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Welcome

00:00:55.930 --> 00:01:00.779

Samer Khan (she/her): Hi, everyone. Thank you so much for joining early. We'll get started shortly.

2

00:01:08.770 --> 00:01:10.299

Kevin Horton: Hey, can you guys hear me?

3

00:01:11.640 --> 00:01:12.030

Paul Mehta: Yes.

4

00:01:12.600 --> 00:01:13.290

Kevin Horton: Okay.

5

00:01:15.180 --> 00:01:16.380

Kevin Horton: Hey, Danielle.

6

00:01:18.040 --> 00:01:22.409

Danielle Boyce: Hi, good morning! Good morning, everyone. Good morning in audience.

7

00:01:30.620 --> 00:01:32.640

Danielle Boyce: We'll get started right at 10.

8

00:05:05.300 --> 00:05:08.909

Danielle Boyce: Good morning, everyone. We'll be getting started right at 10.

9

00:05:09.800 --> 00:05:21.340

Danielle Boyce: We will be using the question and answer as a way of communicating, so feel free to use that as questions arise, and we'll be monitoring

10

00:05:21.540 --> 00:05:22.960

Danielle Boyce: your questions?

11

00:05:23.120 --> 00:05:35.569

Danielle Boyce: as we go, and try to make sure we answer all of them. If you're using eye gaze technology or some other assistive device, we have tested it with someone who uses eye gaze technology, but if you're not sure.

12

00:05:35.780 --> 00:05:48.719

Danielle Boyce: Please feel free to, put your, where your location or some other information in that Q&A. It'll only go to the panelists, and we can confirm with you that it worked.

13

00:05:53.030 --> 00:06:02.450

Danielle Boyce: And if for some reason it does not work, we will have an email address that will be monitored. And I'll repeat this at the top of the meeting as well.

14

00:06:02.610 --> 00:06:05.680

Danielle Boyce: And we'll share that email address with you momentarily.

15

00:07:51.940 --> 00:07:58.659

Danielle Boyce: Thank you so much, Lynn. I received your message that your eye gaze is working. I appreciate your confirmation.

16

00:07:59.190 --> 00:08:00.980

Danielle Boyce: And so nice to see you.

17

00:08:30.770 --> 00:08:32.839

Danielle Boyce: Hey, we're gonna get started.

18

00:08:33.380 --> 00:08:44.749

Danielle Boyce: here pretty soon, and I know that some of the participants today, this is your first meeting for the CDC ALS National Registry, so welcome.

19

00:08:45.020 --> 00:09:01.870

Danielle Boyce: We're going to be using the question and answer feature for the webinar to communicate with you, so if you have any questions throughout the meeting, please do not be shy, put them in the Q&A feature. And if you're wondering if you are doing it correctly, please feel free to

20

00:09:02.330 --> 00:09:10.019

Danielle Boyce: Put something in there as a question, even if it's not a question, your location or something like that, and we can confirm that we received it.

21

00:09:12.490 --> 00:09:14.440

Danielle Boyce: We'll get started in about 3 minutes.

22

00:10:41.550 --> 00:10:50.669

Danielle Boyce: Wonderful. I see, Sassy, thank you very much for being here. Confirmed we received your message, and the Q&A works.

23

00:10:51.180 --> 00:10:54.570

Danielle Boyce: And I'm receiving a few others, too, so it looks like it's working.

24

00:10:54.690 --> 00:10:57.110

Danielle Boyce: Good morning, Becky from Philadelphia.

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00:10:59.320 --> 00:11:02.689

Danielle Boyce: I actually have a house outside of Philadelphia in Ambler.

26

00:11:06.060 --> 00:11:12.789

Danielle Boyce: And yes, everyone except the panelists, I believe, are muted and have cameras off.

27

00:11:13.030 --> 00:11:20.429

Danielle Boyce: And so if someone is, a panelist, they're... or presenting, their camera will be on.

28

00:11:21.400 --> 00:11:22.979

Danielle Boyce: Oh, Plymouth meeting.

29

00:11:24.600 --> 00:11:27.140

Danielle Boyce: Hello! Hi, Steven Finger! Hi!

30

00:11:27.940 --> 00:11:29.369

Danielle Boyce: So good to see you!

31

00:11:34.480 --> 00:11:36.070

Danielle Boyce: Alright, it's 10 o'clock.

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00:11:37.220 --> 00:11:39.690

Danielle Boyce: Trying not to be late.

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00:11:40.230 --> 00:11:41.220

Danielle Boyce: Welcome!

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00:11:42.320 --> 00:11:43.939

Danielle Boyce: Welcome, we're,

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00:11:44.130 --> 00:11:53.599

Danielle Boyce: playing a fun exercise, feel free to put your location or say hello in the Q&A, just to confirm that you know how to access that.

36

00:11:55.090 --> 00:12:05.800

Danielle Boyce: And Summer will put an email address that we can use in the chat if you have trouble. If you have technical difficulties, hopefully you'll be able to access an email.

37

00:12:05.930 --> 00:12:21.129

Danielle Boyce: email account and be able to contact us for technical difficulties if you have any. I'm Danielle Boyce. I should introduce myself first. I'm Danielle Boyce. I am the Director of Data Science and Biomedical Informatics at the ALS Therapy Development Institute.

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00:12:21.310 --> 00:12:34.890

Danielle Boyce: And I'm also on faculty in the Biomedical Informatics and Data Science section at Johns Hopkins University School of Medicine, and I am delighted to be the moderator of this meeting.

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00:12:35.050 --> 00:12:40.490

Danielle Boyce: And we have a lot of really exciting speakers here today.

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00:12:40.850 --> 00:12:47.559

Danielle Boyce: Hello, I'm looking at the... I'm looking at the webinar chat here. Good morning. Hey, Lauren.

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00:12:47.660 --> 00:13:02.520

Danielle Boyce: Hi, Becky. And Becky asks, will this recordings for both days be available afterward? There will be a summary that will be distributed, and I think, Paul and team will be able to, to answer that, question, specifically, later.

42

00:13:03.800 --> 00:13:17.609

Danielle Boyce: I'm just looking at the chat here. So I am... I was taught well from the ALS community. I know some of you are using eye gaze technology, really want to make sure that you're able to communicate, so the way we are choosing to do that is through the webinar.

43

00:13:17.940 --> 00:13:19.649

Danielle Boyce: Q&A feature.

44

00:13:21.450 --> 00:13:24.859

Danielle Boyce: So you should be able to ask questions.

45

00:13:24.980 --> 00:13:35.019

Danielle Boyce: And if you're concerned that, that you're not able to do it, let us know. I'm gonna... I'm gonna try to answer all of you. I see someone named Sarah, who has

46

00:13:35.730 --> 00:13:39.729

Danielle Boyce: has indicated she is here, and so I'm confirming that.

47

00:13:40.610 --> 00:13:44.069

Danielle Boyce: So please, just as we wait for people to get settled in.

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00:13:45.540 --> 00:13:47.510

Danielle Boyce: Feel free to test that out.

49

00:13:48.120 --> 00:13:51.950

Danielle Boyce: We have someone joining us from the morning car line.

50

00:13:53.930 --> 00:13:56.999

Danielle Boyce: We have, Carol from ALSTDI.

51

00:13:57.340 --> 00:13:58.430

Danielle Boyce: Hi, Carol.

52

00:13:58.630 --> 00:14:00.729

Danielle Boyce: Eric from North Carolina.

53

00:14:01.510 --> 00:14:03.960

Danielle Boyce: So, people are coming from all over the place.

54

00:14:05.460 --> 00:14:11.289

Danielle Boyce: So, I can give you a brief overview of the next couple of days and what to expect.

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00:14:12.830 --> 00:14:15.130

Danielle Boyce: You should have received an agenda.

56

00:14:15.510 --> 00:14:17.220

Danielle Boyce: In... in an email.

57

00:14:17.410 --> 00:14:31.809

Danielle Boyce: And if you don't have that, let Summer, the host, you should be able to see in the webinar chat, you should be able to reach out to the hosts and panelists and let her know, please, and we can make sure that you have a copy of that.

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00:14:32.240 --> 00:14:34.609

Danielle Boyce: But to summarize, the next...

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00:14:34.770 --> 00:14:47.920

Danielle Boyce: two days, so we're going to be today until, let's see, about 4 p.m, and the same tomorrow, about 10 to 4. And today, we're going to start off with opening remarks from Dr. Bernstein.

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00:14:48.420 --> 00:14:55.469

Danielle Boyce: who is the Director of the National Center for Environmental Health Agency for Toxic Substances and Disease Registry.

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00:14:56.130 --> 00:15:03.449

Danielle Boyce: And then, Dr. Mehta is going to give us an update of the registry, the state of the registry for this year.

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00:15:03.690 --> 00:15:11.120

Danielle Boyce: And then, some presentations from the partners. We'll have representatives from the ALS Association.

63

00:15:11.220 --> 00:15:14.499

Danielle Boyce: We have Les Turner ALS Foundation.

64

00:15:14.610 --> 00:15:19.419

Danielle Boyce: We have Muscular Dystrophy Association and Team Gleason.

65

00:15:20.210 --> 00:15:27.029

Danielle Boyce: And then, Dr. Ostra will be, sharing about the Temple University Post-Mortem Corps Partnership.

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00:15:27.450 --> 00:15:36.630

Danielle Boyce: And then around 1230, we'll have a break for lunch, but while these presentations are going, please do not hesitate to use that webinar Q&A.

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00:15:37.210 --> 00:15:39.979

Danielle Boyce: And we would be,

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00:15:40.200 --> 00:15:49.849

Danielle Boyce: happy to answer questions. If they're appropriate to answer live, we'll do that. We can save them for our presenters and group them up later. We want to make sure all of your questions are answered.

69

00:15:51.200 --> 00:15:53.929

Danielle Boyce: And then after lunch, at 1.30,

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00:15:54.610 --> 00:16:02.209

Danielle Boyce: We will have, some talks about the, ALS registry-funded research presentations. Well, here we go.

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00:16:02.860 --> 00:16:12.269

Danielle Boyce: Perfect. So we will have, interactions between the microbiome, metabolome, and immune system. That would be, University of Michigan.

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00:16:13.160 --> 00:16:31.549

Danielle Boyce: And then we are going to have a presentation by Dr. Fernando Vieira at ALS Therapy Development Institute, my co-PI on that project, talking about our risk factor study. Then Dr. Mark Weisskopf will be speaking about military exposures.

73

00:16:31.610 --> 00:16:38.390

Danielle Boyce: And Dr. Goutman, representing University of Michigan, again, Occupational Risk and Prevention Studies.

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00:16:38.480 --> 00:16:39.800

Danielle Boyce: for ALS,

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00:16:40.290 --> 00:17:05.160

Danielle Boyce: And then finally, before we close for the end of the day, we'll have some discussion at the very end to kind of catch up with some of those questions that you might have, and talk about some key points that we learned along the way. But before that, we will have representation from Xing Song from University of Missouri Columbia. Really interesting. I'm interested in this because I'm an informaticist, so in particular, I'm very interested in this.

76

00:17:05.160 --> 00:17:10.250

Danielle Boyce: Multimodal, database, for multi, marker discovery.

77

00:17:10.250 --> 00:17:11.430

Danielle Boyce: In ALS.

78

00:17:11.750 --> 00:17:21.980

Danielle Boyce: So that's day one, and then we'll have some Q&A, and if there's anything that carries over between day one and day two, we will be sure to catalog all of your questions.

79

00:17:22.270 --> 00:17:26.340

Danielle Boyce: And, and, try to have them answered, tomorrow at some point.

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00:17:26.960 --> 00:17:29.469

Danielle Boyce: Or reach out to you directly, if that's appropriate.

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00:17:30.150 --> 00:17:38.470

Danielle Boyce: Yeah, so attendees, as this slideshow, attendees are in listen-only mode without audio or video capabilities, so if you have questions, just go ahead and put them in the Q&A.

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00:17:38.780 --> 00:17:51.790

Danielle Boyce: And, if you're a panelist, please mute yourself when you're not presenting. I know I always need a reminder for that. And we can always remind you as well. And the meeting is recorded for purposes of transcription only.

83

00:17:51.840 --> 00:18:07.630

Danielle Boyce: Oh, here we go, and so if you're having any technical issues, please email als at cdc.gov. My concern was this, if you're using eye gaze technology, even though we did test this previously to make sure someone using eye gaze would be able to participate in the Q&A,

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00:18:07.630 --> 00:18:17.910

Danielle Boyce: for whatever reason, if you have trouble doing that, if you're a person living with ALS, and you need to use the eye gaze technology to communicate, my fear was that you wouldn't have a way to tell us that.

85

00:18:17.910 --> 00:18:19.989

Danielle Boyce: If the Q&A doesn't work.

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00:18:19.990 --> 00:18:31.809

Danielle Boyce: So, we have this email address that you can use that will be monitored today, so if you have any problems at all, please use that email if you can, and we would be glad to follow up with you.

87

00:18:32.880 --> 00:18:37.770

Danielle Boyce: So then tomorrow, we're, we're going to start again,

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00:18:38.430 --> 00:18:47.079

Danielle Boyce: Zoom sign in at 945, and we'll kick off at 10, and I'll make some welcome remarks at that time, and we'll do some... some technical checks.

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00:18:47.180 --> 00:18:59.890

Danielle Boyce: And then we're going to have another set of presentations for ALS registry-funded research presentations, and then we'll break for lunch at 1215.

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00:19:00.640 --> 00:19:02.539

Danielle Boyce: And I will review all of the...

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00:19:02.670 --> 00:19:11.759

Danielle Boyce: the presentations, ahead of time tomorrow, just like I did today with today's presentations. And then we'll break for lunch around 12.15, come back around 1.30,

92

00:19:12.080 --> 00:19:19.300

Danielle Boyce: And then the National ALS Registry and ALS Association will talk about their incentives pilot project.

93

00:19:19.770 --> 00:19:37.169

Danielle Boyce: And then, a very important, very, to me, very meaningful presentation, will be at 2 p.m. Eastern, and that is Living with ALS Testimonies from Patients and Caregivers, people living with ALS, and caregivers, and so we have a really great panel set up.

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00:19:37.170 --> 00:19:55.340

Danielle Boyce: Tomorrow, and... and you'll have an opportunity for Q&A. So, sometimes we don't stay for the whole meeting after the science ends, but I really encourage you to stay for the full meeting, because to me, this is where I learn the most, when people with lived experience talk about their experiences interacting with the research.

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00:19:55.340 --> 00:20:10.339

Danielle Boyce: systems, interacting with the registry, but also the ecosystem at large, talking about their experiences in clinic, giving us ideas as to how to improve recruitment and retention in studies, telling us what research questions matter to them.

96

00:20:10.560 --> 00:20:16.039

Danielle Boyce: And so I think that's going to be really valuable for anyone in this ecosystem working in research.

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00:20:17.680 --> 00:20:21.049

Danielle Boyce: Alright, so I'm checking the chat again, the questions.

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00:20:21.270 --> 00:20:24.250

Danielle Boyce: Let's see, mice... Let's see...

99

00:20:27.880 --> 00:20:33.549

Danielle Boyce: All right, so some people are saying that the Zoom overview is kind of stuck, and it's not showing.

100

00:20:33.550 --> 00:20:33.990

Samer Khan (she/her): two of these.

101

00:20:33.990 --> 00:20:37.140

Danielle Boyce: agenda. Yeah, I'm not seeing that either.

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00:20:37.140 --> 00:20:41.510

Samer Khan (she/her): Yeah, the Day 2 agenda will be shown tomorrow. Okay, yeah.

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00:20:41.720 --> 00:20:44.070

Danielle Boyce: So that's... there's nothing... yeah.

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00:20:44.070 --> 00:20:44.650

Samer Khan (she/her): Yeah.

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00:20:44.650 --> 00:21:00.429

Danielle Boyce: Somebody's asking, will both days be available afterwards? I think somebody from the CDC might want to comment on how that works, but I believe there's going to be a transcript, but we're... they can't release a recording because there might be unpublished, research. Is that... is that right?

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00:21:01.050 --> 00:21:10.279

Paul Mehta: Yeah, typically what we do is we'll go ahead and have a transcript. We don't typically release the video, it's just used for internal purposes, just to do the recording itself.

107

00:21:12.680 --> 00:21:13.500

Danielle Boyce: Okay.

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00:21:14.200 --> 00:21:20.699

Danielle Boyce: So I'm just going to check a few more questions, and then if, Dr. Bernstein doesn't mind going a little early.

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00:21:21.090 --> 00:21:25.490

Danielle Boyce: We will be, ready to start, with your presentation.

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00:21:28.090 --> 00:21:31.720

Danielle Boyce: That's okay. Okay, I'm just gonna... just gonna...

111

00:21:31.920 --> 00:21:36.590

Danielle Boyce: monitor the chat just a little bit more, check my Q&As.

112

00:21:36.860 --> 00:21:40.509

Danielle Boyce: I don't want to miss anything. Okay, looks like we're good.

113

00:21:41.020 --> 00:21:42.429

Danielle Boyce: Very good.

114

00:21:45.400 --> 00:21:46.500

Danielle Boyce: Very good.

115

00:21:46.680 --> 00:21:48.079

Danielle Boyce: Thank you so much.

Opening Remarks - Dr. Aaron Bernstein

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00:21:48.280 --> 00:21:53.910

Dr. Aaron Bernstein: Thank you, Danielle, and... Pleasure to be with you all again this year.

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00:21:54.060 --> 00:21:59.990

Dr. Aaron Bernstein: I'm Ari Bernstein, I direct ATSDR and the National Center for Environmental Health at CDC.

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00:22:00.080 --> 00:22:16.360

Dr. Aaron Bernstein: And I am as excited as ever to be with you today for the annual ALS registry meeting. I want to be sure to thank a bunch of folks who helped get us together for this long-awaited meeting.

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00:22:16.420 --> 00:22:22.149

Dr. Aaron Bernstein: Particularly our ATSDR team, Kevin, Paul, Jamie, and Ted, among many others.

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00:22:22.150 --> 00:22:39.710

Dr. Aaron Bernstein: Danielle, I want to extend a specific thanks to you for once again serving as our moderator. I think you're in your second year. I think everyone here can recognize just from her opening remarks that she is a full-fledged, card-carrying member of the ALS community.

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00:22:39.850 --> 00:22:50.749

Dr. Aaron Bernstein: There are probably fewer than 6 degrees of separation to her in that community, and we are so fortunate to have her, because of that,

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00:22:50.820 --> 00:23:01.100

Dr. Aaron Bernstein: close-knit fabric that you are a great part of, Danielle, to lead us through our meeting. So, thank you so much.

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00:23:01.470 --> 00:23:17.169

Dr. Aaron Bernstein: As we all know, the ALS registry is a landmark public health initiative, which is really designed to support scientists in the United States, as well as around the world.

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00:23:17.550 --> 00:23:28.010

Dr. Aaron Bernstein: To better understand the disease, so that we can find better treatments, and of course, ideally, hopefully one day prevent the disease altogether.

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00:23:28.260 --> 00:23:41.389

Dr. Aaron Bernstein: Since the last time we met, we've learned a lot, and I keep tabs on the science here, and it's encouraging. It's obviously not where we want to be.

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00:23:41.390 --> 00:23:49.899

Dr. Aaron Bernstein: Ideally, but there is progress, over and over again, I'm excited by what I see in the trajectory we're headed in.

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00:23:50.240 --> 00:24:02.619

Dr. Aaron Bernstein: Danielle gave a really great overview of both the who and the what of what will be presented over the next few days that will cover a good amount of those discoveries, and of course, I would underscore

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00:24:02.650 --> 00:24:13.730

Dr. Aaron Bernstein: what Danielle mentioned about the need to think, beyond discovery. I know as a, as a pediatrician that so much of both

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00:24:13.880 --> 00:24:18.929

Dr. Aaron Bernstein: The treatment and prevention of disease has to do with the community around the people who

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00:24:18.970 --> 00:24:34.190

Dr. Aaron Bernstein: are affected, and so I'm very grateful that we have time dedicated to hear from those voices. I do want to take just a moment to highlight some of the things Danielle spoke to

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00:24:34.860 --> 00:24:42.000

Dr. Aaron Bernstein: primarily because, as she did, I want to make sure people don't miss some key, key things.

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00:24:42.100 --> 00:24:59.149

Dr. Aaron Bernstein: The first, of course, is that I want to make sure everyone knows there'll be an opportunity to hear directly from our ATSDR ALS team about what's been going on with the registry, the recent research findings and publications, as well as new partnerships, and you'll have opportunities to ask questions of our team.

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00:24:59.150 --> 00:25:13.859

Dr. Aaron Bernstein: As Danielle mentioned, we'll hear from grantees of the registry and the work they've been up to. There are a suite of new initiatives that have been launched since the last time we met.

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00:25:13.930 --> 00:25:27.500

Dr. Aaron Bernstein: There are new research grants, there's the biopository, biorepository Partnership with Temple. There's even a project in Texas, a pilot project, to encourage greater participation in the registry.

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00:25:28.100 --> 00:25:36.210

Dr. Aaron Bernstein: As per usual, we'll hear from the ALS organizations that are partners of the registry, learn about their work.

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00:25:36.370 --> 00:25:41.360

Dr. Aaron Bernstein: And, of course, from people living with ALS,

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00:25:41.420 --> 00:25:58.440

Dr. Aaron Bernstein: And I, you know, think the who here is often as important as the what. I'm always encouraged when we bring together, people who are studying a disease, with the people living with a disease, and,

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00:25:58.600 --> 00:26:02.900

Dr. Aaron Bernstein: There's no question that we all benefit when that happens.

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00:26:05.540 --> 00:26:22.259

Dr. Aaron Bernstein: We'll be sure to give the latest data we have about ALS epidemiology, the current state of affairs, where we think incidents and prevalence may be in a decade or less than a decade off.

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00:26:22.610 --> 00:26:26.060

Dr. Aaron Bernstein: And so there's plenty to cover.

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00:26:26.170 --> 00:26:41.129

Dr. Aaron Bernstein: And so, before I dive in, I want to emphasize, as I do each year, that the success of the registry in reaching its goals really depends on the collaborative spirit that's embodied here among us all.

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00:26:41.340 --> 00:26:53.000

Dr. Aaron Bernstein: The people living with ALS are very much at the center of that. They're caregivers, the clinicians who care for them, the researchers who are studying how the disease may

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00:26:53.000 --> 00:27:02.279

Dr. Aaron Bernstein: may occur, as well as how we can better treat it. The organizations that advocate for research and care of

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00:27:02.280 --> 00:27:09.010

Dr. Aaron Bernstein: people with ALS and the broader communities that surround people with ALS.

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00:27:10.880 --> 00:27:18.830

Dr. Aaron Bernstein: The success here depends on all of us, and that means every step we take forward is a success.

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00:27:18.940 --> 00:27:37.579

Dr. Aaron Bernstein: that can be reflected in each of us. And so I'm really deeply grateful that you all are here for this meeting. I am grateful for the work that you continue to do in this arena. Please do share your thoughts, questions, and feedback throughout the meeting, and of course, beyond.

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00:27:37.620 --> 00:27:43.870

Dr. Aaron Bernstein: As we work together, to ensure the registry's, continued success.

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00:27:44.010 --> 00:27:47.130

Dr. Aaron Bernstein: To evolve it and, improve it.

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00:27:47.290 --> 00:27:52.899

Dr. Aaron Bernstein: So, welcome, to the 2026 National ALS Registry Meeting.

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00:27:53.140 --> 00:27:58.260

Dr. Aaron Bernstein: Thanks for being here, and I will turn it back to Danielle. Thanks again.

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00:27:59.070 --> 00:28:10.899

Danielle Boyce: Thank you so much, Dr. Bernstein, and thank you for your kind words. I love working and being in the ALS community so much, and I hope it comes across in the next few days.

152

00:28:11.160 --> 00:28:18.010

Danielle Boyce: Okay, so next up, is, the... is a presentation by Paul Mehta.

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00:28:18.130 --> 00:28:26.660

Danielle Boyce: He's going to give the National ALS Registry update. Dr. Mehta is the principal investigator of the National ALS Registry.

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00:28:26.660 --> 00:28:44.090

Danielle Boyce: Registries and surveillance section at OIA, Agency for Toxic Substances and Disease Registry. And so, Dr. Mehta oversees the registry and all of its programs, and so if you have questions about the registry, he's the one you ask. So, please take it from here, Dr. Mehta.

National ALS Registry Update - Paul Mehta, MD

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00:28:44.660 --> 00:29:09.610

Paul Mehta: Thank you, Danielle, and thank you for hosting, and thank you, Dr. Bernstein, for your opening remarks. Once again, thank you, everyone, for joining. First, I want to apologize, we wanted to have this meeting last October, but there was a government shutdown, which actually ended up pushing everything back, and then we were trying to do it in late fall, or sorry, late winter. That also was not possible due to reasons of logistics, but thank you for your patience, and thank you for joining us

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00:29:09.610 --> 00:29:11.520

Paul Mehta: for the, 2026 meeting.

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00:29:11.520 --> 00:29:13.020

Paul Mehta: Next slide, please.

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00:29:15.750 --> 00:29:18.790

Paul Mehta: I've got no disclosures. Next slide, please.

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00:29:19.240 --> 00:29:34.249

Paul Mehta: So this is the, outline of the presentation. Gonna be talking about the Act, how we came here, as in terms of our foundation and so forth, and what we do, our purpose, our mission, and so forth. We'll talk about the publications and the research findings from ourselves, as well as our partners.

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Paul Mehta: We'll also talk about our resources that we currently have and those updates, one being the notification system, as well as the National Analyst Biorepository.

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Paul Mehta: We'll talk about the enhancements the registry is going to be doing in the future, as well as the public engagement sessions that we have done, and you'll be hearing from these individuals living with ALS today and tomorrow as well, as well as talking about the funded research we do, an overview, as well as the impact of the registry. Next slide, please.

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00:30:05.170 --> 00:30:29.530

Paul Mehta: So, just kind of talking about where we came from. So, the registry was launched back in October 2010. This October will be 16 years of the registry. I've been very, very blessed to be part of, 13 years with the registry as of October 1st, so this is certainly a very, very important endeavor. So, we have a multifold purpose in the registry. We do a lot more than just count ALS cases, like I like to say. We look at the,

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00:30:29.530 --> 00:30:35.869

Paul Mehta: Epidemiology of ALS, incidence, prevalence, mortality, who gets the disease, demographics of disease itself.

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00:30:35.870 --> 00:31:00.830

Paul Mehta: And also, very importantly, to figure out exactly what causes ALS, the risk factors and the etiologies. We currently have over 21,000 enrolled individuals since we started back in October 2010, so this actually is probably the largest ALS registry in the world. I don't know of any other registry out there, domestically or even in Europe, that has this many individuals who actually participated. And I'd also like to say the registry

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00:31:00.830 --> 00:31:07.280

Paul Mehta: is of buying those, living with ALS. I mean, it is, it is for those individuals. Next slide, please.

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00:31:09.530 --> 00:31:10.489

Paul Mehta: So, I'm gonna...

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00:31:10.640 --> 00:31:34.420

Paul Mehta: jump into the findings that we're talking about, and these are just kind of, like, very, very high-level overview findings. All these publications can be found, and a lot of them will be actually discuss today and tomorrow by our funded grantees as well. So what

I'm going to be giving you is just a very, very highlight overview of the findings that we've actually come across, and we've actually published, since 2025, as well as 2026.

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00:31:34.420 --> 00:31:41.950

Paul Mehta: One of the most important ones was, looking at the actual number of cases from 2022 to 20... through 2030.

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Paul Mehta: And so we wanted to go ahead and have it kind of like a projection of number of cases, that we feel will be, will be coming forth in the future. So what we actually found was, from 2020 to 2030, we're looking at actually an increase of probably 10% number of cases. So what that means is, in 2022, there's about 36,000 cases, I'm sorry, 32,000 cases in 2022,

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00:32:04.920 --> 00:32:29.330

Paul Mehta: And this will increase to 36,000 cases by 2030. We'll also release projections for 2030 to 2035 as well in the near future, and that will also, you know, as in terms of an increase as well, we'll be seeing that too. And the reason why we're seeing these increases is because of the fact that the population is aging. So as the population is aging, individuals are getting ALS. So therefore, the prevalence will be increasing.

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Paul Mehta: Next slide, please.

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00:32:34.470 --> 00:32:58.459

Paul Mehta: The other finding we actually... was just published, actually, just a few days ago, was looking at mortality. So, MND mortality in the U.S. from 2010 to 2023. It looks at the demographics, the geographic, and the temporal analysis of ALS. And this... the objective, like I mentioned, was looking at the MND, and MND typically... when it comes to MND, about 80% or more of the cases of ALS, which encompass MND, are actually ALS cases, so...

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00:32:58.460 --> 00:33:23.289

Paul Mehta: motor neuron disease, ALS, encompasses, like I said, over 80% of that, that fraction right there. And so what we found right here, we found the overall national MND mortality to be about 2.07 per 100,000 per population. The rates were highest in those who were 80 and above, as well as non-Hispanics, as well as males. The states which are located in the northern part of the country have the highest rates

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00:33:23.510 --> 00:33:33.750

Paul Mehta: As well as compared to the mid-tier states. And the states ranged from 3.07 in Vermont to 1.41 in Hawaii when it came to mortality.

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00:33:33.890 --> 00:33:50.719

Paul Mehta: These actually kind of, it's kind of interesting. So we also published incidence at the state level, as well as prevalence at the state level, and so this is very similar as in terms of the findings, where we're looking at a north-to-south gradient, both in mortality, as well as in incidence, as well as in prevalence as well. Next slide, please.

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00:33:53.030 --> 00:34:08.829

Paul Mehta: So, moving over to different topics, so we also published, some works regarding head injury and ALS, and so this is also data from the registry itself. And we looked at, life... we examined lifetime head injuries among those individuals in the registry itself.

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Paul Mehta: And it was a cross-sectional analysis of over 3,000 individuals, and almost 57% experienced a head injury. And what we found was head injuries occurring in childhood and early adulthood, actually increased the odds of getting ALS later in life, so it was in terms of being diagnosed before the age of 60.

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00:34:26.139 --> 00:34:50.279

Paul Mehta: So those individuals having a head injury in childhood and early adulthood, it, from our findings, increased the odds of being diagnosed before the age of 60. So that certainly is really, really interesting, and more research has to be done in that area, because when it comes to head injuries, we're seeing a lot of this, kind of like in the media. There's a player from the Tennessee Titans who was recently diagnosed with ALS as well, and so this kind of...

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00:34:50.280 --> 00:34:58.270

Paul Mehta: you know, comes about, I mean, is there something related to head injuries in sports, or some other areas as well? So it's certainly very, very interesting, and definitely more research has to be done.

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Paul Mehta: The other area I mentioned just briefly, momentarily, was the fact that we also looked at incidents of all 50 states in the U.S. This is the first time we actually have done incidents in the U.S, and so what we found was, as in terms of geographic variations in the U.S, so the rates ranged from .65 per 100,000 in Alaska to 2.25 in Vermont.

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00:35:22.010 --> 00:35:34.189

Paul Mehta: With the overall instance being 1.44 per 100,000. Once again, New England and the Upper Midwest, so the northern part of the U.S, had higher incidence rates than the, than the southern portions of the country.

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00:35:34.190 --> 00:35:35.800

Paul Mehta: Next slide, please.

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00:35:37.880 --> 00:35:45.939

Paul Mehta: We also looked at, place of death in patients with MND and associated comorbidities during, the pandemic.

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00:35:45.940 --> 00:36:10.919

Paul Mehta: And this is also data from the registry as well. And so we went ahead and looked at places of death among patients with MND during the COVID-19 pandemic. And what we found was MND deaths actually at home increased 54% versus 45% pre-COVID. So we're not sure exactly why that was occurring. It could be access to care, it could be a lot of other stuff happening as well, so certainly there are some areas of concern there, which we're

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00:36:10.920 --> 00:36:18.429

Paul Mehta: happening when you have reduced access of care, you can certainly, you know, portend a poorer prognosis of those individuals at home.

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00:36:18.460 --> 00:36:35.729

Paul Mehta: And we also saw an increase in diabetes as well, as opposed to those who were, you know, during the pre-pandemic and so forth. So it's certainly very interesting, like I mentioned, the fact that, I mean, this particular event, which affected the entire globe, also impacted ALS patients as well.

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Paul Mehta: The other thing we also looked at was the diagnostic difference between military veterans and non-veterans, and these are also data from the National ALS Registry.

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Paul Mehta: And from here, we compared diagnostic characteristics between military vets and non-vets who enrolled in the registry. And what we found were veterans were older and reported longer intervals from symptom onset to ALS diagnosis.

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00:36:56.040 --> 00:37:19.040

Paul Mehta: They're also more likely to report difficulty swallowing, as well as having falls, as well as use of non-invasive breathing equipment, too. So, like I said, I mean, before, when it comes to access to care, this could also be an access to care with the veteran population as well. So there's differences as in terms of those who get their care through the VA, as opposed to not going to the VA as well. So it's certainly really interesting findings that we're seeing.

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Paul Mehta: Next slide, please.

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Paul Mehta: The other, work we were... we did was, comparison of demographics, so these were also data from the registry and clinical trials data. So, this is actually the PROACT database, which is a very, very large, ALS clinical trials database, so we actually went ahead and compared our data set, to PROACT. And PROACT's been around for a long, long time. It's kind of like a, like a...

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00:37:47.240 --> 00:37:56.009

Paul Mehta: like I mentioned, a pooled resource of open access, so what happens is from clinical trials, when they're occurring or when they're over, they'll go ahead and give their data voluntarily into the PROACT database.

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Paul Mehta: And so what we found was a greater percentage of younger individuals

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Paul Mehta: But a smaller percentage of older individuals, were represented in Proact when compared to the registry itself, so that's certainly interesting. When it comes to enrollment for minority races, that was greater in the registry than the actual PROACT data.

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00:38:15.030 --> 00:38:38.760

Paul Mehta: We also found some differences in age distribution, as well as, like I mentioned, minority representation, both in PRO Act, as well as the registry populations. So, the registry historically has always been a higher socioeconomic demographic group, so the fact that we were a little bit more diverse than Proact certainly is very interesting. The other stuff we looked at was metal-induced genotoxic

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00:38:38.760 --> 00:39:03.720

Paul Mehta: events, and looking for possible distinction between sporadic and familial ALS. That certainly was a very interesting finding. These were also done internally as well. And so, we looked at the evidence linking environmental metal exposure to ALS, as well as looking at, for example, genotoxicity as well. So, what we found was, in familial ALS, metal exposures may worsen the effect of inherited mutations

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00:39:03.720 --> 00:39:18.279

Paul Mehta: And sporadic ALS environmental exposures may actually play a larger role in initiating disease processes in individuals who are more susceptible. So this certainly was a... like I said, I mean, it's a very, very high-level report, so I definitely would,

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00:39:18.280 --> 00:39:25.079

Paul Mehta: you know, read the actual article itself for a much more deeper dive on exactly what we found. Next slide, please.

