
Sarah Cornell: That led to another hip fracture, which led to her bone density worsening. She sustained a vertebral compression fracture when I hit a pothole while I was driving her to a doctor's appointment next.

278
00:48:07.630 --> 00:48:15.879
Sarah Cornell: By the time she was able to try to stand again, she developed stress fractures in both of her heels simply from standing up.

279
00:48:15.970 --> 00:48:29.019
Sarah Cornell: And all of that time in a wheelchair and off of her feet led to scoliosis, which became quite severe. And so this summer, Cora is facing a massive surgery.

280
00:48:29.460 --> 00:48:35.959
Sarah Cornell: And, you know, last year alone, Cora had 144 medical appointments.

281
00:48:36.190 --> 00:48:43.689
Sarah Cornell: So, this is what delayed diagnosis can still cost many years later when you think the worst is behind you. It costs…

282
00:48:44.010 --> 00:48:53.399
Sarah Cornell: your childhood. It costs school time. It costs mobility. It, you know, takes away from ordinary family life.

283
00:48:53.510 --> 00:49:04.500
Sarah Cornell: And, you know, delayed diagnosis is not just costly on the personal level for families. I would be remiss if I didn't note all that it cost the healthcare system.

284
00:49:04.660 --> 00:49:23.909
Sarah Cornell: schools are employers. It's amazing my husband and I are still employed. You know, all of this meant more emergency care, more specialty visits, more rehabilitation, more surgeries, more

missed work, more educational disruption, and more, education support.

285
00:49:23.950 --> 00:49:25.400
Sarah Cornell: So, you know.

286
00:49:25.640 --> 00:49:36.459
Sarah Cornell: Earlier diagnosis can, you know, save brain, can get you the best treatment, but it can also prevent avoidable, downstream costs.

287
00:49:36.980 --> 00:49:39.630
Sarah Cornell: Cora, do you want to jump in, babe?

288
00:49:45.470 --> 00:49:54.219
Cora Cornell: My bones keep breaking because I've had to be in a wheelchair for almost 2 years. My immune system doesn't work.

289
00:49:54.430 --> 00:49:57.479
Cora Cornell: It means I'm allergic to everything.

290
00:49:57.630 --> 00:50:09.570
Cora Cornell: Eggs, tree nuts, bananas, avocados, celi, watermelon, and much more, while my body is so busy attacking food.

291
00:50:09.570 --> 00:50:18.179
Cora Cornell: It doesn't fight off viruses or bacteria. I have to wear a mask whenever I'm in public, and it's so hard.

292
00:50:32.950 --> 00:50:33.630
Sarah Cornell: Core.

293
00:50:36.260 --> 00:50:37.190
Cora Cornell: That's all we have.

294
00:50:40.750 --> 00:50:49.389
Sarah Cornell: Okay, well, cora told me, also, that,

295
00:50:49.460 --> 00:51:04.269
Sarah Cornell: Between the mask and the wheelchair, that some people

treat her as though she's invisible, and that activities at school are also often very inaccessible for her.

296
00:51:04.350 --> 00:51:10.739
Sarah Cornell: And, you know, school is really difficult. Certain subjects, like math.

297
00:51:10.760 --> 00:51:21.799
Sarah Cornell: are very difficult, because of the impact of MLD and the transplant, the chemo, but also because she has to miss so much school.

298
00:51:21.800 --> 00:51:35.700
Sarah Cornell: And Cora does physical therapy, every single day for hours, hours, because she really wants strong bones and to be able to walk again.

299
00:51:35.720 --> 00:51:38.960
Sarah Cornell: Core wears leg braces.

300
00:51:39.170 --> 00:51:48.300
Sarah Cornell: And she wears a back brace 22 hours a day. She hates it. Hates it. She never complains about anything but that back brace.

301
00:51:48.450 --> 00:52:06.100
Sarah Cornell: But she did it because she didn't want to have spinal surgery, but we just found out last week that she has to have spinal fusion this summer anyway. And, you know, Cora has expressed just how frustrating and difficult all of that is.

302
00:52:06.260 --> 00:52:18.439
Sarah Cornell: But, you know, she wanted to stress for you that she still really enjoys life, she just wishes she could spend more of it being a kid.

303
00:52:18.440 --> 00:52:29.330
Sarah Cornell: She is, you know, in some ways, much like other children. Cora loves… oh, there she is, standing with her broken heels and in her back brace.

304
00:52:29.460 --> 00:52:41.940

Sarah Cornell: Cora loves horseback riding so much, and she loves all animals, so you can see her here with her best friend, feeding some sloths, hanging out with a snake.

305
00:52:42.050 --> 00:52:44.700
Sarah Cornell: And a crawfish…

306
00:52:44.780 --> 00:53:02.779
Sarah Cornell: Cora likes… likes feeding swans, she has discovered a love of fishing, she loves to read, she especially enjoys graphic novels, and she just absolutely loves to hang out with her friends.

307
00:53:02.890 --> 00:53:13.960
Sarah Cornell: But Cora really wants the next children born with MLD to spend more time playing than at the doctor's office, like her.

308
00:53:14.580 --> 00:53:22.840
Sarah Cornell: So… Quora's 10th Rebirthday, her transplant anniversary, was actually last week.

309
00:53:23.120 --> 00:53:35.350
Sarah Cornell: And I am profoundly grateful for this past decade with her. I cannot tell you how blessed, lucky, privileged I feel to have been her mother, and to have had this time with her.

310
00:53:35.640 --> 00:53:54.739
Sarah Cornell: But anniversaries bring thoughts of lasts with them as well. The last time she walked? Independently. The last time we went a week without multiple appointments, hours and hours and hours at doctors' offices. The last season or holiday before fractures changed everything for us.

311
00:53:54.820 --> 00:53:58.109
Sarah Cornell: And you know, then there are the what-ifs, which are almost worse.

312
00:53:58.450 --> 00:54:02.089
Sarah Cornell: What if Cora had been diagnosed at birth?

313
00:54:02.240 --> 00:54:16.840
Sarah Cornell: What if she had received gene therapy before symptoms?

What would her body be like today? Her lung function, her bones? But more importantly, her experiences? What would her childhood have been?

314
00:54:17.140 --> 00:54:19.430
Sarah Cornell: We cannot change that for Quora.

315
00:54:20.390 --> 00:54:23.149
Sarah Cornell: But you all can change it for the next child.

316
00:54:23.570 --> 00:54:36.710
Sarah Cornell: Public health, to my mind, exists, so families don't need extraordinary luck, privilege, relentless self-advocacy, and access to elite institutions to simply give their child a chance.

317
00:54:36.940 --> 00:54:46.460
Sarah Cornell: Newborn screening, creates something rare disease families almost never have time. Time for diagnosis, time for treatment.

318
00:54:46.640 --> 00:54:55.050
Sarah Cornell: Time to save their child's childhood. So, today, Cora and I want to ask you to focus on firsts.

319
00:54:55.240 --> 00:55:06.979
Sarah Cornell: The first Montana baby with MLD to be identified before they show symptoms. The first family spared a diagnostic odyssey like ours. The first baby.

320
00:55:06.980 --> 00:55:18.539
Sarah Cornell: who gets the safest treatment path at the exact right time. And overall, the first future that is protected because you acted.

321
00:55:19.040 --> 00:55:20.000
Sarah Cornell: Cora?

322
00:55:21.030 --> 00:55:22.339
Sarah Cornell: Hey, Cora Babes!

323
00:55:25.080 --> 00:55:27.689

Sarah Cornell: Do you want to thank them for listening to you?

324
00:55:29.480 --> 00:55:30.660
Sarah Cornell: your story?

325
00:55:31.510 --> 00:55:33.729
Cora Cornell: Thank you.

326
00:55:34.480 --> 00:55:36.519
Sarah Cornell: Is there anything else you want to say, babe?

327
00:55:36.800 --> 00:55:37.750
Cora Cornell: No.

328
00:55:37.750 --> 00:55:39.360
Sarah Cornell: Okay, thank you, Cora.

329
00:55:42.850 --> 00:55:44.559
Sarah Cornell: Corey, do you want to log off?

330
00:55:47.170 --> 00:55:48.219
Sarah Cornell: Bye, baby!

331
00:55:49.260 --> 00:55:50.250
Shelly Eagen: Thank you.

332
00:55:50.840 --> 00:55:51.480
Sarah Cornell: Thanks.

333
00:55:51.680 --> 00:55:53.030
Sarah Cornell: Thank you, everyone.

334
00:56:00.040 --> 00:56:09.720
Mikaela Miller: Thank you, Sarah, so much for taking the time to be here, and please make sure to share with Cora that we are so grateful for her to share her story with us as well.

335
00:56:09.960 --> 00:56:10.560

Sarah Cornell: Thank you.

336
00:56:12.950 --> 00:56:17.860
Mikaela Miller: I am going to, go ahead and share my screen again.

337
00:56:21.740 --> 00:56:31.020
Mikaela Miller: While I'm doing that, Shelly, would you like to go ahead and introduce our SME? I believe we have Dr. Von Kaski here.

338
00:56:31.020 --> 00:56:45.019
Shelly Eagen: Yeah, so Dr. Josh Gronkowski is a professor of pediatrics at the University of Utah School of Medicine and Primary Children's Hospital, Chief of the Division of Pediatric Neurology, and Director of the Center for Personalized Medicine.

339
00:56:45.020 --> 00:56:55.069
Shelly Eagen: After graduating from Harvard College, she spent a year on a Fulbright Fellowship in Vienna, Austria, followed by MD and PhD training at UCSD.

340
00:56:55.320 --> 00:57:05.979
Shelly Eagen: Dr. Bronkowski is a physician-scientist with interest in clinical and bench research, including the pathophysiology, outcomes, and treatments for leukodystrophies, including MLD.

341
00:57:05.980 --> 00:57:15.709
Shelly Eagen: Since 2006, Dr. Bonkowski has personally mentored more than 90 trainees, more than half of whom are women or underrepresented minority trainees.

342
00:57:15.710 --> 00:57:34.739
Shelly Eagen: Together with his wife, a pediatric infectious disease physician, he juggles his personal and professional responsibilities. In his quote-unquote spare time, he enjoys camping with his daughter, building a quasi-functional radio telescope with his sons, and trail running. Thank you, Dr. Bonkowski, for joining us.

343
00:57:36.860 --> 00:57:39.869
Josh Bonkowsky: Thanks, everybody, for the invitation.

344
00:57:40.210 --> 00:57:52.520

Josh Bonkowsky: I really appreciated the story from the Cornell family, that's really a hard act to follow. I have some slides to present, is it okay if I try and share them from my computer? Is that okay?

345
00:57:53.140 --> 00:57:54.930
Mikaela Miller: Yeah, let me,

346
00:57:56.120 --> 00:58:03.590
Mikaela Miller: back out here. If you go ahead on your screen, it should ask for permission to Stephanie, and she'll approve that. There we go.

347
00:58:07.230 --> 00:58:09.020
Josh Bonkowsky: Does that seem okay for folks?

348
00:58:09.520 --> 00:58:11.310
Shelly Eagen: Yes, looks great, thank you.

349
00:58:11.660 --> 00:58:29.009
Josh Bonkowsky: Great, so I'll talk briefly about, I mean, you've already heard, from the Cornell family just about their journey and the difficulties they faced. I'll talk, at a more kind of medical scientific level about MLD as a disease, about the treatments,

350
00:58:29.010 --> 00:58:33.200
Josh Bonkowsky: And a little bit about the newborn screening and how it interacts with the medical system.

351
00:58:33.680 --> 00:58:37.829
Josh Bonkowsky: Let's see if I can make this work…

352
00:58:48.480 --> 00:58:52.149
Josh Bonkowsky: So, MLD is a…

353
00:58:52.290 --> 00:59:04.880
Josh Bonkowsky: type of condition called a leukodystrophy. So leukodystrophy is just the fancy term for any disease that affects the white matter of the brain. In MLD, in this case, we're talking about metachromatic leukodystrophy.

354
00:59:05.010 --> 00:59:16.080
Josh Bonkowsky: There are hundreds of different kinds of leukodystrophies, but the reason we are here today is because MLG matters, because there's a treatment available, and that treatment is time-sensitive.

355
00:59:17.460 --> 00:59:30.430
Josh Bonkowsky: So the white matter of the brain is composed of different types of cells, and it's important because it basically acts as the insulation for the nerve signals traveling back and forth, and so if you were to

356
00:59:30.430 --> 00:59:42.359
Josh Bonkowsky: pick up a brain and hold it, and you're looking at it, the white matter looks white, and the gray matter, which are the nerve cells, looks gray. So that's… that's what white and gray matter are when you're talking about the brain.

357
00:59:43.760 --> 01:00:03.049
Josh Bonkowsky: So MLD, or metacromatic leukodystrophy, is caused by, gene… a gene that gets affected, or a gene that's mutated, called ARSA, or aryosulfatase. It's autosomal recessive, the condition, which means that both copies of the gene have to be affected, so usually,

358
01:00:03.190 --> 01:00:13.660
Josh Bonkowsky: in most situations, one parent carries one copy that's affected, but the other copy is fine, so that parent is fine. Same thing, the other parent also has one affected copy, but

359
01:00:13.660 --> 01:00:26.820
Josh Bonkowsky: They have… and so… but they have an unaffected copy, so they're fine, but when they have a child, they have a 1 in 4 chance of both passing on, the mutated copy, leaving their child affected by the condition.

360
01:00:27.070 --> 01:00:32.820
Josh Bonkowsky: The MLD occurs about… in about 1 in 40,000 live births.

361
01:00:33.170 --> 01:00:49.719
Josh Bonkowsky: the way the gene acts, the function of the gene is that it works in something called the lysosome, and there's a picture

of a lysosome on the right there inside the cell. It's a… it's, this little purple thing right here. The lysosome kind of acts as a,

362
01:00:50.050 --> 01:01:02.020
Josh Bonkowsky: as a part of the cell that kind of is involved in breakdown and metabolism of different parts of the cell, and so if it stops working, everything kind of backs up. So it'd be like if your kitchen sink

363
01:01:02.050 --> 01:01:11.729
Josh Bonkowsky: And you had to pass everything through the kitchen sink to get out of the house. If it stopped working, the whole cell starts to get affected because it's no longer taking care of.

364
01:01:11.770 --> 01:01:14.839
Josh Bonkowsky: Of getting rid of toxins or other bad things from the cell.

365
01:01:15.200 --> 01:01:29.309
Josh Bonkowsky: And then the, function of the gene ARSA is to make a protein called aryl sulfatase, and so if it's not working, you're left with something called aryl sulfatase deficiency. So again, these are just all the fancy terms that go along with, with MLD.

366
01:01:31.220 --> 01:01:36.919
Josh Bonkowsky: So, we've already heard, like, a great example of how someone with MLD can be affected.

367
01:01:37.180 --> 01:01:54.309
Josh Bonkowsky: I thought this… I have briefly presented a patient we… a family we took care of, so a 16-year-old girl came in because she's having a little bit of school difficulty, and her walking was getting worse, and in kind of retrospect, the family realized that these symptoms had kind of been building up over the previous year.

368
01:01:54.350 --> 01:02:08.860
Josh Bonkowsky: She'd been previously totally healthy, there was no family history of anything at all, so kind of out of the blue. And then, she ended up getting an MRI, and then based on the MRI, as I'll talk about in a minute, she had testing for MLD, which confirmed that she had an MLD.

369

01:02:09.220 --> 01:02:18.560
Josh Bonkowsky: We tested other people in the family then at that point, and also found that her younger siblings, also had MLD. And so, the first child,

370
01:02:18.650 --> 01:02:30.110
Josh Bonkowsky: did end up going through the bone marrow transplant process, and so she was treated. However, by the time we treated her, she was already far enough along where

371
01:02:30.220 --> 01:02:36.169
Josh Bonkowsky: The treatment wasn't really effective until she got worse and worse, and eventually she passed away about a year after the transplant.

372
01:02:36.610 --> 01:02:41.309
Josh Bonkowsky: Her two younger siblings also had the transplant, the bone marrow transplant.

373
01:02:41.470 --> 01:02:57.189
Josh Bonkowsky: The slightly… the next, younger sibling already had been a little bit affected when she… when we first diagnosed her, and so she's still alive, but she's been quite affected, so the transplant's been effective at saving her life, but unfortunately she's continued to have symptoms.

374
01:02:57.360 --> 01:03:11.949
Josh Bonkowsky: And then the third youngest sibling was asymptomatic at the time we diagnosed them, and now as an adult, working and living independently. I think they're working as a, as a carpenter, if I remember correctly, and so they're doing great.

375
01:03:12.150 --> 01:03:22.980
Josh Bonkowsky: And so, really, making the diagnosis matters, both for just, like, being able to survive it all, and it also matters in terms of timing for, for how effective they're going to be.

376
01:03:24.450 --> 01:03:37.130
Josh Bonkowsky: So, MLD is kind of a tricky condition because, when, when people first are diagnosed, they are asymptomatic, so the kid looks totally fine, or the infant looks totally fine.

377

01:03:37.210 --> 01:03:47.000
Josh Bonkowsky: But the symptoms, kind of creep up. They're often kind of non-specific. It's hard to tell what's going on, and so oftentimes that means that it takes a while to figure out a diagnosis.

378
01:03:48.130 --> 01:04:02.799
Josh Bonkowsky: So, the features of MLD are pretty well understood, and so the MRI, shown here at the top, is very characteristic when someone starts to have disease symptoms. So, this is the MRI picture.

379
01:04:02.800 --> 01:04:10.209
Josh Bonkowsky: And usually both sides of the brain are involved, so it's symmetric, and it has kind of this back part of the brain being affected first.

380
01:04:12.270 --> 01:04:28.929
Josh Bonkowsky: different, depending on when MLD starts in a person, so the age of onset means that different ages of onset have different symptoms, so the symptoms can include a neuropathy, just like a diabetic neuropathy, but a neuropathy caused by MLD.

381
01:04:29.100 --> 01:04:40.219
Josh Bonkowsky: Often they can have gallbladder disease, so that's something that people sometimes first have gallbladder disease before they get diagnosed. It can also cause developmental delay and seizures, and so this is, like, a little,

382
01:04:40.590 --> 01:04:49.519
Josh Bonkowsky: Picture of the different kinds of symptoms that can affect a person, but again, it's very variable depending on when the person has the disease onset start.

383
01:04:51.080 --> 01:05:10.319
Josh Bonkowsky: So, MLD diagnosis, it's very clearly defined, like, how you confirm or make the diagnosis, and so, a key step is genetic testing. Really, based on, you know, living in 2026, now I eventually get a genome sequencing, but there's other options as well, such as an exome or a panel test.

384
01:05:10.650 --> 01:05:13.679
Josh Bonkowsky: And we understand really well, based on what

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01:05:14.000 --> 01:05:26.689
Josh Bonkowsky: type of mutation is in the ARCID gene, what the risk is for the person. There's also a really good community of leukodystrophy and MLD experts who communicate frequently if they find, like, a new

386
01:05:26.850 --> 01:05:32.209
Josh Bonkowsky: mutation that has been seen before to try and figure out, like, what is the risk? So one step is genetic testing.

387
01:05:32.330 --> 01:05:45.769
Josh Bonkowsky: Another test is to send the… is to send testing for LLE, or leukocyte lysosomal enzyme testing, and that helps figure out the level ARSA, because that's… that's also kind of a key step for knowing

388
01:05:45.940 --> 01:05:49.220
Josh Bonkowsky: How much time do we have before the disease really kicks in?

389
01:05:49.550 --> 01:06:08.020
Josh Bonkowsky: And then also, as part of the confirmatory testing, we send a urine test for urine sulfatides. So, the key test is the genetic testing, but it's kind of the full workup. We also do these other two steps just to kind of put the whole puzzle together to understand, timing, and kind of speed of treatment.

390
01:06:09.110 --> 01:06:20.790
Josh Bonkowsky: With MLD care, it's really important to see somebody who, understands MLD and leukodystrophies. They're kind of scattered around in a few different places, and the reason is that there's

391
01:06:20.830 --> 01:06:36.210
Josh Bonkowsky: subtleties, kind of, in care, for what should be done. And then, for a family or patient diagnosed with family, they need ongoing follow-up, of course, with, like, their pediatrician or family care doctor, just for kind of routine childhood stuff.

392
01:06:36.210 --> 01:06:53.269
Josh Bonkowsky: but also usually with either the leukodystrophy specialist, or locally, if there's a pediatric neurologist or geneticist available to kind of help manage care. And then the key thing is, of course, to do treatment, and the treatment is really

time-sensitive, and so that's why it ends up being that newborn screening is so critical.

393
01:06:53.990 --> 01:07:03.459
Josh Bonkowsky: So, diagnosis ends up being urgent. There's a narrow window of time between symptom onset, and then after which treatment's not effective. So, basically.

394
01:07:03.610 --> 01:07:20.420
Josh Bonkowsky: kind of just depending on the age of the child, you have about 2 to 6 months from the time symptoms start to the time that the treatment becomes too late to be effective. If you do a bone marrow transplant after someone's too affected, as I kind of illustrated in that example, the treatment, the bone marrow transplant is not effective.

395
01:07:20.460 --> 01:07:24.430
Josh Bonkowsky: The person in the family just experiences worsening disease and they pass away.

396
01:07:24.730 --> 01:07:32.679
Josh Bonkowsky: If you don't treat, then you have progressive disability and death, and so treatments, you have to do the treatment, and then the treatment is essentially curative.

397
01:07:34.900 --> 01:07:45.269
Josh Bonkowsky: there's different kinds of MLD, and this is a little bit confusing, based on the age of onset, and that age of onset is kind of defined by the genetic

398
01:07:45.380 --> 01:07:53.670
Josh Bonkowsky: variant in the ARSA gene, and so the different kinds are called LI, or late infantile.

399
01:07:53.800 --> 01:08:08.840
Josh Bonkowsky: EJ, or early juvenile, late juvenile, or adult onset. And so really, particularly with newborn screening, we're particularly trying to pay attention to the late infantile and early juvenile types, but with that information, we would be also picking up

400
01:08:09.350 --> 01:08:13.910
Josh Bonkowsky: People who won't have disease till later on, such as

late juvenile or adult onset.

401
01:08:14.300 --> 01:08:20.480
Josh Bonkowsky: With late infantile or early juvenile, obviously the time window is very, very tight, and so it becomes super urgent.

402
01:08:20.920 --> 01:08:30.000
Josh Bonkowsky: With late juvenile, there's a little bit longer window, so it's still urgent, but not like an emergency as it is for late infantile or early juvenile.

403
01:08:31.460 --> 01:08:32.149
Josh Bonkowsky: Ugh.

404
01:08:34.950 --> 01:08:49.749
Josh Bonkowsky: So, late infantile is the most common type, and so that's why newborn screening becomes so critical. The types and ages are a little bit of a generalization. They help us kind of define categories, but then you still need to talk to an expert to really, like, figure out which type of,

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01:08:49.810 --> 01:09:00.369
Josh Bonkowsky: MLD that they have, and the genotype then kind of gets linked to how much of that enzyme activity they have, and that's why the leukocyte lysosome enzyme testing is necessary.