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00:39:27.200 --> 00:39:50.890

Paul Mehta: So another thing we looked at, and this was through our funded colleagues at the University of Michigan, and Dr. Petal, I believe, will be presenting today or tomorrow on these particular findings, or similar. So, University of Michigan looked at air pollution and disease progression, and so this is certainly interesting. They looked at over 500... nearly 500 people with ALS for about 15 years to see whether air pollution affected how

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00:39:50.890 --> 00:40:15.540

Paul Mehta: the disease progressed. And what they found was that people with higher long-term exposure to certain types of air pollution, especially black carbon from traffic, as well as nitrate pollution linked to agriculture, tend to lose their functional... their physical

function faster, as well as with lower exposure levels, too. So this actually may suggest that air pollutants may actually worsen ALS progression. So which certainly, obviously, is something that can be mitigated

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00:40:15.540 --> 00:40:29.570

Paul Mehta: By reducing pollution levels and so forth in this particular cohort. The other one is, the... what's the University of Michigan? Again, looking at, the exposure to cyanobacteria and ALS. Cyanobacteria's been around for a long time. It's been one of those,

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00:40:29.930 --> 00:40:54.859

Paul Mehta: research topics, it always kind of pops up, and we actually, you know, we encourage funding in cyanobacteria because it is pretty, you know, as in terms of bodies of water, it can be found there, and if the exposure is occurring, it can also be mitigated as well. But what the group at University of Michigan found, they found a connection between living near harmful algal blooms and a reduced life expectancy. That certainly is very interesting, as well as also very worrisome as well.

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00:40:55.120 --> 00:41:09.110

Paul Mehta: And those individuals with ALS living within 5 kilometers, of a harmful algal bloom, had a shorter survival. So that's certainly also interesting, too. And that exposure, translated into actually .89 years of shorter survival.

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Paul Mehta: Next slide, please.

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Paul Mehta: Moving along, this is also University of Michigan... I'm sorry, this is, I'm sorry,

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00:41:17.410 --> 00:41:42.400

Paul Mehta: Karolinska Group. Sorry, my apologies, I think the PI is wrong right there, but this is Karolinska Group out of Stockholm, Sweden, and they'll be presenting as well. And what they looked at, was the association between cardiometabolic diseases and risk and progression of MND in Sweden. So, just to kind of quickly step back, Sweden is a very, very robust healthcare infrastructure, and you'll probably learn more about it when they actually present.

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Paul Mehta: And that certainly is very interesting because they're... they have tons of data, a lot more data than certainly what we have in a fragmented healthcare system. In Sweden, you can actually look at and measure individuals from the time they're probably born to the time when they pass away from all the data they actually collect.

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Paul Mehta: So that's very, very interesting. So, and what they found was, when they looked up these cardiometabolic disease and how it influences ALS risk and progression, they found that,

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Paul Mehta: that they were not associated with increased ALS risk, while type 2 diabetes and hypercholesterolemia were associated with lower risk.

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Paul Mehta: So, we've also seen reports and research on where those with type 2 or those who have a higher BMI tend to be a little bit more protective of ALS, so certainly that's very interesting when it comes to looking at the cardiac health as well as the BMI health and status of individuals with ALS.

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00:42:34.910 --> 00:42:53.090

Paul Mehta: The other one we funded was through Dartmouth College, and that looked at both GWAS as well as TWAS to look... to better understand the genetic risk factors of ALS. And this was from a population group study of 435 ALS cases in northern New England as well as Ohio.

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00:42:53.090 --> 00:43:01.319

Paul Mehta: And what they actually found was a missense variant of the TDP gene itself. So that certainly is very interesting. Next slide, please.

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00:43:04.710 --> 00:43:29.380

Paul Mehta: So, this is looking at the pending publications we currently have. So, you know, we're a small group, but we're actually a very, very active group. We actually do a lot of publications. Last year, I think we had, I think, over 10 publications from the team itself. So these are some of the works we're currently working on. The instance of ALS in the veteran population, is currently with a journal. And so just kind of stepping back, there's been more

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Paul Mehta: discussion among Congress to have the registry and the VA have a closer partnership when it comes to looking at the veteran population to see exactly what risk factors are impacting them. Those who are vets get ALS at pretty much... or they're at risk, at double the risk of getting ALS than those who are non-veterans, and that certainly is very concerning. So we're kind of, like, also, like I mentioned, not pivoting, but also

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Paul Mehta: going to be expanding and looking at the veteran population. And some of these other publications I'm going to mention, they also look at the veteran population, too.

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00:44:02.350 --> 00:44:15.460

Paul Mehta: There's also a publication that will be presented by the AILA Association, as well as our colleague Rashma Pajani, looking at the monetary incentives, of those individuals. So we gave them a small,

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Paul Mehta: monetary to actually register, as well as to take the surveys, and what we found was actually very, very encouraging, exactly, as in terms of the return of investment and the number of individuals who actually registered. So that was very interesting. And our colleague Moon Han is also looking at the prevalence of a gene variant in ALS, and so, this is really interesting, working with Dr. Brian Traynor at the NIH regarding this particular analysis, and we'll be publishing that as well.

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00:44:40.970 --> 00:45:04.420

Paul Mehta: Also looking at military survival, military service and survival among persons with ALS, and that is with the journal right now. The next one, the multidisciplinary Clinic Attendance and Patterns of Care, was just actually published just, just yesterday. That's with ALS FTD, and, we can go ahead and give you the actual link, in the chat, and I'll go ahead and send that out momentarily after my talk.

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00:45:04.420 --> 00:45:09.059

Paul Mehta: So you can actually have that particular article, but that was actually just published, yesterday.

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Paul Mehta: The other one we're looking at is occupational exposures to rodenticide and the survival.

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Paul Mehta: As well as looking at smoking as the effect modifier, between, military service and so forth. So that's certainly really interesting stuff that we're currently doing, and we're looking forward to getting these published, as well.

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Paul Mehta: Another one where we were looking at was looking at the actual clinical comparison and demographic characteristics of ALS in the cohort in Hawaii. So the Hawaiian cohort actually tends to be a little bit more ethnically diverse, and so we wanted to kind of do a demographic comparison exactly, you know, looking at our registry data, as well as those in Hawaii to see exactly, to kind of compare and contrast

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Paul Mehta: we are seeing. We're also, looking at, geographic clustering, in Virginia. So last year, or this year, we actually got a request from Virginia regarding number of ALS cases that they were seeing, and so we actually went to Virginia, got their data, had a discussion with the local health department, so this is really interesting. This will be the first time we're actually publishing,

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00:46:15.430 --> 00:46:26.670

Paul Mehta: data on a possible... when it comes to ALS clusters in a state such as Virginia or any other state. So this is very, very interesting findings that we have. Next slide, please.

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00:46:29.090 --> 00:46:39.059

Paul Mehta: So, a pivoting, topic, so the, research notification mechanism, that's been, doing very well. We currently have, over 85 organizations have actually used it.

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Paul Mehta: And this includes a lot of,

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Paul Mehta: Pharma companies and so forth. The Healy Platform trial, which has been one of the largest trials run by MGH, and it's modeled after the cancer trials, is also using our system to kind of go ahead and get the word out to ALS patients as well.

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Paul Mehta: We're also working for the Act for ALS group, Dr. James Berry and Dr. Robert Bowser. That's the ALS Research Consortium. They're actually... we actually partner with them to help, increase awareness for their research consortium, and so that's really one of our ways to partner with, that particular group, and that's funded by the NIH. We're also working with, Perlenia to kind of go ahead and get their, the word out regarding their Phase III

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00:47:20.130 --> 00:47:42.849

Paul Mehta: clinical trial for predapine, and that certainly is really interesting. We also had a request from Neuralink, and Neuralink is using a brain-computer interface, so, which is really, really cutting-edge technology, using BCI to see exactly if that could potentially help and improve the daily living of those with ALS. And there's also other ones we were working on, looking at decision

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Paul Mehta: factors in Medicare enrollment for those living with ALS.

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Paul Mehta: Next slide, please.

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00:47:49.880 --> 00:48:13.689

Paul Mehta: So, regarding the biorepository update, so I just want to let you guys know, last year, we were not able to get the biorepository contract funded, and there was a lot of reasons for that, which I don't need to go into. But that, right now, the biorepository is currently on hold. We're waiting for the contract to be released, so we can have vendors go ahead and bid on it for the upcoming funding cycle.

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Paul Mehta: So, but even that, we're, we're still actively, taking requests, and we're kind of, like, putting those aside, for future release of specimens and so forth. But, but so that's one of our major, areas for, for, for our, in terms of getting the biorepository funded and getting it up and running again. But this was, unfortunately, we are currently on a hiatus with the biorepository.

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Paul Mehta: But like I said, regardless, we are still answering a lot of emails from researchers, probably 2 or 3 on a weekly basis regarding specimens and so forth. And... but fortunately, our colleagues at Temple University, they were recently funded, or will be funded very soon, and they help augment the biorepository with their samples as well, and Dr. Lyle Ostro

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Paul Mehta: We'll be talking about that as well. But some of the areas that, you know, so since, October 2024 and through, August, 2025, so the biorepository,

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00:49:08.260 --> 00:49:28.589

Paul Mehta: was kind of put in suspense, as of October 1st, of last year, so 2025, so we... so August 31st is kind of like the last date when we kind of cut off for applications and so forth. Like I mentioned, a lot of the, requests we're getting are for biomarkers, as well as different sorts of areas they want to look at.

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00:49:28.590 --> 00:49:43.430

Paul Mehta: and so forth. A lot of the omics are certainly very, very popular as well, and the requested samples are PBMCs, plasma RNA, CIRM, and so forth. And so, this is certainly, like I said, I mean, you know, we are currently in suspense, but we're looking to go ahead and get started very soon again.

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Paul Mehta: Next slide, please.

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Paul Mehta: And so these are some of the enhancements we are currently in discussion, and so what we want to do is certainly, you know, make the registry more robust.

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Paul Mehta: And certainly, talking about the incentivized program that... which will be presented today by the ALS Association, that certainly is really important. If this is something which is, you know, the return of investment is there, and we want to go and, you know, roll this out in other states, that certainly is a possibility. Texas was the one that we actually was the pilot state, and this discussion, having this done not only in Texas, but other states such as, let's say, California.

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Paul Mehta: in New York and Florida.

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Paul Mehta: And so that's certainly really, really interesting. We're also looking to potentially, add juvenile ALS. Those would be cases under the age of 18, as well as genetic carriers and controls as well.

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Paul Mehta: It would require additional funding as well. The genetic carriers, we're actually, working with, and the legacy, Jean Swidler, and so forth. We actually talked to her and got her input as well, and so forth, this way, because she's a carrier, and so she's very, very passionate about what she's doing and so forth, and so we want to kind of get their input as well. We also want to restart post-mortem collections within a couple years. That certainly is really important for us to start doing post-mortem

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00:50:58.080 --> 00:51:16.539

Paul Mehta: again, post-mortems are very, very, very, very valuable for researchers, the tissue, the CSF, and so forth, and we want to go ahead and resume that. We currently have close to 60 who've already done post-mortem, but we want to go in and obviously increase that number with the new, with the new contract action the next couple of years.

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Paul Mehta: We also want to look at, healthcare records. EHR certainly is really important, and this is...

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Paul Mehta: Where our partnership with ALSTDI through their grant has been very, very fruitful. They actually have this system to go in and get electronic health records, and patients will go in and opt in to share these health records with the registry. And so this will allow us to get a lot more detailed records about ALS patients, past medical history, past medications, and so forth.

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00:51:44.730 --> 00:52:02.439

Paul Mehta: And from that, we can make certain connections to their risk factor surveys, and so it would definitely make the registry a much more robust area when it comes to data availability for researchers. And I mentioned regarding, well, we work with the state of Virginia on potential cases of elevated cases, and that's a publication.

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00:52:02.650 --> 00:52:15.830

Paul Mehta: That will be, which is with a journal right now, should be coming out very soon, but that's another area where we're partnering with states, and these states come to us if there's a particular concern or a question they have on ALS cases, occurring in their backyards.

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00:52:16.050 --> 00:52:30.739

Paul Mehta: And then, like I mentioned, we also want to look at the burden of ALS on veterans. This has been much more, I mentioned earlier, Congress has kind of tasked us to kind of look at this more closely with our VA partners, and we want to go and do that as well.

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Paul Mehta: Next slide, please.

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00:52:34.570 --> 00:52:59.049

Paul Mehta: So, we also had public engagement sessions this past year as well, and I want to thank those individuals for their input. Like I mentioned, the registries of Buying for those living with ALS, and their input is extremely, extremely valuable. And I want to thank Pat Muradolin, Charles Todd, Stacey Farber, Brian Wilson, and Doug Butchard as well, for their input. And like I mentioned, this allows those with ALS to kind of provide feedback and provide guidance on the registry and

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00:52:59.050 --> 00:53:02.950

Paul Mehta: And to see, you know, down the road where they, you know, where they want us to go.

253

00:53:02.980 --> 00:53:04.789

Paul Mehta: Next slide, please.

254

00:53:07.080 --> 00:53:20.700

Paul Mehta: So, jumping, regarding the funding of our new grants. So, like, every year we do, we do, we try to fund new grants, and so we have a funding opportunity now, so that is released, and we invite researchers to go ahead and apply.

255

00:53:20.700 --> 00:53:36.270

Paul Mehta: And so, in the fall of 2025, we funded 4 new grants, for a total of 31. And some of these grants, like I mentioned, will be discussed today and tomorrow by our researchers themselves. University of Michigan, Dr. Steven Goutman, looking at spectral flow cytometry.

256

00:53:36.360 --> 00:54:01.299

Paul Mehta: Dr. Stommel at Dartmouth, looking at veterans as in terms of why they're having twice the risk of developing ALS compared to civilians. We also funded, VCU as well, and this is kind of related to the hotspots which there were seeing in Virginia as well, so that was certainly an opportunity to have a grant that was funded, to kind of also, you know, expand the areas of research and concern, or research

257

00:54:01.360 --> 00:54:16.240

Paul Mehta: And as well, looking at the areas of concerns in Virginia. And we also funded Washington University, Dr. Susan Turtles, as in terms of looking at air pollutants at the census tract level, and how that impacts ALS. Next slide, please.

258

00:54:17.720 --> 00:54:32.479

Paul Mehta: This kind of gives you, like, a pie chart regarding, the overview of our funding itself, exactly what we're funding. So about 23... 23% of the funding is looking at environmental exposures, biomarkers is, like, around 19%, risk factors are 19%.

259

00:54:32.480 --> 00:54:53.189

Paul Mehta: air pollution, about 16%, genomics, about 10%, microbiome, about 7%, and veteran population is about 6%. Obviously, every year, this pie chart will kind of adjust itself as we get more, applications and potentially fund more new grants, so this will certainly adjust every year. But these are certainly the areas that the registry's covering.

260

00:54:53.510 --> 00:54:54.799

Paul Mehta: Next slide, please.

261

00:54:56.380 --> 00:55:18.899

Paul Mehta: And we also have a new opportunity announcement, actually, that was released this June of 2026. Our times, the timetables were kind of shifted, because there were some extra reviews that had to be done, and so normally this would have been released back in, January, but with the delay, it was released, back in June. And so it's currently in the process of looking at these applications coming in.

262

00:55:18.900 --> 00:55:31.210

Paul Mehta: And funding them. Hopefully, we can fund 1 to 3 this fiscal year, which our fiscal year ends October, sorry, September 30th. And so, and the areas we're covering are also established research, novel topics.

263

00:55:31.210 --> 00:55:39.039

Paul Mehta: underrepresentation of communities such as veterans, as well as looking at the Guam Collection as well, which is currently housed, at Temple.

264

00:55:39.300 --> 00:55:40.759

Paul Mehta: Next slide, please.

265

00:55:43.730 --> 00:56:08.720

Paul Mehta: And this, these next two slides I'm going to talk about are funding for FY24 and FY25. So, in FY24, we received about \$8 million, and you may be asking the question, well, Congress gave you \$10 million, how come you only get \$8 million? So, a lot of those, a lot of the, that \$2 million or so, goes to other parts of CDC for the working capital fund and so forth. But as you can see, the bulk of our funding goes towards research

266

00:56:08.720 --> 00:56:18.750

Paul Mehta: activities at 64%, personnel, outreach, education, and so forth. But this allows, like I said, I mean, we're grateful for all the monies the taxpayers give to us.

267

00:56:18.750 --> 00:56:28.030

Paul Mehta: And so, for us, our role is very, very careful with the monies we spend to make sure we maximize value and so forth, but this is a... right here is an overview of the FY24 funding.

268

00:56:28.170 --> 00:56:29.680

Paul Mehta: Next slide, please.

269

00:56:30.920 --> 00:56:33.059

Paul Mehta: So the FY25, we...

270

00:56:33.060 --> 00:56:54.000

Paul Mehta: received slightly less at 7.9, but the percentages were slightly adjusted, but in general, they're pretty much in line in FY24, even though there's a slight decrease. As you can still see, research activities encompass 60% and so forth, and so that's certainly, like I mentioned, the bulk of our funding goes out for research activities.

271

00:56:54.190 --> 00:56:55.759

Paul Mehta: Next slide, please.

272

00:56:57.060 --> 00:57:14.280

Paul Mehta: So, just kind of like, you know, wrapping up, like I said, you know, we do a lot more than just count ALS cases. Yes, we are registry at heart, but we have our biorepository. We look at the epidemiology of ALS in the U.S, work with partner organizations such as ALS Association, Team Gleason, ALS,

273

00:57:14.640 --> 00:57:22.179

Paul Mehta: United, as well as, Les Turner, and then as well as, Team Gleason as well. As well as MDA too, I'm sorry.

274

00:57:22.180 --> 00:57:47.120

Paul Mehta: And so these are partners which actually help convey the important work we're doing, as well as inform and educate those ALS patients who want to join the registry and provide their information to us, as well as researchers. We have survey data. We currently have 18 risk factor surveys, and we're probably approaching over 130,000 completed risk factor surveys, and all these data we're currently working on, or those have been already

275

00:57:47.120 --> 00:57:52.160

Paul Mehta: release in the form of publications and so forth. Or these data go to researchers who request it.

276

00:57:52.270 --> 00:57:56.439

Paul Mehta: Our notification system is very robust, and it's been extremely successful.

277

00:57:56.440 --> 00:58:20.529

Paul Mehta: As well as the research that we fund. Like I mentioned, we currently fund 31 institutions since we started. We're hoping to fund more this year as well, increasing that

count as well, and so the research that we fund helps answers, or helps, you know, answer the questions about ALS risk factors as well as etiologies, which is really important. Like Dr. Bernstein mentioned, you know, our hope, like everyone in the ALS community, is to figure out what causes ALS,

278

00:58:20.530 --> 00:58:24.740

Paul Mehta: mitigate ALS, and obviously down the road, prevent ALS.

279

00:58:25.620 --> 00:58:26.900

Paul Mehta: Next slide, please.

280

00:58:28.410 --> 00:58:53.249

Paul Mehta: So, just this is kind of the impact of the registry itself. So, like I mentioned, we are the largest ALS registry probably in the world, having over 20,000 ALS patients who've actually volunteered their data. We work with pharma companies across the board, as well as academia, to support their clinical trials, as well as their epidemiological studies. We partner with the leading ALS patient organizations out there, and that certainly is really important to kind of go ahead and get the word out regarding what

281

00:58:53.250 --> 00:59:18.049

Paul Mehta: we do, and we're also advancing ALS research through the biorepository when it comes to biomarkers, genetics, as well as environmental exposures as well. And then we're also funding research. You know, we're obviously a smaller player than some of the other institutions out there, which have a larger budget when it comes to funding research, but we, you know, do what we can with what we have, and so we go ahead and, like I said, get these monies out the door when it comes to looking at what

282

00:59:18.050 --> 00:59:23.370

Paul Mehta: Whether it's cytobacteria, organic pollutants, genetics, and other topics as well.

283

00:59:23.370 --> 00:59:48.280

Paul Mehta: And then, you know, and finally, you know, we're trying to, you know, measure as well as convey to the public, you know, the burden of ALS. Those with ALS, it is a life-changing condition, disease, and it's certainly something that, you know, we here at the Registry take at heart. You know, we want to go ahead and find out what causes ALS, we want to get the data out and the findings out, and that certainly is part of our mission, is to go ahead and serve the ALS community when it comes to getting

284

00:59:48.280 --> 00:59:54.379

Paul Mehta: our publications out, as well as funding research, as well as, like I said, mitigating ALS down the road.

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00:59:54.870 --> 00:59:56.650

Paul Mehta: Next slide, please.

286

00:59:58.300 --> 01:00:01.629

Paul Mehta: That's... that's my presentation. Happy to answer your questions.

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01:00:04.370 --> 01:00:23.629

Danielle Boyce: Thank you so much, Dr. Mehta. I... I know I feel like I have a good, kind of, understanding, you know, big picture overview of this program and what to expect over the next 2 days, so that was really helpful for me, and I learned some other things that I didn't know before, so...

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01:00:24.050 --> 01:00:28.280

Danielle Boyce: Thank you very much, and I want to just take a beat, we're a little ahead of schedule.

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01:00:28.280 --> 01:00:48.649

Danielle Boyce: And I want to give everyone a chance to get the next speaker's slides set up, but if you have any top-of-mind questions that you haven't already asked, I noticed a lot of Q&A already in the registry team answering those questions, but if you have anything that's on, you know, top of mind, please do put it in the Q&A.

290

01:00:48.820 --> 01:01:00.760

Danielle Boyce: And we can either answer, live, or we can answer as we go through the following presentations, or save it to the end of the day when we have some time at the end.

291

01:01:00.810 --> 01:01:19.789

Danielle Boyce: And also, I did notice a few people used the chat to contact the hosts and panelists directly with their questions. If that was missed, because there's lots going on in

that chat, please ask again in the Q&A if your question wasn't answered yet. We want to make sure that everyone's questions are answered.

292

01:01:23.620 --> 01:01:24.560

Danielle Boyce: Okay.

293

01:01:25.890 --> 01:01:31.989

Danielle Boyce: So, coming up next, if you're ready, Patty, Wanna make sure.

294

01:01:32.640 --> 01:01:33.930

Danielle Boyce: You're here and ready?

295

01:01:34.350 --> 01:01:39.060

Danielle Boyce: Please join me in welcoming... you ready? Okay, good.

296

01:01:39.060 --> 01:01:40.850

Danielle Boyce: Thank you for being flexible.

297

01:01:40.850 --> 01:02:00.269

Danielle Boyce: It's unlike me to be so early, usually I'm running late, so I'm impressed with myself for keeping on time. Please join me in welcoming Patricia Patty Stanko. I'm so glad to see you, Patty, haven't seen you in a long time. Associate Director of Mission Engagement at the ALS Association.

298

01:02:00.570 --> 01:02:09.859

Danielle Boyce: In her role, Patty supports efforts related to the National ALS Registry, with a focus on increasing awareness, education, and participation.

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01:02:09.900 --> 01:02:34.260

Danielle Boyce: So that's what you'll be hearing about today. Before stepping into her current position, Patty served in both care services and advocacy with the ALS Association's Florida team, where she worked closely with individuals and families affected by ALS at multidisciplinary clinics, support groups, and on the Hill, and in Washington, D.C. So Patty brings a strong commitment to advancing the mission

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01:02:34.260 --> 01:02:42.239

Danielle Boyce: of the ALS Association and the National ALS Registry. And it is a great honor to have you here, Patty. I will turn it over to you. Thank you.

National ALS Registry Partner's Presentations

ALS Association - Patricia Stanco, MHS

301

01:02:43.300 --> 01:02:44.890

Patricia Stanco, MHS: Thank you so much!

302

01:02:46.660 --> 01:02:48.589

Patricia Stanco, MHS: Give this other slides up.

303

01:02:49.600 --> 01:02:50.790

Patricia Stanco, MHS: Can't see.

304

01:02:52.460 --> 01:02:56.969

Danielle Boyce: Yes, they're up, it's, on the first slide, our mission, I can see.

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01:02:57.920 --> 01:03:00.619

Patricia Stanco, MHS: Okay, let me just put this...

306

01:03:01.740 --> 01:03:05.820

Patricia Stanco, MHS: Let me put this over here. Okay, I can't... Hmm.

307

01:03:06.510 --> 01:03:13.299

Patricia Stanco, MHS: Okay, I just can't see what slide we're on, so I'll just assume that we're gonna go in the same order.

308

01:03:13.850 --> 01:03:15.460

Patricia Stanco, MHS: Let me get this up.

309

01:03:20.620 --> 01:03:34.210

Patricia Stanco, MHS: Okay, so thank you. Thank you so much. It's a pleasure to be here. We greatly appreciate everyone who is in attendance today, and thank you for taking the time out of your schedules to learn more about the National ALS Registry.

310

01:03:34.210 --> 01:03:46.179

Patricia Stanco, MHS: The CDC and the National ALS Registry do tremendous work, as you'll hear throughout today and tomorrow, and the outstanding presentations that have been scheduled, over these days.

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01:03:46.740 --> 01:04:02.889

Patricia Stanco, MHS: But none of us do the work we do alone, and that includes the registry, so I'm very grateful that they've made the space for its partners to share a little bit about the work we do and how we work together to advance this very important mission. Next slide.

312

01:04:05.570 --> 01:04:11.019

Patricia Stanco, MHS: So our mission, simply put, is to make ALS livable and to cure it.

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01:04:11.230 --> 01:04:24.240

Patricia Stanco, MHS: What we mean by making ALS livable is that people who are diagnosed with ALS will be able to live longer lives, have improved quality of life, and also prevent loved ones from ever getting ALS.

314

01:04:24.440 --> 01:04:37.150

Patricia Stanco, MHS: Our commitment is that every person living with ALS, regardless of where they live, should be able to access high-quality care and effective treatments. And we use three pillars to work towards these goals.

315

01:04:37.330 --> 01:04:44.840

Patricia Stanco, MHS: Local care and support, national advocacy, and global research. So I'm just going to go through each of those briefly.

316

01:04:46.070 --> 01:04:47.630

Patricia Stanco, MHS: Next slide.

317

01:04:51.380 --> 01:05:06.129

Patricia Stanco, MHS: So, care and support is at the heart of our mission to make ALS livable. Across the entire U.S, the ALS Association works alongside people who are living with ALS and their families to help them navigate every stage of the journey.

318

01:05:06.670 --> 01:05:14.509

Patricia Stanco, MHS: Clinically, that support includes helping people to access specialized care through ALS multidisciplinary clinics.

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01:05:14.990 --> 01:05:25.660

Patricia Stanco, MHS: On the emotional and social side, it includes connecting individuals and caregivers with national, local, and specialized support groups that help to reduce isolation.

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01:05:25.980 --> 01:05:42.609

Patricia Stanco, MHS: As examples, we have support groups that are based on geography or location, being newly diagnosed, being a young adult who's living with ALS, caregiver groups, veterans groups, groups for people who are using communication devices, and others.

321

01:05:43.060 --> 01:05:46.939

Patricia Stanco, MHS: We also loan and provide access to medical equipment.

322

01:05:48.020 --> 01:05:59.280

Patricia Stanco, MHS: And assistive technology. That can help improve safety, communication, quality of life. We also offer grants that can help to ease some of the financial burden that often comes with living with ALS.

323

01:05:59.460 --> 01:06:09.590

Patricia Stanco, MHS: Together, all of these services are designed to meet people where they are, surround them with support, and help to ensure that no one has to face ALS alone.

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01:06:12.610 --> 01:06:16.529

Patricia Stanco, MHS: Next slide should be on nationwide advocacy.

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01:06:18.060 --> 01:06:22.640

Patricia Stanco, MHS: Advocacy is another essential part of how we make ALS livable.

326

01:06:22.640 --> 01:06:39.609

Patricia Stanco, MHS: Our advocacy work happens at both the state and federal levels, where we work to increase funding for ALS research, care and support services, and to secure stronger policies that improve access, protect needs, and reduce the burdens for people living with ALS and their families.

327

01:06:40.100 --> 01:06:55.300

Patricia Stanco, MHS: Some recent state advocacy wins, as you can see on the box to the left of the slide, are increasing state appropriations by almost 50%, passing state bills to increase access and affordability of health insurance.

328

01:06:55.550 --> 01:06:59.059

Patricia Stanco, MHS: And protecting against genetic discrimination.

329

01:06:59.460 --> 01:07:12.029

Patricia Stanco, MHS: And some recent federal wins, and this is for the entire ALS community that all worked for this, securing funding for reauthorization of the Act for ALS Act.

330

01:07:12.170 --> 01:07:18.429

Patricia Stanco, MHS: And we're also looking at legislation to enhance the benefits for families of veterans who are affected by ALS.

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01:07:18.690 --> 01:07:34.120

Patricia Stanco, MHS: So there's a QR code on the screen if you're interested in getting involved to join our advocacy network. You can sign up to receive email action alerts, which make it simple to contact elected officials when your action can help to advance better policies and increase support.

332

01:07:35.300 --> 01:07:36.390

Patricia Stanco, MHS: Next slide.

333

01:07:39.200 --> 01:07:51.650

Patricia Stanco, MHS: A few quick facts about our robust research program. We're investing over \$27 million to support 79 active research projects in 20 states, Puerto Rico, and 12 other countries.

334

01:07:51.850 --> 01:08:00.760

Patricia Stanco, MHS: And since the Ice Bucket Challenge took place back in 2014, we've committed over \$163 million to support nearly 600 research projects.

335

01:08:00.890 --> 01:08:19.430

Patricia Stanco, MHS: We've also funded over 100 postdoctoral fellows and have a strong retention rate for researchers who stay in the field of ALS. This is something, anytime I'm at a conference and I get to speak with ALS researchers, I always ask them, how long have you been researching ALS? And I'm just always amazed by the commitment.

336

01:08:19.540 --> 01:08:23.470

Patricia Stanco, MHS: And how people stay with ALS once they start researching it.

337

01:08:23.899 --> 01:08:24.870

Patricia Stanco, MHS: Next slide.

338

01:08:31.569 --> 01:08:40.429

Patricia Stanco, MHS: So, I think this has an animation in it, so if you just want to make sure that all three columns are going... are showing on the screen, we should have three.

339

01:08:40.910 --> 01:08:46.150

Patricia Stanco, MHS: Graphics that might be... Easier just to see all of them at once.

340

01:08:46.430 --> 01:08:55.159

Patricia Stanco, MHS: So for our research pathways, when we talk about research at the ALS Association, our work happens in several important ways.

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01:08:55.270 --> 01:09:02.820

Patricia Stanco, MHS: First, we fund research, and we do that by investing in promising projects, researchers, and scientific ideas.

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01:09:03.290 --> 01:09:20.759

Patricia Stanco, MHS: We also conduct our own in-house research through our Focus Survey program, and that program gathers experiences and insights from people who are living with ALS and caregivers to better understand the needs, priorities, and the real-world impact of ALS.

343

01:09:21.310 --> 01:09:37.070

Patricia Stanco, MHS: And finally, we partner on research, and this includes our collaboration with the National ALS Registry, because working together helps to increase awareness about the registry, broaden and increase participation, and ultimately strengthens the data.

344

01:09:37.979 --> 01:09:46.699

Patricia Stanco, MHS: Next slide is a little bit more about our focus survey program, and there's a QR code on the slide as well.

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01:09:46.930 --> 01:09:57.090

Patricia Stanco, MHS: If you are interested, this is something that's open to people who are living with ALS, as well as caregivers, and some of the topics that have been

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01:09:57.140 --> 01:10:08.110

Patricia Stanco, MHS: surveyed recently are listed there, and this program made a big difference when the seat elevation for power wheelchairs got approved.

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01:10:08.330 --> 01:10:17.030

Patricia Stanco, MHS: Focus Survey data was used to help advocate for that change, so it can really make a very meaningful difference in the world.

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01:10:17.920 --> 01:10:19.070

Patricia Stanco, MHS: Next slide.

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01:10:21.160 --> 01:10:31.099

Patricia Stanco, MHS: So, when we talk about partnering with the National ALS Registry, I'm going to just touch on four highlights of the main ways that we do that.

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01:10:31.180 --> 01:10:42.349

Patricia Stanco, MHS: So we're going to talk about partner... in our partnership, in-person outreach, registry training, enrollment volunteers, and the incentive pilot that Paul mentioned in his remarks.

351

01:10:43.140 --> 01:10:53.809

Patricia Stanco, MHS: But before I do that, I do just want to tell a quick story that someone told me about that really illustrates why any of this even matters at all.

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01:10:54.240 --> 01:11:02.990

Patricia Stanco, MHS: So, a colleague of mine met with a person who'd been diagnosed with ALS, and it took a long time to get the diagnosis, like, we're talking almost 2 years.

353

01:11:03.700 --> 01:11:11.099

Patricia Stanco, MHS: And they had hand weakness, and so they were referred for carpal tunnel syndrome and had surgery.

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01:11:12.210 --> 01:11:23.390

Patricia Stanco, MHS: And just had to keep going around until they finally got this diagnosis. And by the time they finally had a name for what was happening, obviously, they were very eager to participate in research.

355

01:11:23.530 --> 01:11:27.139

Patricia Stanco, MHS: But they quickly learned, as so many people do, that

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01:11:27.520 --> 01:11:34.599

Patricia Stanco, MHS: Some studies, a lot of studies, have limitations, and if you've had symptoms for a certain period of time.

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01:11:34.830 --> 01:11:37.709

Patricia Stanco, MHS: Sometimes you don't qualify for that particular study.

358

01:11:38.810 --> 01:11:42.639

Patricia Stanco, MHS: So... they learned about the ALS registry.

359

01:11:42.800 --> 01:11:46.890

Patricia Stanco, MHS: From my colleague at the clinic visit, and they were like, you know.

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01:11:47.290 --> 01:11:52.999

Patricia Stanco, MHS: fine, I can do that. I can answer some risk factor survey questions, and they even contributed,

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01:11:53.130 --> 01:11:55.430

Patricia Stanco, MHS: A sample to the biorepository.

362

01:11:56.110 --> 01:12:01.289

Patricia Stanco, MHS: They also signed up, For those research alerts that Paul mentioned.

363

01:12:01.780 --> 01:12:19.419

Patricia Stanco, MHS: And one of the emails came through, and they got a notification about a symptom management study, and they were actually looking at if strengthening... strengthening the chest wall muscles could help delay having to use non-invasive ventilation. And they qualified for that study. And so.

364

01:12:19.780 --> 01:12:28.520

Patricia Stanco, MHS: I just wanted to share that, because for that person, the registry actually became more than just a database. It became a pathway back to research.