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01:09:00.529 --> 01:09:17.430
Josh Bonkowsky: And then, at this point now, we have a… we… The specialists kind of have a lot of information, understanding, like, what is the risk for somebody based on what their gene is, what their genotype, what kind of mutation they have, and also based on their enzyme activity.

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01:09:17.580 --> 01:09:23.619
Josh Bonkowsky: And then you can see here, there's kind of an overview of the different clinical subtypes and the kind of symptoms that they have, and so…

408
01:09:23.760 --> 01:09:36.400
Josh Bonkowsky: Late infantile, often the symptoms are pretty nonspecific, like delayed development, and then, like, someone, an adult, for example, might have more of a neuropsychiatric symptoms.

409
01:09:38.120 --> 01:09:56.229
Josh Bonkowsky: So, to summarize treatment, there's been, several, very comprehensive studies just published, a little over a year ago, about how to, diagnose someone, how to do monitoring, and then how to do treatment. So that's, those two publications right there.

410
01:09:56.490 --> 01:09:58.330
Josh Bonkowsky: And then to summarize treatment.

411
01:09:58.490 --> 01:10:12.800
Josh Bonkowsky: If it's late infant… if it's someone with late infantile or early juvenile subtype, so basically anyone under a few years of age, then they should get this treatment called RSSL, which I'll talk about in a few minutes.

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01:10:12.900 --> 01:10:19.340
Josh Bonkowsky: Whereas if it's late… someone who's older, lead juvenile, or adult onset, then a standard bone marrow transplant.

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01:10:20.090 --> 01:10:26.099
Josh Bonkowsky: Again, the timing is really critical, because for the late infantile, for the infants.

414
01:10:26.210 --> 01:10:33.889
Josh Bonkowsky: the RCSL or any treatment, only works if they're pre-symptomatic. Once they become symptomatic, the treatment becomes ineffective.

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01:10:34.070 --> 01:10:37.030
Josh Bonkowsky: With early juvenile, the wind is a little bit longer.

416
01:10:37.190 --> 01:10:42.740
Josh Bonkowsky: Ideally pre-symptomatic, but you have a little bit longer if they… if you diagnose someone after they're already symptomatic.

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01:10:43.950 --> 01:10:51.480
Josh Bonkowsky: So one treatment is a bone marrow transplant, or which also… which is also sometimes called HSCT, hematopoietic stem cell transplant.

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01:10:51.630 --> 01:11:01.099
Josh Bonkowsky: Again, it's only effective if the disease is cut early enough, and it's, at this point, it's indicated for the late juvenile and adult forms.

419
01:11:01.280 --> 01:11:19.009
Josh Bonkowsky: However, it's a non… bone marrow transplant, it's a non-trivial thing, as you kind of heard. Like, if someone just walked in today, like, if I asked for a bone marrow transplant today, my overall mortality in about a year is about 15%, so it's a big deal to go through a bone marrow transplant.

420
01:11:19.240 --> 01:11:25.079
Josh Bonkowsky: Of course, if you don't go through the bone marrow transplant, then mortality is 100%, so that's why the risk is worthwhile.

421
01:11:26.930 --> 01:11:39.160
Josh Bonkowsky: So, just some caveats about bone marrow transplant. It's only effective if you catch the disease early, that's why newborn screening is so critical, and there's still the risk that there can be some progression of motor symptoms.

422
01:11:39.400 --> 01:11:48.680
Josh Bonkowsky: One issue that we've run into is that there's sometimes not donors available for minority patients, and then the gene therapy still becomes a critical option.

423
01:11:50.440 --> 01:11:54.150
Josh Bonkowsky: Second treatment is, what you've heard about called Arsisel.

424
01:11:54.210 --> 01:12:06.710
Josh Bonkowsky: also call it… the commercial name is Lenmeldi, or, the kind of the generic name is the titular darsogene AutoTem cell, so a little bit of a mouthful there. So, it is a gene therapy.

425
01:12:06.710 --> 01:12:19.909
Josh Bonkowsky: But it's also a form of bone marrow transplant, so it's a little bit confusing. So the way it works is that instead of having a donor, as you have in a standard bone marrow transplant, use

your own, or the patient's own cells to do the transplant.

426
01:12:20.110 --> 01:12:32.009
Josh Bonkowsky: But it's a gene therapy because you use the patient's own cells and infect them, basically, with a virus that supplies the missing gene. And then you take those cells and put them back into the patient.

427
01:12:32.300 --> 01:12:41.899
Josh Bonkowsky: Person still has to go through chemotherapy, they still have to go through the bone marrow transplant process, but it seems to work overall much better than a standard bone marrow transplant process.

428
01:12:42.060 --> 01:12:55.370
Josh Bonkowsky: It is FDA approved. It's, currently available at specialized treatment centers. So, for example, it's available, like, in Minnesota, in Los Angeles, in Salt Lake City, in Boston.

429
01:12:55.370 --> 01:13:03.699
Josh Bonkowsky: I think probably in Philadelphia, so there's kind of some centers scattered across the country that offer this treatment for MLD.

430
01:13:04.630 --> 01:13:14.200
Josh Bonkowsky: And it's indicated for the late infantile and early juvenile subtypes, the, the, gene therapy RCL version.

431
01:13:14.600 --> 01:13:26.130
Josh Bonkowsky: So this is not, it's not for free, unfortunately, so if you just get a bone marrow transplant, it costs about a million dollars, roughly. The RSA cell costs $4.25 million, so it's quite expensive.

432
01:13:26.580 --> 01:13:34.109
Josh Bonkowsky: There's a very comprehensive review by this group called ICER, the Institute for Clinical and Economic Review.

433
01:13:34.360 --> 01:13:47.209
Josh Bonkowsky: Who determined the health benefit, just at a pure, kind of, financial cost basis to be almost $4 million. And so you can see that the drug company has very cleverly priced the…

434
01:13:47.400 --> 01:13:51.969
Josh Bonkowsky: The, price just slightly over the, kind of health benefit cost.

435
01:13:53.530 --> 01:13:59.060
Josh Bonkowsky: So this is a little bit complicated, and it's probably more into the weeds than we really need to go into.

436
01:13:59.060 --> 01:14:20.200
Josh Bonkowsky: But it shows the benefits both of transplant on the left, so these slides show both survival of transplanted versus non-transplanted, people with MLD, but also, kind of more importantly, if you're transplanted, it really preserves cognitive function, whereas if you're not transplanted, then you, your cognitive function just declines with age.

437
01:14:20.470 --> 01:14:23.240
Josh Bonkowsky: On the right are,

438
01:14:23.810 --> 01:14:29.959
Josh Bonkowsky: late infantile and early juvenile MLD kids who went through transplant, so first of all, survival is very good.

439
01:14:29.990 --> 01:14:47.529
Josh Bonkowsky: But then really critically, on the right-hand side, you can see that the, cognitive function is just, really spectacular. So it's, so it just shows both survival being very helpful for the transplant and RSSL, and also the outcomes being very good.

440
01:14:49.600 --> 01:15:06.609
Josh Bonkowsky: So, the newborn screening process usually, depending, you know, different labs have different ways they do it, but typically there's kind of a first-tier screening that uses, like, a mass spec assay. Usually, depending on, again, on the individual state lab, it can be added to the existing newborn screening platform.

441
01:15:06.610 --> 01:15:13.389
Josh Bonkowsky: It's looking at the sulfatides, which kind of build up in MLD, and it can be done in the dried blood spot.

442

01:15:13.700 --> 01:15:29.600
Josh Bonkowsky: And then a lot of labs use a second-tier assay where they measure the RSA activity before, and sometimes that's either, like, in parallel or, instead of, kind of timing to send to refer them to a specialist.

443
01:15:31.530 --> 01:15:46.119
Josh Bonkowsky: Once a specialist gets contacted, what would they do? So they would see the infant in the family and clinic, they would do a neurologic and general exam, they would also be arranging a brain MRI, which is usually… an infant would be normal.

444
01:15:46.120 --> 01:15:57.289
Josh Bonkowsky: They'd also do something called an EMG or slash NCB. This is nerve conduction velocity testing. The reason is that MLD affects the peripheral nerves as well, so it's kind of part of the general workup.

445
01:15:58.190 --> 01:16:13.679
Josh Bonkowsky: the person would send the diagnostic confirmatory testing, which would be, for example, whole genome sequencing, the urine sulfatide test, and the leukocyte lysosomal enzyme testing. That's all necessary to kind of confirm the genotype findings on the genome sequencing, and to kind of make sure we understand

446
01:16:13.680 --> 01:16:18.949
Josh Bonkowsky: What age of onset the MLD would be… would have.

447
01:16:19.020 --> 01:16:31.709
Josh Bonkowsky: And then also, it's usually a good idea at that point to talk to the bone marrow transplant team so they can start to prep in case we're going to bone marrow transplant or to, the, gene therapy RSSL treatment.

448
01:16:32.240 --> 01:16:42.479
Josh Bonkowsky: In addition to just treating the patient, there are implications for the family. So, like, if there's other siblings, are they at risk? They're trying to do, what is… what's called cascade testing.

449
01:16:42.530 --> 01:16:58.239
Josh Bonkowsky: And then, importantly, this really has, like, a downstream impact for the family to think about future pregnancies,

because IVF, you can often tell the insurance company, like, would you rather do IVF so the family doesn't have another child affected by MLD?

450
01:16:58.290 --> 01:17:08.729
Josh Bonkowsky: Or would you rather kind of gamble that you will be spending millions of dollars for if another child is affected by MLD? So, we often talk to the families about,

451
01:17:08.840 --> 01:17:11.380
Josh Bonkowsky: Talking to their insurance companies about IVF.

452
01:17:11.790 --> 01:17:28.209
Josh Bonkowsky: So, why this kind of summary? Like, why newborn screening for MLD? So, MLD is treatable, the treatment is effective, and the treatment's only effective if the disease is copied before symptoms, and the most common type are infants who are affected by MLD, the late infantile type.

453
01:17:28.360 --> 01:17:30.130
Josh Bonkowsky: And then,

454
01:17:30.430 --> 01:17:42.550
Josh Bonkowsky: our ability to find and detect patients is not very good, really, because the symptoms are tricky. This is a map showing in the United States where people get diagnosed with MLD and other leukodystrophies.

455
01:17:42.660 --> 01:17:59.760
Josh Bonkowsky: And so, if it's yellow, it means no one was diagnosed there. And it's not because no one lives there, it's because no one… it's because we missed the diagnosis. So basically, it's only if you're kind of lucky, so to speak, and live near a major hospital center that you can get diagnosed, which means we're missing lots of people who should be diagnosed.

456
01:18:01.060 --> 01:18:07.960
Josh Bonkowsky: And, thanks so much for listening to me. Hopefully, I went kind of quick, but I'm happy to take any questions.

457
01:18:13.320 --> 01:18:36.570
Mikaela Miller: I was gonna hop in here, I think we're gonna take a

quick break, and then we're gonna go into the lab discussion, but if you're available, Dr. Bonkowski, we do have a discussion period, I would say in about 30 minutes or so, and it would be great if you're available to stay on for that. I'm sure the committee will have a lot of questions, but if you're not,

458
01:18:36.820 --> 01:18:48.379
Mikaela Miller: yeah, I think maybe we should take a moment here so the committee does have a chance to ask you some questions. Are you able to stay on for that, or do you have another, engagement to get to?

459
01:18:48.510 --> 01:18:52.920
Josh Bonkowsky: What time would the restart be? Sorry, I wasn't quite sure.

460
01:18:52.920 --> 01:19:06.210
Mikaela Miller: Well, I'm thinking we'll take a 10-minute break since we're halfway through the meeting, and then our lab presentation we have scheduled for about 20 minutes or so, so I would say the discussion will start in about 30 minutes.

461
01:19:06.870 --> 01:19:10.509
Josh Bonkowsky: Sure, that should be… that should work well for me, if that's okay with… for everybody.

462
01:19:10.740 --> 01:19:24.900
Mikaela Miller: Yeah, that would be wonderful. Okay, well, I kind of promised everyone a break about halfway through this meeting, so let's take a quick 10-minute break, refill waters and whatnot. You're welcome to just turn your camera off and then mute yourself.

463
01:19:24.900 --> 01:19:33.900
Mikaela Miller: And then I'll come back and kind of get us all back together, and we'll have Jeannie and Nikki from the Montana State Lab, present.

464
01:29:37.710 --> 01:29:42.360
Mikaela Miller: Alright, everyone, we're kind of right at that 10-minute mark.

465
01:29:44.200 --> 01:29:50.919

Mikaela Miller: Once I see a few more cameras on, I'll go ahead and get us started, so I know a few more of us are here.

466
01:29:54.480 --> 01:29:59.540
Lynne Wood: And I apologize, I won't be able to start my camera up, I've been having technical difficulties. Sorry, guys.

467
01:29:59.610 --> 01:30:06.730
Mikaela Miller: Thank you. Yeah, at least I know you're here, I just didn't want to get started. If I saw cameras off, to me, that means maybe…

468
01:30:08.210 --> 01:30:17.189
Mikaela Miller: Oh, there we go. I see lots of people here. Okay, well, Jeannie and Nikki, do you both, want to go ahead and start?

469
01:30:19.800 --> 01:30:20.840
Jeanne Lee: Yeah.

470
01:30:21.150 --> 01:30:23.959
Jeanne Lee: Do you, have some slides, too?

471
01:30:24.390 --> 01:30:29.270
Mikaela Miller: I do, let me… Share my screen again here.

472
01:30:35.820 --> 01:30:39.400
Jeanne Lee: Alright, so I'm gonna… I'll get started.

473
01:30:39.990 --> 01:30:57.530
Jeanne Lee: So, hi again, everyone. Thank you for coming back, and, thank you for the, presentations, from Dr. Borkowski and, the family presentation from, the Cornell family.

474
01:30:58.100 --> 01:31:17.440
Jeanne Lee: I'm Jeannie Lee, and I supervise newborn screening and serology at the Montana Public Health Laboratory. Before I begin today, I just want to briefly remind you about newborn screening in Montana. We currently have 32 conditions on the panel.

475
01:31:17.440 --> 01:31:23.970

Jeanne Lee: 7 of the conditions are screened right here in the public health laboratory.

476
01:31:23.970 --> 01:31:35.359
Jeanne Lee: And the other 25 conditions are tested at the Wisconsin State Lab of Hygiene, where they can perform mass spectrometry testing inexpensively.

477
01:31:35.530 --> 01:31:43.059
Jeanne Lee: The cost of the newborn screening panel is currently $161.80.

478
01:31:44.470 --> 01:31:50.579
Jeanne Lee: Today, I will provide you with testing considerations for MLD.

479
01:31:51.050 --> 01:32:09.480
Jeanne Lee: You may remember me telling you, at, during our last nomination that when evaluating whether to take on new tests, there are many factors to consider, such as instrumentation, methodological expertise.

480
01:32:09.580 --> 01:32:13.679
Jeanne Lee: whether the test is FDA approved, and cost.

481
01:32:14.240 --> 01:32:20.520
Jeanne Lee: For MLD, a major concern is the lack of an FDA-approved test.

482
01:32:20.890 --> 01:32:33.169
Jeanne Lee: although Montana Code does not preclude the Advisory Committee from adding the condition when there's not an FDA-approved test.

483
01:32:33.760 --> 01:32:38.849
Jeanne Lee: I just want to touch on what it means when there's no FDA-approved test.

484
01:32:39.330 --> 01:32:51.359
Jeanne Lee: When no FDA-approved test is available, a laboratory must develop its own test, which we call an LDT, or Laboratory Developed

Test.

485
01:32:52.300 --> 01:33:04.159
Jeanne Lee: The difference between LDTs and FDA-approved tests comes down to the verification and validation processes used to implement the assay.

486
01:33:04.460 --> 01:33:10.220
Jeanne Lee: An FDA-approved test has already undergone rigorous studies.

487
01:33:10.530 --> 01:33:22.280
Jeanne Lee: Of screening performance, including false negative and false positive studies, Precision, sensitivity, and reproducibility assays.

488
01:33:22.640 --> 01:33:25.360
Jeanne Lee: Interference studies, and so forth.

489
01:33:25.560 --> 01:33:40.389
Jeanne Lee: With an LDT, all of that needs to be done by the laboratory, which can take an extensive period of time to develop and evaluate, as there is no outside party reviewing the data.

490
01:33:41.520 --> 01:33:48.829
Jeanne Lee: Mae Baker at the Wisconsin State Laboratory of Hygiene is working on an assay for MLD.

491
01:33:49.230 --> 01:34:01.300
Jeanne Lee: She hopes to have it developed by the end of the year, although I do not know what that means as far as her validation studies and when those would be completed.

492
01:34:02.200 --> 01:34:09.529
Jeanne Lee: I also do not know what the cost of screening MLD will be once her assay is validated.

493
01:34:10.000 --> 01:34:17.670
Jeanne Lee: I'll be seeing Mae Baker at the beginning of May, and so I hope I'll be getting some clarification from her then.

494
01:34:18.360 --> 01:34:38.060
Jeanne Lee: I'll now turn over to Nikki Gosin, and she will give you some information about long-term follow… or sorry, short-term follow-up considerations following a positive screen for MLD. And then when she's finished, we're happy to answer any questions that you have.

495
01:34:40.750 --> 01:34:54.420
Nikki Goosen: Yeah, thanks, Jeannie. Yeah, so I'm Nikki Gosin. I do the short-term follow-up for Montana. I work with Jeannie in the laboratory as well, so I do have a laboratory background.

496
01:34:55.080 --> 01:35:12.099
Nikki Goosen: So here in Montana, we have about 11,000 births a year. So after we get a screen-positive result on the newborn screen, my responsibility is to make sure the primary care provider, you know, knows about that result.

497
01:35:12.100 --> 01:35:30.070
Nikki Goosen: knows what the appropriate recommendations are, and depending on the condition, it might be, you know, a consult with one of the specialists around the state, you know, whether that's pediatric endocrinology, one of our… excuse me, metabolic specialists,

498
01:35:30.250 --> 01:35:31.820
Nikki Goosen: Anything like that.

499
01:35:32.320 --> 01:35:41.780
Nikki Goosen: So, for MLD, I just kind of want to briefly go through the short-term follow-up, and what that would entail for Montana babies.

500
01:35:42.310 --> 01:35:48.360
Nikki Goosen: So once we get a positive result, we would immediately inform primary care provider.

501
01:35:48.570 --> 01:36:04.639
Nikki Goosen: We would also get Shodare involved right away. We've got a metabolic team there, and they help assist with, test recommendations, and then helping to, you know, interpret those tests after they come back for primary care providers.

502

01:36:05.340 --> 01:36:20.970
Nikki Goosen: So here in Montana, all of these tests are going to be send-outs, so it's going to be the ARSA leukocyte enzyme assay, urine sulfatides, and then the urine glycosaminoglycans.

503
01:36:21.110 --> 01:36:23.120
Nikki Goosen: Mayo does all of those tests.

504
01:36:23.420 --> 01:36:26.519
Nikki Goosen: It's whole blood specimens, urine specimen.

505
01:36:26.920 --> 01:36:35.720
Nikki Goosen: As for the molecular genetic testing, we're pretty fortunate here in Helena that Chader is literally just down the street from us.

506
01:36:35.920 --> 01:36:45.740
Nikki Goosen: So we can send, you know, a blood slot from that initial screen over to them right away, so they can take care of our molecular testing right away.

507
01:36:46.560 --> 01:36:55.819
Nikki Goosen: Once all of that comes back, you know, depending on those results, we would then get our neurologists involved, pediatric neurology.

508
01:36:56.220 --> 01:37:03.919
Nikki Goosen: And then from that point, you know, I step away, you know, no longer short-term.

509
01:37:04.070 --> 01:37:08.749
Nikki Goosen: And then, you know, they go from there for… You know, further care.

510
01:37:10.210 --> 01:37:16.590
Nikki Goosen: Let's see… yeah, and that… that's about all I have for follow-up in Montana.

511
01:37:22.030 --> 01:37:23.590
Mikaela Miller: Okay, so…

512
01:37:23.610 --> 01:37:31.689
Mikaela Miller: Next, we have the discussion, so I think we're gonna go ahead and just jump right into that. If anyone has questions,

513
01:37:31.690 --> 01:37:49.070
Mikaela Miller: For anyone who presented today, as far as our… for committee members have any questions for anyone who presented today, and then also, please let me know if you need me to jump back in the slides at all, I'm happy to do that. But I will pass it off to Shelly and Jen to go ahead and lead the discussion.

514
01:37:49.530 --> 01:38:07.399
Shelly Eagen: Yeah, great, thank you. So we'll go ahead and open up the discussion. I will go ahead and jump in first. I have a few questions, but I'll just start with one. With there not being an FDA-approved test right now, and there are states that are screening.

515
01:38:07.520 --> 01:38:25.490
Shelly Eagen: And it also was recently added to the RESP, which means there's going to be additional states that have to incorporate this as part of that agreement. Is there any knowledge amongst, the SME, or is there any knowledge about what those states are currently using?

516
01:38:30.130 --> 01:38:40.720
Abe Elias: I can, I can… actually, I can talk a little bit about that, and actually, I have also a question then for Dr. Wonkowski on that, because I think a big part

517
01:38:40.720 --> 01:38:58.050
Abe Elias: of the, you know, of the consideration is really, that MLD is one of the… is the really… one of the most recent additions, and, there is actually very good screening, but the screening is still being worked out, and I… I… so the… the…

518
01:38:58.050 --> 01:39:06.340
Abe Elias: issue with… with the screening is, the metabolic screening, is that you, you know, there are different ways, and I think, Nikki

519
01:39:06.700 --> 01:39:18.569
Abe Elias: in that, in that schematic that she had, there was urine… there was sulfatites, and there was also the ARSA activity. It's, it's really important that, there is a…

520
01:39:18.690 --> 01:39:24.670
Abe Elias: an, a… Good screening for the sulfatides that are

521
01:39:24.700 --> 01:39:41.420
Abe Elias: to measure. So to have that, because one of the issues with the ARSA gene is there are many pseudo-deficiency alleles. In fact, the pseudodeficiency, you know, alleles are probably about 10 times more common than the regular alleles.

522
01:39:41.420 --> 01:39:44.889
Abe Elias: And so, to avoid,

523
01:39:44.890 --> 01:39:58.350
Abe Elias: lots of false positives in the initial screening, and that then would have to sort out with a second tier. You want to really… you really need to, use the testing that is,

524
01:39:58.510 --> 01:40:08.180
Abe Elias: both sensitive and specific, and, and, the, the, the double mass spec, that, that you can use to,

525
01:40:08.440 --> 01:40:13.339
Abe Elias: to, to detect, sulfur tides.