365

01:12:28.710 --> 01:12:35.870

Patricia Stanco, MHS: And also a way to contribute meaningfully, after even... even after other doors had seemingly been closed.

366

01:12:38.200 --> 01:12:42.479

Patricia Stanco, MHS: So let's go to the next slide, which should say Outreach at the top.

367

01:12:44.170 --> 01:12:52.649

Patricia Stanco, MHS: Face-to-face, in-person outreach is the cornerstone of our registry efforts. This past year, we've conducted over 300 outreach trips.

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01:12:52.900 --> 01:12:58.189

Patricia Stanco, MHS: to visit people living with ALS, support groups, clinics, home health agencies.

369

01:12:58.380 --> 01:13:07.979

Patricia Stanco, MHS: Healthcare providers, neurology practices, skilled nursing facilities, hospitals, Walk to Defeat ALS events, health fairs, veterans clinics, and more.

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01:13:08.340 --> 01:13:23.180

Patricia Stanco, MHS: Repeated exposure to the registry is important, because the right time to reach someone to talk about the registry might not be at the time of diagnosis, and it might not be during times when there's a lot of other things going on.

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01:13:23.540 --> 01:13:35.229

Patricia Stanco, MHS: So, by continuing to share the registry in different settings and at different points along the journey, we ensure that the right information is available when people are ready and open to taking action.

372

01:13:37.160 --> 01:13:38.270

Patricia Stanco, MHS: Next slide.

373

01:13:39.610 --> 01:13:47.999

Patricia Stanco, MHS: Registry training has become an increasingly important part of how we embed registry awareness into our everyday work.

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01:13:48.740 --> 01:14:03.470

Patricia Stanco, MHS: To date, we've trained more than 300 staff across all of our departments on the National ALS Registry, so that they have a thorough understanding of how important it is and why it matters, and how to weave it into their daily interactions.

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01:14:03.800 --> 01:14:11.190

Patricia Stanco, MHS: We're also seeing strong interest from ALS multidisciplinary clinics that we partner with. We have an annual survey that goes out.

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01:14:11.360 --> 01:14:24.760

Patricia Stanco, MHS: And we asked, you know, are you talking about the registry, and would you be interested in a virtual training? Or a train-the-trainer on the registry for your clinic team? And we've gotten a really positive response.

377

01:14:24.930 --> 01:14:37.880

Patricia Stanco, MHS: to that request. So, these trainings help our staff and clinic staff to better understand, again, why this is important and the crucial role that we can all play in increasing awareness and participation.

378

01:14:37.890 --> 01:14:44.959

Patricia Stanco, MHS: And the resources and materials that are available to share with people who are living with ALS, their caregivers, and their families.

379

01:14:45.030 --> 01:14:50.189

Patricia Stanco, MHS: The goal is to make registry education accessible, consistent, and repeatable.

380

01:14:50.470 --> 01:15:03.569

Patricia Stanco, MHS: And again, because we all develop... when we have trusted relationships, that's where you want to hear about the registry from someone that you already have a relationship with, not someone new coming into your circle of support.

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01:15:05.710 --> 01:15:13.330

Patricia Stanco, MHS: Next slide is going to talk about our next initiative, which is a program with trained volunteers.

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01:15:13.510 --> 01:15:28.770

Patricia Stanco, MHS: And I touched on this program two years ago when we had our last annual meeting with the registry. It's now available nationwide, and anyone in the audience who's interested, there's a QR code there that you can scan, or there's a website to get more information.

383

01:15:29.450 --> 01:15:47.540

Patricia Stanco, MHS: We now have five volunteers who are assisting people with ALS. Two of them are bilingual and are fluent in Spanish. All of our volunteers have been background checked, and they all have a personal connection to ALS, so they really understand the challenges of this diagnosis and the importance of research.

384

01:15:48.500 --> 01:15:52.790

Patricia Stanco, MHS: They provide assistance virtually, either by video chat or by phone.

385

01:15:52.900 --> 01:15:56.619

Patricia Stanco, MHS: And, we had someone who...

386

01:15:56.680 --> 01:16:02.100

Patricia Stanco, MHS: Really wanted to participate, but didn't have a computer, wasn't tech-savvy.

387

01:16:02.140 --> 01:16:17.899

Patricia Stanco, MHS: The only connection to the internet they had was through their smartphone, and they didn't want to complete the entire risk factor module surveys on their phone, so they connected with a volunteer who helped talk them through it, and they did it all by phone, and

388

01:16:17.900 --> 01:16:22.260

Patricia Stanco, MHS: person was, it didn't take that... they broke it up into a couple different sessions.

389

01:16:22.330 --> 01:16:39.670

Patricia Stanco, MHS: I think it was about 4 times they met, about a half hour each, and they got it done, so it's great. That resource is available. These volunteers can just help get you started, they can take you through from beginning to end, or they can just answer questions, if you're not sure how to navigate the process.

390

01:16:40.970 --> 01:16:46.479

Patricia Stanco, MHS: And the next slide is going to talk about our incentive pilot that, again, Paul mentioned.

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01:16:46.680 --> 01:16:52.370

Patricia Stanco, MHS: So, this was designed to better understand if offering a gift card incentive

392

01:16:52.390 --> 01:17:04.829

Patricia Stanco, MHS: could help to get more people to participate in the registry. It's a well-established practice in health research. It had never been tried in ALS or with the registry. So the idea was simple, you know, could we...

393

01:17:04.830 --> 01:17:22.000

Patricia Stanco, MHS: could doing this move the needle? Could we see a result that was measurable and meaningful? So we tested this approach as part of our broader registry strategy, alongside outreach, education, and enrollment support, to see if,

394

01:17:22.000 --> 01:17:38.459

Patricia Stanco, MHS: see what would happen, and I can't... spoiler alert, it worked, but you'll have to join tomorrow afternoon to hear just how successful it was. Reshma and I are going to go over all of the details, what we learned, and how the results can inform future engagement efforts.

395

01:17:38.460 --> 01:17:49.910

Patricia Stanco, MHS: We're also developing a manuscript with the registry for publication, and we're also going to be presenting a poster at the ALS Association's upcoming ALS Nexus conference.

396

01:17:50.620 --> 01:17:52.090

Patricia Stanco, MHS: Next slide.

397

01:17:52.410 --> 01:18:11.130

Patricia Stanco, MHS: So, speaking of ALS Nexus, it is coming up next week, so if you're interested in learning more or joining us, please visit alsnexus.org. A reminder that for people living with ALS and a caregiver, registration is completely free. There's no charge to attend either in person

398

01:18:11.130 --> 01:18:20.259

Patricia Stanco, MHS: or virtually. And, we'd love to have you join the broader ALS community to connect, collaborate, and change the future of ALS. If you do

399

01:18:20.260 --> 01:18:25.170

Patricia Stanco, MHS: Decide to attend, please stop by and see our incentive poster in the poster hall.

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01:18:25.960 --> 01:18:27.290

Patricia Stanco, MHS: Thank you so much.

401

01:18:32.690 --> 01:18:41.419

Danielle Boyce: Thank you so much, Patty. I learned a lot, from that, and I... it also teed up, like you said, tomorrow very...

402

01:18:41.420 --> 01:18:51.980

Danielle Boyce: Very well, because, you know, I think all of us who work in research are always interested in how to recruit and retain better, and whether incentives work. I mean, that's not just something in ALS, that's across

403

01:18:51.980 --> 01:19:03.979

Danielle Boyce: you know, all research, so I think this is, you know, could be a model for, for, you know, across many domains, and so for that reason, I think it's, really, really, really interesting. I think a lot of people want to tune in for that.

404

01:19:03.990 --> 01:19:27.420

Danielle Boyce: And so we do have some time before, Lauren Webb is going to present, and so I was thinking we could maybe catch up with some of the Q&A, you and Paul, both, and maybe starting, with Paul, and let folks enter into the Q&A. But while that's, while everyone's getting their questions together and, you're looking over what has already been asked, I do have the.

405

01:19:27.420 --> 01:19:38.019

Danielle Boyce: the sad job to report that, Mr. Brian Wilson has passed away. I just found this out from Pat Dolan and the IMALS legislative

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01:19:38.020 --> 01:19:57.910

Danielle Boyce: team, Pat forwarded that message after seeing that we had acknowledged Brian's, efforts for the listening sessions. And, you know, I think that I wanted to share that, A, to honor Mr. Wilson and make sure that we all learn more about his remarkable advocacy, but also to highlight the ALS clock.

407

01:19:58.030 --> 01:20:14.460

Danielle Boyce: Because I met with him as part of this preparation not long ago. And the last time I moderated this meeting, I received word that the great Sandy Morris had passed away, during the time of the meeting.

408

01:20:14.460 --> 01:20:37.110

Danielle Boyce: And, and it, and so, that is not a coincidence. That is the ALS clock, and it is, it, it, it is on all of us to work with this sense of urgency, that, that, that these, tragic losses, have highlighted for us. And so, I just wanted us all to take a moment to, think about Mr. Wilson and his family.

409

01:20:40.460 --> 01:20:52.469

Danielle Boyce: Okay, so, Paul, would you like to start and kind of summarize? I know a lot of questions have been answered directly, but I don't know if there are things that you would like to highlight, or outstanding questions that you would like to answer.

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01:20:58.420 --> 01:21:00.190

Danielle Boyce: Paul, I can't hear you.

411

01:21:02.550 --> 01:21:05.109

Danielle Boyce: I... Am I the only one?

412

01:21:05.110 --> 01:21:06.289

Paul Mehta: Can you hear me now?

413

01:21:06.480 --> 01:21:07.580

Danielle Boyce: Yes, I can hear you.

414

01:21:07.580 --> 01:21:15.520

Paul Mehta: Sorry about that. We got a question from Beth Anderson. Her question is, any chance states could be funded to collect statewide

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01:21:15.680 --> 01:21:29.150

Paul Mehta: registries. So that certainly is a really interesting question. So right now, the only states that currently have a registry or one in place are Massachusetts, Vermont, Maine, Michigan, and California.

416

01:21:29.150 --> 01:21:34.559

Paul Mehta: So those are the 5 states. Michigan just recently brought the registry online, and

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01:21:34.560 --> 01:21:55.620

Paul Mehta: A lot of these states are in different degrees of collecting cases and so forth. So, this sort of question is, in terms of, you know, funding states and helping them out, has been done previously in, for example, the newborn screening model that CDC has, where funds go to newborn screenings across the country and so forth.

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01:21:55.800 --> 01:22:13.629

Paul Mehta: The question is, right now, you know, is resources. We don't have the resources currently to go ahead and provide any sort of funding for states at this time. But like I mentioned, I mean, this sort of model has been used in other diseases before, so it is not out of the possibility that that could be done in the future.

419

01:22:14.230 --> 01:22:27.790

Paul Mehta: Let's see, one other question is, from MC Colette. How do you pay the partner organizations annually? How much do you pay the partner organizations annually? How do you measure the performance, results, and self-enrollment?

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01:22:28.040 --> 01:22:39.229

Paul Mehta: That's a really, really good question. So, what we pay for the partner organizations, is our partnership with them, and it varies regarding the size of the organization, as well as the scope.

421

01:22:39.710 --> 01:23:03.859

Paul Mehta: So it's not going to be a, you know, one-size-fits-all. It varies. And we do measure their performance regarding us in terms of, you know, the metrics and so forth, and that's provided to us on a monthly basis. Please keep in mind, we can't make anyone register, so this is just information the ALS Association, MDA, Team Gleason, Les Turner, that they provide to ALS.

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01:23:03.860 --> 01:23:22.039

Paul Mehta: Patients, you know, in their, in their, in their catchment area, in their territories, and so forth. But so we can't make anybody certainly go ahead and register, but we do certainly measure their performance and work with them closely, provide them materials,

go to their events to talk and so forth to go ahead and increase enrollment and get the word out.

423

01:23:22.750 --> 01:23:28.699

Paul Mehta: Anonymous attendee, how about a clinic bonus based on percentage enrolled PALS?

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01:23:28.700 --> 01:23:46.400

Paul Mehta: That certainly is an interesting question. I think, you know, we don't work directly with the clinics themselves, we're working more with the organization. So, for example, Les Turner, has a Northwest ALS clinic, Northwestern ALS Clinic, in their backyard that they partner with, and so we work with the organizations themselves.

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01:23:46.400 --> 01:23:55.099

Paul Mehta: We don't have the resources or any sort of clinic bonus. The ad for ALS, which I believe has about 35 to 37

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01:23:55.100 --> 01:24:13.030

Paul Mehta: clinics across the country they work with directly, and they do provide monies for them to get enrolled, and so forth. And I believe, if I'm not mistaken, I think they wanted to enroll close to 2,000 individuals, with ALS, as well as, carriers, and controls as well.

427

01:24:13.260 --> 01:24:29.020

Paul Mehta: to kind of go ahead and expand research in those areas, especially when it comes to basic sciences and so forth, as well as biomarkers. They certainly have the capacity, we don't have the capacity to go ahead and give out any sort of monies at this time to clinics.

428

01:24:29.350 --> 01:24:48.670

Paul Mehta: Let's see, will presenter slides be available? We don't typically have slides available. We have a, for example, like an executive summary as well as notes and so forth, but a lot of the times, those slides are incorporated inside the executive summary as well as the meeting notes itself, so you don't see all the slides, but you see some of the slides here.

429

01:24:50.510 --> 01:24:58.309

Paul Mehta: Where can we access the full agenda of the meeting? We could certainly put that in the chat, so we can put the agenda on the chat itself.

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01:24:58.730 --> 01:25:07.979

Paul Mehta: Oh, Tiffany Carr said, New York and New Jersey both passed legislation for a state-based registry. That's really interesting. I did not know that. That's interesting information.

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01:25:08.260 --> 01:25:13.350

Paul Mehta: Let's see, and moving along, I think there's...

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01:25:13.730 --> 01:25:22.329

Paul Mehta: Other questions were already answered in the Q&A by the team itself, so I'm not sure if anybody else has any other questions for myself or Patty.

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01:25:26.910 --> 01:25:33.060

Danielle Boyce: Looks like, Song put that in the chat, if, if... To everyone, the agenda.

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01:25:36.120 --> 01:25:42.530

Danielle Boyce: Thank you so much. I'm just going to give a minute or so with the chat to see if anything else comes in for Paul or Patty.

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01:25:46.260 --> 01:25:49.580

Danielle Boyce: I'm just scrolling through to see what hasn't been answered.

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01:26:02.900 --> 01:26:19.089

Danielle Boyce: I'm looking at this question here about publishing a list of each study funded. I don't think... did we fully answer? No, we didn't, that just came in. Each study funded, what researchers, and most importantly, what they actually concluded, and how it advances ALS research. I can answer part of that, in that

437

01:26:19.200 --> 01:26:38.399

Danielle Boyce: We... that's what you're going to be learning about this afternoon and tomorrow, is... is the funded research studies and what they have learned so far, or what they have concluded if their research is, grant is coming to an end. I don't know if, Paul wants to comment any more on that.

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01:26:38.620 --> 01:26:42.399

Paul Mehta: Yeah, so, I'm putting in the actual response,

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01:26:42.400 --> 01:27:04.219

Paul Mehta: the, link which shows all the studies that we currently fund, all the grantees and so forth, and that's on our website. It tells you the ASHA study name, institution, the investigator name, as well as the period of funding as well. We don't have, so we also... what we do is we also have our publications, and these publications are from our partners who've actually,

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01:27:04.520 --> 01:27:12.199

Paul Mehta: are being funded and so forth, and that certainly can vary, and let me just put that link in there as well, so you can see that link, too.

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01:27:12.200 --> 01:27:37.140

Paul Mehta: And... and this right here shows you exactly, the publications that we currently have, and so forth. So, I mean, our goal, obviously, is whenever someone is funded, is to have a, you know, as in terms of, you know, a period publication, the findings themselves, and those are certainly, you know, we actually, put on our website when it comes to the publications themselves. We also work with our partner groups to kind of do the social

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01:27:37.140 --> 01:28:01.609

Paul Mehta: media to kind of get the word out. Our social media has been somewhat curtailed, and so we can't do a lot of the social media we were in the past doing, and so we kind of rely upon our partners to kind of get the word out regarding new publications and so forth. There was another question that was answered, but I just want to kind of highlight that question regarding the biorepository, and kind of give you more information.

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01:28:02.160 --> 01:28:08.979

Paul Mehta: So, with the change of administration, there was some stuff that was done, and which resulted in certain contract staff being let go.

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01:28:08.980 --> 01:28:33.809

Paul Mehta: It was called reduction in force, and so when that happened, a lot of those staff members were let go, and that impacted what we could or could not fund last fiscal year. We provided justifications and so forth, but keep in mind, you know, CDC is a very

large organization, and so having, you know, that particular group of individuals who were servicing a large organization such as CDC, we had to kind of prioritize exactly who was

445

01:28:33.810 --> 01:28:45.600

Paul Mehta: getting funded. Rest assured, we, you know, we put our justifications forth and so forth, to get the biopostory funded, but last year, it just wasn't possible, and so our hope is to get it funded this year.

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01:28:50.250 --> 01:29:00.070

Danielle Boyce: Thank you very much, to, to Patty again, for that presentation, and I look forward to seeing you again for Part 2 tomorrow. And... and as for the,

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01:29:00.330 --> 01:29:24.240

Danielle Boyce: the manuscripts. I can speak for the ALSTDI-funded projects. We have, as Dr. Vieira will talk more about this afternoon, we have two preprints, which means they're under review, but they're publicly available, including the electronic health records pipeline that Dr. Mehta had shared and touched upon in his presentation. We have two preprints there, and we have one under review

448

01:29:24.240 --> 01:29:47.709

Danielle Boyce: for, again, work with, our, with collaborators on the OMOP Common Data Model, and, those, that has been submitted to ALS FTD Journal, and so you can reach out to me anytime, and I'd be glad to share, what, what we have learned as a result of, our funding. So, and I think most of our presenters would be glad to share anything that they have, studied as well.

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01:29:48.170 --> 01:30:09.910

Danielle Boyce: Okay, so next up, I'm so glad to see Lauren Webb, Chief Advocacy and Outreach Officer. She is dedicated to, for, Les Turner, I'm sorry, Les Turner ALS Foundation. She's dedicated to forging links between policymaking and service delivery, so patients and families receive not just care, but hope.

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01:30:10.310 --> 01:30:18.599

Danielle Boyce: With a master's degree in social work from the University of Chicago, she has worked in the neuromuscular community for over 25 years.

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01:30:19.000 --> 01:30:29.049

Danielle Boyce: Providing patient, direct patient care, coordinating clinical trials, and overseeing the Muscular Dystrophy Association's nationwide care center network.

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01:30:29.600 --> 01:30:41.359

Danielle Boyce: At the Les Turner ALS Foundation, she leads efforts to provide innovative, compassionate support services with emphasis on health literacy, access, and patient-centered care.

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01:30:41.680 --> 01:30:45.440

Danielle Boyce: Thank you so much, Lauren, I will let you take it from here.

Les Turner ALS Foundation - Lauren Webb

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01:30:45.440 --> 01:30:57.650

Lauren Webb, Les Turner ALS Foundation: Well, thank you so much, Danielle. I really appreciated hearing, what the work that the ALS Association is doing and their efforts and focus. So, next slide, please.

455

01:31:00.020 --> 01:31:07.839

Lauren Webb, Les Turner ALS Foundation: So the Les Turner A. Les Foundation was, founded in 1977, so next year we will be celebrating our 50th

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01:31:07.880 --> 01:31:23.519

Lauren Webb, Les Turner ALS Foundation: anniversary, and our focus is to provide comprehensive care, for people living with ALS, and we fund research at Northwestern. In 2025, we gave over a million dollars to support the

457

01:31:23.640 --> 01:31:26.759

Lauren Webb, Les Turner ALS Foundation: Center at Northwestern. Next page.

458

01:31:29.100 --> 01:31:45.690

Lauren Webb, Les Turner ALS Foundation: So our priorities for the National ALS Registry was the continued emphasis on concierge approach. And so, you know, we're different in that we have 6 people who are members of our team, who are all focused on really providing the comprehensive

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01:31:45.690 --> 01:31:55.669

Lauren Webb, Les Turner ALS Foundation: care and support that families need, and they, engage with families often, and frequently have conversations about the ALS registry.

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01:31:55.770 --> 01:32:15.109

Lauren Webb, Les Turner ALS Foundation: In 2025, we trained over 70 community health workers, and this was a part of a new initiative, to be able to have more coverage, across the state of Illinois to increase, registry numbers in the state, and so you'll learn a little bit more later in the slide about that.

461

01:32:15.340 --> 01:32:25.520

Lauren Webb, Les Turner ALS Foundation: And then the other thing that we did, during these two years, since we last presented, is we, launched a new case management system. So we,

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01:32:25.630 --> 01:32:34.699

Lauren Webb, Les Turner ALS Foundation: It's been going very well, and our team is learning a lot, and we are continuously learning from that to adjust our outreach strategies.

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01:32:34.880 --> 01:32:42.130

Lauren Webb, Les Turner ALS Foundation: And again, we continue to collaborate with people with lived experience and other stakeholders, to address some of the challenges.

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01:32:43.150 --> 01:32:44.219

Lauren Webb, Les Turner ALS Foundation: Next slide.

465

01:32:46.740 --> 01:33:02.709

Lauren Webb, Les Turner ALS Foundation: So, Carla Gallagher, who you can't see her face here, who's handing, the folder, is our dedicated National ALS Registry Associates. She really provides one-on-one support at clinic, and then... and then she assigns,

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01:33:02.710 --> 01:33:07.680

Lauren Webb, Les Turner ALS Foundation: The support, service coordinators to work one-on-one with the families.

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01:33:07.690 --> 01:33:17.129

Lauren Webb, Les Turner ALS Foundation: And so, sometimes CARA enrolls people directly, at clinic, and other times that is done in partnership with people.

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01:33:17.200 --> 01:33:20.549

Lauren Webb, Les Turner ALS Foundation: And their subsequent, visits in between clinic.

469

01:33:20.750 --> 01:33:35.269

Lauren Webb, Les Turner ALS Foundation: But we do know that, that personal encouragement really makes a big difference, and, you know, families are... have a lot going on. They might not have the time or the energy, to do the enrollment, and so, working

470

01:33:35.270 --> 01:33:43.409

Lauren Webb, Les Turner ALS Foundation: In collaboration with our support service coordinators, I think really helps, to support the families. And one of the things that we do is

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01:33:43.410 --> 01:33:54.919

Lauren Webb, Les Turner ALS Foundation: By, providing care and support for families in other areas, then, you know, sometimes that assists them with, an opportunity to,

472

01:33:54.940 --> 01:33:56.369

Lauren Webb, Les Turner ALS Foundation: Complete their surveys.

473

01:33:56.650 --> 01:34:08.190

Lauren Webb, Les Turner ALS Foundation: So again, having that personalized, support helps to overcome some of these obstacles, you know, around technology and, you know, around actual enrollment.

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01:34:08.500 --> 01:34:09.450

Lauren Webb, Les Turner ALS Foundation: Next slide.

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01:34:10.780 --> 01:34:18.470

Lauren Webb, Les Turner ALS Foundation: So, in here is a picture of Dr. Coleman and, Matt Green, at our,

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01:34:18.670 --> 01:34:32.990

Lauren Webb, Les Turner ALS Foundation: at our Lois and Celia ALS Clinic at Northwestern Medicine. It is the first and largest multidisciplinary clinic in the U.S, and we have the highest number of neurologists and dedicated, pulmonologists in the Chicagoland area.

477

01:34:33.230 --> 01:34:48.180

Lauren Webb, Les Turner ALS Foundation: And we work really well with the Center in terms of accessing enrollment to clinical research and dedicated, clinical trial coordinators. In fact, we funded, a Accelerating Centers of Excellence,

478

01:34:48.270 --> 01:35:07.829

Lauren Webb, Les Turner ALS Foundation: initiative, and we found that that helped to increase, enrollment into clinical research by funding the care infrastructure, the research infrastructure. So, through those funds, they were able to hire more, clinical research, coordinators at the hospital.

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01:35:08.200 --> 01:35:17.040

Lauren Webb, Les Turner ALS Foundation: And again, we provide this no-cost coordinated support from our center... from our ALS support service coordinators. Next slide.

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01:35:18.500 --> 01:35:35.530

Lauren Webb, Les Turner ALS Foundation: So the, here's a link, or a QR code, to our ALS clinical research, and we always include the National ALS Registry, as part of this page, so when we're talking about clinical research and redirecting families to this site.

481

01:35:35.530 --> 01:35:40.959

Lauren Webb, Les Turner ALS Foundation: They are also able to see information about the registry. Next slide.

482

01:35:42.860 --> 01:35:54.989

Lauren Webb, Les Turner ALS Foundation: So, oh, I'm not sure why this slide is different. It looked fine on my slide. But, as you can see, the Les Turner ALS Foundation, helps to answer questions about ALS,

483

01:35:55.000 --> 01:36:08.110

Lauren Webb, Les Turner ALS Foundation: And the registry is a really, nice way to engage with people and learning more about them, about their history. Our team really focuses on completion of risk factor surveys.

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01:36:08.110 --> 01:36:18.999

Lauren Webb, Les Turner ALS Foundation: And so, you know, through the information that Paul presented earlier, you know, we're able to have those discussions with families based upon

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01:36:19.170 --> 01:36:22.750

Lauren Webb, Les Turner ALS Foundation: Based upon some of the registry results.

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01:36:22.810 --> 01:36:33.410

Lauren Webb, Les Turner ALS Foundation: So, we provide emotional support. We have, support groups, that focus on caregivers. We have, people living with ALS.

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01:36:33.410 --> 01:36:52.869

Lauren Webb, Les Turner ALS Foundation: And caregiver groups. We also have a young caregiver, group, so those, over the age of 18 to 35, so that really provides a nice way of connecting, and I'll... I can drop in the chat a link to our support groups. And then we also offer a very comprehensive, bereavement program as well.

488

01:36:52.970 --> 01:37:06.110

Lauren Webb, Les Turner ALS Foundation: Again, we assist with recommendations, to help with daily living. In fact, Anne-Marie, who is one of our Director of Community Education, she provides one-on-one support for

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01:37:06.110 --> 01:37:14.439

Lauren Webb, Les Turner ALS Foundation: People are working with the foundation to help them, overcome some of those technology obstacles that I spoke about earlier.

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01:37:14.440 --> 01:37:31.810

Lauren Webb, Les Turner ALS Foundation: So we really do see, you know, brain... brainstorming in partnership with people living with ALS, giving them the tools that they need so that they can continue to participate in online clinical research, engage with their family.

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01:37:31.810 --> 01:37:35.790

Lauren Webb, Les Turner ALS Foundation: And have all the appropriate access as their needs change.

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01:37:35.980 --> 01:37:52.870

Lauren Webb, Les Turner ALS Foundation: We also provide equipment, loans and need-based grants, as well as care coordination and, guidance on, other federal programs, and we really help families, you know, assisting them with planning.

493

01:37:52.870 --> 01:38:02.559

Lauren Webb, Les Turner ALS Foundation: And later, I think in September, we're going to be launching our ALS, palliative and, hospice care guides. Next slide.

494

01:38:04.310 --> 01:38:20.380

Lauren Webb, Les Turner ALS Foundation: So, we talked a little bit, earlier about some of our online tools, and we just recently launched a tracheostomy and invasive mechanical ventilation campaign, and we had a really wonderful engagement

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01:38:20.380 --> 01:38:24.620

Lauren Webb, Les Turner ALS Foundation: With, the community on this tool. This was, in fact.

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01:38:24.660 --> 01:38:34.619

Lauren Webb, Les Turner ALS Foundation: A module that, the community wanted, when we first launched our tools in, in, early 2021.

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01:38:34.790 --> 01:38:43.210

Lauren Webb, Les Turner ALS Foundation: So we're really proud of this new initiative, for the, driving the conversation, so our ALS decision tools

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01:38:43.260 --> 01:38:55.840

Lauren Webb, Les Turner ALS Foundation: It's an interactive tool that explains treatment options, and then it allows for reflection, on certain questions, so people can have an informed conversation

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01:38:55.840 --> 01:39:05.400

Lauren Webb, Les Turner ALS Foundation: With their loved ones and with their clinicians. So I highly encourage, folks, if you haven't, to please check out our ALS decision tool.

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01:39:05.790 --> 01:39:06.780

Lauren Webb, Les Turner ALS Foundation: Next slide.

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01:39:08.980 --> 01:39:19.449

Lauren Webb, Les Turner ALS Foundation: And then this is our comprehensive, guides that we offer, and I wanted to point out, we have an ALS and Participating in clinical research guide.

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01:39:19.530 --> 01:39:24.530

Lauren Webb, Les Turner ALS Foundation: That, highlights the National AALS Registry.

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01:39:24.530 --> 01:39:41.310

Lauren Webb, Les Turner ALS Foundation: And redirects people to register, at the CDC. And so, you know, that's a printed material that we, provide for families, and, not only in our area, but across the country, we have clinicians who request our materials because

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01:39:41.350 --> 01:39:53.539

Lauren Webb, Les Turner ALS Foundation: Of the way that they're designed in terms of, easy to read, graphics, pictures, it really helps families learn more and ask questions, so please check that out.

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01:39:53.610 --> 01:39:54.590

Lauren Webb, Les Turner ALS Foundation: Next slide.

506

01:39:56.070 --> 01:40:15.490

Lauren Webb, Les Turner ALS Foundation: Again, this is part of some of our, initiatives that we started in 2025. Anne-Marie Doyle, our Community Education Director, you know, has been doing some podcasts. We've been working more closely with LHIPCO, which is our palliative

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01:40:15.490 --> 01:40:27.470

Lauren Webb, Les Turner ALS Foundation: care organization in Illinois. And we've been doing some unique things with, rural health outreach, as well, and so we are working with the Illinois Public, Health

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01:40:27.470 --> 01:40:33.230

Lauren Webb, Les Turner ALS Foundation: Association to really learn more about the community and about some of their needs.

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01:40:33.230 --> 01:40:47.759

Lauren Webb, Les Turner ALS Foundation: And in fact, I spoke, at a meeting in June and very southern Illinois, and so we're... we're learning more about what the needs in the rural communities are and what that looks like, and of course.

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01:40:47.760 --> 01:40:55.170

Lauren Webb, Les Turner ALS Foundation: in all of these, meetings or engagements, we talk about the CDC registry, and we highlight that.

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01:40:55.270 --> 01:41:05.449

Lauren Webb, Les Turner ALS Foundation: And again, Anne-Marie's doing a very interesting project, training community health workers to learn more about ALS, and our goal is to really help, with

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01:41:05.720 --> 01:41:17.660

Lauren Webb, Les Turner ALS Foundation: expedite, and improve, rapid, diagnosis, so we have more pathways, to get people, to ALS centers, across the state.

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01:41:17.850 --> 01:41:27.770

Lauren Webb, Les Turner ALS Foundation: And, one of the ways that we think will help is by educating, people who are working directly in different communities. Next slide.

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01:41:29.780 --> 01:41:43.770

Lauren Webb, Les Turner ALS Foundation: So, I know there was questions about metrics, so I'm just gonna report out, on... I spent time with an Excel spreadsheet calculating all the monthly, items for us, what we report on.

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01:41:43.820 --> 01:41:55.549

Lauren Webb, Les Turner ALS Foundation: We had, 100... we average about 104 direct encounters per month. This also includes our support groups, as well as, the, engagements.

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01:41:55.550 --> 01:42:06.229

Lauren Webb, Les Turner ALS Foundation: one-on-one engagements with, family members. We have an average of 9 toolkits that are distributed per month. That's the physical. We only count the physical,

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01:42:06.860 --> 01:42:17.800

Lauren Webb, Les Turner ALS Foundation: folders that we hand out, and and then we also continue to place an emphasis on completion of surveys, during these visits. So.

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01:42:17.910 --> 01:42:30.070

Lauren Webb, Les Turner ALS Foundation: It's not just a one conversation, it's a continuous conversation with families, so that way we can really dive into the data and learn more about these risk factors. Next slide, please.

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01:42:31.360 --> 01:42:50.489

Lauren Webb, Les Turner ALS Foundation: So, you know, and again, another initiative of ours was to, really focus on increasing some of our metrics, and you'll see, on the... these two pages, that we have here, we've increased our website, engagement, with, about the registry.

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01:42:50.490 --> 01:43:01.279

Lauren Webb, Les Turner ALS Foundation: And we really, will continue to look for new ways in which to improve that, whether it's social media engagement, or,

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01:43:01.590 --> 01:43:04.129

Lauren Webb, Les Turner ALS Foundation: engagement in other ways. Next slide.

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01:43:05.950 --> 01:43:25.129

Lauren Webb, Les Turner ALS Foundation: So, I just wanted to show this, couple of pictures. We, promoted, the National ALS Registry at our walk, and the CDC always joins us, which we really enjoy having their presence, to really, work a booth and have communications with

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01:43:25.130 --> 01:43:30.629

Lauren Webb, Les Turner ALS Foundation: our clinical researchers, our basic science researchers, it's a really nice event.

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01:43:30.820 --> 01:43:39.980

Lauren Webb, Les Turner ALS Foundation: And then we launched... we had our, Les Turner Symposium, in 2025, and we had over 305 attendees.

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01:43:40.590 --> 01:43:47.509

Lauren Webb, Les Turner ALS Foundation: So we promoted the registry both virtually and in person, through slides, and we also had a table. Next slide.

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01:43:48.600 --> 01:43:58.629

Lauren Webb, Les Turner ALS Foundation: So what was really beautiful about, our, symposium in 2024 was we had an opportunity, to,

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01:43:58.660 --> 01:44:12.670

Lauren Webb, Les Turner ALS Foundation: take photos of, two amazing people who serve on our Support Services Committee, Melissa and Barbara. And so, with those photos, you'll be seeing their, their pictures and their stories.

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01:44:12.670 --> 01:44:24.149

Lauren Webb, Les Turner ALS Foundation: Attached to the National ALS Registry. We also, promote the registry through the Our Foundation newsletters. In fact, we just,

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01:44:24.160 --> 01:44:36.170

Lauren Webb, Les Turner ALS Foundation: Had a newsletter go out in August. We have about 48,000 newsletter subscribers, and then, I believe it was in 2025, Anne-Marie started adding information

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01:44:36.410 --> 01:44:47.270

Lauren Webb, Les Turner ALS Foundation: To, the ALS Learning Series, about the CDC registry to our ALS Learning Series in our opening remarks. So,

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01:44:47.510 --> 01:45:01.250

Lauren Webb, Les Turner ALS Foundation: I think what is really important, and that we've learned over the years, is that we have to incorporate the National ALS Registry into all aspects of our work. It's been an honor and a privilege to work with families and to learn

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01:45:01.250 --> 01:45:10.580

Lauren Webb, Les Turner ALS Foundation: More, with my team about ways in which to improve the registry, engagement, and outreach. And I just wanted to... next slide, please.

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01:45:10.830 --> 01:45:18.780

Lauren Webb, Les Turner ALS Foundation: I just wanted to thank the people living with ALS and their families for all the time and energy that they put into,

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01:45:18.910 --> 01:45:22.230

Lauren Webb, Les Turner ALS Foundation: Completing surveys and,

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01:45:22.650 --> 01:45:34.439

Lauren Webb, Les Turner ALS Foundation: And I think it's really important, sessions like this to be able to highlight how impactful the registry is. So thank you. And I apologize for my little guest appearance.

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01:45:36.860 --> 01:45:58.859

Danielle Boyce: That's okay. Lauren, we... you might... I have four at home, so there might be a few of those on my end, too. No worries. Humanizes it, right? Thank you, Lauren. And, you know, one thing that never really occurred to me that I took away from what you said was, this could... the registry is an opportunity for clinicians to learn more about

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01:45:58.860 --> 01:46:13.599

Danielle Boyce: about the people with ALS and their caregivers and their families, maybe asking questions that they had not asked in clinic, and so I hadn't even really considered that, but it sounds like that kind of partnership could be really useful for more than just research.

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01:46:13.600 --> 01:46:16.320

Lauren Webb, Les Turner ALS Foundation: Yeah, I mean, it just drives that,

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01:46:16.430 --> 01:46:26.819

Lauren Webb, Les Turner ALS Foundation: relationship, and it opens up additional conversation, and it's part of, you know, supporting people in the communities that they serve. So, thank you so much, Danielle.

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01:46:26.820 --> 01:46:49.959

Danielle Boyce: Yeah, yeah, thanks, thanks a lot, Lauren. And so we're going to hold questions for this until after the next couple of presenters, but if you have any questions for Lauren, please put them in the Q&A, and we will answer them at the end, or live, depending on the nature of the question. Okay, so next up, it is my great pleasure to introduce Peyton Neverett.

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01:46:49.960 --> 01:46:55.839

Danielle Boyce: She has been with the MDA for 13 years, and is the Care Center Network Director.

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01:46:55.840 --> 01:47:14.060

Danielle Boyce: She provides strategic and technical assistance to sites within the care center network and works collaboratively within MDA and among community partners, sharing information and resources that are relevant to clinicians, members, and families. Thank you so much for joining us, Peyton. I'm going to turn it over to you now.

Muscular Dystrophy Association (MDA) - Peyton Navarrete

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01:47:14.590 --> 01:47:23.290

Peyton Navarrete: Thank you so much, Danielle. And thank you to the ALS Registry Team for hosting this meeting. I'm glad we were able to all come together again after having a year off.

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01:47:23.480 --> 01:47:30.240

Peyton Navarrete: So for this presentation, I'm going to walk you all through our MDA programs and how we connect our members

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01:47:30.420 --> 01:47:37.569

Peyton Navarrete: connect with our members, and really detail some of the ways that we weave education about the ALS registry throughout their journey.

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01:47:37.570 --> 01:47:59.150

Peyton Navarrete: We all know, and you've heard from the other partners as well, it's not something that you just talk about once, and then you're done talking about it. You really... you have to find when they're ready on their journey to join something like the ALS registry, and so we do our best to try and, sprinkle it through all of our programs, really, so that when they're ready to do it, the information is available to them.

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01:47:59.160 --> 01:48:00.319

Peyton Navarrete: Next slide, please.

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01:48:03.310 --> 01:48:17.889

Peyton Navarrete: So, MDA's mission is to empower the people that we serve to live longer, more independent lives. For over 75 years, MDA has led the way in accelerating research, advancing care, and advocating for the support of MDA families.

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01:48:17.920 --> 01:48:28.729

Peyton Navarrete: We unite researchers, clinicians, advocates, and families to speed the pace of discovery, improve access to expert care, and ensure inclusion in every aspect of life.

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01:48:29.090 --> 01:48:45.429

Peyton Navarrete: What's different about MDA is that we are, we've always used the term an umbrella organization, but we really, we work across disease-specific boundaries within the neuromuscular space, because research breakthroughs in one disease can really help fuel progress in others.

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01:48:45.430 --> 01:48:53.649

Peyton Navarrete: Our mission is to give people that we... give the people we serve the tools and opportunities that they need to live longer and more independent lives.

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01:48:53.660 --> 01:48:54.979

Peyton Navarrete: Next slide, please.

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01:48:57.150 --> 01:49:09.730

Peyton Navarrete: We take a multifaceted approach to what we do, aiming for impacts greater than just the sum of its parts. So, through these 6 channels, our efforts focus on having a positive impact on the people we seek to support.

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01:49:09.840 --> 01:49:17.809

Peyton Navarrete: We foster unity through engagement with families, volunteers, local institutions, and organizational partners across the U.S.

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01:49:18.130 --> 01:49:38.070

Peyton Navarrete: Our research department is very robust, and I'll go a little bit more in detail with them on the next slide. Our MDA Advocacy Department is dedicated to do everything... dedicated to doing everything in their power to advocate for public policies and programs that empower everyone living with a neuromuscular disease.

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01:49:38.070 --> 01:49:41.189

Peyton Navarrete: And together, we ensure that our collective voice is heard.

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01:49:41.990 --> 01:49:53.399

Peyton Navarrete: Our access to care involves our MDA Care Center network. It spans the nation and Puerto Rico, and I will go into much more detail on this in the coming slide.

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01:49:53.560 --> 01:50:09.709

Peyton Navarrete: We offer quite a bit of education, both for the community, individuals, and their families living with neuromuscular disease, but also, to clinicians and, CE-accredited webinars and things like that to help ensure that they have the information that they need.

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01:50:10.060 --> 01:50:27.209

Peyton Navarrete: Our recreation offers... offerings include MDA Summer Camp, which is for individuals under 17 and under, but also our Family Weekends. And really, our family weekends started within the last few years and are open to all individuals and their families, not just for kids.

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01:50:27.390 --> 01:50:37.240

Peyton Navarrete: Finally, engagement when our families and individuals and community can all come together to show, the support and be here. Next slide, please.

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01:50:39.980 --> 01:50:54.479

Peyton Navarrete: SWAMDA is the largest non-governmental funder of neuromuscular research in our country. Since our inception, we have invested more than \$1.1 billion in neuromuscular research, and we are aggressively working to advance therapy development

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01:50:54.480 --> 01:51:02.850

Peyton Navarrete: Through innovative research at universities and industry, and along with the collection of healthcare data, and seeing where that takes us.

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01:51:03.200 --> 01:51:13.350

Peyton Navarrete: We currently have 18 active ALS grants, and again, our funding model... our model of funding research across diseases means that

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01:51:13.430 --> 01:51:31.510

Peyton Navarrete: findings within one disease can help enable the progress in others. This is... this slide shows the... what we are funding out, but that we also very much talk about the ALS registry with our family and support team, and I will go into that in just a little bit. Next slide, please.

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01:51:35.330 --> 01:51:46.339

Peyton Navarrete: MDA's National Care Center Network serves as a platform through which there's an opportunity for both MDA staff and MDA Care Center clinicians to connect with the ALS community.

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01:51:46.700 --> 01:51:51.459

Peyton Navarrete: We have more than 150 Care Center Network sites, as I mentioned before.

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01:51:51.480 --> 01:52:06.730

Peyton Navarrete: 47 of those are designated as an MDA ALS care center, which offers best-in-class care. The MDA ALS Care Center is a designation above an MDA Care Center, because of the additional work that they do with ALS.

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01:52:06.730 --> 01:52:20.519

Peyton Navarrete: But that's not to discount our other care centers. Many, many of them also see ALS patients. It's about a... just over 120 care center network sites see ALS patients.

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01:52:20.540 --> 01:52:25.599

Peyton Navarrete: Either in their ALS specialty clinic, or as part of their neuromuscular disease clinics.

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01:52:25.810 --> 01:52:41.030

Peyton Navarrete: We've surveyed them in the past, and nearly 80% of them are actively sharing information about the ALS registry. Even if MDA's not able to be there in person, or we miss somebody when we do our post-clinic follow-up.

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01:52:41.030 --> 01:52:47.469

Peyton Navarrete: We want to make sure that the information about the registry is being shared at our multidisciplinary care centers.

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01:52:47.470 --> 01:52:50.589

Peyton Navarrete: And... and we do have a very robust

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01:52:50.590 --> 01:53:00.619

Peyton Navarrete: set of sites that are doing that. We will also continue to work with all of our sites to ensure that that registration information is available for individuals when they need it.

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01:53:01.290 --> 01:53:02.510

Peyton Navarrete: Next slide, please.

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01:53:04.780 --> 01:53:13.950

Peyton Navarrete: So what happens at an MDA Care Center visit? You heard from the previous two, speakers the talking about a multidisciplinary clinic, and so

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01:53:14.130 --> 01:53:21.230

Peyton Navarrete: In addition to having a highly qualified neurologist or physiatrist, patients are seen by a variety of additional specialists.

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01:53:21.440 --> 01:53:33.360

Peyton Navarrete: A PT, OT, genetic counseling, speech and language, social services. Woven into all of this is our family and... the MDA's family and clinical services staff.

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01:53:33.360 --> 01:53:42.599

Peyton Navarrete: We often follow up with, individuals after they're seen at a care center to see if we can provide additional resources, materials, updates.

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01:53:42.760 --> 01:53:46.610

Peyton Navarrete: As part of their journey.

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01:53:46.850 --> 01:54:02.849

Peyton Navarrete: This helps us provide a number of touchpoints with their families, with individuals and their families, and we're able to provide education and information, call-out initiatives and additional, resources, as mentioned.

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01:54:04.180 --> 01:54:14.020

Peyton Navarrete: Additionally, we use this care center network infrastructure to provide promotional and educational information to, newly diagnosed ALS

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01:54:14.180 --> 01:54:19.060

Peyton Navarrete: Folks, as well as, any caregivers, families, or supports that are there.

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01:54:19.730 --> 01:54:20.959

Peyton Navarrete: Next slide, please.

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01:54:23.730 --> 01:54:28.820

Peyton Navarrete: Another, avenue here at MDA is our advocacy initiatives and programs.

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01:54:28.890 --> 01:54:45.050

Peyton Navarrete: On screen, you'll see our 2026 priorities includes things like care therapies, accelerating therapy development, and empowerment of the individual. The link on this first graphic will take you directly to our Action Center, where it's very easy to get involved.

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01:54:45.450 --> 01:54:58.940

Peyton Navarrete: Our advocacy department has grown in recent years, and we participate in quite a few unified efforts with other organizations. The great example this year is the Act for ALS Reauthorization Act.

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01:54:58.940 --> 01:55:05.579

Peyton Navarrete: Where more than 25 ALS organizations came together to successfully pass versions in both the House and the Senate.

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01:55:05.580 --> 01:55:17.920

Peyton Navarrete: Right now, there's a little bit of differences between those versions that are being reconciled before it can be sent to the President. But really, that just shows the power of what happens when we can all come together with a united voice.

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01:55:18.820 --> 01:55:35.240

Peyton Navarrete: This last graphic, shows our Advocacy Institute. It's open to all and provides skills and updates on issues from Capitol Hill to other agencies. And if you're not able to attend the Advocacy Institute when it's live, recordings are available on our website.

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01:55:35.970 --> 01:55:37.120

Peyton Navarrete: Next slide, please.

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01:55:39.790 --> 01:55:48.939

Peyton Navarrete: We have quite a few ways that we can... that you all can connect with MDA, and that we can connect with our community. We're committed to providing

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01:55:49.150 --> 01:55:55.590

Peyton Navarrete: Compassionate care and quality education and connections throughout the neuromuscular journey.

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01:55:55.660 --> 01:56:13.969

Peyton Navarrete: Mda staff members across the organization are able to directly interact and make these meaningful connections, where they can share resources, things... they are constantly sharing the ALS registry information when it comes up. Our National Resource Center includes a team of resource specialists.

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01:56:14.400 --> 01:56:26.599

Peyton Navarrete: Who can connect you to either resources within MDA, and if it's something that we cannot assist with, we have quite the robust resource list, and we can send you, a list of those.

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01:56:27.240 --> 01:56:28.530

Peyton Navarrete: Next slide, please.

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01:56:31.040 --> 01:56:43.639

Peyton Navarrete: Our family support team really is the bread and butter of outreach to our families. I've mentioned some of the touchpoints within the care centers. They listen to experiences, they share connections.

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01:56:43.740 --> 01:56:52.320

Peyton Navarrete: And in the past few years, we've launched a number of new connection programs to help facilitate and share knowledge within the community.

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01:56:52.430 --> 01:57:02.319

Peyton Navarrete: We... I believe it was a year or two ago, we launched an MDA community support group specifically geared towards individuals with ALS and those supporting them.

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01:57:02.470 --> 01:57:13.149

Peyton Navarrete: Our peer connections allows the MDA support... the family support team to connect individuals one-on-one with another member that

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01:57:13.410 --> 01:57:33.350

Peyton Navarrete: may have a similar situation, or may be able to, just provide that peer support that's different, than somebody from MDS... MDA, pardon me. Our gene therapy support network is specifically designed to help individuals and families navigate the very rapidly changing gene therapy landscape.

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01:57:33.720 --> 01:57:49.369

Peyton Navarrete: Our MDA Connect program is a really cool program where we can... an individual can schedule a face-to-face video call with a specialist, at a time that fits for them. We know that everybody's lives are busy.

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01:57:49.370 --> 01:58:01.170

Peyton Navarrete: And especially care center visits can be particularly busy, and so we want to make sure that we can meet individuals in their time and on... with a modality that works for them.

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01:58:01.420 --> 01:58:02.750

Peyton Navarrete: Next slide, please.

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01:58:07.120 --> 01:58:17.259

Peyton Navarrete: Our education department has also expanded significantly. The four programs listed here have a ton of print and online resources available.

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01:58:17.280 --> 01:58:28.100

Peyton Navarrete: Each of the opportunities... each of these opportunities provide a touchpoint for MDA to connect with the neuromuscular and ALS community and share information pertinent to them.

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01:58:28.310 --> 01:58:44.950

Peyton Navarrete: The first one here, the MDA Engaged Symposiums, are held, I believe we have four a year. These are in-person events, and I was able to attend the one last fall in Stanford, and while we have small, disease-specific tracks.

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01:58:44.950 --> 01:58:51.889

Peyton Navarrete: There's also a lot of information that is shared as a whole to the neuromuscular clinic, or to the neuromuscular community.

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01:58:52.220 --> 01:59:00.820

Peyton Navarrete: I was the one holding down the MGA resource table at that event, and it was great to be able to connect one-on-one with individuals at that.

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01:59:00.870 --> 01:59:19.240

Peyton Navarrete: Shared quite a few ALS registry folders, even though... and it was interesting, because a lot of times people told me, oh yes, I saw that folder, I don't know where it went. And so, this is where we meet them in that moment, and if they saw it before, and maybe they cast it aside, here's a new opportunity to share that with them.

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01:59:19.280 --> 01:59:24.129

Peyton Navarrete: I'll go a little bit more in detail on a few of these programs. Next slide, please.

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01:59:28.500 --> 01:59:38.419

Peyton Navarrete: This year's Virtual Learning Spotlight on ALS took place in May. It was hosted live with the components you see here on the screen, and then it's available on demand afterwards.

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01:59:38.600 --> 01:59:49.029

Peyton Navarrete: The comprehensive Learning Series focused on ALS, and it covered the latest research updates, treatment strategies, and supportive care options for those living with ALS.

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01:59:49.930 --> 01:59:50.860

Peyton Navarrete: Next slide.

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01:59:54.390 --> 02:00:11.550

Peyton Navarrete: So just last week, we held our Next Steps seminar for newly diagnosed ALS patients and families. The Next Steps seminar, we have several different, seminars in this series, but the... currently, the newly diagnosed ALS one is held once a year.

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02:00:11.640 --> 02:00:23.910

Peyton Navarrete: And that's to capture a very robust community and try and get as many people within that webinar as possible. There are potentially plans to expand, but we don't have anything set in place at this point.

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02:00:24.050 --> 02:00:37.050

Peyton Navarrete: It is currently a one-day virtual program. It's a mix of on-demand viewing, live presentation, and discussion, along with a roadmap for participants, so from diagnosis to all that comes next.

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02:00:37.330 --> 02:00:44.080

Peyton Navarrete: The ALS registry materials are discussed within this, and shared as a very important resource.

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02:00:44.830 --> 02:00:46.139

Peyton Navarrete: Next slide, please.

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02:00:49.580 --> 02:00:57.010

Peyton Navarrete: Finally, I wanted to highlight our Quest Media platform, which now includes a Quest podcast and blog in addition to Quest Magazine.

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02:00:57.250 --> 02:01:16.500

Peyton Navarrete: Hopefully, individuals or partners have seen our Quest magazine before. It's been in print for more than 25 years. It was established as a national flagship quarterly resource for individuals and families affected by neuromuscular disease, and it is a wealth of information. It has individual stories, it has

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02:01:16.570 --> 02:01:35.240

Peyton Navarrete: industry information, it has research updates. We continued... with the continued expansion of these platforms and adding in the podcasts and the blogs and, all of those things, we can really connect directly to the patient, provider, and research communities.

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02:01:35.350 --> 02:01:49.079

Peyton Navarrete: You'll see here in this picture, the registry is featured prominently on the inside back cover of the print magazine each quarter, and members of the registry team have participated both in print articles and blog articles in the past.

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02:01:49.530 --> 02:01:50.740

Peyton Navarrete: Next slide, please.

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02:01:55.000 --> 02:02:11.100

Peyton Navarrete: MDA has a very busy digital community. It is robust and thriving, and these are just a few of the ways we actively engage with individuals, families, community, and industry partners across these platforms. We know that the digital world is

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02:02:11.330 --> 02:02:17.100

Peyton Navarrete: kind of where everybody is now, and we want to make sure that we are available to all. Next slide, please.

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02:02:19.620 --> 02:02:27.600

Peyton Navarrete: These are the links to all of those, digital platforms, so that if you are not already following MDA, these are available to you.

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02:02:29.790 --> 02:02:31.310

Peyton Navarrete: Next slide, please.

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02:02:33.590 --> 02:02:47.900

Peyton Navarrete: And I wanted just to provide a few contact updates. These can go out in an email off, so afterwards, if you are interested, I have Meredith Donovan, our Senior Director, my contact information, our Resource Center, as well as our advocacy team.

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02:02:48.790 --> 02:02:51.700

Peyton Navarrete: And that is all for MDA. Thank you very much.

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02:02:52.400 --> 02:03:15.849

Danielle Boyce: Thanks so much, Peyton. Yeah, Lauren in the chat had mentioned, the digital work, the Quest resource, and, you know, what I come away when I'm, you know, talking today with all of you partners is just the deep connections in the community and the importance of meeting people where they are, in the research process, and just how important it is to really understand

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02:03:15.850 --> 02:03:26.910

Danielle Boyce: the community, the population, the challenges that they face in participating in research, and that's where this partnership can really come in. And I really appreciate that and appreciate you.

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02:03:26.910 --> 02:03:50.059

Danielle Boyce: And speaking of deep expertise, our next speaker is Adina Bradshaw, Chief Impact Officer at Team Gleason, who drives innovative, person-centered solutions for people living with ALS. Now, remember earlier when I was talking about the eye gaze technology and making sure everyone with eye gaze could use the Zoom Q&A,

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02:03:50.060 --> 02:04:05.259

Danielle Boyce: This is the group that pioneered that work and advocates for that work, among many other things. And so, a speech-language pathologist with 20-plus years in assistive technology, she collaborates with tech leaders, universities.

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02:04:05.260 --> 02:04:14.920

Danielle Boyce: industry and healthcare providers to advance evidence-based care and technology. Thank you so much for coming today. Adina. I'm going to turn it over to you.

Team Gleason - Adina Bradshaw

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02:04:15.700 --> 02:04:33.239

Adina Bradshaw: Thank you so much. It's, hard to follow Patty and Lauren and Peyton. I have enjoyed every conversation we've had on the partner meetings, when I've joined in, and being, Team Gleason, being a partner to the CDC, ATSDR ALS registry has been

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02:04:33.240 --> 02:04:50.229

Adina Bradshaw: a joy for me. I know it's not much to say a joy in these situations, but I've learned so much from this community and enjoyed speaking about what the registry does with our staff and with the community, so thank you again all for being here and for inviting us.

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02:04:52.180 --> 02:05:02.550

Adina Bradshaw: I'm not sure. I've learned, that some people outside of the South don't know much about Team Gleason, so I'm going to give a little bit of an overview about what we do, and...

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02:05:02.750 --> 02:05:14.140

Adina Bradshaw: hopefully finish up in 7 minutes. As, you know, I'm a Dean of Bradshaw. I oversee our program services, innovation, partnership, education, training, and clinical

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02:05:14.180 --> 02:05:31.489

Adina Bradshaw: support, and then Kelly Beater, is often on our calls, and some of you may have spoken with her. She, facilitates our virtual support groups, she facilitates our, Team Gleason Presents quarterly webinars, and she is, a wealth of knowledge for our

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02:05:31.490 --> 02:05:40.500

Adina Bradshaw: community. She also coordinates our respite care program that provides respite services and funding to people in multiple states in the United States.

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02:05:40.610 --> 02:05:41.980

Adina Bradshaw: Next slide.

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02:05:43.120 --> 02:05:56.370

Adina Bradshaw: So, Team Gleason, our mission is to improve the life for people living with ALS and those who care for them by delivering innovative technology and equipment, as well as providing an empowering and improved life experience.

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02:05:56.780 --> 02:06:09.480

Adina Bradshaw: And Steve's vision when he started the organization, in September will be 15 years. We'll be celebrating our 15-year anniversary. He believes that until there's a cure for ALS, technology is a cure.

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02:06:09.650 --> 02:06:19.590

Adina Bradshaw: So, we believe our vision is a world where people living with ALS have the resources and opportunities not to just continue to live, but continue to live productive, purposeful, and meaningful lives.

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02:06:20.000 --> 02:06:38.390

Adina Bradshaw: And then the technology, obviously, hopefully, will help them. So, since our inception, Team Gleason has provided over \$40 million in adventure, technology, equipment, and care services to people living in the ALS... living with ALS in the United States, since we were founded in 2011.

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02:06:38.820 --> 02:06:49.950

Adina Bradshaw: We are a 503 nonprofit, and our demand for services has grown significantly over even just the past 5 years as technology has become more

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02:06:49.950 --> 02:07:00.009

Adina Bradshaw: mainstream and available and affordable. Over the past 5 years, our requests for services have increased by 105%.

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02:07:00.010 --> 02:07:02.240

Adina Bradshaw: And...

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02:07:02.710 --> 02:07:10.470

Adina Bradshaw: we strive to provide whatever equipment or services that we can for the community. You can go to the next slide.

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02:07:10.890 --> 02:07:12.699

Adina Bradshaw: I'll try to run through these little quick.

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02:07:12.730 --> 02:07:31.719

Adina Bradshaw: Next slide. There we go. So, some of the services that we provide, we are a little bit different than the other partners in that we do focus on the technology, innovation, equipment, support, and the adventures, and then advocacy and awareness, more so than research. So...

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02:07:33.520 --> 02:07:41.929

Adina Bradshaw: We want to be the bright spot in the journey for everyone living with ALS and their care partners, so we want to provide those tools and resources for them.

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02:07:42.440 --> 02:07:48.019

Adina Bradshaw: And that is including eye gaze technology, grants for,

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02:07:48.240 --> 02:08:10.459

Adina Bradshaw: co-pays for insurance, if insurance doesn't pay for the full equipment. We have a loaner program, a robust loaner program, that we provide portable power wheelchairs for people living with ALS. They can request the wheelchair, and we send it to them in a box, and we tell them to keep the box, and when they no longer need it, they can send it back to us, and then we can send it to another community member.

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02:08:10.460 --> 02:08:15.039

Adina Bradshaw: That may need it. We provide shower chairs and alternative drive controls.

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02:08:15.330 --> 02:08:27.090

Adina Bradshaw: loaner pieces of equipment. We fund voice preservation services and the actual voice, because the cost of the voice, can be more expensive. We will also

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02:08:27.120 --> 02:08:41.029

Adina Bradshaw: walk through, or support people through the voice preservation process, which can be, somewhat daunting, when a lot of information is being, thrown at you. And so.

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02:08:41.590 --> 02:08:53.570

Adina Bradshaw: Often, in these sessions, when someone requests services from us, we will go through and identify what services they need, and talk to them about the registry once they've received their services.

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02:08:53.570 --> 02:09:02.960

Adina Bradshaw: Additionally, anytime someone requests services from Team Gleason, they receive an email, with a, a packet, it's like a welcome packet.

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02:09:02.960 --> 02:09:13.900

Adina Bradshaw: That talks about our services, and the flyer for the registry is included in that, so that we can follow up when we do speak to our staff, the community member on the phone.

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02:09:13.900 --> 02:09:23.020

Adina Bradshaw: We have 23 staff members, and about 7 staff members are fulfilling requests daily. Each of them,

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02:09:23.060 --> 02:09:27.419

Adina Bradshaw: Has about... oh gosh, we maintain a caseload of over 100.

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02:09:27.920 --> 02:09:35.399

Adina Bradshaw: Calls, interactions per week, and we receive over 800 requests for services, every month.

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02:09:35.640 --> 02:09:40.020

Adina Bradshaw: try to run through this quick, because I know we have some time.

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02:09:40.660 --> 02:09:43.289

Danielle Boyce: Please take your time. Sorry, Adina, please take your time.

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02:09:43.290 --> 02:09:43.820

Adina Bradshaw: Very good.

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02:09:44.340 --> 02:09:47.159

Adina Bradshaw: So,

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02:09:48.070 --> 02:10:01.319

Adina Bradshaw: I'll go through a little bit of our services then when we have a little bit more slowly. Voice banking and message banking, or voice preservation. The voice preservation services and technology have,

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02:10:01.890 --> 02:10:15.060

Adina Bradshaw: grown and changed very rapidly in the past 3 years, so there's, we, we are committed to ensuring that anybody with ALS who would like to preserve their voice

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02:10:15.180 --> 02:10:34.500

Adina Bradshaw: has the solutions and opportunities and education to do that, so that if and when they do need to use that voice on a piece of technology, if they do lose their ability to speak, they have something that sounds like them, that is part of their autonomy and part of your, identity. And so, we will...

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02:10:34.500 --> 02:10:37.479

Adina Bradshaw: Educate, and,

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02:10:37.890 --> 02:10:46.849

Adina Bradshaw: support through that process. At any point in the journey, we have people that come to us right as, you know, a couple days after they've been diagnosed, if they've been

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02:10:47.120 --> 02:10:54.670

Adina Bradshaw: heard about Team Gleason from their ALS clinic, and then we have people who, a little bit later on, their voices might be changing, and we have some people who

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02:10:54.670 --> 02:11:08.779

Adina Bradshaw: need to use previous recordings to create a voice, and we, provide all the education technology solution to do that. If somebody needs a recorder or a headset in order to do the recordings, we'll do it. We often meet with them virtually.

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02:11:08.900 --> 02:11:13.039

Adina Bradshaw: Because there's just a lot of information, and we want to be able to help them with that.

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02:11:13.250 --> 02:11:25.740

Adina Bradshaw: Access, to, solutions, so we provide guidance on alternative access methods for augmented alternative communication systems, speech generating devices,

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02:11:25.740 --> 02:11:35.219

Adina Bradshaw: keyboards, mice for, communication technology. We will provide that equipment to them so that, again, if they... if you

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02:11:35.710 --> 02:11:40.429

Adina Bradshaw: Want to continue to work or use the computer,

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02:11:40.740 --> 02:11:57.419

Adina Bradshaw: anything you want to do in the community, environment, you have that technology to do that. In addition to these services, we also partner with DME companies, CRT, technology companies, to,

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02:11:57.480 --> 02:12:04.099

Adina Bradshaw: innovate and improve access to the technology, so, Apple Personal Voice.

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02:12:04.280 --> 02:12:10.019

Adina Bradshaw: We worked with them. We are part of the Speech Accessibility Project that's,

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02:12:10.490 --> 02:12:20.790

Adina Bradshaw: Funded by, several big tech companies to improve access to, speech-to-text, or speech communication devices, or... sorry.

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02:12:22.440 --> 02:12:39.029

Adina Bradshaw: speech devices where, if you have atypical speech, you can still control your Amazon Alexa or Google to watch what I say, and you... or Siri, even if your speech may, have atypical speech patterns. We also partner with the,

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02:12:39.360 --> 02:12:53.000

Adina Bradshaw: Thank you, Lynn. We also partner with the, brain-computer interface, and, implantable brain-computer interface, vendors, and we are a part of the IBCICCC.

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02:12:53.240 --> 02:13:00.050

Adina Bradshaw: Which is a collaborative community of researchers and, community

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02:13:00.430 --> 02:13:14.940

Adina Bradshaw: Advocates and people living with speech mobility and communication disabilities to ensure that the brain-computer interface technology that is developed is developed with the consumer or the user in mind.

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02:13:15.080 --> 02:13:31.150

Adina Bradshaw: And that there are outcomes for it. So, we are often involved with a lot of the development of the technology that many of you are aware of. Advocacy awareness, we are, just like all of our peers, we are grateful.

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02:13:31.640 --> 02:13:51.160

Adina Bradshaw: to see the Act for ALS, move forward and advocate for that. Locally, I think there was a question if what we're doing, if any of the organizations are working to mandate reporting. In Louisiana, Team Gleason has been involved with, trying to get a

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02:13:51.310 --> 02:13:55.880

Adina Bradshaw: Registry and mandated reporting in the state there.

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02:13:56.090 --> 02:14:00.390

Adina Bradshaw: We've had conversations with them. And then...

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02:14:00.900 --> 02:14:07.650

Adina Bradshaw: We also have our Adventures Program. The Adventures Program started because Steve and Michelle love to

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02:14:07.650 --> 02:14:23.090

Adina Bradshaw: be out in the, outdoors and traveling, and they wanted everyone to have that opportunity, too. So, we plan and document experiences for people living with ALS and their loved ones, while using this platform to,

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02:14:23.560 --> 02:14:29.180

Adina Bradshaw: create a broader public awareness about ALS and,

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02:14:29.560 --> 02:14:37.099

Adina Bradshaw: and the progression. The adventures range from world excursions to milestone celebrations,

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02:14:37.280 --> 02:14:49.450

Adina Bradshaw: with friends and families, we send people to the Super Bowl, and then the adventures not only create these lasting memories, but, advocate for awareness for people living with ALS.

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02:14:49.880 --> 02:15:06.780

Adina Bradshaw: Monthly, we have virtual community gatherings where people with ALS, their caregivers connect, share experiences, receive resources, and those are led by Kelly, and Kelly speaks about the ALS registry in every single one of her community,

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02:15:06.790 --> 02:15:21.859

Adina Bradshaw: community groups, and there are local community groups in Louisiana, and then there are also national groups, for caregivers, and children, and then people living with ALS. Some of our advocacy efforts are

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02:15:22.390 --> 02:15:32.870

Adina Bradshaw: still relevant today. In 2015, we passed the Act for, Steve Gleason, Act, which ensures Medicare coverage for essential communication devices.

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02:15:33.170 --> 02:15:35.420

Adina Bradshaw: And then,

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02:15:35.920 --> 02:15:52.849

Adina Bradshaw: In 2024, Steve received the Arthur Ashe Award for Courage at the ESPYs, and he received the Congressional Gold Medal. So we are continuing to advocate, for legislation that provides financial

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02:15:53.080 --> 02:15:55.010

Adina Bradshaw: and research.

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02:15:55.410 --> 02:15:58.930

Adina Bradshaw: support for people living with ALS.

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02:15:59.660 --> 02:16:18.890

Adina Bradshaw: Next slide, let me go real quick. There we go. If you are not familiar with Team Gleason, or you know someone who might want to get... connect with us or receive assistance, you can request assistance on our website. We also recently moved to a new system.

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02:16:18.890 --> 02:16:30.430

Adina Bradshaw: I think Peyton mentioned it, or Lauren. And so, to request services, you would go to our portal, our website, click Needs Assistant, and then apply for assistance.

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02:16:30.430 --> 02:16:40.529

Adina Bradshaw: And then we will... our staff members will reach out to the assistant, and the person needing assistance, or their care partner, and request more information and discuss our services.

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02:16:40.820 --> 02:16:43.499

Adina Bradshaw: I do want to mention,

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02:16:43.850 --> 02:16:56.469

Adina Bradshaw: one at the outreach, I know there was a mention that there was much social media that we could be done. I was just looking at some of our reporting metrics, and we did a post on social media, Facebook,

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02:16:56.620 --> 02:16:59.900

Adina Bradshaw: in June, for the...

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02:17:01.709 --> 02:17:18.259

Adina Bradshaw: let's see... CDC registry, and our posts typically range, in terms of views and engagement. We have over 12,000 views, with usually a couple hundred clicks or engagement in them, so we've been really trying to,

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02:17:19.959 --> 02:17:30.239

Adina Bradshaw: use our social media platform and our connection with the community to discuss and share about the registry also. Go ahead, next slide, I'll go quickly.

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02:17:30.480 --> 02:17:49.980

Adina Bradshaw: So, our outreach plans, we have an email that goes out to 16,000 people, it is our quarterly PALS newsletter. And in the newsletter, we talk about our services, we share information with our partners, and the registry is always

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02:17:49.980 --> 02:17:52.450

Adina Bradshaw: Listed in there, and that went out last week.

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02:17:52.450 --> 02:18:04.809

Adina Bradshaw: We typically have over a 50% open rate in that. Our social media is very active, and we always enjoy receiving questions and interacting with the community that way.

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02:18:04.920 --> 02:18:18.920

Adina Bradshaw: We attend multiple national assistive technology research, and, industry conferences every year, and we mention or talk about the registry in each one, and, hand out

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02:18:19.440 --> 02:18:25.920

Adina Bradshaw: our flyers and information clinic. Team Gleason has a very small clinic in our office, but

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02:18:25.920 --> 02:18:42.660

Adina Bradshaw: In October of 2026, we will be opening the Ochsner Neuroscience Institute with the Ochsner Health System. We will have a suite inside of their main building, and that is also where the ALS Multidisciplinary Clinic will be.

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02:18:42.660 --> 02:18:47.269

Adina Bradshaw: So we will be participating in the multidisciplinary Clinic,

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02:18:47.780 --> 02:18:54.240

Adina Bradshaw: Days. When they have those... those days, we'll have a staff member there, plus we will have our...

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02:18:54.320 --> 02:19:03.999

Adina Bradshaw: In the Team Gleason Suite, we will have all of the technology that we would typically show, and so we are... we will be able to, in real time, work with

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02:19:04.049 --> 02:19:17.969

Adina Bradshaw: the community members who are at the multidisciplinary clinic, and then provide a continuity of care to move from the multidisciplinary clinic to supporting the out... if they have any outpatient services. We can also support the OTs, PTs.