526
01:40:13.400 --> 01:40:22.339
Abe Elias: It's actually quite good, but it's… it's not readily available. It's being developed, because even though there are

527
01:40:22.340 --> 01:40:33.740
Abe Elias: There are now a number of states that have added it. Most of them are actually still in the process of developing it, and so that is really the… in order to do,

528
01:40:33.740 --> 01:40:44.660
Abe Elias: an efficient and, screening, you really have to, have to rely on the, on the, on the accurate and so sensitive and, and specific,

529
01:40:44.740 --> 01:41:01.380

Abe Elias: detection of these metabolites through double mass spec. And I actually wanted to ask, Dr. Bonkowski a little bit if… I'm not sure if you're able to talk about it, when you, you know, when you… in Utah, when you, kind of considered that condition and then decided.

530
01:41:01.380 --> 01:41:21.829
Abe Elias: to, to go, to, to, to implement or to, to, decide it for it. What were kind of the discussions with the public health? I assume that you're… that the public health lab has that set up and, and has it set up so that it can maybe multiplex it. Can you talk a little bit about those concerns or, or discussions you had?

531
01:41:22.760 --> 01:41:36.430
Josh Bonkowsky: Yeah, that's a good point. So I don't know the technical details in terms of what the state testing lab is doing, but I think the same concern was about this, pseudo-deficiency problem that could have a high false positive rate, and trying to

532
01:41:36.430 --> 01:41:50.460
Josh Bonkowsky: weed those out before it hit the family. What we've done in the past, there's this other condition you're probably familiar with, ALD, adrenal leukodystrophy.

533
01:41:50.580 --> 01:41:52.469
Josh Bonkowsky: And,

534
01:41:53.010 --> 01:42:03.890
Josh Bonkowsky: What we've done is we've decided to be more… that we'd rather, know about potential patients and have a higher false positive rate, and weed people out.

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01:42:04.040 --> 01:42:16.739
Josh Bonkowsky: afterwards than to miss people. So we've kind of, biased ourselves to that side of the equation, but I think it's a little bit of a judgment call for each state lab, how they want to balance that.

536
01:42:20.920 --> 01:42:22.309
Abe Elias: Thanks, thanks, everyone.

537
01:42:28.040 --> 01:42:29.330
Shelly Eagen: Anybody else?

538
01:42:29.600 --> 01:42:30.490
Shelly Eagen: Go ahead and jump.

539
01:42:31.750 --> 01:42:37.570
Jeanne Lee: I… I guess I was gonna jump in a little bit, too. Shelly. There are some…

540
01:42:37.730 --> 01:42:40.090
Jeanne Lee: Tests that are…

541
01:42:40.200 --> 01:42:55.250
Jeanne Lee: I'm going to be submitted to the FDA. I think maybe towards the end of 2026. I'm aware of, two different companies that are submitting

542
01:42:55.390 --> 01:43:07.529
Jeanne Lee: assays for FDA approval. And I… and I'm not quite sure, like, how long that FDA approval process is for assays.

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01:43:10.880 --> 01:43:11.639
Shelly Eagen: Alright, thank you.

544
01:43:17.860 --> 01:43:22.310
Shelly Eagen: I have some other questions, if nobody else has questions here.

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01:43:22.850 --> 01:43:31.420
Shelly Eagen: Let's see… so, one of the… you had talked about needing the RSA activity. I'm curious if that is on the same…

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01:43:31.570 --> 01:43:45.269
Shelly Eagen: blood spot that's already going to be used, or if we're going to be doing another punch. I know we've talked about real estate in the past, and how much we're using up, so I was curious if that would be using the same blood spot, or if that's another punch card.

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01:43:53.630 --> 01:43:56.140
Jeanne Lee: Nikki, do you have a feel for that?

548
01:43:56.490 --> 01:44:00.000
Jeanne Lee: ARSA activity, if that was a new draw.

549
01:44:00.160 --> 01:44:11.290
Nikki Goosen: Well, so for me, mine would be more on, like, the diagnostic end for the Mayo send-out, but I think if, if Wisconsin performed that test.

550
01:44:12.620 --> 01:44:18.699
Nikki Goosen: I guess I don't know if it's a mass spec test, or if it's… well, it's enzyme activity.

551
01:44:18.950 --> 01:44:26.920
Nikki Goosen: Yeah, I'm not sure. It just depends. If it was still on the same platform, I imagine, you know, they could use the same punch.

552
01:44:27.080 --> 01:44:30.810
Nikki Goosen: But if it's a different platform, it would require an additional…

553
01:44:31.190 --> 01:44:34.569
Nikki Goosen: additional sample. Well, additional punch, I should say.

554
01:44:35.900 --> 01:44:47.419
Abe Elias: So, you know, I… so, it depends… so part of the difficulty, I think, we have, I think, in this discussion is that there is, that Wisconsin currently is still

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01:44:47.480 --> 01:44:57.830
Abe Elias: developing, the test. So, there is a possibility for them, if they decide to do so, to, you know, have the initial mass spec, and then

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01:44:57.830 --> 01:45:08.050
Abe Elias: reflex directly, we have that with some of the other metabolic conditions, biochemical, reflex directly to a second-tier test, which could be ARSA activity.

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01:45:08.200 --> 01:45:11.640
Abe Elias: so there are…

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01:45:11.680 --> 01:45:34.849
Abe Elias: That's not always… so, you can develop a mass spec test that is so specific, actually, with the urine sulfatides, that you have a low, you know, a low false positive rate, and then what happens is that they, the initial sulfatides are flagged as abnormal.

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01:45:34.850 --> 01:45:52.320
Abe Elias: And then what hap… what happens then on the short-term follow-up that Nikki just mentioned is that you would, on a different blood spot, sorry, on a different… on a new blood draw and urine, you basically develop… you detect ARSA activity and the urine sulfatite as a conformation.

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01:45:52.460 --> 01:46:13.269
Abe Elias: Nikki mentioned that one thing that we would have, we're actually developing this as part of a, of a grant, right now for Pompeii, or we already have validated it for Pompeii and, and, and, XALD is, because we're so, we, what we could do,

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01:46:13.270 --> 01:46:16.909
Abe Elias: In addition, to really, to…

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01:46:18.570 --> 01:46:43.530
Abe Elias: to accelerate the process is we can, from a blood spot, we could directly extract DNA and do the molecular testing, rather than… what Nikki just presented there, the molecular testing as a third tier, if you will, that's just a general suggestion that's often done, but where it's possible, including in New York, for example, they do molecular testing early on, and I say

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01:46:43.530 --> 01:46:50.710
Abe Elias: about molecular testing is that you circumvent the problem of pseudodeficiency alleles. So the genotyping is very important

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01:46:50.710 --> 01:47:07.100
Abe Elias: in that sulfotides and molecular testing are probably the most important part of that, that aspect. So, so we could, you know, and this could actually be done from a blood spot, meaning that we could have the results within,

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01:47:07.100 --> 01:47:10.810

Abe Elias: Really, within a few… within a few days. And…

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01:47:10.820 --> 01:47:29.130
Abe Elias: The… the… again, the problem is… the initial problem is the initial test, the initial screening test, to work that out, and the way how we are set up right now, we're really dependent… be dependent on, a, you know, an efficient test, from… from Wisconsin.

567
01:47:29.550 --> 01:47:34.889
Abe Elias: Jeannie, is that, kind of, from that aspect, would that… is that correct?

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01:47:37.100 --> 01:47:39.580
Jeanne Lee: Yeah, I think so.

569
01:47:40.100 --> 01:47:47.540
Jeanne Lee: I… yeah, I don't really know what… what she has in the works. When I spoke with her, she just…

570
01:47:47.750 --> 01:48:04.289
Jeanne Lee: She just said, that she was developing an assay, so I, you know, I don't know how complex it is. I, I do think that she was going to try to multiplex it with XALD, so,

571
01:48:05.040 --> 01:48:11.529
Jeanne Lee: So yeah, I just… I hope to learn more from her, in early May, just…

572
01:48:11.840 --> 01:48:31.650
Jeanne Lee: just to get a feel for, what she has planned. I was actually quite surprised that she was already, starting to develop an assay, and, and she's just cute. She says, of course I am, I'm Mae Baker. So, so…

573
01:48:31.970 --> 01:48:36.820
Jeanne Lee: I, you know, she… she's great, and she knows her stuff, so,

574
01:48:36.960 --> 01:48:41.469
Jeanne Lee: hopefully… hopefully I'll learn some more here next month.

575
01:48:45.020 --> 01:48:49.229
Shelly Eagen: I echo that. Mae Baker is wonderful. I worked with her when I was in Wisconsin.

576
01:48:51.150 --> 01:48:53.580
Shelly Eagen: Anybody else have questions?

577
01:48:54.360 --> 01:49:13.690
Lynne Wood: Sorry that I don't have my raise hand feature, I know I'm supposed to use it, but, just to make sure that I understand what everyone's been saying so far, our biggest challenge would be that right now, an FDA-approved or, like, standardized measurement doesn't necessarily exist. There have been places that have worked around it.

578
01:49:13.700 --> 01:49:21.339
Lynne Wood: Some of the things that have been proposed have been waiting to see, how Wisconsin designs this new test.

579
01:49:21.340 --> 01:49:33.800
Lynne Wood: It sounds like maybe waiting to see what happens with some of these FDA-approved tests coming at the end of the year, or Abe, if I understood you correctly, it sounds like you're maybe proposing that rather than doing the…

580
01:49:33.800 --> 01:49:45.210
Lynne Wood: initial screening with the ARSA, and then getting the urine sulfatides, like, was outlined in some of the, stuff we've seen, going straight to molecular testing.

581
01:49:45.810 --> 01:50:02.990
Abe Elias: No, not exactly, Lynn. So the initial screening would still be dependent on the sulfatides. That's a, that's actually a very good test, but it's a tricky test. It's not a… it's, because you really have to, the, the, the, the,

582
01:50:03.350 --> 01:50:21.050
Abe Elias: the diagnostic or screening, you know, window is narrow, so it's not easy to develop, and as I mentioned, there are really only a few labs who have started doing that, so you can't necessarily, you know, depend on a

583

01:50:21.100 --> 01:50:28.490
Abe Elias: on a broad community, basically. But what I was mentioning is that the second-year testing

584
01:50:28.490 --> 01:50:52.500
Abe Elias: the molecular testing, actually bringing that in earlier, rather than as a third tier, is actually a very, I think, very good choice, because that together… because that takes care for many of the questions of the pseudodeficiency alleles. Not as a screening, really, but both as a confirmation, but also, to… because the ARSA activity

585
01:50:52.710 --> 01:51:10.290
Abe Elias: If it's positive, the one thing that you cannot exclude is the possibility of pseudodeficiency are alleles there. But, but again, if the screening is well done, if the screening of using the sulfatites is,

586
01:51:10.320 --> 01:51:24.109
Abe Elias: is well done. You actually… the pseudodeficiencies are not a big problem. It's not like, because you can… the… the range is, or it's specific enough to…

587
01:51:24.110 --> 01:51:34.239
Abe Elias: really reduce that, that otherwise what you could expect, a high, you know, a high, false positive rate. But you still need to, need to address it.

588
01:51:35.000 --> 01:51:49.369
Lynne Wood: So, it sounds like it's more still using the sulfatides, but then rather than the molecular testing being step 3 in the algorithm, it's just step 2, and we don't worry about the ARSA to figure out pseudodeficiency alleles and things like that.

589
01:51:50.250 --> 01:52:00.420
Abe Elias: I would use the ALSA, you know, the ALSA as a second-tier testing, also, and urine sulfatides, but, you wouldn't have to rely only on that, so you have that… Okay.

590
01:52:00.420 --> 01:52:15.970
Abe Elias: testing, potentially also earlier, because you wouldn't have to wait for another blood draw. You know, as you know, in Montana, sometimes, you know, the patients, they live very far, they live remotely, the, the

591
01:52:16.820 --> 01:52:17.910
Abe Elias: the,

592
01:52:18.060 --> 01:52:27.909
Abe Elias: The blood draw and then sending it to the lab is sometimes a challenge, so that the molecular testing would circumvent that.