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02:19:17.969 --> 02:19:25.900

Adina Bradshaw: And speech pathologists for the outpatient services within that one narrow clinic. And if you're not familiar with the Ochsner Health System.

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02:19:25.930 --> 02:19:29.949

Adina Bradshaw: It is one of the largest health systems in the South?

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02:19:30.670 --> 02:19:46.430

Adina Bradshaw: East, area, and serves, Mississippi, Alabama, Texas, and Louisiana. So we are very excited to move into that space. This is, and very excited to be able to continue the work we're doing on a larger scale.

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02:19:46.620 --> 02:20:03.109

Adina Bradshaw: I already explained the support groups. We have webinars, like, Team Gleason Presents, that are available on our YouTube channel. You can watch any of those recordings. Our outreach calls, we will, provide, again, the services, our

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02:20:03.110 --> 02:20:19.640

Adina Bradshaw: 7 to 10 staff members, when they call people to talk about our services, they will, again, at the right point, mention, again, the registry and talk people through, any information and questions they have, and then the registry is also listed on our website.

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02:20:19.920 --> 02:20:21.080

Adina Bradshaw: Next slide.

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02:20:21.780 --> 02:20:24.039

Adina Bradshaw: And then this is how you can reach us.

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02:20:25.610 --> 02:20:28.740

Adina Bradshaw: And if you have any other questions.

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02:20:28.840 --> 02:20:37.569

Adina Bradshaw: Feel free to reach out. I did not put my email address on here, I apologize. But, thank you all again. It is an honor to be here with you.

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02:20:39.020 --> 02:20:58.899

Danielle Boyce: Thank you so much, Adina, and if you have any questions for Adina about Team Gleason, or the efforts with Team Gleason and the registry, or any of our other partners so far who've presented, please put them in the Q&A if you haven't already. If we don't get a chance to answer your questions before lunch, we will try to get to them later in the day.

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02:20:58.980 --> 02:21:00.380

Danielle Boyce: Thank you so much.

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02:21:01.140 --> 02:21:14.920

Danielle Boyce: Next, we have a great pleasure to have Dr. Lyle Ostro. He is a neurologist for ALS and muscle disorder researcher and director of Temple Neuromuscular Pathology Lab.

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02:21:15.080 --> 02:21:24.780

Danielle Boyce: and the Temple ALS Postmortem Corps, and Guamanian ALS PDC Resources. He serves as a scientific advisory boards for everything ALS,

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02:21:24.800 --> 02:21:38.660

Danielle Boyce: and the ALS Network, and the board of directors of the ALS Hope Foundation. He is also the long-standing chair of the programmatic Panel for the Department of Defense ALS Research Program, or ALSRP.

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02:21:38.700 --> 02:21:45.050

Danielle Boyce: The largest dedicated annual funder, \$40 million a year, of ALS therapeutic discovery and validation.

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02:21:45.150 --> 02:21:58.539

Danielle Boyce: He led ALSRP efforts to develop and refine funding mechanisms to support the development of new, innovative therapeutic ideas, emphasize biomarker development, and encourage open data and resource sharing.

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02:21:58.540 --> 02:22:16.189

Danielle Boyce: He has ALS research grant funding from NIH, serves on several ALS steering committees and review panels, and is widely recognized for his clinical leadership, translational research, and commitment to improving care and accelerating therapies for ALS. Please go ahead, Dr. Ostrom.

Temple University Postmortem Core Partnership - Lyle W. Ostrow, MD, PhD

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02:22:17.220 --> 02:22:35.930

Lyle W. Ostrow MD PhD, Temple LKSOM: Thank you. Really, really glad to be here, really wonderful to see everybody and to hear everybody's talks. I want to just point out on my disclosures, as you mentioned, I have funding from, for this effort, from the CDC, from

everything else, and from NIH, but then also... actually, can you guys see my mouse? Hold on a second.

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02:22:36.380 --> 02:22:38.449

Lyle W. Ostrow MD PhD, Temple LKSOM: How do I point to slides?

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02:22:38.840 --> 02:22:39.550

Lyle W. Ostrow MD PhD, Temple LKSOM: Let's see.

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02:22:40.490 --> 02:22:42.760

Lyle W. Ostrow MD PhD, Temple LKSOM: Can you see it now, or no? Nothing?

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02:22:43.130 --> 02:22:46.299

Samer Khan (she/her): Sorry, I'm screen sharing your slides. Okay.

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02:22:46.300 --> 02:22:53.640

Lyle W. Ostrow MD PhD, Temple LKSOM: Yeah, so there's not a way I can do it, that's fine. Yeah. But just on the bottom there, I wanted to point out that, you know, Paul mentioned that there was, you know, this...

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02:22:53.710 --> 02:23:04.550

Lyle W. Ostrow MD PhD, Temple LKSOM: a funding pause because of what was going on in the government, and ALS Hope Foundation actually really graciously stepped in during that pause to fund these efforts, and

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02:23:04.550 --> 02:23:14.319

Lyle W. Ostrow MD PhD, Temple LKSOM: You know, at any given time, we're working with labs around the world, and if they hadn't done that, you know, all of those projects would have had to stop, because

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02:23:14.470 --> 02:23:26.460

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, these are ongoing efforts, ongoing work, and ALS Hope Foundation and also Temple itself really stepped in in a big way to make sure that things could continue during that funding pause. You can go to the next slide.

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02:23:27.550 --> 02:23:46.460

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, you know, I'm going to talk about why this matters, why we do this, what's the big deal, how we work, and specifically how the funding from the CDC enables us to do things differently than others, and why I think that matters, how we work with research teams around the world, and then I'm also going to talk a little bit specifically about this

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02:23:46.460 --> 02:23:54.480

Lyle W. Ostrow MD PhD, Temple LKSOM: resource these samples and data from the island of Guam, from the epidemic of ALS and Parkinson's dementia.

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02:23:54.610 --> 02:23:59.729

Lyle W. Ostrow MD PhD, Temple LKSOM: That the CDC has facilitated so that we can make them available. So, next slide.

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02:24:00.970 --> 02:24:14.410

Lyle W. Ostrow MD PhD, Temple LKSOM: So, you know, I don't have to tell you guys this, I mean, ALS is a clinical diagnosis, right? So, and aside from the small portion of people who have a genetic mutation, you know, it... your diagnosis depends on your neurologist saying you have ALS, and

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02:24:15.250 --> 02:24:26.550

Lyle W. Ostrow MD PhD, Temple LKSOM: We know that the biology in different people with ALS is different. I mean, obviously, the clinical picture is different, people progress very differently, but the underlying abnormalities in their biology is also quite different.

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02:24:26.550 --> 02:24:42.260

Lyle W. Ostrow MD PhD, Temple LKSOM: And this is a problem, right? It's a problem for trials, it's a problem for understanding how somebody's changing over time. You know, if I have a clinical trial of a blood pressure medicine, I can tell that somebody's blood pressure go up or down. If I have a clinical trial for diabetes, I can see, like, what happened to their blood sugars.

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02:24:42.550 --> 02:24:56.229

Lyle W. Ostrow MD PhD, Temple LKSOM: if I have a clinical trial for cancer, for a particular kind of cancer, maybe I stick a needle into the tumor and get out some tissue, and then I

can use, you know, the molecular analysis of that tissue to decide who gets which drugs, and

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02:24:56.230 --> 02:25:07.950

Lyle W. Ostrow MD PhD, Temple LKSOM: And I can certainly see if the tumor gets bigger or smaller when I treat somebody. And these are all things that we, you know, can't really do in ALS. We can't take somebody's brain out, but we know

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02:25:07.980 --> 02:25:12.210

Lyle W. Ostrow MD PhD, Temple LKSOM: that there's very different abnormalities in different people. Next slide.

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02:25:13.880 --> 02:25:16.110

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, you know, that's where this...

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02:25:16.110 --> 02:25:37.190

Lyle W. Ostrow MD PhD, Temple LKSOM: this idea of having these autopsy tissues really comes in. And, you know, on the left there, you see there's that little mouse, and as you guys know, like, in the lab, we study this disease with different kinds of models. Maybe we have a mouse that has a genetic type of ALS, or maybe we take, you know, cells from people living with this disease, and we have a way to turn them into brain cells and study them in a dish.

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02:25:37.190 --> 02:25:37.920

Lyle W. Ostrow MD PhD, Temple LKSOM: But...

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02:25:38.050 --> 02:25:50.750

Lyle W. Ostrow MD PhD, Temple LKSOM: But more often than not, those tests that we're doing in the lab are on a particular biological abnormality, like, you know, mitochondria, or oxidative stress, or some particular thing that cells do. And

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02:25:51.030 --> 02:26:07.109

Lyle W. Ostrow MD PhD, Temple LKSOM: And when we take it to clinical trials, we know, as I said, that different people, different stages of disease, different people with ALS, have different abnormalities, and we need to be able to figure out which drugs to give to which people, and, you know, and how to tell if we're affecting the biology we want to affect.

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02:26:07.340 --> 02:26:10.190

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, that's where having these tissues comes in.

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02:26:10.360 --> 02:26:27.219

Lyle W. Ostrow MD PhD, Temple LKSOM: Now, that picture, that second picture of the apple, so what do we actually do in lab? Like, let's say we have cells, or we have mice that have ALS, right? You know, we have our disease, and we have our normal, and we look for something that's different between them. And sometimes it's obvious, like, you know, you can clearly see that an orange is not an apple.

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02:26:27.730 --> 02:26:39.750

Lyle W. Ostrow MD PhD, Temple LKSOM: sometimes it's less obvious. Sometimes, like, that's, you know, two different types of apples, right? And maybe it's hard to tell that they're different, but maybe if I grind them up and do some molecular analysis, or look at their different sorts of ingredients.

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02:26:39.750 --> 02:26:52.090

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, make applesauce, I can analyze that, and I can tell the difference. And then I have some experiment in a lab where I try and figure out, if I give a drug, can I make that one that has disease look like the one that doesn't have disease?

765

02:26:52.280 --> 02:27:02.170

Lyle W. Ostrow MD PhD, Temple LKSOM: And, you know, in this analogy of apples are nerve cells, right, or motor neurons, let's say, you know, let's say that I have an apple orchard, and I have a sick apple tree, and...

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02:27:02.300 --> 02:27:06.619

Lyle W. Ostrow MD PhD, Temple LKSOM: The apples are falling off the tree, and they're dying, and they're, you know, lying on the grass outside.

767

02:27:07.410 --> 02:27:09.640

Lyle W. Ostrow MD PhD, Temple LKSOM: One of the things we think about a lot is.

768

02:27:09.980 --> 02:27:20.850

Lyle W. Ostrow MD PhD, Temple LKSOM: how do I know, like, if I look at the apples that are left on the tree, maybe those aren't the ones to be looking at, because maybe they are protected somehow. Maybe those are the resistant ones. Maybe I need to look at the ones on the grass.

769

02:27:20.870 --> 02:27:33.919

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, the point is that the other thing that we need, besides the tissues, is the really detailed pathology. We need people to look under a microscope and be able to characterize what is... what's abnormal and how abnormal is it.

770

02:27:33.930 --> 02:27:52.240

Lyle W. Ostrow MD PhD, Temple LKSOM: Right? So that we can tell, are we looking at, you know, end-stage disease, or mild disease, or disease that affects neurons, or a different kind of cell? And that stuff varies in every person, actually within a person. A different part of the nervous system might look very different from another part. So, you know, that sort of rigorous analysis lets us then

771

02:27:52.240 --> 02:27:59.030

Lyle W. Ostrow MD PhD, Temple LKSOM: correlate studies that we do on the tissue with what actually is going on. You know, are the apples on the tree? Are the apples on the ground?

772

02:27:59.430 --> 02:28:02.260

Lyle W. Ostrow MD PhD, Temple LKSOM: But our brain isn't...

773

02:28:02.420 --> 02:28:08.749

Lyle W. Ostrow MD PhD, Temple LKSOM: one type of cell, right? It's not just apples. It's not, you know, just neurons. There's all kinds of stuff in there. It's more like apple pie.

774

02:28:09.110 --> 02:28:16.600

Lyle W. Ostrow MD PhD, Temple LKSOM: And the crazy thing is that as ALS progresses, the ratios of those different things change, so it's like the, you know, ingredients in your pie changing.

775

02:28:16.740 --> 02:28:25.620

Lyle W. Ostrow MD PhD, Temple LKSOM: And if you grind up the pie, maybe, and measure something, maybe the measurement just changes because there's less apple and there's more, you know, sugar, or I don't know.

776

02:28:26.310 --> 02:28:41.919

Lyle W. Ostrow MD PhD, Temple LKSOM: And then we talk a lot about things that we measure in blood, or we measure in spinal fluid, and we have to figure out, do those things matter? And they're not that different than that ice cream there that's melting on that piece of pie, right? It's sort of going by the tissues and the cells and picking something up, and we're measuring something in it.

777

02:28:42.070 --> 02:28:51.679

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, having these tissues and having the detailed pathology and the clinical records and the genetics lets us figure this stuff out, lets us figure out what's important.

778

02:28:51.710 --> 02:29:06.119

Lyle W. Ostrow MD PhD, Temple LKSOM: And then we can try and figure out, so what can we measure during life that might correlate with this? For example, you know, we collect muscle specimens from all of these autopsies, and is there something I can see in somebody's muscle that correlates with what I see in their brain? Next slide.

779

02:29:08.030 --> 02:29:17.499

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, you know, in 2012, I founded this post-mortem core at Johns Hopkins, and in 2013, we created a multi-centered effort that was funded by Target ALS.

780

02:29:17.520 --> 02:29:36.089

Lyle W. Ostrow MD PhD, Temple LKSOM: five and later six different centers. And, you know, we directed it out of Hopkins, and that effort, obviously, is still ongoing and doing some really amazing things. It's so wonderful to see. As it progressed, as it got bigger, you know, as the critical mass got bigger and we were working with hundreds of labs everywhere.

781

02:29:36.090 --> 02:29:45.049

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, as the... sort of the site that was directing it, what we found was that we were spending most of our time on admin and regulatory stuff, kind of, you know, it's a...

782

02:29:45.050 --> 02:30:04.190

Lyle W. Ostrow MD PhD, Temple LKSOM: the downside of having a federated model across many centers is that you have... every time there's a new project, there's all these hoops that you have to jump through with the different centers, and, you know, it was really taking a lot of effort, and as most academic efforts are, we don't really have the admin that we perhaps need. So, you know.

783

02:30:04.190 --> 02:30:19.940

Lyle W. Ostrow MD PhD, Temple LKSOM: with funding from the registry in 2021, we separated from that effort, which is still ongoing, and we formed a fully independent academic core. And the reason we did this is it let us just focus on helping researchers, right? Rather than spending all of our time, sort of.

784

02:30:19.940 --> 02:30:30.559

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, making sure that everything was getting done across all these sites in the same way, and that all the regulatory stuff was going. We could literally just focus on whatever we needed to do to accelerate the research.

785

02:30:30.640 --> 02:30:46.649

Lyle W. Ostrow MD PhD, Temple LKSOM: And then in 2023, this effort moved to Temple. I relocated my own clinic and my own lab to Temple. And right around that same time, Paul and the team at the registry were contacted by Dr. Gerudo, who had been

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02:30:46.700 --> 02:30:59.279

Lyle W. Ostrow MD PhD, Temple LKSOM: curating this collection, which we'll talk about in a moment, of these samples from Guam, and... and they then helped us to incorporate those samples into our resource, which we'll talk about in a moment.

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02:30:59.580 --> 02:31:00.570

Lyle W. Ostrow MD PhD, Temple LKSOM: And...

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02:31:01.610 --> 02:31:14.839

Lyle W. Ostrow MD PhD, Temple LKSOM: And then, fast forward to today, as Paul mentioned, we're right in the process right now, this... actually, I think this week, of finalizing the agreement to be able to move this effort on forward. Next slide.

789

02:31:14.960 --> 02:31:34.150

Lyle W. Ostrow MD PhD, Temple LKSOM: Oh, I... wait, actually go back for one sec. There's an important sentence at the bottom there. So this Guam collection that I'm going to talk about, you know, started as an NIH collection that was transferred to Dr. Gerudo and then to Temple, and so the only reason we have these resources is because a whole lot of people over a whole lot of years did a lot of work, and so we're very gracious for... or grateful for all of that. Next slide.

790

02:31:35.400 --> 02:31:50.379

Lyle W. Ostrow MD PhD, Temple LKSOM: And so what do we do, right? So, you know, when somebody has an autopsy normally, maybe they take one or two pieces of the motor cortex, which is what an ALS researcher might want, and, you know, and that brain can only get used by one or two experiments, and that just doesn't cut it, you know?

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02:31:50.600 --> 02:31:57.219

Lyle W. Ostrow MD PhD, Temple LKSOM: every time this damn disease wins... I mean, I'm a... I'm an ALS neurologist, right? I don't... I don't like the fact that... that...

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02:31:57.250 --> 02:32:04.849

Lyle W. Ostrow MD PhD, Temple LKSOM: this disease still beats us, and every time it does, I want to do everything I can so that eventually.

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02:32:04.870 --> 02:32:23.530

Lyle W. Ostrow MD PhD, Temple LKSOM: we win. And certainly, anytime that somebody makes this ultimate donation, we're going to make sure that their tissues and their data is used for as much science as possible. And so, you know, the way that we do this creates a maximum number. Each single autopsy gets used by thousands of experiments, and

794

02:32:23.530 --> 02:32:48.460

Lyle W. Ostrow MD PhD, Temple LKSOM: And everything we do is designed to provide this information and these samples as quickly as possible. And that sentence at the bottom there, like, this is the thing that the CDC funding lets us do, because I don't have to worry about me, right? This isn't about me. You know, it's not about a paper, or getting a grant, or being famous, or all that kind of baloney. Because of this funding that we have, we can just focus on doing whatever we can to accelerate every research project.

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02:32:48.460 --> 02:32:51.940

Lyle W. Ostrow MD PhD, Temple LKSOM: And, and really, you know, spend our time doing that. Next slide.

796

02:32:53.380 --> 02:32:56.080

Lyle W. Ostrow MD PhD, Temple LKSOM: And, and so what do we do? You know, we, we, we...

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02:32:56.510 --> 02:33:01.700

Lyle W. Ostrow MD PhD, Temple LKSOM: Every time that we do one of these research dissections, which, by the way, we built the standard operating procedures

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02:33:01.700 --> 02:33:22.789

Lyle W. Ostrow MD PhD, Temple LKSOM: for these by surveying the research community, and we've done this a few times now over these years, to make sure that we were meeting their needs, to make sure we were providing the right samples, prepared the right way, stored the right way, the right data, and as many as possible. And so we, you know, there are... if you count up all the blocks and the individual pieces of tissue and the slides from one autopsy, it's thousands.

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02:33:22.790 --> 02:33:24.210

Lyle W. Ostrow MD PhD, Temple LKSOM: Not one or two.

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02:33:24.210 --> 02:33:30.150

Lyle W. Ostrow MD PhD, Temple LKSOM: And all of it is linked to this very rigorous data, and it's all done the same way. Next slide.

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02:33:31.930 --> 02:33:39.029

Lyle W. Ostrow MD PhD, Temple LKSOM: And, you know, and this is important, too, because I don't know what's gonna work. We actually, we say yes to everybody, we don't say no. But...

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02:33:39.090 --> 02:33:59.439

Lyle W. Ostrow MD PhD, Temple LKSOM: we do this responsibly, and we make sure that the experiments are going to work, and we work very closely with researchers, so if they have an assay, a test in a lab, that they don't know if it works yet, we help them debug that,

right? We send test sample sets. Maybe, let's say that you have a project that has to do with a certain protein in the brain, you know, that's involved in ALS,

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02:33:59.440 --> 02:34:09.080

Lyle W. Ostrow MD PhD, Temple LKSOM: Well, we can send blinded samples that either have a whole lot of that protein or none of that protein, because we have the pathology, and we have the clinical data, we have the genomics.

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02:34:09.080 --> 02:34:14.929

Lyle W. Ostrow MD PhD, Temple LKSOM: And so we make these black-white sample sets, and we, you know, figure out how to make experiments work.

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02:34:14.980 --> 02:34:24.509

Lyle W. Ostrow MD PhD, Temple LKSOM: We work very closely, and the reason for that is that blue box at the bottom, right? Again, none of this would be possible without the generosity of people who make this donation. Next slide.

806

02:34:25.770 --> 02:34:34.139

Lyle W. Ostrow MD PhD, Temple LKSOM: And, you know, so most of our time is actually spent on Zoom, even way before the pandemic, like 2013, because this is what we do. We...

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02:34:34.250 --> 02:34:51.090

Lyle W. Ostrow MD PhD, Temple LKSOM: We do this on a rolling basis, there's no delay. Somebody sends us a request for samples. Within two weeks, we've scheduled a Zoom, and we are working with them. And whoever they are, let's say it's a postdoc in some lab somewhere, you know, we want to do what we can to get them what they need quickly. And oftentimes.

808

02:34:51.090 --> 02:35:07.330

Lyle W. Ostrow MD PhD, Temple LKSOM: We can do that by actually fostering collaborations with other labs that are already working with us, right? And partly that's because a lot of these labs return the data to us, and every time they do that, it makes the resource better, it makes it more useful for other people, and, you know, really becomes this kind of global lab.

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02:35:07.330 --> 02:35:13.059

Lyle W. Ostrow MD PhD, Temple LKSOM: All of this is provided, you know, free to academic researchers. There is a very small, what's called a transmittal fee.

810

02:35:13.060 --> 02:35:18.200

Lyle W. Ostrow MD PhD, Temple LKSOM: for industry, which is basically covering costs of processing and shipping and that kind of thing. Next slide.

811

02:35:18.970 --> 02:35:25.920

Lyle W. Ostrow MD PhD, Temple LKSOM: And I'm not gonna talk about this, but we have a, like, actually a four-page handout that we send to everybody, kind of, before the first Zoom with us.

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02:35:25.950 --> 02:35:42.600

Lyle W. Ostrow MD PhD, Temple LKSOM: That goes over the sorts of things that we consider when we talk to them, and try to figure out, you know, what are the best samples for their idea? How are we going to figure it out? What's the best comparison? Is it better to use regions of the brain that aren't involved in ALS and compare them to ones that are, or

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02:35:42.640 --> 02:35:55.770

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, compare from different people of different kinds of ALS, and that orange sentence at the bottom there, you know, we think really hard about how can we screw up the experiment? Like, what are the things that could possibly go wrong? And, you know, we test them. Next slide.

814

02:35:58.450 --> 02:36:10.049

Lyle W. Ostrow MD PhD, Temple LKSOM: Oop, it froze. Next slide, there you go. And at any given time, you know, we're probably working with, I don't know, 20, 25 active projects, but this was just kind of for amusement. I asked... I gave

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02:36:10.050 --> 02:36:34.620

Lyle W. Ostrow MD PhD, Temple LKSOM: Claude, like, the, you know, 25 or 30 papers from the last 3 years that I could find, and... or that I know about, I should say, and said, hey, what are these about? And now recognize current ongoing active projects, like, a lot of them haven't published yet, but this was... this was what Claude said right now is most of the... that know those publications, and it's kind of cool. It's definitely true. That top left one, there's a lot that's not published, but, you know, we're working with, say.

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02:36:34.620 --> 02:36:40.459

Lyle W. Ostrow MD PhD, Temple LKSOM: companies who are, you know, thinking of having trials, upcoming trials, targeting these downstream

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02:36:40.590 --> 02:36:47.400

Lyle W. Ostrow MD PhD, Temple LKSOM: abnormal proteins that result when TDP43 isn't doing what it's supposed to do. And how are we working with them? We're helping try to figure out

818

02:36:47.700 --> 02:37:04.709

Lyle W. Ostrow MD PhD, Temple LKSOM: can you make an assay that might work in blood or in muscle that measures these things? So much like they do in cancer, when you have a trial and you give somebody the drug, you can tell, you know, did I have an effect? Did it go up? Did it go down? There's a lot of focus on neuroimmunology right now, as you guys know.

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02:37:04.710 --> 02:37:11.259

Lyle W. Ostrow MD PhD, Temple LKSOM: that molecular subtype, so that's what I was talking about, figuring out can we define different flavors of ALS, different...

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02:37:11.260 --> 02:37:19.810

Lyle W. Ostrow MD PhD, Temple LKSOM: Types of abnormalities, and then if we can define those in the brain, can we find things that correlate with that, that you can measure during life? Like, say, a muscle biopsy, or blood, or spinal fluid?

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02:37:20.190 --> 02:37:21.370

Lyle W. Ostrow MD PhD, Temple LKSOM: Next slide.

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02:37:22.810 --> 02:37:41.049

Lyle W. Ostrow MD PhD, Temple LKSOM: So, we actually... I know some of you probably join. Once a month, I do these things with Terry for Everything ALS, these Citizens Research sessions where, you know, our tagline is that you don't have to be a scientist to think critically, and it really is true. And so, every ALS Hope Foundation newsletter, we feature one of these projects, and

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02:37:41.590 --> 02:37:42.490

Lyle W. Ostrow MD PhD, Temple LKSOM: And...

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02:37:43.160 --> 02:38:01.219

Lyle W. Ostrow MD PhD, Temple LKSOM: the... by the way, the newsletter also has been on hiatus for the past few months, but it's about to start back up, too. You know, and those examples there, like, that looks like alphabet soup, right? Like, look at those ridiculous words. But we really do our best to try and explain this in a way that's digestible, and I wish I should have put the picture, but the one on the left there, that's, you know, Dr. Zhu.

825

02:38:01.220 --> 02:38:10.330

Lyle W. Ostrow MD PhD, Temple LKSOM: This is this project about MG53 that we've been doing, and if you read that last sentence, it says, the green spots in the muscles are the abnormal clumps, right? So we really try to

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02:38:10.370 --> 02:38:20.109

Lyle W. Ostrow MD PhD, Temple LKSOM: to explain this stuff and show pictures in ways that are useful, because, you know, it's the people who are making this donation who really deserve to hear what came from it. Next slide.

827

02:38:21.660 --> 02:38:35.969

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, what's this... what's the deal with this Guam collection that I mentioned a few times? So... so, next slide. So, on the island of Guam, in the 1940s and 50s, there was an epidemic. 10% of the deaths on the island of Guam at that time were due to ALS.

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02:38:36.380 --> 02:38:40.449

Lyle W. Ostrow MD PhD, Temple LKSOM: 10% of the deaths were due to something called Parkinson's Dementia Complex.

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02:38:40.750 --> 02:38:42.220

Lyle W. Ostrow MD PhD, Temple LKSOM: In a, you know.

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02:38:42.220 --> 02:39:05.949

Lyle W. Ostrow MD PhD, Temple LKSOM: families, some people might get one, some might get the other, some might get all three, some might get nothing. This went for many, many decades, and, you know, the NIH set up this center on the island of Guam in the 1950s, and they collected everything. They collected serial blood, they went into the schools and did hearing tests on the children, and EEGs, and hair samples, and they analyzed the dirt in the soil, and the, you know, the water sources, and

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02:39:05.950 --> 02:39:16.240

Lyle W. Ostrow MD PhD, Temple LKSOM: Because the idea was that this must be some sort of, you know, something environmental or an engagement, something where the environment interacting with a genetically susceptible population, nobody really knew.

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02:39:16.810 --> 02:39:20.250

Lyle W. Ostrow MD PhD, Temple LKSOM: they recorded all this data. All of this was sent to us, by the way, and

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02:39:21.950 --> 02:39:23.119

Lyle W. Ostrow MD PhD, Temple LKSOM: I just showed that.

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02:39:23.280 --> 02:39:33.100

Lyle W. Ostrow MD PhD, Temple LKSOM: map there on the right, because right now we're working with a couple researchers who have a hypothesis related to different, you know, things that are freshwater exposures, and the,

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02:39:33.120 --> 02:39:47.829

Lyle W. Ostrow MD PhD, Temple LKSOM: the geology of Guam is different in different areas, and we have, with these samples, you know, the villages that the peoples lived in, and the villages that they were born in, and what their water source was, and what the soil was like, and all of this is part of this collection. Next slide.

836

02:39:49.280 --> 02:40:08.660

Lyle W. Ostrow MD PhD, Temple LKSOM: And I think last year, or the year before, when I presented this, I showed you guys this whole rogues gallery of the ridiculous thing that showed up when we said yes to accept this, because basically, it was truckloads of paper records and freezers full of specimens, all labeled differently, all dissected differently, and, you know, buckets of fixed tissues, hundreds of brains, and, you know.

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02:40:08.660 --> 02:40:18.499

Lyle W. Ostrow MD PhD, Temple LKSOM: And it was all paper, and it was all differently labeled, and we've spent, you know, the past couple years re-dissecting, going through every sample, every block.

838

02:40:18.730 --> 02:40:30.460

Lyle W. Ostrow MD PhD, Temple LKSOM: all the paper records, and really decoding them, and linking them, and figuring out who's related to who, and what data goes for which, and all the things that we need to do so that we're sharing the samples now, linked to the data. Next slide.

839

02:40:31.330 --> 02:40:36.709

Lyle W. Ostrow MD PhD, Temple LKSOM: And this is just, I mean, like, that box on the... I mean, you gotta realize, like, we... it was honestly, like.

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02:40:36.710 --> 02:40:59.410

Lyle W. Ostrow MD PhD, Temple LKSOM: dog-eared boxes of paper like that, and we had to go through and figure out what was what. The cool thing is that we were able to link, you know, so we know who's related to who, right? And one of the things we weren't expecting... so there's a whole lot of people who have both a control and a case file, and you know why? Because they started collecting blood and data on people who they thought were controls, and while they were doing that, they converted to ALS, or to Parkinson's Dementia Complex.

841

02:40:59.410 --> 02:41:01.809

Lyle W. Ostrow MD PhD, Temple LKSOM: And they kept collecting from them. Next slide.

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02:41:02.950 --> 02:41:20.819

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, roughly, this is what's available sample-wise. There's a little over 300 autopsies. There's over 15,000 tubes of serum from 4,500 people. There's a limited amount of CSF. As I said, you know, among all the data, we have all the clinical records, all the family trees.

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02:41:20.820 --> 02:41:40.459

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, all the villages that they lived in, all that kind of thing. That red box there is just to highlight one thing that a lot of these... a lot of post-mortem tissue and, you know, biofluid cords are missing are controls, and not only does this one have a whole lot of controls, but the controls are often family members, right? And so there really are good controls for the people who are the cases. Next slide.

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02:41:41.230 --> 02:42:00.870

Lyle W. Ostrow MD PhD, Temple LKSOM: And just to show you, like, when they arrived, those are tackle boxes, and they were just literally tackle boxes packed with serum

samples, and they were all labeled differently. And we went through, and we have painstakingly reorganized and re-boxed, and relabeled and re-inventoried everything. And in doing so, what we discovered that's so amazing is there are

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02:42:01.080 --> 02:42:15.580

Lyle W. Ostrow MD PhD, Temple LKSOM: over 100 people who started out as healthy controls and later became disease, and we have serial blood draws on them, right? And for a selection of them, we have tissues after they died. And so we can measure things in the blood that

846

02:42:15.580 --> 02:42:23.569

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, and compare before and after they develop disease, and then compare to, you know, the tissues after they die. Next slide.

847

02:42:25.030 --> 02:42:37.859

Lyle W. Ostrow MD PhD, Temple LKSOM: And so... but at the same time, these are archival samples, right? Some of these are from the 50s and 60s and, you know, even the 40s. They're pretty old. And so the first things that we wanted to do was figure out what kinds of data

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02:42:37.880 --> 02:42:51.120

Lyle W. Ostrow MD PhD, Temple LKSOM: are reliable? What do they work for? And we have a lot of little pilot projects going on that are kind of getting at this, and I've just given three examples here. So one of them is with Brain Chemistry Labs, who also has worked with the ALS,

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02:42:51.120 --> 02:43:14.190

Lyle W. Ostrow MD PhD, Temple LKSOM: ATSDR team. But, you know, they're developing this microRNA panel as an ALS diagnostic, and we sent them a blinded set of this CIRA, and remarkably, they all passed QC. There was microRNA in every sample that was reliable, that, you know, met the criteria that they have for usable samples. We purposely sent them samples that we thought were screwed up, ones that had lost volume because maybe the lids weren't on tight.

850

02:43:14.190 --> 02:43:27.539

Lyle W. Ostrow MD PhD, Temple LKSOM: A couple that we knew had been dehydrated and rehydrated. And so... and we did this all blind, but we were able to tell there were a couple samples that had been degraded, and they were the ones that we expected.

851

02:43:28.020 --> 02:43:51.210

Lyle W. Ostrow MD PhD, Temple LKSOM: that MG53, that project that I showed you, a picture from the Hope Foundation newsletter, you know, we were working with our standard ALS tissues and using these protein measurements called ELISAs. We had the ELISAs, and so we said, hey, that's a specific protein, let's see if we can measure that specific protein and if it's consistent in these samples. And not only was it consistent, it's undetectable in the controls, it's elevated in every ALS sample.

852

02:43:51.210 --> 02:43:53.390

Lyle W. Ostrow MD PhD, Temple LKSOM: We haven't...

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02:43:53.400 --> 02:44:05.189

Lyle W. Ostrow MD PhD, Temple LKSOM: We have more data on this now, but we, you know, we try to save these longitudinal samples because they're scarce, but at least in one person that we looked, an early versus a late sample, the concentration changed.

854

02:44:05.550 --> 02:44:21.869

Lyle W. Ostrow MD PhD, Temple LKSOM: Just recently, we've started a project with a team at University of Nebraska and some other places, looking at a particular type of virus and viral antibodies, and in all cases, these archival samples are producing reliable and data that meets QC. Next slide.

855

02:44:22.640 --> 02:44:32.360

Lyle W. Ostrow MD PhD, Temple LKSOM: This is just about this, actually, I don't know if you guys are... some of them are on the Zoom right now, but they're waiting for information from me today, because they just got their preliminary data, and I haven't sent them

856

02:44:33.040 --> 02:44:36.309

Lyle W. Ostrow MD PhD, Temple LKSOM: all the uncoated data yet, but I'm going to today.

857

02:44:36.310 --> 02:44:59.490

Lyle W. Ostrow MD PhD, Temple LKSOM: But just to give an example of how having this village data and this geography data can help, because this is a virus that has to do, you know, is in certain freshwater sources, and oh, by the way, it might also vary seasonally, and we have the seasons that these serum samples were collected in, like, was it the rainy

season or the dry season? But what you're seeing on the right there is, in the pilot sample set that we created to just test what's feasible.

858

02:44:59.490 --> 02:45:05.039

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, we took ALS, Parkinson's, and controls, and some that were started out as controls and became converters.