593
01:52:28.230 --> 01:52:34.700
Lynne Wood: Yeah, that makes sense, thank you. So, it's not that we're taking away a step, we're just merging step 2 and step 3.

594
01:52:40.680 --> 01:52:42.779
Lynne Wood: And…

595
01:52:46.600 --> 01:52:48.030
Jennifer Banna: Lynn, go ahead and finish.

596
01:52:48.690 --> 01:52:52.359
Lynne Wood: Oh, I actually had another question, so you should go ahead, I saw your hand up.

597
01:52:52.360 --> 01:52:52.850
Jennifer Banna: Oh, you're.

598
01:52:52.850 --> 01:52:53.979
Lynne Wood: We're actually following the rules.

599
01:52:54.040 --> 01:52:55.860
Jennifer Banna: Well, I…

600
01:52:56.450 --> 01:53:10.459
Jennifer Banna: That's funny. I'm not known to be a real follower. I… so I had a follow-up question. We talk about sometimes the newborn screening and late onset, and which things are on the newborn screen. I just wanted, clarification.

601
01:53:10.520 --> 01:53:21.820
Jennifer Banna: Dr. Bonkowski, about that. I couldn't tell if you were

saying that the ones that are caught on the newborn screen could also be late onset or early onset, or if we're only catching a certain group.

602
01:53:23.800 --> 01:53:40.949
Josh Bonkowsky: Yeah, that's kind of confusing. The, the most common kind is late infantile, which is the one that would… which would be… so, let me say it again. All the kinds would be picked up, but late infantile is the most common kind, so it'd be the one that we see the most often.

603
01:53:42.070 --> 01:53:57.480
Josh Bonkowsky: And then, even for the ones that have later onset, they, we try and take them to transplant before they become symptomatic, so there's, like, a little bit of, like, trying to figure out what that… when is that exactly.

604
01:53:57.480 --> 01:54:07.489
Jennifer Banna: Okay, so it's different than some of the other late-onset things that happen that are on newborn screen now, where it's not caught on the newborn screen, and then there's a later onset

605
01:54:07.530 --> 01:54:20.899
Jennifer Banna: I'm sorry, am I saying that clearly? There's some things we screen for now that we've had people talk about that they had later onset, but the testing that's done on newborns doesn't catch the later onset conditions. In this case, we might say to some families, your child

606
01:54:20.970 --> 01:54:27.320
Jennifer Banna: is… doesn't have the Motel or whatever, but you're gonna have to get on this, because later it's gonna be a problem. Is that… did I get it?

607
01:54:27.430 --> 01:54:30.069
Josh Bonkowsky: Yeah, that's a good, way to say it.

608
01:54:30.070 --> 01:54:31.070
Jennifer Banna: Thank you.

609
01:54:36.260 --> 01:54:38.659
Shelly Eagen: Lynn, did you want to ask your other question?

610
01:54:39.160 --> 01:54:40.320
Shelly Eagen: Oh, art.

611
01:54:41.710 --> 01:54:47.290
Lynne Wood: Sure, I don't know that this is the time to ask it, though. It might be that I'm supposed to ask it later in the meeting, but…

612
01:54:49.060 --> 01:55:05.940
Lynne Wood: it seems like there's some pretty compelling data, and it's been added to the RASP for, you know, screening for MLD, but it sounds like the infrastructure and technology isn't quite as fleshed out as some of the other, conditions we've seen brought to the committee.

613
01:55:05.950 --> 01:55:09.140
Lynne Wood: Are we ever able to, like.

614
01:55:09.850 --> 01:55:16.910
Lynne Wood: Pause, get more information about, like, what technologies are going to be available, and then…

615
01:55:17.180 --> 01:55:23.960
Lynne Wood: make our decision? I mean, it could be that by the time we vote at the next meeting, we have all this information, but I almost…

616
01:55:25.670 --> 01:55:28.859
Lynne Wood: you know, I think the questions that often come up

617
01:55:29.160 --> 01:55:40.100
Lynne Wood: have been, like, well, gosh, the real estate question, the how much is it gonna cost, the families question, and it sounds like we don't have those pieces of information just yet.

618
01:55:48.750 --> 01:55:56.900
Josh Bonkowsky: Well, not to step in where I don't know anything, but, the… I guess the newborn screening testing side, I'd have to defer to…

619
01:55:56.930 --> 01:56:10.519

Josh Bonkowsky: the lab experts, because I certainly don't understand the technical complexities there, but I think once the, once a kit is handed to us, I think that pathway is really clear, so I think, it's… I think it's more just is the,

620
01:56:10.550 --> 01:56:14.259
Josh Bonkowsky: Newborn screen testing component fleshed out enough.

621
01:56:15.680 --> 01:56:16.889
Lynne Wood: Yeah, exactly.

622
01:56:22.490 --> 01:56:24.640
Shelly Eagen: Dr. Elias, go ahead.

623
01:56:27.030 --> 01:56:45.080
Abe Elias: I just have a follow-up to Dr. Bonkowski from earlier Jen's question about, you know, the different types of MLD, and Dr. Bonkowski, in terms of, you know, I think you made the point, and that seems to be really that for the gene therapy.

624
01:56:45.080 --> 01:56:50.630
Abe Elias: It's really important to have pre-symptomatic. Are there…

625
01:56:50.650 --> 01:56:52.970
Abe Elias: Are there spec… are there,

626
01:56:53.490 --> 01:57:05.010
Abe Elias: criteria that are… specific criteria that can be followed, and… and who… who makes that decision, basically? How… how does… how does that workflow once you have

627
01:57:05.030 --> 01:57:17.530
Abe Elias: Actually, I'm independent now, I'm not from… only from the newborn screening, and I'm asking because, you know, I think what the Connell family earlier just, described.

628
01:57:17.530 --> 01:57:40.999
Abe Elias: really that heartbreaking, long, you know, diagnostic odyssey that they experienced, you know, it was in 2014. Today, that likely would be different somewhat, because we do, even with non-specific neurodevelopmental, you know, manifestations, we do early,

whole genome, whole exome sequencing, and usually have diagnosis, very quickly.

629
01:57:41.000 --> 01:57:44.160
Abe Elias: However, I think you made the point that

630
01:57:44.220 --> 01:57:53.039
Abe Elias: that even then, it might be already too late. So I guess, are there, specific criteria, to…

631
01:57:53.170 --> 01:57:54.589
Abe Elias: Kind of determine that.

632
01:57:56.090 --> 01:57:58.040
Josh Bonkowsky: Yeah, so the,

633
01:57:58.210 --> 01:58:17.769
Josh Bonkowsky: the things… so the, the approval to use RCCL, the gene therapy in the late infidel and early juvenile subtypes is pretty tightly regulated in that they have to have a normal neurologic exam by a pediatric neurologist,

634
01:58:17.770 --> 01:58:23.899
Josh Bonkowsky: and they can't have MRI involvement, and…

635
01:58:24.420 --> 01:58:44.330
Josh Bonkowsky: And so that… and so then… and that's kind of regulated because of both the insurance companies don't want to pay for something that's too late to be effective, and then I think, I mean, not to speak on Orchard's behalf, the company that makes the RSSL, but because of their FDA approval, they've been quite,

636
01:58:44.450 --> 01:58:46.630
Josh Bonkowsky: You know, conscientious about

637
01:58:46.750 --> 01:58:51.819
Josh Bonkowsky: The same process, just making sure that they're not giving to people for whom it's too late to be effective.

638
01:58:52.430 --> 01:58:57.930

Josh Bonkowsky: Does that answer your question? Just making sure I'm not going on.

639
01:58:58.110 --> 01:59:09.279
Abe Elias: Yeah, so it seems like that… so really no MRI involvement, and so if you have MRI involvement, you would not qualify for the RSSL.

640
01:59:10.040 --> 01:59:12.169
Josh Bonkowsky: For the late infantile subtype, yeah.

641
01:59:12.170 --> 01:59:13.909
Abe Elias: delete infertile, yeah. Okay.

642
01:59:23.560 --> 01:59:24.740
Shelly Eagen: Nikki, go ahead.

643
01:59:25.700 --> 01:59:41.019
Nikki Goosen: Yeah, I just wanted to kind of speak to, the real estate issue for spots. We recently did just change our, collection cards for Montana. We went from 5 spots to 8 spots.

644
01:59:41.290 --> 01:59:44.909
Nikki Goosen: So we do have those additional 3 spots.

645
01:59:46.140 --> 01:59:54.360
Nikki Goosen: We don't always get 8 quality spots, but now, you know, we are collecting more specimen on those babies.

646
01:59:57.030 --> 01:59:58.050
Shelly Eagen: Thank you.

647
01:59:58.050 --> 01:59:58.700
Nikki Goosen: Yeah.

648
01:59:59.120 --> 01:59:59.850
Shelly Eagen: Jen?

649
02:00:00.400 --> 02:00:05.159

Jennifer Banna: I just wanted to follow up on, what Dr. Wood was saying.

650
02:00:05.440 --> 02:00:16.979
Jennifer Banna: about the labs being ready or not ready, because I'm not sure we've had this situation before, where we were like, well, what will happen if we recommend it? But it takes so long to go through the process, and then also the governor

651
02:00:17.130 --> 02:00:35.750
Jennifer Banna: can not recommend it, because we're just making a recommendation to him, so I'm interested in what other… how other people in the committee feel about not knowing exactly how that testing is going to go, and… and voting anyway, and letting that work itself out, or if it seems important, because I can kind of see both pieces.

652
02:00:50.630 --> 02:00:59.060
Jeanne Lee: I… so, I guess maybe to try to… Add.

653
02:01:00.350 --> 02:01:01.780
Jeanne Lee: Add more to that.

654
02:01:02.250 --> 02:01:09.070
Jeanne Lee: Jen, is I… I think that's kind of why…

655
02:01:09.840 --> 02:01:17.449
Jeanne Lee: You are the advisory committee, that you are having to make these difficult decisions.

656
02:01:17.790 --> 02:01:27.270
Jeanne Lee: And, and… and the director is going to, take your recommendation.

657
02:01:27.600 --> 02:01:40.710
Jeanne Lee: So, and really, you know, Dr. Wood, this kind of fits into your question, too. You know, if there are too many questions,

658
02:01:41.190 --> 02:01:42.440
Jeanne Lee: you know…

659
02:01:43.210 --> 02:01:51.759
Jeanne Lee: We can do things like have another meeting to, you know, get more information, before you make a decision.

660
02:01:52.030 --> 02:02:02.700
Jeanne Lee: But really, it's up to the advisory committee to ask all the questions that you have,

661
02:02:02.990 --> 02:02:05.549
Jeanne Lee: You know, how's the,

662
02:02:06.760 --> 02:02:14.759
Jeanne Lee: You know, have our group try to find those answers for you, so you… so you can make those

663
02:02:15.090 --> 02:02:16.340
Jeanne Lee: decisions.

664
02:02:24.190 --> 02:02:25.459
Shelly Eagen: Jacqueline, go ahead.

665
02:02:26.850 --> 02:02:31.469
Jacqueline Isaly: Yeah, so I'm not a voting member, but just to kind of clarify.

666
02:02:31.850 --> 02:02:50.279
Jacqueline Isaly: When we write the recommendation letters to the director, we do include all the details and information about, like, what this will do to our testing process, and what that will look like. So, if we don't know all of those details, we would then have to explain that

667
02:02:50.320 --> 02:02:53.880
Jacqueline Isaly: That that is the current case for this one, and so that…

668
02:02:53.910 --> 02:03:12.919
Jacqueline Isaly: would be potentially, you know, taken into consideration when then the director's office is considering the recommendation for approval or not approving. So that is just to

clarify, that's kind of part of what… the information that we, include on the recommendation.

669
02:03:15.660 --> 02:03:29.040
Lynne Wood: How… and it sounds like the meeting with May Baker is coming up pretty soon. It sounds like FDA approval for some of the more standardized newborn screening tests that might be more nationally available are coming in a couple of months.

670
02:03:29.040 --> 02:03:36.399
Lynne Wood: do you guys have any estimates for, like, how soon we'll have that information? I guess I want to try and thread the needle where, like.

671
02:03:36.600 --> 02:03:48.909
Lynne Wood: you know, I feel like the argument for screening is quite compelling, but if we're gonna recommend it, we also need to have a good plan for, like, well, okay, what does this mean for the rest of the screen? You know, how do we factor this in?

672
02:03:48.910 --> 02:03:58.119
Lynne Wood: if other things come down the pipeline, and then, like, how is it going to roll out? Because it sounds like if we get the newborn screening process right.

673
02:03:58.120 --> 02:04:09.360
Lynne Wood: the actual treatment, if we do it early, would be relatively streamlined at one of these big centers. How soon do you think we'll know some of these things, in a way that

674
02:04:09.510 --> 02:04:14.499
Lynne Wood: Would inform the director and the people who accept our recommendations.

675
02:04:15.550 --> 02:04:16.460
Lynne Wood: She's gone.

676
02:04:25.820 --> 02:04:30.399
Jeanne Lee: I, you know, I… Those are good questions.

677
02:04:30.540 --> 02:04:49.289

Jeanne Lee: Dr. Wood, and I, you know, I'm hoping that we'll learn more over the next month or so. As far as, like, her assay… as Mae Baker's assay development, I mean, I don't really know

678
02:04:49.470 --> 02:04:59.890
Jeanne Lee: Where she is in that process, nor what it means for when screening, like, an implementation date.

679
02:05:00.010 --> 02:05:08.269
Jeanne Lee: So, so hopefully we'll get some of those answers,

680
02:05:08.440 --> 02:05:11.490
Jeanne Lee: You know, over the next couple of months.

681
02:05:13.610 --> 02:05:22.369
Jeanne Lee: You know, and there's many other states that are in, you know, this same situation. Like, when a condition is added to the rust.

682
02:05:22.580 --> 02:05:31.410
Jeanne Lee: There are some states that automatically have to align to the RUSP, and so, you know, that puts them in a position

683
02:05:31.570 --> 02:05:37.810
Jeanne Lee: Where they either have to figure out how to, develop an assay.

684
02:05:38.030 --> 02:05:43.950
Jeanne Lee: Or, wait for, an assay to do… to be developed.

685
02:05:44.150 --> 02:05:55.989
Jeanne Lee: I… I don't… I, I think that can take years, and, I, I do feel like…

686
02:05:56.160 --> 02:05:59.329
Jeanne Lee: You know, if…

687
02:05:59.560 --> 02:06:08.640
Jeanne Lee: If a condition's added to the panel, it, you know, it doesn't… it doesn't mean you get to start screening at 6 months from

when you

688
02:06:09.110 --> 02:06:20.009
Jeanne Lee: vote it. And I… you guys have seen that already. You know, the rulemaking process takes time, you know, assay development takes time.

689
02:06:20.110 --> 02:06:29.830
Jeanne Lee: So… so it may, you know, it may take a couple of years, for… or 18 months.

690
02:06:30.290 --> 02:06:33.209
Jeanne Lee: To actually begin screening.

691
02:06:34.840 --> 02:06:47.509
Lynne Wood: And then a follow-up, and then I promise I will stop monopolizing everybody's time. Let's say if we, like, game it out both ways. Scenario one, we recommend before we…

692
02:06:47.620 --> 02:06:56.129
Lynne Wood: have a really clear path of, like, here's how we're going to screen, here is what it will cost, here is where it will go on the spot.

693
02:06:56.470 --> 02:07:12.549
Lynne Wood: if we get turned down, I could see if… or foresee a scenario where, hey, it means now MLD ends up back of the line, and some of these other conditions that are in line maybe get approved sooner, and actually screening for MLD gets set back even further. Maybe not. You know, maybe if we've…

694
02:07:12.730 --> 02:07:25.370
Lynne Wood: applied, it gets turned down, and then this technology comes along. Maybe that ends up being a fast track, and we don't actually lose that much time in rolling the screening out. Scenario two, we…

695
02:07:25.370 --> 02:07:40.900
Lynne Wood: wait until we have a little bit of this information, potentially, like, within a couple of months. I think generally when we were voting on these, conditions after a meeting like this, it's generally at that next quarterly meeting anyway, to say, hey, like.

696
02:07:40.900 --> 02:07:52.749
Lynne Wood: is this okay? You know, maybe we hold… gather that information then when we're all together, and then can kind of hold the vote once we have more info, and then would also foreseeably

697
02:07:52.750 --> 02:07:57.459
Lynne Wood: have more practical, logistical information to give the director.

698
02:07:57.970 --> 02:07:59.740
Lynne Wood: So, knowing that we're sort of…

699
02:07:59.900 --> 02:08:10.459
Lynne Wood: delaying things on the front end in hopes that it gets less delayed on the back end, if that makes sense. Do you think that's an accurate way of thinking about it, or do you think I have that wrong?

700
02:08:17.880 --> 02:08:26.820
Jeanne Lee: I think that you are thinking about it, in the right way with those two scenarios.

701
02:08:27.160 --> 02:08:37.320
Jeanne Lee: I, we'll… we'll just have to see. I… I don't have an easy answer for you today.

702
02:08:42.670 --> 02:08:59.019
Lynne Wood: It looks like there's something in the chat that, the advisory committee can schedule, like, other meetings and things like that, so it sounds like maybe if there was hot-off-the-presses news, even in between the quarterly meetings, we might be able to hear back on it. But it sounds like

703
02:08:59.280 --> 02:09:10.670
Lynne Wood: I guess my impression is that we'll just kind of have to go with our gut as far as, like, do we gamble on recommending now, or do we wait? And we don't have a lot of information to guide us.

704
02:09:13.740 --> 02:09:15.379
Shelly Eagen: Dr. Bromkowski, go ahead.

705
02:09:16.670 --> 02:09:25.910
Josh Bonkowsky: I guess, since several states are screening already, I guess, it seems like we should have fairly good confidence that it's,

706
02:09:26.100 --> 02:09:32.260
Josh Bonkowsky: technically doable, is that… does that seem accurate, or…

707
02:09:33.820 --> 02:09:51.079
Lynne Wood: I think technically doable, yes, but how we do it here, I think, is the question. You know, for example, I think we only do 7 of our own screens here, and we send the rest out to Wisconsin. I think if we were to have to, like, parse out the newborn screens to yet a third state, I mean, maybe that's more doable than it seems.

708
02:09:51.080 --> 02:09:56.720
Lynne Wood: But it might be a bit of a… a lift, as far as our health infrastructure.

709
02:10:00.250 --> 02:10:08.440
Jeanne Lee: And I guess I'd add to that, Dr. Wood, that that may increase the cost of the screen even more.

710
02:10:08.540 --> 02:10:16.520
Jeanne Lee: If… if you were… if we were looking at shipping a blood spot to a third state,

711
02:10:17.620 --> 02:10:22.320
Jeanne Lee: That… that could be a pretty significant increase in cost.

712
02:10:28.300 --> 02:10:29.410
Shelly Eagen: Dr. Elias?

713
02:10:33.010 --> 02:10:51.129
Abe Elias: Yeah, just to follow up on this, I mean, I think, as Dr. Bokovsky said, it's technically feasible, and, it just has to be developed, and one thing is that the screening is really the, based on, on a mass spec technology, so,

714

02:10:53.220 --> 02:11:08.870
Abe Elias: that's where, we really are dependent, on a lab that does that, and Wisconsin does a wonderful job in certainly in doing that. It's just, they're… they currently don't have that test on their menu,

715
02:11:09.140 --> 02:11:25.680
Abe Elias: It certainly might be. I think it would be interesting to see, Ginny, when you meet with May, just to kind of see where they are. One thing never to forget is that if a lab decides to develop a test, you know, they usually,

716
02:11:26.440 --> 02:11:36.189
Abe Elias: have a timeline, a projected timeline. That timeline can change, however, because there might be unexpected, you know, unexpected,

717
02:11:36.190 --> 02:11:51.489
Abe Elias: outcomes of the preliminary validation, and so on. So, there's just some uncertainty, I think, there. One thing I actually wanted to ask, Dr. Momkowski is just to… has Utah started to screen now? Have you already started screening?

718
02:11:52.200 --> 02:11:55.509
Josh Bonkowsky: No, I think, they're setting up the…

719
02:11:56.150 --> 02:12:09.739
Josh Bonkowsky: they're both setting up the essays, and then also we have to go through a, legislative, budget approval process, and that only happens once a year, so it's, like, can't happen again until January of 2027.

720
02:12:13.360 --> 02:12:14.400
Abe Elias: Weird things.

721
02:12:18.760 --> 02:12:31.420
Shelly Eagen: I just would clarification… want a clarification from Dr. Brunkowski on one thing. You had talked about approximately 2 to 6 months having that narrow timeframe before patients are deemed to be too affected.

722
02:12:31.420 --> 02:12:40.819
Shelly Eagen: And you made mention of… is it based purely on MRI

findings, or is there other things that go into play there to say that somebody's too advanced or too affected?

723
02:12:41.290 --> 02:12:49.410
Josh Bonkowsky: It's also, that, in that time period, patients start to become symptomatic, on a neurologic exam, and so.

724
02:12:49.570 --> 02:13:02.810
Josh Bonkowsky: Especially with a late infantile, it's really quite fast, like, in the first… like, they might seem totally normal if you saw them at 2 months of age, but by the time they're, like, 4 or 5 months of age, they might already, like.

725
02:13:03.300 --> 02:13:04.980
Josh Bonkowsky: I have findings on exam.

726
02:13:09.250 --> 02:13:17.909
Shelly Eagen: So I guess, like, is it based on the severity of symptoms, or the number of symptoms, or that plus MRI findings, or…

727
02:13:18.450 --> 02:13:26.029
Josh Bonkowsky: So, anything, any involvements puts you into the disqualification… disqualification category.

728
02:13:26.030 --> 02:13:27.350
Shelly Eagen: Okay, thank you.

729
02:13:33.420 --> 02:13:35.489
Shelly Eagen: Any additional questions?

730
02:13:36.640 --> 02:13:38.060
Shelly Eagen: our discussions.

731
02:13:39.930 --> 02:13:40.880
Shelly Eagen: Nikki?

732
02:13:42.920 --> 02:13:50.280
Nikki Goosen: Yeah, this… Dr. Wood, I think you maybe would be able to answer this question, or Dr. Bunkowski,

733
02:13:50.760 --> 02:14:04.270
Nikki Goosen: So, for Pompei disease, one of the things we kind of ran into for the diagnostic workup, was the challenge of getting a pediatric cardiologist involved right away for the echo, and the EKG.

734
02:14:04.540 --> 02:14:05.770
Nikki Goosen: for…

735
02:14:06.050 --> 02:14:19.960
Nikki Goosen: for this condition, to get an MRI done, would that need to be, you know, specifically at, you know, a facility, you know, with you, or is that something they could get done, you know.

736
02:14:20.020 --> 02:14:26.150
Nikki Goosen: anywhere in Montana, and then, you know, you could look at it, you know, gosh.