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02:45:05.040 --> 02:45:12.189

Lyle W. Ostrow MD PhD, Temple LKSOM: And we specifically did it as a geographical sampling around the island, and specifically tried to match different

860

02:45:12.190 --> 02:45:25.160

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, fresh water characteristics and different soil characteristics, and this is the kind of thing that you can do with these samples, and there it shows... so it's Dr. Patty and Petro Carlson down again. Those are the team that's doing this work.

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02:45:25.310 --> 02:45:28.260

Lyle W. Ostrow MD PhD, Temple LKSOM: By the way, it's going to be presented in...

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02:45:28.530 --> 02:45:34.719

Lyle W. Ostrow MD PhD, Temple LKSOM: posters by them at the NEOS meeting and the MNDA meeting, so stay tuned for that. Next slide.

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02:45:36.530 --> 02:45:42.630

Lyle W. Ostrow MD PhD, Temple LKSOM: And so, that picture on the right there is just, Catherine and Catherine, Wilsbach and

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02:45:42.840 --> 02:46:07.700

Lyle W. Ostrow MD PhD, Temple LKSOM: excuse me, Kathleen Wilsbach and Catherine Gallo are the two people who did all this work to organize it. Those pictures on the right, like, when we originally took things out of these freezers, they were all different kinds of dissected and labeled in containers, and we've now gone through and systematically organized and re-dissected all of it. And so what comes next? We're working with some collaborators right now to plan this comprehensive effort to really use rigorous modern neuropathology and

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02:46:07.700 --> 02:46:13.300

Lyle W. Ostrow MD PhD, Temple LKSOM: You know, genomics, proteomics, in an organized fashion, to...

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02:46:13.760 --> 02:46:29.390

Lyle W. Ostrow MD PhD, Temple LKSOM: to do things that weren't available back in the 50s and 60s, and to take all these paper records and, you know, really get them scanned in at scale, get everything linked, and make all of this data available. And so I hope to be able to tell you more about that soon.

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02:46:29.650 --> 02:46:30.910

Lyle W. Ostrow MD PhD, Temple LKSOM: Next slide.

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02:46:31.740 --> 02:46:50.240

Lyle W. Ostrow MD PhD, Temple LKSOM: So, if there's researchers on the call, or if there's people on the call who just want to talk to me, I'm always happy to talk about anything ALS. My email's on the bottom there, but as I said, we say yes to everyone. Send me an email. We will send you a request form. Send it back to us. We will then, right away, schedule a Zoom with you, and we will work with you to make sure that

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02:46:50.240 --> 02:47:03.560

Lyle W. Ostrow MD PhD, Temple LKSOM: that we're sending you the best samples and the best data. And the reason we're able to do this is this funding from the CDC. The reason we're able to just make sure that we are prioritizing getting everybody's experiments to work, it's not about us, it's not about, you know.

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02:47:04.190 --> 02:47:13.799

Lyle W. Ostrow MD PhD, Temple LKSOM: our own papers or grants or anything like that. And, you know, our goal is not to ship you a box, like it says there. We're not just saying, okay, here's the samples, go nuts.

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02:47:13.800 --> 02:47:24.739

Lyle W. Ostrow MD PhD, Temple LKSOM: we're gonna keep working with you, we're gonna send samples in, you know, sequential sets as the project evolves to make sure that we're doing whatever we can to make it work. I would also just highlight that,

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02:47:24.770 --> 02:47:33.900

Lyle W. Ostrow MD PhD, Temple LKSOM: the registry, you know, once a year has a request for research proposals that's evaluate risk factors for ALS, and they've now added a, a,

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02:47:34.610 --> 02:47:44.589

Lyle W. Ostrow MD PhD, Temple LKSOM: particular call-out in that to ask for people who are doing research on Guamani and on this epidemic in Guam, because it really is the most

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02:47:44.760 --> 02:47:59.529

Lyle W. Ostrow MD PhD, Temple LKSOM: the largest, most well-characterized, you know, epidemic of these neurodegenerative diseases that's ever been in existence, and so there's funding that people can apply for, and of course, we are then going to provide whatever samples and data you need. Next slide.

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02:48:00.360 --> 02:48:14.439

Lyle W. Ostrow MD PhD, Temple LKSOM: So, you know, again, I mentioned that Temple and ALSO Foundation stepped up big time during this funding gap. Thank you, obviously, to the CDC for this funding. Kathleen and Catherine are the people who really do all the work. John Fury and Terry Hammond-Patterson's lab also is a tremendous help.

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02:48:14.440 --> 02:48:31.130

Lyle W. Ostrow MD PhD, Temple LKSOM: I want to actually just say thank you to the prior stewards of this Guam collection, and that was, you know, the whole team at NIH. By the way, we also have all the raw data from every experiment they ever did, and we're going to link and scan that in, too. Dr. Gerudo, who's the one who had this collection at Binghamton before us, Sarah Stoll was his

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02:48:31.130 --> 02:48:36.500

Lyle W. Ostrow MD PhD, Temple LKSOM: Graduate student, she's still doing research in this area, and really did a whole lot of the work to characterize this stuff.

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02:48:36.500 --> 02:48:53.020

Lyle W. Ostrow MD PhD, Temple LKSOM: I do want to say there's one thing that's missing from this slide that really is important, and I've been thinking about this a lot, which is that we really need to reach out to the Chamorro people, and they need to be involved with this, because, you know, much like, you know, nothing about us without us, we're very good at that in ALS now, which is really amazing to say.

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02:48:53.020 --> 02:48:59.159

Lyle W. Ostrow MD PhD, Temple LKSOM: We... we need... we need their input in this, and we need them to be involved and engaged, and so I'm going to work on that.

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02:48:59.670 --> 02:49:02.660

Lyle W. Ostrow MD PhD, Temple LKSOM: Thank you guys very much, and that's all I got.

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02:49:04.180 --> 02:49:11.740

Danielle Boyce: Thank you so much. That was terrific. And we're heading into lunchtime, we're a few minutes over,

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02:49:11.980 --> 02:49:26.869

Danielle Boyce: It was worth it. I think we got a lot done this morning, and I really appreciate you all. So, when you come back at 1.30, we're going to start our presentations from the National ALS Registry Funded research projects.

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02:49:27.250 --> 02:49:29.809

Danielle Boyce: Thank you so much, and I'll see you back here at 1.30.

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03:39:08.430 --> 03:39:11.880

Danielle Boyce: Hello, and welcome back. We're going to get started at 1.30.

National ALS Registry Funded Research Presentations

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03:40:19.130 --> 03:40:24.610

Danielle Boyce: Looks like there are a lot of great questions in the Q&A, and keep those coming, and

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03:40:24.820 --> 03:40:30.640

Danielle Boyce: We're going to have some open discussion after the scientific presentations this afternoon.

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03:41:31.210 --> 03:41:32.889

Danielle Boyce: Hey, welcome back!

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03:41:33.350 --> 03:41:35.170

Danielle Boyce: To our afternoon session.

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03:41:36.280 --> 03:41:44.279

Danielle Boyce: So this afternoon, we're going to have a series of presentations from the National ALS Registry-funded researchers.

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03:41:44.730 --> 03:41:50.240

Danielle Boyce: And we're going to start today with Dr. Ben Murdock. So nice to see you.

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03:41:50.420 --> 03:41:58.649

Danielle Boyce: Dr. Benjamin Murdock is a research associate professor at the University of Michigan, studying the role of the immune system in ALS.

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03:41:59.210 --> 03:42:15.080

Danielle Boyce: After receiving his PhD in immunology from the University of Michigan in 2010, he worked for several years examining the mechanisms by which fungal pathogens in the lungs result in asthma or persistent fungal infections due to immune dysregulation.

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03:42:15.480 --> 03:42:28.419

Danielle Boyce: In 2014, he joined the U of N Department of Neurology, examining how the immune system impacts neurodegenerative disease such as ALS, Alzheimer's disease, and diabetic neuropathy.

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03:42:28.750 --> 03:42:36.669

Danielle Boyce: We're so glad to have you, Dr. Murdock, and whenever your slides appear, the floor is yours.

Interactions between the microbiome, metabolome, and immune system
as underlying mechanisms of ALS pathogenesis

University of Michigan - Benjamin Murdock, PhD

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03:42:36.670 --> 03:42:39.970

Ben Murdock: Alright, well, thank you so much, and thank you, as always, for having me.

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03:42:39.970 --> 03:43:04.610

Ben Murdock: So my work, at least for the registry CDC project, is... looks at sort of the intersection between the microbiome, the immune system, and ALS pathogenesis. And so, because it kind of looks at many different kind of factors and kind of sits at this intersection, I'm going to kind of take you on a whirlwind tour with some of the background. I might not have the time to kind of go into the detail that I normally would.

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03:43:04.610 --> 03:43:11.000

Ben Murdock: So if there's any questions about it, feel free, obviously, after the talk, to, to ask me. Next slide, please.

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03:43:14.160 --> 03:43:16.270

Danielle Boyce: I'm sorry, I don't see the slides yet.

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03:43:16.270 --> 03:43:18.650

Ben Murdock: Oh, I can see it, I don't know if.

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03:43:18.650 --> 03:43:19.750

Danielle Boyce: Oh, you can see them? Okay.

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03:43:19.750 --> 03:43:22.620

Ben Murdock: I can see them, I'm not sure about other people.

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03:43:24.070 --> 03:43:30.529

Ben Murdock: So for the first section, I'm going to talk a little bit about the, the gut-brain access. Next slide, please.

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03:43:32.140 --> 03:43:51.519

Ben Murdock: So, it may seem a little far-fetched or counterintuitive, but there's actually a very strong link between the microbiome and the central nervous system, and that's known as the gut-brain axis. For people who aren't familiar with the term microbiome, it just kind of represents all the living organisms within the gut itself.

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03:43:51.520 --> 03:43:57.509

Ben Murdock: You... in this case, we're talking primarily about bacteria, but if you imagine, for instance, a forest.

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03:43:57.510 --> 03:44:14.949

Ben Murdock: And you say, well, what's living in the forest? Well, there's trees, there's ferns, there's plants, there's squirrels, every animal you can imagine. So when you say, like, the forest, you're kind of talking about everything that's in there, both the plants and the animals. And when we say the microbiome, that's kind of what we mean, too, is everything that's within the gut.

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03:44:14.950 --> 03:44:39.029

Ben Murdock: And so even though it's somewhat counterintuitive, it's been shown again and again and again that there is a very strong link between the central nervous system and the gut, because a healthy microbiome helps maintain homeostasis through the release of a number of different metabolites that go into the blood and then traffic to the central nervous system. There's neurotransmitter metabolites, ones that help with brain function.

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03:44:39.030 --> 03:44:49.760

Ben Murdock: And then, as we'll see when we get into kind of the immune system, there's also factors that influence immune function in the body as well. Next slide, please.

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03:44:50.770 --> 03:45:02.490

Ben Murdock: So, you can imagine, though, that if you get dysregulation or disruption of the gut, that if it's linked to the brain and the central nervous system, you can also see effects there as well, and this is what's been seen in a number of diseases.

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03:45:02.490 --> 03:45:27.189

Ben Murdock: So, for instance, with dysbiosis, often the epithelial layer in the gut breaks down, so that's the layer that basically separates the bacteria from the rest of your body. You get different metabolites entering the bloodstream, often endotoxins, so these are basically toxins produced by bacteria that you don't want. And that can affect transmission of the neurons, neuronal health, things like that.

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03:45:27.190 --> 03:45:29.169

Ben Murdock: Next slide, please.

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03:45:30.200 --> 03:45:36.449

Ben Murdock: And this isn't just theoretical. This has been seen in a number of neurodegenerative conditions.

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03:45:36.450 --> 03:45:59.900

Ben Murdock: Before. So, again, I don't have time to go into all the details, this is just... I'm cherry-picking, you know, some of these studies to kind of make a point. But one of the things, for instance, in Alzheimer's disease that's been found in a study in 2017, about 10 years ago, was that if you take a healthy control individual and you track them over time as they get Alzheimer's, what happens is you have a normal, healthy microbiota, or microbiome.

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03:45:59.900 --> 03:46:04.049

Ben Murdock: When you're in control before onset of disease, and then as disease progresses.

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03:46:04.050 --> 03:46:17.360

Ben Murdock: even before you get amyloid deposition in the brain, you see microbiota changes within the gut. And then as you get further along, as disease gets more severe, you see bigger and bigger changes. And what you really kind of see is that

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03:46:17.360 --> 03:46:25.309

Ben Murdock: Bacteria that are associated with a more pro-inflammatory phenotype, so more inflammation, more destruction, become more common in the gut.

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03:46:25.310 --> 03:46:37.669

Ben Murdock: And then bacteria that are protective and are anti-inflammatory go down. And so you see this sort of shift in the balance between anti- and pro-inflammatory bacteria that coincide with disease progression. Next slide, please.

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03:46:37.880 --> 03:46:57.239

Ben Murdock: And this isn't just relegated to Alzheimer's, other neurodegenerative diseases have been... this has been found as well. So, for instance, Parkinson's disease, you see changes in polysaccharide and short-chain fatty acids, you see decreases in neuroprotective molecules, increases in toxic metabolites.

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03:46:57.240 --> 03:47:15.650

Ben Murdock: dysregulated immune signaling, that sort of thing. So this has been seen in a number of different neurodegenerative disorders. So we're not kind of inventing this ourselves, this isn't just some wild idea that we had on our own. We're kind of following in the footsteps of studies that have been done by other researchers in the neurodegenerative field. Next slide, please.

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03:47:16.260 --> 03:47:20.999

Ben Murdock: Okay, so what about the microbiome in ALS? Does it have a role? Next slide, please.

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03:47:22.040 --> 03:47:38.310

Ben Murdock: So again, I'm cherry-picking a few slides, or a few papers. You know, I apologize, I have to kind of get through this in a timely fashion. But we'll start in mice and some of the exciting findings that other people have had. So, this was a big paper that came out in 2019 in Nature, which is one of the kind of the big, you know.

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03:47:38.580 --> 03:47:45.820

Ben Murdock: big, big journals that everyone kind of wants to get into. And what this group did is they looked in mice, so this isn't in people, this is in mice.

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03:47:45.820 --> 03:48:05.260

Ben Murdock: But they found not only did they see microbiome disruptions in ALS mice, but what they found is that there were certain populations that were more associated with disease progression. So, for instance, the one they particularly focused on was A. mucinophila, which has also been linked to a number of other diseases as well, or the lack thereof of this bacteria.

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03:48:05.260 --> 03:48:25.150

Ben Murdock: And what they found was that not only did this bacteria decrease over the course of the lifespan of ALS mice, but as you can see down there on the bottom, in some mice, it was completely absent altogether. So, already they're kind of finding a potential candidate that may be contributing to disease, disease progression pathology. Next slide, please.

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03:48:25.450 --> 03:48:44.369

Ben Murdock: And they followed this up by actually manipulating this particular bacteria. So, this is kind of a busy slide, but if you just look at the red and the blue lines, the blue line

represents a regular wild... or regular SOD1 ALS mouse, so this is a mouse that's receiving no treatment whatsoever.

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03:48:44.400 --> 03:48:59.180

Ben Murdock: And then the red line represents mice that received a mucinophila, so they actually reconstituted this bacteria. They gave this bacteria back to the mice to try and affect disease progression. And what you can see is that it slowed disease progression there on the left.

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03:48:59.180 --> 03:49:23.209

Ben Murdock: And on the right... in the right panel, you can see that it actually extended the lifespan of ALS mice, suggesting that this bacteria may actually play a central role, in disease pathology. And so, one of the things, before we go forward, I think I kind of forgot to mention this, I want to emphasize, is I think most of the people who are in this field, we don't think that necessarily the microbiome is the cause of ALS, we don't think it's the end-all, be-all. Sometimes I get that question, so I don't want to give that impression.

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03:49:23.210 --> 03:49:48.179

Ben Murdock: But one of the things, both with the microbiome and the immune system, is we think that the way it reacts and the sort of baseline, you know, functionality you have can dramatically affect disease progression. And so one of the things we're trying to do with both the immune system and the microbiome is can we find something that we can change? Can we find something that we can fix so we can slow disease and give patients a longer lifespan?

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03:49:48.180 --> 03:49:49.970

Ben Murdock: span, essentially. Next slide, please.

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03:49:50.860 --> 03:50:12.310

Ben Murdock: So this is a study that we did about the same year. It's a little bit different, but one of the things we did see that kind of validates those findings was we looked at A. mucinophila and found basically the exact same thing, in our mice at the end of disease. So we found that ALS mice were... this bacteria was pretty much absent and was only found in control mice.

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03:50:12.310 --> 03:50:13.960

Ben Murdock: Next slide, please.

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03:50:14.060 --> 03:50:36.919

Ben Murdock: But one of the things we did that was unique, I believe, and kind of different than that previous study, was we did a time course. What we wanted to do is we wanted to see, you know, at what point do we see dysregulation in the immune system? What point do we see dysregulation in the microbiome? And sort of to our surprise, we actually found that the microbiome was dysregulated from day one. We didn't start,

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03:50:36.920 --> 03:50:41.110

Ben Murdock: tracking changes in the microbiome until the day we got the mice from Jackson Labs.

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03:50:41.110 --> 03:50:49.589

Ben Murdock: And we could see dysbiosis even as the mice got to us, and that continued through the lifespan of the mice, and as you can see there from this figure from that paper.

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03:50:49.590 --> 03:51:08.940

Ben Murdock: That actually, preceded both muscle atrophy, so actually disease onset, so preceded something you would see in the clinic, and also preceded changes in the immune system, which suggests that if there is a link between the microbiome and the immune system, it may actually be upstream of immune changes, but we're not entirely sure yet. Next slide, please.

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03:51:09.850 --> 03:51:34.530

Ben Murdock: And finally, to kind of bring this back to the immune system and link the two, again, this is a busy figure, but one of the things we did is we did a correlative analysis where we looked at whether or not the immune system and immune metrics were associated at all with the microbiome and the top, kind of, 20 bacterial populations found in the gut. And so, again, this is very busy, but if you look at the two red boxes down there, what you can see is the box on the left

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03:51:34.530 --> 03:51:56.939

Ben Murdock: represents immune markers in the peripheral blood, and the box on the right represents immune markers in the central nervous system and the spinal cord. And what you can see is that while it's a little light, there are very significant associations between these bacterial populations and the immune system, suggesting that they're not acting independently, that they are acting in concert and potentially contributing to disease progression.

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03:51:56.970 --> 03:51:58.260

Ben Murdock: Next slide, please.

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03:51:58.890 --> 03:52:07.830

Ben Murdock: Okay, so that's in mice, that's all well and good, but mice are mice, and often that doesn't translate to people, so what about, humans... human studies, then?

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03:52:07.830 --> 03:52:19.609

Ben Murdock: This is from one we published a couple years ago. Again, other groups have done similar studies as well. In fact, I think some of them are on the call right now and listening to this, so I don't want to imply that we're the only people looking at this.

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03:52:19.610 --> 03:52:27.809

Ben Murdock: But this is a study we did a couple years ago and found that, for instance, at a baseline analysis of people who have ALS versus healthy controls.

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03:52:27.810 --> 03:52:52.659

Ben Murdock: What we found was that there was a reduction in bacterial diversity, so this is often a metric of bacterial health, so as you see disruption in the microbiome, basically the more diverse populations are basically destroyed or lost, and so you see this sort of over-representation of certain bacterial populations. And so these are just three different statistical models that we

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03:52:52.660 --> 03:53:05.449

Ben Murdock: used, or methods to determine whether there were changes, and what you can see is in all three, we actually saw less diversity, suggesting that there is a significant alteration of the microbiome in ALS patients compared to controls. Next slide, please.

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03:53:06.440 --> 03:53:24.119

Ben Murdock: And this just kind of furthers hammers that down. So what we did was we looked at the bacterial populations using multiple markers at once. So this is what's known as, for people who aren't in the field, dimensional reduction. It's a way to create a, basically, a two-dimensional plot of a whole bunch of different variables. So you have, you know.

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03:53:24.330 --> 03:53:39.710

Ben Murdock: dozens, hundreds of variables. This is a way to kind of boil it down into something that your brain can visually see much easier. And what you can see is that there's a shift in the bacterial populations within the microbiome of ALS patients versus controls. So.

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03:53:39.780 --> 03:53:51.730

Ben Murdock: ALS patients, essentially, their microbiome is different than what you would see in a healthy control, so we don't think we're just barking up the wrong tree. We think there are very significant differences between the two groups. Next slide, please.

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03:53:52.400 --> 03:54:01.249

Ben Murdock: And perhaps most importantly, one of the things we found was that the relative abundance of microbes producing butyrate are down in ALS.

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03:54:01.250 --> 03:54:21.850

Ben Murdock: Relative to control. So, butyrate is one of the main metabolites produced by bacteria in the gut, and it's been shown over and over again now, and it made kind of a splash when it came out a number of years ago, that it's highly anti-inflammatory. So, it has very strong potential for reducing inflammation and keeping the immune system in check.

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03:54:21.850 --> 03:54:35.780

Ben Murdock: And what you can see here is that as... as ALS progresses, and when a person has ALS, they actually have less of the bacteria that produce this protective, metabolite. So this, again, goes to the idea that the immune... the...

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03:54:35.780 --> 03:54:41.309

Ben Murdock: microbiome is dysregulated in ALS relative to healthy controls. Next slide, please.

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03:54:42.980 --> 03:54:55.150

Ben Murdock: Okay, so how does the immune system factor in there? So, I'm an immunologist by training. I'm very excited by this project, and, you know, I love bringing in the microbiome. I've actually kind of been

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03:54:55.150 --> 03:55:11.350

Ben Murdock: tertiary involved in the microbiome for a number of years, even before this project. But in my heart and in my training, I'm an immunologist, and so what I really

wanted to do was bring all this together and look at how this might affect the immune system and the interactions as it pertains to ALS. Next slide, please.

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03:55:12.900 --> 03:55:20.200

Ben Murdock: Alright, so just to give you a little bit of a project overview for what we're doing for the registry and the CDC,

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03:55:20.200 --> 03:55:33.629

Ben Murdock: Essentially, what we're doing is we're looking at the microbiome and trying to link it to various factors that we're also collecting as well. So, one of these is obviously clinical metrics, so survival, disease progression rates, site of onset, things like that.

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03:55:33.680 --> 03:55:40.419

Ben Murdock: But we're also looking at the immune system, and I don't have time to look at the... or talk about this today, but the metabolites in the blood.

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03:55:40.460 --> 03:56:04.300

Ben Murdock: And so, what we're really trying to do is see whether or not, when we examine these gut microbes and their abundance, are they associated with survival? Are they associated with changes in disease progression rate? But just as excitingly, or just as importantly, we're also looking at whether they're going to be associated with immune markers, and can that explain how the immune system may be contributing to disease progression? Do we see disruptions of the microbiome?

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03:56:04.300 --> 03:56:09.520

Ben Murdock: Does that then affect the immune system, and then does the immune system in turn affect disease progression?

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03:56:09.520 --> 03:56:31.789

Ben Murdock: And there are a number of different markers we'll be looking at. We have 148 markers in a separate study that I won't be able to get into today, as well as C for T cell expression. However, one of the things I will be talking about today is neutrophils and their expression and their activity, because that's one of the main cell types we think may be involved, and I'll explain why in just a few slides. Next slide, please.

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03:56:33.120 --> 03:56:43.010

Ben Murdock: Alright, so just to give you kind of a total number, we actually have been very good about collecting and recruiting people. We've had, over a thousand people consent, and we've collected a grand total of

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03:56:43.010 --> 03:57:07.050

Ben Murdock: samples from over 500 individuals, and then over 100 individuals have provided multiple samples over several time points, and that'll allow us to do kinetic analyses, which we've done before with just the immune system, so we're very excited about that. On top of that, we're also looking at the microbiome, which is the fungal pathogens, or fungal organisms within the gut. I don't have time to talk about that today, but that's something we've added on at the last minute that's going to be integrated in the study.

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03:57:07.050 --> 03:57:08.240

Ben Murdock: Next slide, please.

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03:57:09.880 --> 03:57:34.839

Ben Murdock: All right, so the immune system, near and dear to my heart. So, one of the reasons we're interested in the immune system is because, and I don't have time to go into today, but we've shown that the immune system is likely highly involved in the pathology and pathogenesis of ALS. The problem, though, is it's complex. It can be both protective and destructive. Early studies that used broad-spectrum immunosuppressive drugs either had no effect, or in some cases.

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03:57:34.840 --> 03:57:37.090

Ben Murdock: In some cases, made people worse.

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03:57:37.140 --> 03:57:49.419

Ben Murdock: So you can't just get rid of the immune system and fix ALS. You actually need to be very specific and kind of know exactly which pathway you're aiming for, and that's kind of what we're aiming for right now. Next slide, please.

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03:57:51.100 --> 03:58:11.050

Ben Murdock: So today, I'm going to be talking a little bit about neutrophils. These are the immune cells that make up the bulk of your white blood cells in the peripheral blood. They're multi-nucleated cells that have a number of ways that they attack pathogens and can damage tissue while they're destroying bacteria. Next slide, please.

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03:58:12.520 --> 03:58:26.469

Ben Murdock: And we're interested in them for a number of reasons, but first and foremost, they've been implicated in neurodegenerative diseases, and they've been shown to be affected by the microbiome. Again, I don't have time to go into every one of these studies, but again, this is not a new idea on our part.

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03:58:26.470 --> 03:58:37.550

Ben Murdock: This is something that has been, you know, postulated and shown in other diseases by other people, and we're kind of following in the footsteps of people who have blazed this trail before. Next slide, please.

967

03:58:39.800 --> 03:59:03.209

Ben Murdock: So, in our hands, we've seen neutrophils crop up again and again and again in our analyses. So, in our study in 2024, what we found was that, neutrophils were the single best predictor of disease progression in ALS patients. So, we created predictive models, and we said, okay, what are the factors that we use to determine whether we think someone's going to be a faster progressor or a slower progressor?

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03:59:03.210 --> 03:59:05.699

Ben Murdock: And again and again, we see neutrophils crop up.

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03:59:05.700 --> 03:59:25.040

Ben Murdock: And in terms of raw survival, in a separate study we did a few years before that, we found that if you have more neutrophils, it's associated with shorter survival, so the yellow line, and then if you have the fewer neutrophils, the red line, you have better survival. But what was really interesting, and I'll go into this a little bit later, was we found this was very specific to women.

970

03:59:25.040 --> 03:59:37.700

Ben Murdock: And what we found was that the neutrophil levels didn't have a huge effect in men, but if you reduced the neutrophil level in women, or if you had women with fewer neutrophils, they had a nearly 2-year survival advantage over women.

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03:59:37.700 --> 03:59:49.580

Ben Murdock: over men, or over the overall population, which is very exciting. It's something we can talk about in the questions and comments at the end, but it's something

that we've been looking into pretty aggressively now for the last few years. Next slide, please.

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03:59:51.390 --> 04:00:06.500

Ben Murdock: All right, so this is... this was all work done by my now-former graduate student, Lilia Baird. She graduated in April, very proud of her. And what she wanted to do was she wanted to figure out, well, exactly what mechanism of neutrophils may be contributing to disease progression.

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04:00:06.500 --> 04:00:18.249

Ben Murdock: And so you can see here from this figure that was published in our study this year, there's a series of activation steps. It's not just that neutrophils are activated or not activated, there's actually a sequential series of steps.

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04:00:18.250 --> 04:00:24.339

Ben Murdock: Whereby they become activated. First, they had to... they show baseline activation, and that's measured by calprotectin levels.

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04:00:24.340 --> 04:00:41.319

Ben Murdock: Then they become migratory, so they're able to get out of the blood and into the tissue. That can be measured by MMP9. And then activities such as granule release or net formation, which I'll talk about in a little bit, that can be measured by either NGAL or double-stranded DNA.

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04:00:41.510 --> 04:00:42.930

Ben Murdock: Next slide, please.

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04:00:43.710 --> 04:00:49.549

Ben Murdock: So what Lilia did is she looked at these levels in the blood of ALS patients relative to controls.

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04:00:49.550 --> 04:01:04.230

Ben Murdock: And what you can see is, pretty much universally, these markers were upregulated in ALS versus control, so both, calprotectin, MMP9, NGAL, and double-stranded DNA, even though double-stranded DNA was kind of just on the border of significance.

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04:01:04.230 --> 04:01:06.849

Ben Murdock: Advance the slide, please, just real quick.

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04:01:06.850 --> 04:01:23.789

Ben Murdock: Yep. But one of the things we found was we found that there was a significant difference in calprotectin. So this is the first stage in activation. We said, oh, great, it must be... it must be that these neutrophils are just slightly more activated in not only ALS patients, but especially women. This must explain what we're seeing.

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04:01:23.790 --> 04:01:26.890

Ben Murdock: And as it turns out... next slide, please.

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04:01:27.410 --> 04:01:36.260

Ben Murdock: when we did, these analyses... sorry, these are supposed to be white blocks, blocking things out, I don't know why they came out yellow.

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04:01:36.420 --> 04:01:59.130

Ben Murdock: when we looked at calprotectin and its effect on survival, so for those of you who don't know, this is a... these are known as hazard ratios. HR stands for hazard ratios. Basically, the higher the hazard ratio over 1, the more dangerous it is, or the more it's associated with disease progression, and the lower it is, so the less it is, or lower than 1, it means it's protective.

984

04:01:59.130 --> 04:02:11.040

Ben Murdock: And so what you can see is that while calprotectin looked like it may have added a little bit of hazard or a little bit of reduced survival in ALS patients, there wasn't anything that reached statistical significance, which

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04:02:11.040 --> 04:02:14.930

Ben Murdock: really kind of surprised us based on our findings. Advance the slide, please.

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04:02:16.720 --> 04:02:29.190

Ben Murdock: And even more surprising was that these other factors weren't impacted as well either. So, when we looked at MMP9 and NGAL, we didn't see any association with survival. So, oh, God, maybe we're barking up the wrong tree.

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04:02:29.440 --> 04:02:37.049

Ben Murdock: Well, advance the slide, please. What we actually found was that double-stranded DNA, which is a marker of neaposis.

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04:02:37.170 --> 04:02:47.739

Ben Murdock: was associated with disease progression. You can see that in the overall population group, but as with the total number of neutrophils in our previous study, you can see this is driven entirely by women.

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04:02:47.880 --> 04:03:01.089

Ben Murdock: So, men are not affected, or, and we're not entirely sure why, are not affected by double-stranded DNA levels or mnitosis, but it's highly associated with disease progression in women. Next slide, please.

990

04:03:01.290 --> 04:03:17.350

Ben Murdock: And just to confirm this, Lilia did a very elegant study where she looked at these cells under a microscope. What she did was she took fresh samples from ALS patients, stained them, and did automatic imaging using some very kind of advanced software that she tweaked.

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04:03:17.350 --> 04:03:35.319

Ben Murdock: And what you can see there in panel A is those are kind of neutrophils that are at rest in the top panel, but then as you go down, you can see netosis. And basically what mettosis is, is the neutrophils actually turn themselves inside out, and basically launch their own DNA, at targets. And so...

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04:03:35.320 --> 04:03:47.710

Ben Murdock: They don't... they usually don't survive this process, but they have a very short half-life, and that's kind of their function, and so one of the things they do is they will actually attack bacteria and just kind of launch their end trails almost at the target.

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04:03:47.710 --> 04:04:03.569

Ben Murdock: And it turns out that this is what's being associated with more rapid disease progression, so what Lily wanted to do was see whether or not ALS neutrophils are more prone to net formation than those from control patients. So if you look at the right set of panels, the graphs.

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04:04:03.570 --> 04:04:24.829

Ben Murdock: You can see at the very bottom, the maximal activation has not changed, so if she took these cells and stimulated them with a stimulant, it's called PMA, to just kind of charge them up and get them revved up and, like, ready to kill, what you can see is that when they're fully activated, there's no difference between ALS and control. So it didn't change the capacity for damage, it didn't change the capacity for violence.

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04:04:24.830 --> 04:04:34.429

Ben Murdock: But when she just looked at them at the spontaneous activation at 2 and 4 hours, what she found was that they were much more activated in ALS patients than in controls.

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04:04:34.430 --> 04:04:56.729

Ben Murdock: And there was a trend toward more in women than in men, but unfortunately, because these studies were very hard to do, they took a lot of time, a lot of effort, and the number of samples that we had were much lower, because these were very time-intensive, we kind of couldn't stratify that. But we did see a trend toward more activation in women, neutrophils from women than in men.

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04:04:56.860 --> 04:04:58.200

Ben Murdock: Next slide, please.

998

04:04:59.340 --> 04:05:15.020

Ben Murdock: So, that kind of brings us to where we are now. What we're trying to do with future directions is basically we're waiting on the data from the microbiome as we speak, so we've actually sent all these samples to the microbiome Corps here at the University of Michigan, and we're waiting on the results.

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04:05:15.120 --> 04:05:17.679

Ben Murdock: And as soon as we get those data back, we're gonna start

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04:05:18.090 --> 04:05:41.250

Ben Murdock: basically associating that with existing data sets, because we have, obviously, clinical data from Stephen Goutman's clinic, he'll be talking a little bit later today, but we also have very deep immunophenotyping, and this figure on the right is actually from a paper that we currently have under review, where we looked at 140, I want to say 8 surface markers in, you know, 8 or 9 different

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04:05:41.250 --> 04:05:42.430

Ben Murdock: immune...

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04:05:42.430 --> 04:05:58.759

Ben Murdock: populations, and we found that there is dysregulation, both up and down dysregulation, in every single immune population that we observed. And so what we really want to do is use these data to kind of create a roadmap and an atlas and figure out exactly what populations

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04:05:58.760 --> 04:06:11.900

Ben Murdock: of bacteria are associated with changes in the immune system and changes in ALS and survival and disease progression and that sort of thing. And so that's where we're going to be going in the future, as soon as we get these data back. So we're very excited.

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04:06:11.900 --> 04:06:19.009

Ben Murdock: hopefully we'll get them back in a week or two, and then we'll kind of be off to the races. So we're very excited about where this is going. Next slide.

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04:06:20.380 --> 04:06:26.099

Ben Murdock: And then, finally, I just want to make sure I thank everyone involved, and this is not everyone involved. It takes a village.

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04:06:26.100 --> 04:06:42.110

Ben Murdock: to do this. This is not a one-man show by any stretch of the imagination. So there are my mentors, there's biostatisticians, bioinformaticians, technicians, there's the clinical coordinators who have to get, you know, people enrolled in the study and, you know, send out sample kits.

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04:06:42.110 --> 04:07:03.379

Ben Murdock: So this was... it took a small army to get this done, and I would be remiss if I didn't thank everyone who... who was involved in this. And of course, I also want to thank my funding. Obviously, the ALS Registry and the CDC, as well as the NIH, Target ALS, ALSA, CREATE, and the Department of Defense. So, thank you. I think I'm on time, and I have a few minutes for questions, I believe.

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04:07:05.900 --> 04:07:17.569

Danielle Boyce: Yes, that was... that was amazing. There is a question in the Q&A, if you can see. Dr. Murdoch, what are your thoughts on NLR as a biomarker for ALS?

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04:07:19.190 --> 04:07:26.929

Ben Murdock: NLR. Right now, I think... so I'm...

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04:07:27.840 --> 04:07:35.599

Ben Murdock: with NLR link, there's actually a couple of NLRs, I mean. Is there a specific one that you are talking about? Sorry.

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04:07:36.290 --> 04:07:41.320

Danielle Boyce: We can, we can table that if it's kind of a longer conversation and get.

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04:07:41.320 --> 04:08:00.240

Ben Murdock: Oh, oh, NLR lymphos... sorry, neutrophil lymphocyte ratio. Okay, no. I think it's been shown consistently to be associated with disease progression, so we've found the NLR is associated with ALS, progression and survival. Other groups have as well.

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04:08:00.240 --> 04:08:04.159

Ben Murdock: I don't know if anyone...

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04:08:04.250 --> 04:08:17.240

Ben Murdock: has used NLR as a pre-onset marker. I would... I think Fang Fang's on the call, you might want to ask her. So she's... she's... she's in Sweden, they've got that absolutely wonderful

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04:08:17.240 --> 04:08:36.420

Ben Murdock: national registry of people that they can use to track people before disease onset that we don't really have in America. I think it's potentially a viable biomarker. Again, I think one of the things that we're consistently running into now, especially with the immune system, and I don't think it's unique to the immune system.

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04:08:36.420 --> 04:08:47.430

Ben Murdock: Is that we're seeing differences based on both sex and age, and so we're actually finding that, for instance, certain markers, whether it's for prediction or, you know, certain mechanisms.

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04:08:47.430 --> 04:08:52.600

Ben Murdock: they actually may be completely different in men or women. So that study I showed you.

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04:08:52.600 --> 04:09:08.709

Ben Murdock: With, the predictive modeling, one of the things we found was that when we associated all these markers with ALS progression, we actually saw primarily neutrophil markers in women, especially older women. Not younger women, but that also could be there's so few of them.

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04:09:08.710 --> 04:09:24.369

Ben Murdock: for which we could do the analysis, the statistical power was very low, but it was almost entirely in women. So, I think NLR is potentially something that could be used as a biomarker, but again, I think we really need to figure out if there are demographic differences and, like, you know.

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04:09:24.810 --> 04:09:29.679

Ben Murdock: basically, who can we use this biomarker in? And I think that's true of...

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04:09:29.790 --> 04:09:43.869

Ben Murdock: honestly, I think maybe all the biomarkers. I think we need to start stratifying people by age, sex, site of onset, whether it's a genetic form. It's a very, very heterogeneous disease, but we tend to treat it as just this one monolithic, like.

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04:09:44.150 --> 04:09:53.159

Ben Murdock: you have ALS, it's like, no, really, it's probably a whole bunch of other kind of sub... sub-diseases and kind of wearing trench coat. So I think we really need to get towards.

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04:09:53.160 --> 04:09:53.510

Danielle Boyce: chillin'.

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04:09:53.510 --> 04:09:58.819

Ben Murdock: medicine, and I think that will help, but I do think NLR could be a viable biomarker down the road.

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04:09:59.940 --> 04:10:13.820

Danielle Boyce: Thank you very, very much, and there are a few other questions. We're going to hold them toward the end of this session, and we greatly appreciate that. I'm fascinated, and my wheels are turning, and that's the whole point of this meeting, so thank you so much, Dr. Murdoch.

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04:10:13.820 --> 04:10:14.950

Ben Murdock: Yes, of course.

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04:10:15.920 --> 04:10:17.330

Danielle Boyce: And next...

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04:10:18.430 --> 04:10:41.949

Danielle Boyce: I am pleased to introduce you to Dr. Fernando Vieira. Full disclosure, I work with Dr. Vieira, and you'll be learning a little bit about my work in the process here. Dr. Fernando Vieira is the CEO and Chief Science Officer at the ALS Therapy Development Institute, or ALSTDI. He has been an ALS researcher since 2001.

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04:10:42.040 --> 04:10:59.009

Danielle Boyce: His ALS research focuses have spanned ALS animal model characterization, preclinical pharmacology, cell biology, human ALS risk factor evaluation, which he'll be talking about today, and human ALS digital biomarker development.

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04:10:59.060 --> 04:11:10.299

Danielle Boyce: He now leads a multidisciplinary team of researchers focused on advancing effective treatments and biomarkers for people with ALS. And I will turn it over to you now, Dr. Vieira.

Assessment of ALS Risk Factors from ALS TDI's Ongoing Natural History Study

ALS Therapy Development Institute - Fernando Vieira, MD

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04:11:11.080 --> 04:11:31.079

Fernando Vieira: Thank you, Danielle, Dr. Boyce. It's a pleasure to see you here. It's a pleasure to be here with the CDC today. Thanks, everybody, for joining, for taking time out, to see what's been a great session so far, and what will prove to be through the day today and tomorrow.

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04:11:32.500 --> 04:11:50.869

Fernando Vieira: I'm going to be telling you today about work that ALS TDI has been doing with the CDC National Registry, ALS National Registry, to try to determine risk factors out of data that we've been collecting through the ALS Research Collaborative. Next slide, please.

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04:11:52.560 --> 04:12:16.680

Fernando Vieira: So today, we'll go through an overview of what the ALS Research Collaborative is to give you some context. I'll walk through some progress that we've made looking at a genome-wide association study derived from the AHRQ study, and exploring risk factor corroboration of a lot of risk factors that have been posited by folks that have been supported.

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04:12:16.680 --> 04:12:24.120

Fernando Vieira: by the ALS Registry over the years, and we'll talk some about upcoming activities and collaborations

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04:12:24.120 --> 04:12:33.289

Fernando Vieira: that are, being spawned from the infrastructure that we're building, thanks to, this grant and this support. Next slide, please.

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04:12:34.500 --> 04:12:58.349

Fernando Vieira: Before I get into that, I'm going to talk about the team that's directly involved in this project. There are a lot of folks who have been making this project work, starting with Dr. Danielle Boyce, who needs no introduction at this point, but she works in the day-to-day here at ALSTDI as our Director of Data Science and Biomedical Informatics, and her own specific focus is on real-world evidence.

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04:12:58.350 --> 04:12:59.139

Fernando Vieira: Go back, please.

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04:13:00.120 --> 04:13:24.190

Fernando Vieira: Thank you. I'd also like to thank and reference, Pat Dolan. Pat Dolan, leads, GEOALS, an organization focused on geospatial and geotemporal data, risk factor data, associated with ALS. He's a person with ALS, he's a lead, an ALS advocate.

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04:13:24.190 --> 04:13:42.319

Fernando Vieira: And really, he brings his expertise to this project in ways that have been fantastic. Gwen Hun, who's our senior data science focused on omics, I'll be presenting work from her on the genome-wide association study. We have administrative support from Veronica and Beth.

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04:13:42.320 --> 04:13:43.700

Fernando Vieira: Next slide, please.

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04:13:45.210 --> 04:13:56.480

Fernando Vieira: Alan Promisiri, who runs the ARC day-to-day operations, so all of the data come through him, from, the generous, participation of, patients involved.

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04:13:56.480 --> 04:14:10.829

Fernando Vieira: Paula Sebastiani, who's also an omics expert, from Tufts, director of Bird, professor of medicine there, and Sean Sullivan, who does, sort of software management, and Hannah Walters, who.

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04:14:10.870 --> 04:14:34.659

Fernando Vieira: As, epidemiologist. A little bit of, background on just ALS TDI in general. We're a non-profit research institute. We're independent. We have, 4 different research teams, located here in the Boston area. Cell biology team, preclinical pharmacology team, and a translational research team. And as,

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04:14:34.670 --> 04:14:51.420

Fernando Vieira: data gain more primacy, sort of big data, in all of these projects. We've now built a data science team led by Dr. Boyce that integrates all of this. Today, I'll be focused on the translational research element and the data science element.

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04:14:51.440 --> 04:14:52.650

Fernando Vieira: Next slide, please.

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04:14:55.510 --> 04:15:06.950

Fernando Vieira: So the ALS Research Collaborative, specifically, so what is it? The ALS Research Collaborative is an ALS natural history study that's been ongoing since 2014.

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04:15:06.950 --> 04:15:31.459

Fernando Vieira: It's focused on biomarker discovery, biomarker validation, and molecular omics. And I'm not talking about it much here, but also cell biology. We collect fibroblasts and lymphoblasts and generate induced pluripotent stem cells from participants in the study. To date, we actually have more than probably 1,800 people,

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04:15:31.460 --> 04:15:55.740

Fernando Vieira: enrolled in the study with ALS, we've been enrolling asymptomatic carriers as well for the last couple of years, along with some healthy controls. But really, the lion's share of the data are from people with ALS diagnoses who have been contributing. More than two-thirds of the participants have shared more than three or more time points worth of data.

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04:15:55.740 --> 04:16:00.969

Fernando Vieira: And those data include everything from ALS functional rating scale, self-assessed.

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04:16:00.970 --> 04:16:17.909

Fernando Vieira: Accelerometry, which I won't talk about much today, but we do a lot of work with actor graph devices on each of the limbs to track limb disease progression, movement disease progression, voice recordings to track bulbar assessment.

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04:16:18.260 --> 04:16:42.759

Fernando Vieira: We have a number of risk factor surveys, which I'll touch on today. Whole genome sequencing. More recently, we've been doing RNA-seq and proteomics, and we've integrated electronic health records. And really importantly, the program used to be called the Precision Medicine Program. We changed it to the ALS Research Collaborative to really highlight the idea that these data are shared.

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04:16:42.820 --> 04:17:02.540

Fernando Vieira: They're shared from the patient participants who are contributing the data to us, and they're shared by us to researchers anywhere around the world, from any type of institution focused on trying to accelerate research for ALS, fundamental target discovery, biomarker, etc. Next slide, please.

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04:17:03.560 --> 04:17:08.660

Fernando Vieira: So, from the perspective of a person with ALS,

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04:17:08.660 --> 04:17:24.609

Fernando Vieira: They're typically, if they're diagnosed with ALS, they might find, the ALS Research Collaborative within 6 months, and so what you're seeing is kind of a timeline from the patient's perspective here, and it's a bit archetypal for participants who join.

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04:17:24.620 --> 04:17:28.090

Fernando Vieira: So often folks find... please, go back?

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04:17:28.290 --> 04:17:42.060

Fernando Vieira: Thank you. So often folks will, join about, 6 months after diagnosis, and then, we ask participants to contribute, data, approximately monthly.

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04:17:42.280 --> 04:17:51.700

Fernando Vieira: So ALS functional rating scale, those digital data that I mentioned. But we also send phlebotomists to people's homes,

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04:17:51.700 --> 04:18:15.259

Fernando Vieira: for quarterly blood draws, and those blood draws are used for the first one, the whole genome sequencing, which I'll talk about, but we also capture whole blood clinical chemistry, complete blood count data, and RNA data, and serum and plasma for proteomics and metabolomics. Those are quarterly.

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04:18:15.340 --> 04:18:30.860

Fernando Vieira: More recently, in the last couple of years, and Dr. Palmetta referenced this during his talk earlier, we integrated a way for participants to contribute their own electronic health records to the

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04:18:31.070 --> 04:18:47.639

Fernando Vieira: ARC database, so they have their own separate consent, where they can, select which elements of their data they can share with us. And, and, Danielle has built, Dr. Boyce has built a pretty incredible pipeline

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04:18:47.640 --> 04:19:10.419

Fernando Vieira: for extracting, loading, and transforming those data, and really extracting value from those. Those data have every... they go back in time, right? So you're not limited to what a participant might remember, or what we're asking. Those data are open, and they might have clinical notes. They can go back, you know, 10 years prior to

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04:19:10.420 --> 04:19:21.369

Fernando Vieira: your ALS diagnosis, and that can be really, really powerful when trying to understand risk factors that might precede the development of ALS. Next slide, please.

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04:19:24.370 --> 04:19:40.799

Fernando Vieira: And so, just for your information, we have drafted a descriptive manuscript of the ALS Research Collaborative data set. It exists as a preprint right now.

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04:19:40.800 --> 04:19:54.869

Fernando Vieira: on Research Square, and really it kind of gives a framework for what we had, at least up until about 1,500 participants. But as the data set continues to grow, this will, continue to be updated.

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04:19:55.030 --> 04:19:56.180

Fernando Vieira: Next slide, please.

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04:19:58.030 --> 04:20:04.949

Fernando Vieira: And, now I'll go in specifically into the CDC grant and the aims and the progress that we've made.

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04:20:05.140 --> 04:20:06.400

Fernando Vieira: Next slide.

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04:20:07.690 --> 04:20:32.109

Fernando Vieira: These are supposed to be white, but, you know, sometimes things transfer when they see a different computer, but we'll see what other interesting colors we get. So the aims were really, when we launched this project with the CDC, was to get a clear understanding of the data that we had, to standardize, clean, and normalize those data.

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04:20:32.150 --> 04:20:34.969

Fernando Vieira: There's a huge amount of work that went into that.

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04:20:34.970 --> 04:20:58.740

Fernando Vieira: Then you need to evaluate the evidence to support or refute existing risk factors that have been previously associated with ALS. We wanted to really see what this particular cohort could show, and what doing that comparison would tell us about our cohort, because it works both ways, and I'll get into that a little bit more when we talk about, like, military, as a risk factor.

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04:20:59.180 --> 04:21:07.770

Fernando Vieira: Then we really wanted to dive into the data to see if we could find new risk factors that hadn't been identified.

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04:21:07.770 --> 04:21:32.680

Fernando Vieira: relating to the age of disease onset or rate of disease progression. I'll talk about that in terms of the genome-wide association study. Really, we focused on risk factors relating to onset and progression, because we're comparing the ALS to itself here. We really weren't comparing to a large database of healthy controls or non-neurological disease controls.

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04:21:32.680 --> 04:21:33.340

Fernando Vieira: controls.

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04:21:33.620 --> 04:21:50.879

Fernando Vieira: And then, really, a huge, effort here was to provide open access data, through the ARC Data Commons and even beyond, so that others could, dive into the data, as well. Next slide, please. Or advance the slide, please.

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04:21:51.340 --> 04:21:55.750

Fernando Vieira: Think... Wow, yeah, some new colors. Next one, please.

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04:21:57.480 --> 04:22:08.509

Fernando Vieira: So, I'm going to start here on efforts to standardize, clean, and normalize the data, and how we're developing a platform to share these data. Next slide.

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04:22:11.720 --> 04:22:35.140

Fernando Vieira: So, the first thing I wanted to mention is another manuscript that, the team put together. This is under the leadership of Daniel Boyce, to really, harmonize, this is a description of the effort to harmonize, ALS research data across two big, actually three big multimodal data sets, using, the OMOP,

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04:22:35.140 --> 04:22:58.289

Fernando Vieira: common data model. The Observational Medical Outcomes Partnership is sort of a common data model across other, disease types, other conditions that make it possible for people to easily, compare data sets. This is a partnership between ALS TDI, ANSWER ALS, and the Critical Path Institute, CPATH,

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04:22:58.550 --> 04:23:06.750

Fernando Vieira: To really take our separate datasets and, build them all into this common data model.

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04:23:06.750 --> 04:23:20.799

Fernando Vieira: and share the data in a unified way. Particularly, ALS TDI and ANSWER ALS have shared our data with this common model on AnswerALS's Neuromind platform.

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04:23:20.800 --> 04:23:38.430

Fernando Vieira: We hear a lot about how data are siloed in the ALS space. I think that is increasingly not the case. I think we're increasingly trying to share data and make it available so that others can make progress. But one key element of that is making those data interoperable.

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04:23:38.430 --> 04:23:50.819

Fernando Vieira: And so, the data science teams, both at ANSWER and at ALSTDI, and more recently CPATH, did a lot of work to make that possible, and so those data are shared now. Next slide, please.

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04:23:51.720 --> 04:23:57.850

Fernando Vieira: And, there's access to this, at, it's, GitHub,

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04:23:57.850 --> 04:24:15.010

Fernando Vieira: alstdi.github.io, I think is the URL for this, where you can really dive into all of the data that have been sort of OMOPIfied, and it points directly to the AnswerALS Neuromine data source as well.

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04:24:15.010 --> 04:24:27.430

Fernando Vieira: So that you can get access to that. And really do recommend that any folks who are wanting to dive in and ask their own research questions do make use of these resources.

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04:24:27.640 --> 04:24:28.880

Fernando Vieira: Next slide, please.

1087

04:24:31.780 --> 04:24:33.129

Fernando Vieira: Advance, please?

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04:24:34.010 --> 04:24:43.639

Fernando Vieira: And so, my next focus will be really, the effort to identify some new possible risk factors that might be related to HALS. Next slide.

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04:24:45.610 --> 04:24:53.730

Fernando Vieira: The first study that I want to focus on is our genome-wide association study.

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04:24:54.060 --> 04:25:03.169

Fernando Vieira: What you're looking at here, the figure on the top is called a Manhattan plot, and what it's actually showing is that across the entire genome.

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04:25:03.170 --> 04:25:26.640

Fernando Vieira: we were able to identify some genes which are significantly associated with disease severity. That is to say that people who harbor these single nucleotide polymorphisms seemed to be at higher risk of having a faster disease progression. This is preliminary data, and it's a relatively small

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04:25:26.760 --> 04:25:33.049

Fernando Vieira: patient population of approximately, 15, people,

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04:25:33.060 --> 04:25:51.399

Fernando Vieira: with ALS, but the genes that we did identify do seem to be clustered around muscle function, neuronal function, and inflammation. And so, we think that, there's, there will be a lot of value in following up on this. Next slide, please.

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04:25:52.510 --> 04:26:03.230

Fernando Vieira: So our next steps on this is really to dive into other datasets to see if we can corroborate it. It's a little bit difficult because our data set is

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04:26:03.310 --> 04:26:27.760

Fernando Vieira: somewhat unique in that we do have a lot of longitudinal data, and so we have a clear sense of who's a fast progresser and who's a slower progressor. Some of the other data sets don't have that, but there is potential to really dive into the answer ALS data set to really see if we can corroborate some of these. We want to clarify the signal structure here, so we want to determine

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04:26:27.760 --> 04:26:52.580

Fernando Vieira: If the association is driven by, like, a specific variant, or are there multiple correlated variants that are really driving the risk of faster disease? And then sort of integrate all of that to see, in terms of understanding of the different biology and the functions of these genes, to see if we can prioritize what to explore in the lab here and beyond in

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04:26:52.580 --> 04:27:09.699

Fernando Vieira: collaboration with others, and then really test the robustness of this. So, we applied, you know, a couple of different statistical methods to find these, SNPs, but we're going to dive in and really confirm that, and that's something that Gwen will be focusing on.

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04:27:10.040 --> 04:27:11.370

Fernando Vieira: Next slide, please.

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04:27:16.230 --> 04:27:35.030

Fernando Vieira: Another point that I wanted to make is I wanted to call out again Pat Dolan and GOALS. So, we worked really, really hard, with Pat to take the ARC dataset and format it, so that we could, understand,

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04:27:35.030 --> 04:27:37.970

Fernando Vieira: Where our participants really are coming from.

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04:27:37.970 --> 04:28:01.599

Fernando Vieira: And so, the data have been formatted into public use microdata areas, or PUMAs, which are U.S. Census statistical geographic units, where they... the sort of clusters have about 100,000 residents, or at least 100,000 residents, and you can use those to explore lots of different population frequencies. And so, we plan to go

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04:28:01.600 --> 04:28:09.610

Fernando Vieira: forward and ask many, many questions about, where people live right now with the disease, but also their location history.

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04:28:09.610 --> 04:28:24.099

Fernando Vieira: and, and potential environmental exposures that might be associated with when a person has been in a particular PUMA. And so we're grateful, to Pat and GOALS for making that possible.

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04:28:24.100 --> 04:28:27.890

Fernando Vieira: The other type of thing that you can do with these data... next slide, please.

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04:28:30.140 --> 04:28:49.050

Fernando Vieira: is sort of ask questions about your own study, and ask questions about, the people who have enrolled in your study. And so what we're looking at here is a map, obviously, of the United States, but there are also, little blue dots. The little blue dots indicate, and, and,

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04:28:49.050 --> 04:28:57.769

Fernando Vieira: the little blue dots indicate AHRQ participants. You can also see the, sort of, the, the red,

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04:28:57.820 --> 04:29:22.669

Fernando Vieira: spots also indicate ARC participants, and the green areas tell you the distance from drive time for those participants to a major ALS clinic. And so what this is telling us is that most of our participants do, in fact, come from areas that are close to major ALS clinics, but we are able to reach people who are outside of those.

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04:29:22.710 --> 04:29:42.190

Fernando Vieira: We really want, the AHRQ study to be able to reach more and more people who are outside of those regions. We want to bring, more, access to research to people, across, the country in all underserved communities. And, so GOALS, really,

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04:29:42.190 --> 04:29:51.460

Fernando Vieira: Has helped us, assess our own study's performance that way, and we can benchmark and show that we're improving or not.

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04:29:52.020 --> 04:29:53.280

Fernando Vieira: Next slide, please.

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04:29:56.700 --> 04:30:19.630

Fernando Vieira: So, the sort of final stretch of this presentation is really focused on, efforts to sort of support or refute risk factors that have been previously associated with ALS. And some of that is going to speak to work, like, that Dr. Murdoch was just describing, Dr. Weisskopf, who we'll talk about a little bit later, Dr. Gautman as well.

1112

04:30:19.630 --> 04:30:32.269

Fernando Vieira: We really looked at some of those markers, the ways that we could within our data set to see, what's supported and where we probably need to gather more data ourselves. Next slide, please.

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04:30:34.900 --> 04:30:35.900

Fernando Vieira: Next slide.

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04:30:38.440 --> 04:30:56.360

Fernando Vieira: So, when we delved into our entire dataset, and all of the different surveys, that we probed, there were a few things that really bubbled up, as, really, potentially key risk factors.

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04:30:56.520 --> 04:31:10.090

Fernando Vieira: Autoimmune comorbidities were really, really high. There was a really significant signal for our patient population, our cohort. We had more than 10% of our cohort reported

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04:31:10.090 --> 04:31:33.740

Fernando Vieira: having some autoimmune disorder compared to, sort of, the age-matched U.S. population of 4.6, age-sex-matched population of 4.6. So that was significant. We also saw, not surprisingly, a significant, increased risk of familial history of ALS. We saw a significant, effect,

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04:31:33.740 --> 04:31:35.780

Fernando Vieira: from smoking,

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04:31:35.780 --> 04:32:00.419

Fernando Vieira: asthma and thyroid disease, we didn't. We did see a significant effect, for... in military, when you looked sort of crudely at it, but when you do age and sex adjustment, we sort of lost that effect. In fact, when we adjusted our population, we actually were underrepresented, and I'll talk about that a little bit more.

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04:32:00.420 --> 04:32:03.000

Fernando Vieira: In the next slides. Next slide, please.

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04:32:03.990 --> 04:32:16.659

Fernando Vieira: And so, like I said, one really clear signal, from autoimmune disease, where we're seeing, frequency about 2 times higher, than the U.S. population.

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04:32:16.660 --> 04:32:31.690

Fernando Vieira: For military service, once we age and sex matched, we actually were lower. We would have expected about 14% of our population to have served in the military, and we're not seeing that. We're seeing about 11.

1122

04:32:31.910 --> 04:32:56.189

Fernando Vieira: And, that, is sort of a point of discussion on what the composition of our, AHRQ study population might be. Is it a socioeconomic limitation? What folks find us, and volunteer and can invest the time and effort, to contribute to our study?

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04:32:56.210 --> 04:32:59.480

Fernando Vieira: I think that's... these are important questions.

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04:32:59.750 --> 04:33:00.990

Fernando Vieira: Next slide, please.

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04:33:03.580 --> 04:33:26.080

Fernando Vieira: Diving a little bit more deeply into the autoimmune disease, yeah, the signal seems to be driven by psoriasis, inflammatory bowel disease seems to be higher, rheumatoid arthritis, and those are really the main contributors. There is also a lupus and multiple sclerosis signal.

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04:33:26.080 --> 04:33:49.150

Fernando Vieira: It's possible that the multiple sclerosis signal, maybe that was misdiagnosis at some point. The cohort that we're looking at is 62% male, but given that autoimmune disease is female predominant in the population, the elevation seems to be a little bit, even more notable, rather than less.

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04:33:49.880 --> 04:33:51.230

Fernando Vieira: Next slide, please.

1128

04:33:53.200 --> 04:34:00.829

Fernando Vieira: Then, just, diving into the military service, it'll be really great to hear from Dr. Mark Weisskopf later.

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04:34:00.830 --> 04:34:25.530

Fernando Vieira: to get his take on this. I know there have been recent publications looking at, specific, domains of service, so, specific, branches, Navy, Army, Air Force, officer versus non. We're looking to dive into those types of questions with deeper understanding, deeper queries into our

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04:34:25.529 --> 04:34:32.800

Fernando Vieira: population to see if we can understand that, because that might actually explain the discrepancy that we're seeing here.

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04:34:33.029 --> 04:34:34.520

Fernando Vieira: Next slide, please.

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04:34:36.660 --> 04:34:59.060

Fernando Vieira: And so, those are kind of questions that we're putting, to this whole community. You know, explanations, cohort composition, sort of the, the, the, ability to measure, single self-reported item, like, age, sex matching, that doesn't necessarily capture the differences.

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04:34:59.060 --> 04:35:05.709

Fernando Vieira: Do we need to standardize beyond age and sex, to really, understand?

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04:35:05.710 --> 04:35:08.119

Fernando Vieira: And,

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04:35:08.450 --> 04:35:21.209

Fernando Vieira: Is there a preferred benchmark from the ALS registry? Is there an adjusted veteran benchmark or external comparator to trust beyond what we're using?

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04:35:22.820 --> 04:35:23.710

Fernando Vieira: Next slide.

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04:35:24.759 --> 04:35:35.309

Fernando Vieira: And so, upcoming projects, for ALSTDI that are really supported, by the work that's been done, through this grant. Next slide.

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04:35:36.130 --> 04:35:59.370

Fernando Vieira: We're going to continue to refresh, the OMOPified data and install the Standard Models Odyssey tools. We've just added a new tranche of data to Neuromine, that's been OMOPified from the ARC dataset. We'll be doing that yearly. We're going to continue to work with GOALS to further,

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04:35:59.369 --> 04:36:04.040

Fernando Vieira: Explore geospatial analysis and place-based exposure layers.

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04:36:04.040 --> 04:36:10.030

Fernando Vieira: We're going to expand our electronic health records, our electronic medical records analysis.

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04:36:10.029 --> 04:36:33.719

Fernando Vieira: piloting an incredible tool that Danielle Boyce has created called Registry Forge that really can extract these data, transform them, and get you to more easily extract these insights. And then we're partnering with Kaiser Permanente to really generate a comparative data set, both for omics, but also clinical data.

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04:36:33.720 --> 04:36:52.359

Fernando Vieira: Some which can go back in time for individuals before they were ever diagnosed with ALS to see if we can find risk factors that might, have predicted, or biomarkers that might have predicted a person developing ALS.

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04:36:52.360 --> 04:36:55.449

Fernando Vieira: And I think I have a little bit of time to take questions.

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04:36:56.450 --> 04:36:57.369

Fernando Vieira: Thank you.

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04:36:58.470 --> 04:37:04.259

Danielle Boyce: Thank you so much, Fernando, and let me see, I think we do have time.

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04:37:04.700 --> 04:37:12.379

Danielle Boyce: For one question, and then we can save the rest for after. Let's see...

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04:37:13.430 --> 04:37:38.210

Danielle Boyce: So this... so one question about autoimmune disease, so I think we're gonna... we can ask that question, but I think it's mostly for the registry. With treatment for some of these autoimmune diseases, is National ALS Registry capable to pick up rates of ALS in subjects with treated autoimmune disease? So, medications. I wonder, Fernando, if

you can comment on, the data that we have in the ARC around treatment, and then we'll let the ALS Registry weigh in after?

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04:37:39.110 --> 04:37:49.820

Fernando Vieira: Yeah, there are a few different ways that we can do that. So, a lot of participants do contribute, their own, medications that they're taking and when they're taking them.

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04:37:49.820 --> 04:38:02.849

Fernando Vieira: So that's one way we get the data. We also can access through their electronic health records. I think one of the things to keep in mind as we're looking at, these potential immune markers is

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04:38:02.960 --> 04:38:08.890

Fernando Vieira: With these comorbidities, are some of the markers actually signs of the other disease?

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04:38:08.890 --> 04:38:33.739

Fernando Vieira: Right? As opposed to the ALS, or how are they interacting with one another? I think that'll be really important going forward. How do the treatments that people are taking also influence those markers? I think that'll be really important going forward. And so, we do plan to dive into those questions. Just one thing to note, the neutrophil lymphocyte ratio, the

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04:38:33.740 --> 04:38:48.810

Fernando Vieira: that was referenced earlier, that's a really clear signal in our data set. And so, it's great when you're seeing multiple, datasets, multiple cohorts really pointing in the same direction. We think the neutrophil signal is really meaningful.

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04:38:50.930 --> 04:39:15.589

Danielle Boyce: Thank you so much, Dr. Vieira, and I'm excited to hear the next speaker also, Dr. Weisskopf, because, as you can see, the military question is very difficult from a data science perspective, from an epidemiology perspective, and I know that I speak for you when I say we're very lucky to have Dr. Weisskopf as an advisor on our project, and to help us to understand the military.

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04:39:15.590 --> 04:39:21.859

Danielle Boyce: side of things as well. So I think it's a perfect segue, into this And our next speaker...

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04:39:22.710 --> 04:39:35.919

Danielle Boyce: Dr. Mark Weisskopf is the Cecil K. and Philip Drinker Professor of Environmental Epidemiology and Physiology at the Harvard Chan School of Public Health and the Departments of Environmental Health and Epidemiology.

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04:39:36.000 --> 04:39:50.750

Danielle Boyce: and director of the Harvard T.H. Chan NIEHS Center for Environmental Health. His work examines environmental influences on brain health across the life course, including ALS specifically. Dr. Weisskopf, I'll turn it over to you. Thank you.

Military exposures and ALS in a large veteran population

President and Fellows of Harvard College - Marc Weisskopf, PhD, ScD

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04:39:51.170 --> 04:40:04.590

Marc Weisskopf: All right, thank you very much, Danielle, and it's great to get... finally have one of these meetings again. Great to see everybody and see all the wonderful presentations. So, as was mentioned, I will talk about work we've been doing under one of the CDC grants.

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04:40:04.590 --> 04:40:15.130

Marc Weisskopf: to look at military and ALS. I will say that because of all of... a combination of problems with European laws and our skipping meetings.

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04:40:15.130 --> 04:40:29.359

Marc Weisskopf: I don't think I ever got to talk about another grant of mine, so if I have time at the end, I'll show you a couple quick things from that prior work also, but we'll start with the military one, I can take questions after that, and we'll see where we are at that point. Next slide, please.

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04:40:29.940 --> 04:40:38.660

Marc Weisskopf: So, I probably don't even need this slide, because most of you are probably aware of the relatively long history now of interest in military service and ALS.

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04:40:38.670 --> 04:40:58.639

Marc Weisskopf: Really starting a couple decades ago with a couple papers out of, the... that followed veterans out of the Gulf War, suggesting they were at higher risk of ALS, and then that was followed by a paper of mine in working with Alberto Escario, looking really at a... not a Gulf War population, but a much more general

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04:40:58.640 --> 04:41:15.220

Marc Weisskopf: population, of, of the U.S, so many of whom were veterans and many of whom weren't, but, it was, in fact all pre-Gulf War, while the Gulf War papers also suggested maybe about a two-fold increased risk of ALS for those who'd been deployed, or,

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04:41:15.220 --> 04:41:27.230

Marc Weisskopf: deployed versus non-deployed or versus U.S. rates, we looked at it in the general population, just any veteran versus non-veteran, and found about a 50% increased risk of ALS.

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04:41:27.230 --> 04:41:35.880

Marc Weisskopf: And that's something that, as many people have alluded to, has been relatively consistently found whenever people have done these kinds of questions and studies.

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04:41:35.880 --> 04:41:48.820

Marc Weisskopf: In that original publication, we saw some variation by branch of service, but of course, it wasn't really designed to go after that. But we really have, as people, again, have alluded to, have struggled to

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04:41:48.820 --> 04:42:06.109

Marc Weisskopf: get to what it is about military service, or being in the military, that may actually affect the risk of ALS. And so this grant that I'll be talking about, that we've been doing work on, is really designed to try and get at that, to get deeper into what is the root cause of why we're seeing this.

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04:42:06.130 --> 04:42:07.809

Marc Weisskopf: Next slide, please.

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04:42:09.190 --> 04:42:14.119

Marc Weisskopf: And so to do that, what we did is we, have been looking at,

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04:42:14.340 --> 04:42:34.320

Marc Weisskopf: VA data, Veterans... Department of Veterans Affairs, and this really initiated because just before we put this in, the VA had, for the very first time, in collaboration with the DoD, created a joint data set where you... they... they were mixing military and veteran data. Turned out that wasn't

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04:42:34.390 --> 04:42:46.680

Marc Weisskopf: exactly everything they'd promised, so there are a lot of issues with that. But, but nonetheless, we were able to work with this Veterans Affairs database, which is where veterans go for,

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04:42:46.680 --> 04:43:04.560

Marc Weisskopf: health benefits, not all veterans, I will say, but they can go here. So it's a very large nationwide database in which we can now search for ALS and look at risk factors for ALS. So that database has over 9 million veterans, you know, all ages, getting care at the VA.

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04:43:04.560 --> 04:43:15.520

Marc Weisskopf: The electronic data, more or less goes from, starts in the 2000s, till now. We, for the purposes of kind of weeding out,

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04:43:15.520 --> 04:43:32.670

Marc Weisskopf: prevalent ALS and really trying to focus on incident ALS, we sort of start any follow-up at least 2 years after someone has entered the VA system, so we have... we can tell that they haven't had ALS or any indication of it for 2 years to sort of enrich for that incident ALS cases rather than prevalent.

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04:43:32.760 --> 04:43:46.179

Marc Weisskopf: And to identify the cases in that database, we use a variety of IC-9 codes, some non-ALS-specific, also ALS-specific, and treatment medication dispensations.

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04:43:46.180 --> 04:43:54.490

Marc Weisskopf: And essentially developed a sort of algorithm that is along the lines of the ATSDR algorithm, not exactly the same as indicated.