737
02:14:26.320 --> 02:14:29.930
Nikki Goosen: You know, from… from Billings, if that makes sense.

738
02:14:29.930 --> 02:14:53.250
Lynne Wood: Yeah, I think there are MRI machines throughout the state. I imagine the reader's comfort at looking at the white matter in infants might vary. I know, like, you know, Kalispell, Missoula, Bozeman, here, we have neuroradiologists that are sort of dedicated to just brain scans, and they're pretty accustomed to looking at pediatric scans.

739
02:14:53.250 --> 02:15:04.789
Lynne Wood: the nice thing about radiology is, even if you get it somewhere outside, as long as it's a good quality skin, you can generally get an over-read, and people can review it after the fact. So, I think the MRI

740
02:15:04.790 --> 02:15:09.819
Lynne Wood: Wouldn't be too big a barrier, as far as a screen here.

741
02:15:11.020 --> 02:15:12.899
Nikki Goosen: Like, thank you.

742

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02:15:20.540 --> 02:15:21.750
Shelly Eagen: Anything else?

743
02:15:21.910 --> 02:15:24.010
Shelly Eagen: Michaela, how are we doing on time?

744
02:15:27.020 --> 02:15:40.529
Mikaela Miller: We're actually slightly ahead of schedule, so, there's
plenty of time here. I normally kind of try to shut this off around
11.40 for public comment, so, we have, like, another

745
02:15:40.760 --> 02:15:46.060
Mikaela Miller: several minutes here. If anyone has anything else,
don't feel like we're running over by any means.

746
02:15:48.840 --> 02:16:05.689
Lynne Wood: I guess the only other thing I would add is maybe more of
a proposal, like, you know, maybe as we're considering this, as soon
as our, colleagues with the lab and everybody have a little bit more
information about the actual screen itself, maybe sharing that with
the committee.

747
02:16:05.690 --> 02:16:21.049
Lynne Wood: I feel like if there's, if maybe we've hit all three of
the points that we were asking about, as far as, like, how would we
get it done, like, what would it mean for, like, a send-out, what
would it cost to families? Like, if we have all that well before the
next meeting, it might be good to know, and then if…

748
02:16:21.050 --> 02:16:34.240
Lynne Wood: you know, we do want to do an interim meeting. I know
that's really tough, getting this many people together in a room, but,
especially if it's something where, hey, we might be able to keep a
vote on schedule

749
02:16:34.540 --> 02:16:39.500
Lynne Wood: by doing an interim follow-up? Would that be something
people are open to?

750
02:16:45.240 --> 02:16:50.009
Shelly Eagen: I would be open to a shorter, meeting in the interim if
we have additional.
```

751
02:16:50.510 --> 02:16:54.100
Shelly Eagen: Information that we're able to gather between now and the vote in the fall.

752
02:16:55.400 --> 02:16:56.480
Jennifer Banna: I would too.

753
02:16:57.480 --> 02:16:58.129
kathy Crowley: Sure.

754
02:17:13.150 --> 02:17:20.200
Shelly Eagen: We'll pause here and let anybody else jump in that has questions or wants to have follow-up discussion about.

755
02:17:30.570 --> 02:17:31.809
Shelly Eagen: Dr. Elias?

756
02:17:32.639 --> 02:17:49.589
Abe Elias: Yeah, question I… maybe for Dr. Bakowsky, but I realize you might not be able to answer this, but have you had discussions with the Public Health Lab in terms of what the costs, additional costs would be for Utah, and do you have a little bit of an idea what that,

757
02:17:49.959 --> 02:17:55.049
Abe Elias: And also maybe the timeline of the development, and so on.

758
02:17:56.059 --> 02:18:04.989
Josh Bonkowsky: I'm not totally sure. I think it was, like, an incremental cost of $5 to $10 per blood spot, but I could be making that up,

759
02:18:05.409 --> 02:18:10.649
Josh Bonkowsky: And… It seemed like they were intending to…

760
02:18:10.989 --> 02:18:18.369
Josh Bonkowsky: Be testing, like, doing internal testing by this fall, and then…

761

02:18:18.559 --> 02:18:22.729
Josh Bonkowsky: Try and roll out in 2027, once they had gone through the legislative approval process.

762
02:18:25.950 --> 02:18:30.589
Abe Elias: And did you say they are planning to, multiplex it with the XALD?

763
02:18:31.150 --> 02:18:36.279
Josh Bonkowsky: I know they're gonna multiplex it, I couldn't tell you exactly. It's some… something they do in the lab, I don't know…

764
02:18:38.920 --> 02:18:39.950
Abe Elias: Thanks.

765
02:19:07.799 --> 02:19:10.929
Shelly Eagen: Well, thanks, everybody, for the discussion.

766
02:19:11.769 --> 02:19:13.639
Shelly Eagen: Is there anything else?

767
02:19:29.389 --> 02:19:32.089
Shelly Eagen: Alright, that does not look like it.

768
02:19:38.529 --> 02:19:49.769
Shelly Eagen: I just want to say thank you again, Dr. Bronkowski, for joining us and being available to help answer our questions and aid in that discussion. Michaela, are we able to go to public comment early?

769
02:19:51.000 --> 02:20:00.089
Mikaela Miller: Yeah, definitely. I do see we have several members of the public here already, so, we can definitely roll into that.

770
02:20:02.080 --> 02:20:12.219
Mikaela Miller: I'm gonna pull up this slide here again, just to remind everyone how that works. So please raise your hand if you would like to make a comment.

771
02:20:12.620 --> 02:20:30.129
Mikaela Miller: I will call on you and give you permission to come off

of mute. Stephanie is going to go ahead and, start a timer, and we'll give you, like, a mini 45-second warning, but we do want to try to stick to that, because I believe we have a few of you here who may like to share.

772
02:20:30.240 --> 02:20:33.310
Mikaela Miller: So yeah, let's go ahead and start.

773
02:20:43.820 --> 02:20:48.189
Mikaela Miller: If anyone from the public would like to say anything, feel free to raise your hand.

774
02:20:59.930 --> 02:21:00.960
Mikaela Miller: Okay.

775
02:21:01.470 --> 02:21:03.440
Mikaela Miller: Let's see, Sushila.

776
02:21:03.720 --> 02:21:04.730
Mikaela Miller: Go ahead.

777
02:21:04.730 --> 02:21:23.070
Susheela Jayaraman: Yeah, thanks so much. Hi, everyone. My name is Sushila Jayaraman. I'm the Associate Director of Diagnostics and Newborn Screening at Orchard Therapeutics. Really great discussion, I really enjoyed listening in to everyone's comments and the presentations, and I just wanted to add a couple of notes. So, as of today.

778
02:21:23.070 --> 02:21:40.709
Susheela Jayaraman: New York, Pennsylvania, and Illinois are all live with their screening, and a couple of additional states are, actively validating and will be live by the end of the year. And then, as you guys have all mentioned, there are a handful of RESPA-lined states that are at various stages of their implementation.

779
02:21:40.710 --> 02:21:46.299
Susheela Jayaraman: As well as a number of states that have it added, or recommended via their advisory committee.

780
02:21:46.350 --> 02:21:54.889

Susheela Jayaraman: And I also wanted to just note that our gene therapy product has been approved in Europe since 2020.

781
02:21:54.890 --> 02:22:12.440
Susheela Jayaraman: So there's a lot of data about the performance of the newborn screening algorithm, as has been recommended by an international consensus group out of Europe. So, Norway has been screening, nationwide for over a year now, and have, their data,

782
02:22:12.440 --> 02:22:31.470
Susheela Jayaraman: was presented recently at the World Symposium, and then there are two ongoing prospective pilots in Germany and Austria. They've published their first 100,000 screens in the New England Journal, and I believe another publication is, in the works for about 300,000 screens that they've performed.

783
02:22:31.630 --> 02:22:37.049
Susheela Jayaraman: through their, through their pilot study. So, just wanted to flag that, though the U.S. is,

784
02:22:37.360 --> 02:22:45.960
Susheela Jayaraman: in kind of the early stages, a lot of work has been done in Europe, and a lot of data coming out of there, so thanks so much. I'll wrap up there.

785
02:22:50.840 --> 02:22:51.730
Mikaela Miller: Thank you.

786
02:22:56.450 --> 02:23:00.570
Mikaela Miller: Would anyone else from the public like to take a moment to share anything?

787
02:23:15.940 --> 02:23:17.130
Mikaela Miller: Okay.

788
02:23:17.890 --> 02:23:29.990
Mikaela Miller: Well, if anything else does come up, I've got an email on the screen here. You're welcome to submit any additional comments to this email, and we will make sure the committee receives those.

789
02:23:30.090 --> 02:23:32.309

Mikaela Miller: Up to 1 hour after the meeting.

790
02:23:36.260 --> 02:23:55.349
Mikaela Miller: I'm gonna roll into next steps here, so we are going to have all of the follow-up materials posted on our website, and I also will email those individually to all of the committee members, so that includes any notes, recordings, etc.

791
02:23:55.350 --> 02:24:12.780
Mikaela Miller: We also, as you heard, have more meetings coming up here, so, normally we have these meetings twice a year, which means the vote for this condition will be held sometime likely in October, is usually when we have the best responses.

792
02:24:12.830 --> 02:24:24.369
Mikaela Miller: But as mentioned earlier, we're happy to hold an additional, potentially shorter meeting if any new information arises. So I just ask if anyone here

793
02:24:24.540 --> 02:24:45.250
Mikaela Miller: has any new information, please feel free to email the website, or me, or Stephanie, and we can make sure to pass all that information off to the committee as well, just so we can all stay on the same page and keep everyone as informed as possible as kind of things arise here before October.

794
02:24:45.250 --> 02:24:47.990
Mikaela Miller: We do have other conditions…

795
02:24:48.070 --> 02:25:02.339
Mikaela Miller: That have been nominated as well, so our October meeting will also likely be this again for a new condition with an SME and a family presenter, along with that MLD vote. So it will be another, kind of, about 3-hour meeting.

796
02:25:05.470 --> 02:25:23.910
Mikaela Miller: And… we go to the next slide here. So, contact information once again, but I just want to say thank you all so much for being here. I'm going to pass it to Shelly, if you'd like to go ahead and wrap it up. I know we're a little early, but I know you all also probably have

797

02:25:24.150 --> 02:25:27.630
Mikaela Miller: Other responsibilities to get to today?

798
02:25:27.820 --> 02:25:41.500
Shelly Eagen: Yeah, so, first of all, thank you again to Sarah and Cora for joining us and sharing their story, and also to Dr. Bonkowski for joining us and providing us all of the information. A huge welcome again to Rose.

799
02:25:41.500 --> 02:25:54.559
Shelly Eagen: We appreciate you being on, even though it's a very inconvenient time. And then, also a big thank you to Shaunaliyah, for your contributions to the committee, and for everybody who was able to join today.

800
02:25:58.180 --> 02:26:04.829
Shelly Eagen: The meeting survey is in the chat, so please click on that to complete that as well.

801
02:26:08.140 --> 02:26:08.860
Mikaela Miller: Yes.

802
02:26:10.370 --> 02:26:12.129
Mikaela Miller: Alright, thank you, everyone.

803
02:26:14.840 --> 02:26:16.250
Mikaela Miller: Have a good day.

804
02:26:16.420 --> 02:26:18.190
Abe Elias: Yeah, you too. Bye-bye.

805
02:26:19.720 --> 02:26:20.470
Abe Elias: Bye, everyone.

806
02:26:21.100 --> 02:26:22.030
Lynne Wood: See ya!

807
02:26:29.560 --> 02:26:32.959
Mikaela Miller: And Stephanie, I'm gonna go ahead and stop the recording as well.