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04:43:54.490 --> 04:44:10.380

Marc Weisskopf: here, and I can go into details about that with people if they want. But having done this, we find over, you know, over 14,000 ALS cases over that time period in the VA database. And for the purposes of our analyses, we use

1177

04:44:10.380 --> 04:44:27.859

Marc Weisskopf: because we use a multiple of indication... multiple indicators of whether someone has ALS, once someone has been defined as a case of ALS and sort of confirmed in that way, we take the first mention of any of those indicators as the index date for the ALS case.

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04:44:28.390 --> 04:44:30.119

Marc Weisskopf: Next slide, please.

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04:44:30.310 --> 04:44:46.659

Marc Weisskopf: So, yeah, so we can... we can... the hopes is to use... is to actually go very deep and get many more exposures related to military experience, but what I'm going to show you today, we've really just started with some of the basics, which is what branch were they in, what military rank did they have, just officer or enlisted?

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04:44:46.660 --> 04:44:51.660

Marc Weisskopf: both sometimes. Length of service, how long they were in.

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04:44:51.660 --> 04:45:04.049

Marc Weisskopf: And and most importantly, this data comes from this dataset called the United States Veteran Eligibility Trends and Statistics data set that we then merge with the VA health data.

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04:45:04.980 --> 04:45:07.129

Marc Weisskopf: Next slide, please.

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04:45:07.780 --> 04:45:30.160

Marc Weisskopf: So, for this analysis, what we essentially do is a sort of typical Cox proportional hazards model, looking at the rate of developing ALS over time. Age is the time scale, so it gets controlled very tightly. The person time, starts, or rather, they're censored at either getting ALS death or age 104, only because, because of, sort of.

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04:45:30.160 --> 04:45:34.980

Marc Weisskopf: When you're in massive datasets like this, there are always some errors going on, and some...

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04:45:34.980 --> 04:45:41.429

Marc Weisskopf: Ages wind up being super old that we were pretty confident are not correct, so we censor everybody at 104.

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04:45:41.430 --> 04:45:57.849

Marc Weisskopf: or the end of follow-up, which for this was September of 2024. We can stratify by sex. Now, of course, in the military, the vast majority of these folks are male, but just because of the size, even among the women, we have a fair amount of ALS cases to look at.

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04:45:57.930 --> 04:46:13.299

Marc Weisskopf: And we can adjust for a variety of factors, most importantly, race and ethnicity. Of course, the sex and age is being controlled, as shown there. And then we can do additional analyses, considering other variables, like smoking or marital status.

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04:46:13.400 --> 04:46:14.889

Marc Weisskopf: Next slide, please.

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04:46:15.820 --> 04:46:39.300

Marc Weisskopf: So, these are results, actually, that were, in fact, just published a little while ago, literally, I think, within the last month or so, in neurology. This is the population that we're looking at for this study, and really just to point out from this slide that that top row shows we've got a lot of ALS cases over this time. The majority of them are in the Army, it's just the largest

1190

04:46:39.300 --> 04:46:40.180

Marc Weisskopf: branch.

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04:46:40.180 --> 04:46:53.339

Marc Weisskopf: But we have a whole lot in all the other branches, and even in just the Coast Guard, I mean, 133 cases there is larger than... or on the order of many studies we wind up seeing in ALS, so you can see the numbers are

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04:46:53.350 --> 04:46:55.299

Marc Weisskopf: are quite large.

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04:46:55.710 --> 04:47:11.090

Marc Weisskopf: other than that, there's not much notable here. I mean, the diagnosis age is perhaps slightly on the high side. I will point out that you might see in the Marines column that they are different for some reason, and I'm still struggling with exactly why they show up different.

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04:47:11.090 --> 04:47:17.360

Marc Weisskopf: in this VA database, getting an earlier diagnosis of ALS, their birth year median is younger.

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04:47:17.360 --> 04:47:26.240

Marc Weisskopf: The age they start in the VA system seems to be younger, and I, for the life of me, have not been able to get a clear answer on why that's the case.

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04:47:26.250 --> 04:47:31.230

Marc Weisskopf: I will say that the diagnosis age of, you know, the late 60s for many of the others.

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04:47:31.230 --> 04:47:54.800

Marc Weisskopf: might strike some as slightly older, but keep in mind that, you know, you only... the VA, you don't go into the VA right after your military service. As I said, many people don't ever enter the VA system for healthcare, and those who do actually don't... often, usually don't enter until many years after their military service, so we're... we're sort of losing a younger set here, which is an important point.

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04:47:55.070 --> 04:48:02.029

Marc Weisskopf: As you can see, that's reflecting the age at start in the VA database, which is in the 50s already for most of these groups.

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04:48:02.590 --> 04:48:08.439

Marc Weisskopf: And then the years of service these folks had, you know, in general, was around 6, 7, 8 years.

1200

04:48:08.780 --> 04:48:18.130

Marc Weisskopf: And again, most of the people are enlisted, but there are officers here as well, which make up the other bulk, and then a number of folks were actually both at some point.

1201

04:48:18.290 --> 04:48:19.900

Marc Weisskopf: Next slide, please.

1202

04:48:21.240 --> 04:48:32.779

Marc Weisskopf: So, just to hit the main results here, we use the Army as the largest one as the reference group. Now, keep in mind, this is different from, certainly, the study I did before, and many studies when they've got

1203

04:48:32.860 --> 04:48:48.660

Marc Weisskopf: military veterans and non-veterans, in that everybody in our group is a veteran. So, they are, in theory, already all at some higher risk, but what we're trying to now do is sort of dive down and see, within that group at higher risk.

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04:48:48.800 --> 04:49:00.920

Marc Weisskopf: are there certain ones that are higher and others that are not? And that can help us sort of hone in on what particular exposures or some kind of factor that might be related to the ALS risk.

1205

04:49:00.920 --> 04:49:09.789

Marc Weisskopf: And so what we've got here is the number of ALS cases in each branch, the number of person years overall that were followed, so that's between cases and non-cases.

1206

04:49:09.790 --> 04:49:23.149

Marc Weisskopf: And then the hazard ratio. So, do these branches differ in their rate of ALS? And in fact, that is exactly what we found with the Air Force, Navy, and Coast Guard largely having higher rates of ALS than folks who had been in the Army.

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04:49:23.160 --> 04:49:38.999

Marc Weisskopf: With the Marines actually showing a significantly lower rate of ALS, which in fact is something that is... has also generally been found in all of the other studies that have looked at this, but the Marines tend to be quite small. So in any single study that has come out before.

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04:49:39.000 --> 04:49:51.569

Marc Weisskopf: there's been this suggestion that they were at a lower risk of ALS, but the numbers were always quite small, so one was never quite sure about this, but in this very large data set, that still seems to be what we're seeing.

1209

04:49:51.660 --> 04:49:59.029

Marc Weisskopf: And yeah, multiple branches, for whatever reason, are actually no different than army.

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04:49:59.750 --> 04:50:04.099

Marc Weisskopf: Although probably most of the multiple branch people include Army, so that's relevant.

1211

04:50:04.900 --> 04:50:06.379

Marc Weisskopf: Next slide, please.

1212

04:50:06.830 --> 04:50:16.740

Marc Weisskopf: So what we also find, is that, again, enlisted men are... or enlisted... this is all men, by the way, that we're looking at, just to stratify there, but the enlisted men

1213

04:50:16.740 --> 04:50:36.190

Marc Weisskopf: most of them are in the Army. Sorry, most of the men in the military were enlisted. But relative to those, officers actually had a higher rate of ALS, with a hazard ratio of 1.63, and if you were both an officer and enlisted, it was about the same as officer, even so slightly higher.

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04:50:36.340 --> 04:50:47.539

Marc Weisskopf: Missing unknown was lower, not exactly clear what that means or who that would be, because rank really typically shouldn't be missing, so it's unclear who those folks are.

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04:50:47.810 --> 04:50:49.920

Marc Weisskopf: Next slide, please.

1216

04:50:51.230 --> 04:51:01.720

Marc Weisskopf: So then we also looked by duration of service in the military, splitting it roughly in quartiles of years of service in the military, and in fact, here, find

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04:51:01.750 --> 04:51:15.610

Marc Weisskopf: possibly an, you know, an odd association in the sense that it tended to go down with more years of service in the military, with the longest servers being at about a 25% lower rate of ALS.

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04:51:15.610 --> 04:51:28.259

Marc Weisskopf: I will say this is a pattern that is, not infrequently seen in occupational epidemiology studies that often relates to a healthy survivor bias, which is that

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04:51:28.260 --> 04:51:42.730

Marc Weisskopf: the people who actually stay in the longest are staying in because they're not having whatever the bad effects might be, that would ultimately lead to ALS, and so they sort of drop out. So this is a...

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04:51:42.730 --> 04:51:49.270

Marc Weisskopf: pattern we do see. Whether that's what this is is not totally clear, but it's certainly similar to that kind of a pattern.

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04:51:49.700 --> 04:51:51.069

Marc Weisskopf: Next slide, please.

1222

04:51:52.300 --> 04:52:09.619

Marc Weisskopf: So, the other thing we explored a little bit was how this related to the age, at which someone got ALS, which is, you know, on the one hand, obviously, it's an age stratification, but keep in mind that what it also is is a sort of

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04:52:09.630 --> 04:52:28.310

Marc Weisskopf: to some degree, very correlated with time since service, because the older you are, in general, means you've been out of the military longer. And what we tend to

find is that the differences by branch are much stronger in the younger age groups, and then it tends to fade. So, if you take Air Force, for example.

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04:52:28.330 --> 04:52:31.880

Marc Weisskopf: The hazard ratio was 1.45 in the youngest group.

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04:52:31.910 --> 04:52:47.339

Marc Weisskopf: Dropping to 1.24, 1.26, and then 1.11 even in the oldest group. Still significant, but of course, that's in part because our numbers are so large, but you can see there's a little bit of this time pattern, going on here. Next slide, please.

1226

04:52:48.430 --> 04:52:58.029

Marc Weisskopf: And with that, I just raised the point that there have been some suggestions of a sort of time-limited effect of this. This was a paper by Horner et al. in 2008, following the Gulf

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04:52:58.260 --> 04:53:03.629

Marc Weisskopf: War and veterans who were deployed or not, with the suggestion from their data that the

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04:53:03.630 --> 04:53:22.529

Marc Weisskopf: sort of effect of having been, having been deployed to the Gulf seemed... on ALS, that sort of increased risk of ALS following that, seemed to decline over the decade after service. And, next slide, or next click, I guess. Yeah, so, I will say we looked at military service in

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04:53:22.530 --> 04:53:23.580

Marc Weisskopf: Denmark.

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04:53:23.580 --> 04:53:46.200

Marc Weisskopf: in the Danish population, which is a slightly different scenario, but also found a sort of suggestion of this as well, which is that while the military... those who served in the military there were at higher, risk of ALS, that also seemed to be larger in the decade following their employment in the military service. So there... there... there is... there may be something to this time aspect of,

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04:53:46.200 --> 04:53:48.169

Marc Weisskopf: Of service, and how long it's been.

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04:53:48.700 --> 04:53:50.429

Marc Weisskopf: Next slide, please.

1233

04:53:51.050 --> 04:54:10.419

Marc Weisskopf: So, additional results on all of this. So, you see the sort of similar decreases by age in association with rank, a little bit less so for officers, but generally similar. As I said, there were many fewer ALS cases among women, because there are just fewer women who served in the military, but we still had 484, so it's a large number, and

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04:54:10.420 --> 04:54:23.219

Marc Weisskopf: roughly speaking, we see the same patterns by branch, although none of them wind up actually being significant, even though the point estimates are, sort of, have a similar pattern to them. Same with officer status and length of service.

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04:54:23.230 --> 04:54:42.570

Marc Weisskopf: The rank pattern between officer and enlisted is pretty much the same across all the branches, if you just look within the branches. And if we specifically look in that... the youngest group I showed you before was 17 to 61, but the prior Horner paper, or a couple prior papers, had focused on veterans less than 45.

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04:54:42.570 --> 04:55:02.319

Marc Weisskopf: And when we restrict even to that group, which is much smaller, we see even higher hazard ratios. So that time aspect seems very important here. And we did some sensitivity analysis. We split these data at 2008, which is when ALS became a presumptive disease, so anybody with ALS who had served in the military got

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04:55:02.320 --> 04:55:21.050

Marc Weisskopf: their care completely covered, regardless of where or when they served. So there's some worry that that might have changed what we're seeing in the VA database, but it was essentially not different by that split. And if we... if we also... if we actually sort of tried to exclude prevalent cases even more conservatively by

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04:55:21.050 --> 04:55:36.299

Marc Weisskopf: requiring that any veteran did not show any sign of ALS for 5 years in the VA system before getting ALS, we essentially saw the same results here. So, that didn't change anything, nor did additional adjustment for smoking and marital status.

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04:55:36.390 --> 04:55:37.710

Marc Weisskopf: Next slide, please.

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04:55:38.680 --> 04:55:54.380

Marc Weisskopf: So, obviously, there's some limitations still to what we're doing here. You know, it's a VA population, so if exposures related to ALS also lead to using VA for other reasons, this could bias true effects towards the null. That is, if some

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04:55:54.510 --> 04:56:09.429

Marc Weisskopf: bad exposure led you to have health problems and ALS, and those health problems brought you into the VA, that could be a potential problem, but it would likely, it would likely make the results look less, less different from null.

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04:56:09.610 --> 04:56:25.230

Marc Weisskopf: You know, there's possible differential use of the VA by branch, but again, this would only bias if it sort of didn't apply to those with ALS, so it's kind of unlikely, especially when we're doing these exclusions where we're only considering people who

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04:56:25.290 --> 04:56:39.369

Marc Weisskopf: are in the VA for a full 5 years before they even develop ALS, so that's unlikely. We were missing about 20% data on rank. Obviously, smaller numbers in women, although patterns were quite similar. We don't have genetic information on these folks.

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04:56:39.370 --> 04:56:57.700

Marc Weisskopf: And then, I guess, I have, again, getting back to the VA system and the typical entry into the VA system, it's well after military service, as we said. It's, you know, they're entering the VA in their late 50s in general, and there are reasons why that could potentially lead to a selection bias if important things are happening before that age.

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04:56:57.700 --> 04:56:59.719

Marc Weisskopf: Right, so that's something to keep in mind.

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04:56:59.760 --> 04:57:01.459

Marc Weisskopf: Next slide, please.

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04:57:02.620 --> 04:57:22.310

Marc Weisskopf: So, in the end, what we are seeing is substantial variation in the rate of ALS by branch rank and length of service. You know, is this related to differences in exposures in those categories? That's one leading theory, and that's what we're trying to now delve into more. Like, are there exposures in the Air Force, Navy, and Coast Guard that

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04:57:22.310 --> 04:57:28.450

Marc Weisskopf: That increase the risk, and they're more exposed in those branches, and that's why we see the higher rates.

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04:57:28.450 --> 04:57:40.840

Marc Weisskopf: One obvious thing that comes to mind is sort of aircraft operations. This is something that had been seen in a smaller study in the Bay Area, where it seemed like people who work on planes or in planes had a higher rate of ALS.

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04:57:40.840 --> 04:57:50.219

Marc Weisskopf: So that's certainly something to consider. Even though, obviously, we think of boats with the Navy and the Coast Guard, they actually... both of them have very high usage of planes as well.

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04:57:50.240 --> 04:57:58.219

Marc Weisskopf: And in fact, my understanding is Coast Guard, you know, percentage-wise, more people in the Coast Guard actually work in and around planes than even in the Air Force.

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04:57:58.610 --> 04:58:08.199

Marc Weisskopf: So, that is something to potentially consider. Higher rate decrease with age, again, this is what I said, this is,

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04:58:08.830 --> 04:58:11.810

Marc Weisskopf: Well, sorry, this, yeah, this could be...

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04:58:11.810 --> 04:58:29.680

Marc Weisskopf: that there is sort of earlier effects of these, whatever the military exposure is, and then as you go longer and longer, you see less of an effect because they've already had the effect they're going to have. As I say, the time aspect I showed you relative to the Gulf and Denmark is sort of similar.

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04:58:29.690 --> 04:58:34.859

Marc Weisskopf: And the reduced hazard ratio of longer service, as I mentioned, may be this kind of healthy survivor effect.

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04:58:35.300 --> 04:58:36.619

Marc Weisskopf: Next slide, please.

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04:58:37.840 --> 04:58:53.009

Marc Weisskopf: Yeah, so let me actually... oh yeah, so I will say that we are... we are... I'll keep going on new stuff. This is not published, but it's something else we've... is part of the grant that we've been doing and looking into, and that is statin use, because we have that information from the VA records.

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04:58:53.010 --> 04:59:10.620

Marc Weisskopf: This is just from a recent, relatively recent meta-analysis. I think there are actually other papers than this on statins and ALS. There's been a lot of interest in this, sort of in both directions, like concern that statins increase the risk of ALS, but some studies have suggested it might lower the risk of ALS.

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04:59:10.720 --> 04:59:19.279

Marc Weisskopf: This meta-analysis and some others have suggested they don't see anything overall, but you can see that the second row there is one of the largest studies, and it

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04:59:19.350 --> 04:59:25.189

Marc Weisskopf: Has very, very narrow confidence intervals and does see a slight reduction.

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04:59:25.190 --> 04:59:40.030

Marc Weisskopf: there was also a recent paper out of Norway that also sort of found a small reduction. So this is still sort of an open question, and it's something that we have data on in the VA, so we decided to sort of explore that as well. Next slide, please.

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04:59:40.060 --> 04:59:50.799

Marc Weisskopf: So it's the same population I told you about, but we're doing it in a slightly different way. Rather than looking at the entire cohort of those 9 million veterans, we take the ALS cases and we match

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04:59:50.800 --> 05:00:00.570

Marc Weisskopf: Controls to them in an incident density sampling way, so they have to be alive when the case was... became a case, and we match them on birth year and sex.

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05:00:00.620 --> 05:00:10.429

Marc Weisskopf: And we essentially select randomly 10 controls for each case, and then we look at their past statin dispensation history from the VA.

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05:00:10.530 --> 05:00:12.050

Marc Weisskopf: Next slide, please.

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05:00:13.460 --> 05:00:27.230

Marc Weisskopf: This is the population, so over 14,000 ALS cases and 146,000 match controls. Not much to point out here, necessarily, other than, again, you see most are male cases.

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05:00:27.230 --> 05:00:40.690

Marc Weisskopf: There's slight differences in smoking status, slight differences in marital status and racial identity, but generally relatively similar. Next slide, please.

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05:00:41.140 --> 05:00:58.020

Marc Weisskopf: And what we are finding, and this is really a work in progress, so this is not published and still ongoing, and we're finalizing it, so take this with, I suppose, a grain of salt. We're still kind of working out the details, but, again, if we exclude statin use in the two years before the index date for ALS to

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05:00:58.020 --> 05:01:02.739

Marc Weisskopf: Sort of make sure we're not, you know, try and avoid issues of reverse causation, where

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05:01:02.740 --> 05:01:14.309

Marc Weisskopf: statin use is being affected by underlying ALS in some way, we see a significantly reduced risk of ALS among statin users, of an odds ratio of 0.77.

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05:01:14.740 --> 05:01:30.410

Marc Weisskopf: And if we, again, extend that even further, like, don't even consider statin use within 5 years before ALS, so this is only statin use earlier than that, we still see the significant, almost 20% reduced odds of ALS in this group.

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05:01:30.670 --> 05:01:32.369

Marc Weisskopf: Next slide, please.

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05:01:33.370 --> 05:01:39.029

Marc Weisskopf: And when we sort of look in the sort of two... so we exclude the first two years before ALS, but

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05:01:39.080 --> 05:01:58.970

Marc Weisskopf: up to 10 years before that, look at use, and how many years they were using statins, we do see some evidence of a dose response, where the more years they were using statins, the lower the risk of ALS going from .92 in just 1 or 2 years of use to .86 with 7 to 8 years of use.

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05:01:59.280 --> 05:02:01.280

Marc Weisskopf: Next slide, please.

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05:02:02.640 --> 05:02:15.019

Marc Weisskopf: Yeah, so that's the end of the sort of military-oriented work. These are the folks that certainly are very important to acknowledge, because they were the team that did a lot of this work, so my collaborators at the VA,

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05:02:15.020 --> 05:02:23.980

Marc Weisskopf: And in particular, the Edith Norse Rogers Memorial Veterans Hospital in Bedford, Massachusetts, Lauren Moo, Donald Miller, Stephen Shirk, and Alex Braga.

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05:02:23.980 --> 05:02:29.829

Marc Weisskopf: And then, some folks on my team at Harvard, Andrea Roberts, Ron Rotem, and Ian Tang.

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05:02:29.960 --> 05:02:38.029

Marc Weisskopf: So I would stop there to take questions, and then if those don't go too long, I would give you a brief indication of the other stuff that I've been doing.

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05:02:39.680 --> 05:02:47.690

Danielle Boyce: Let's have one question, from the audience, and then we can save the rest of the questions, for later, so... because I'm curious what else you have.

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05:02:47.690 --> 05:02:48.040

Marc Weisskopf: Sure.

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05:02:48.040 --> 05:02:59.960

Danielle Boyce: So, selfishly, I want to hear what else. So, from, MC Colett, Dr. W, is the million veteran project data of any help in your work? Thank you.

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05:02:59.960 --> 05:03:24.949

Marc Weisskopf: So, well, yes and no. No in the sense that I have not yet linked with it in any way, but absolutely, it would be incredible, and I am trying to make inroads, and if anyone, you or anyone else could help, it would be hugely valuable. I would love to see how many of their folks we have in our database, how many ALS cases they have in theirs, and if we could combine the genetics with the sort of environmental, not just

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05:03:24.950 --> 05:03:26.909

Marc Weisskopf: what I've shown you here, but the other stuff.

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05:03:26.910 --> 05:03:32.730

Marc Weisskopf: we're trying to get, would be really powerful. So, so I'm really hoping we can do that at some point.

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05:03:33.330 --> 05:03:40.279

Marc Weisskopf: it seems a little tricky to get into the MVP, but I'm trying, and any help from anyone on this call would be

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05:03:41.000 --> 05:03:42.969

Marc Weisskopf: Be much appreciated.

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05:03:43.470 --> 05:03:55.820

Danielle Boyce: Thank you so much. If you wouldn't mind spending the next few minutes sharing the additional research, that would be great. And if you have questions, we can... please put them in the Q&A, and we'll circle back to them later.

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05:03:56.070 --> 05:04:02.089

Marc Weisskopf: Okay, sure, so I'll try in the next 8 minutes or so. So, I guess next slide.

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05:04:02.130 --> 05:04:20.989

Marc Weisskopf: All right, so I... this is a new title slide, because this was my prior grant that's over now, but because of issues of getting samples out of Europe under new laws, things got really delayed, and then we didn't have these meetings, so I couldn't present to you. But it was... it was really trying to look at pre-disease biomarkers of persistent organic pollutants, a proteomic set, and ALS. Next slide.

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05:04:23.170 --> 05:04:36.889

Marc Weisskopf: So, the work... the aspects of this work that I'm going to show you today really just focus... we were actually looking at two cohorts, one in Finland, one in Denmark, but I'll be talking about the Danish work just now. That's the more recent stuff.

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05:04:36.940 --> 05:04:53.090

Marc Weisskopf: This is the Danish Diet, Cancer, and Health Study cohort, Danish EPIC, that was set up in the mid-90s when they recruited almost 60,000 people, who were 50 to 64 at the time, and collected blood from them at that time.

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05:04:53.090 --> 05:05:02.589

Marc Weisskopf: And the cohort was really set up as a cardiovascular, you know, they were more interested in cardiovascular outcomes, but given that it is there, and that they have,

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05:05:02.700 --> 05:05:13.429

Marc Weisskopf: registry systems in Denmark, what we could do is take the members of this cohort and then use the registry systems to see whether... who among them developed ALS.

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05:05:13.430 --> 05:05:23.859

Marc Weisskopf: And so, in 2017, we did that and identified 166 ALS cases among those roughly 60,000 people who were recruited at baseline.

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05:05:23.860 --> 05:05:33.889

Marc Weisskopf: Through linkage with their national hospital registry, and matched two controls per case. So we did this, nested case control study within this large cohort.

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05:05:33.890 --> 05:05:50.040

Marc Weisskopf: And the advantage here is that we had blood samples from well before the ALS developed, because I don't believe anybody had ALS at the time of baseline, but had they had it, we would not have included them. So we only included people who developed ALS

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05:05:50.040 --> 05:06:04.110

Marc Weisskopf: post-enrollment in this study. And those plasma samples were stored at, in fact, minus 150 since then, on an average of about 13 years before ALS developed, and up to 23 years before.

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05:06:04.250 --> 05:06:11.679

Marc Weisskopf: So we took advantage of those samples to both measure persistent organic pollutants that were in the samples.

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05:06:11.690 --> 05:06:24.009

Marc Weisskopf: at that early stage, as well as a proteomic panel, the OLINX target 96 neurology, and some other panels. I'm going to focus on just one thing, one proteome that we got out of that.

1301

05:06:24.010 --> 05:06:35.079

Marc Weisskopf: And then we, essentially did a Cox proportional hazards to see, sort of, what's the rate of developing ALS over time under different scenarios, but also looked at how those biomarkers changed.

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05:06:35.680 --> 05:06:37.359

Marc Weisskopf: Next slide, please.

1303

05:06:38.260 --> 05:06:50.660

Marc Weisskopf: So very quickly, since I don't have much time just to cut to the chase, what we were looking at, we focused on neurofilament light chain because of all of the interest, of course, that that has generated already. Now, most of the work on NFL,

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05:06:50.660 --> 05:06:59.440

Marc Weisskopf: has been done, really, probably most of it has been done in ALS cases already, comparing ALS cases to controls and samples taken from ALS cases.

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05:06:59.440 --> 05:07:11.820

Marc Weisskopf: There's much less work on samples from before disease onset. And the reason that's important is that after disease, of course, the disease can cause all sorts of changes that may affect these things. So what we'd like to know is.

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05:07:11.820 --> 05:07:24.050

Marc Weisskopf: did those changes happen before the disease occurred? But even the few studies that looked at samples before disease have all been within a few years before the disease, maybe up to 5-ish, I think.

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05:07:24.050 --> 05:07:34.389

Marc Weisskopf: But we had a scenario where we had samples from much, much earlier than, than, than that. Actually, I think some of the prior ones have looked in more years, maybe out to 10 or so, but often.

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05:07:34.390 --> 05:07:45.849

Marc Weisskopf: With small, very small numbers when you get out that early. And what we actually found is that if you use NFL expression levels, in the plasma from this O-Link panel.

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05:07:45.850 --> 05:07:59.449

Marc Weisskopf: that, first of all, the top row there is all cases and controls, and you can see that the odds for ALS are higher when NFL is higher, and that's generally what people have found, even when they've looked at samples before, within about

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05:07:59.550 --> 05:08:07.679

Marc Weisskopf: As I say, it's usually within about, at most, 5 years before ALS. And, next slide, please. Or next click, rather.

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05:08:10.530 --> 05:08:26.070

Marc Weisskopf: Right, so the... actually, I should have said the second row there shows, if we just look at NFL and the people who had their sample collected within 5 years of developing ALS, we see a very strong association with ALS, as some others have as well.

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05:08:26.070 --> 05:08:37.650

Marc Weisskopf: But what we have that hasn't really been seen before is that when we look at the people whose blood samples were collected 5... at least 5 years before ALS, and up to 14.6, which is...

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05:08:37.650 --> 05:08:47.059

Marc Weisskopf: the median split between 5 and the highest number we had, which was 23. We still see a significant increased,

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05:08:47.160 --> 05:08:57.220

Marc Weisskopf: risk of ALS when NFL is elevated. And if you're out at more than 14.6 years, it's still elevated, but not significant. Next click, please.

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05:08:58.010 --> 05:09:02.759

Marc Weisskopf: And it seems roughly similar between males and females. Next click.

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05:09:03.480 --> 05:09:26.109

Marc Weisskopf: If... what I've plot... what we've plotted here that's... that's in another study, they plotted it similarly, that's why we did it this way. This is the ratio of NFL between cases and controls. So anything above 1 says that the cases have higher levels of NFL than the controls. And the numbers on the x-axis here, 0 is when ALS diagnosis occurs.

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05:09:26.110 --> 05:09:50.000

Marc Weisskopf: And minus 5 is 5 years before that, minus 10 is 10 years before that, etc. And so you can see that in the 5 years before ALS, the NFL is pretty dramatically raised, and that's higher than controls, and that is something that generally people have suggested before. But what we're seeing is that that ratio is elevated significantly. The gray band around the red line is sort of our confidence limits of this.

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05:09:50.030 --> 05:09:55.239

Marc Weisskopf: is significantly elevated even back to about 15 years before ALS onset.

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05:09:55.350 --> 05:09:57.689

Marc Weisskopf: Next slide, please.

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05:09:58.200 --> 05:10:15.920

Marc Weisskopf: And so we could use this in our models to do these predictions, the area under the curve, to see how well the NFL level is actually predicting getting ALS. And the green line is the NFL levels in the model, you know, when you're just looking within 5 years of ALS. But next click, please.

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05:10:16.370 --> 05:10:36.069

Marc Weisskopf: Yeah, the... that one, that's the less than 5, and maybe next click? I'm forgetting what's on the next one. Nope, let's go back one. Sorry. That's the within 5 years, that's the green one, but the 5 to 14.6 is the light blue there, and it's an area under the curve of .63. Not... not massive, but it is certainly suggesting that things are changing.

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05:10:36.070 --> 05:10:38.880

Marc Weisskopf: This is under review at the moment. Next slide, please.

1323

05:10:39.400 --> 05:10:53.119

Marc Weisskopf: So yeah, so basically from this, and that was a quick run-through of it, but it seems like we're getting this NFL-level increase, you know, up to 15 years before, well before we generally thought, so things seem to be changing very early in the body.

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05:10:53.120 --> 05:11:01.450

Marc Weisskopf: You know, and this is just one proteomic signal, but, you know, it raises the possibility that maybe we can identify risk somewhat earlier.

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05:11:01.470 --> 05:11:14.229

Marc Weisskopf: If you go to the next slide, I'll give the other one very quickly. We also looked at the persistent organic pollutants, found many of them related to... this is survival with ALS. These are all individual models. Next click.

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05:11:14.380 --> 05:11:19.829

Marc Weisskopf: This is the same population. You can see a lot of them elevated, but they're correlated. Next click.

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05:11:20.210 --> 05:11:32.820

Marc Weisskopf: These things are very highly correlated, so on the next click, we used a regression method to sort of select out ones that seem to be driving this effect, or the association we're seeing. Next click.

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05:11:32.900 --> 05:11:47.929

Marc Weisskopf: Using something called ElasticNet that picked out, seemed to suggest that the hexachlorobenzene and chlorine were driving this association the most. So we created, next click, an environmental risk score using those two.

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05:11:47.930 --> 05:11:58.580

Marc Weisskopf: That found a very, high hazard ratio for ALS for people who were higher on this sort of combination of hexachlorobenzene and chlorine. Next slide.

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05:11:58.580 --> 05:12:18.550

Marc Weisskopf: This is the last one, that if you were... essentially, what we found here is that if you were one standard deviation higher in that combination of chlorine and hexachlorobenzene, your survival was about a year less than if... than someone with a lower combination of those two. And that's it. Okay, getting it in right out. These are the collaborators that helped with all of that.

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05:12:18.550 --> 05:12:31.790

Danielle Boyce: Thank you. No, thank you so much, and now I want to pick your brain about lots of things, including the Kaiser study that Dr. Vieira mentioned that we're working on with folks who have not developed ALS yet, and we have samples from them, and so...

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05:12:31.790 --> 05:12:45.920

Danielle Boyce: Now, yeah, so very, very, very exciting stuff. So, please put any questions that you have in the Q&A, and, we'll come back to them. And also, if, Dr. Weisskopf, if there's any that you want to answer directly, if you can see them, feel free to do that as well, and that goes for all of our panelists.

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05:12:45.920 --> 05:12:54.329

Danielle Boyce: Next, we have a pre-recorded, presentation, from Dr. Steven Goutman.

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05:12:54.810 --> 05:13:10.470

Danielle Boyce: And, he is an associate professor of neurology at Michigan Medicine and director of the ALS Clinic and ALS Center of Excellence. His research focuses on uncovering the causes of ALS, particularly environmental risk factors, so continuing that theme.

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05:13:10.720 --> 05:13:30.050

Danielle Boyce: and has identified associations between ALS and exposures, such as organochlorine pesticides. Dr. Gautman also helps direct the University of Michigan ALS Biorepository, which provides essential resources to ALS researchers, and so we are going to play that recording next. Thank you very much.

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05:13:31.380 --> 05:13:35.079

Samer Khan (she/her): Thanks, Danielle. I'm gonna hit play. Let me know if the volume's okay.

Establishing the Cohort for Occupational Risk and Prevention Studies - for Amyotrophic Lateral Sclerosis (ALS CORPS) (Prerecorded) University of Michigan - Stephen Goutman, MD

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05:13:37.310 --> 05:13:41.930

Stephen Goutman: Hi, it's so great to be with you today. I'm Stephen Goutman, I'm an associate professor of neurology

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05:13:41.930 --> 05:14:01.380

Stephen Goutman: At University of Michigan, I'm also the Harriet Hiller Research Professor, Director of the Stanford Morris ALS Clinic, and Associate Director of the Scott Pringer ALS Center. Thank you for allowing me to talk to you today about our study, titled Establishing the Cohort for Occupational Risk and Prevention Studies for Amyotrophic Lateral Sclerosis. It's really a pleasure. Sorry I cannot be with you in person, but I'm actually

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05:14:01.380 --> 05:14:04.540

Stephen Goutman: in clinic today, seeing, people living with ALS.

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05:14:06.550 --> 05:14:12.699

Stephen Goutman: Before I start, let me give you a little bit of background about what led us to propose and carry out this study.

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05:14:13.100 --> 05:14:14.830

Stephen Goutman: We know that ALS is...

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05:14:14.850 --> 05:14:34.439

Stephen Goutman: the result of what's called the gene-time environment hypothesis. Under this idea, people have some underlying genetic susceptibility to disease, and as they age, there's cellular damage. And if one has insufficient amount of environmental exposures, it pushes one over the threshold where it leads to this self-perpetuating disease process. And ultimately, this

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05:14:34.730 --> 05:14:37.740

Stephen Goutman: this development of the disease ALS.

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05:14:38.610 --> 05:14:55.709

Stephen Goutman: But we also know that ALS starts prior to clinical symptoms, so if we use this model that was proposed by Dr. Al-Shalabi and Dr. Hardiman, and we superimpose it on this model that was proposed by Dr. Benatar, we have this idea that there's this susceptibility period to disease, and then ALS starts

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05:14:55.900 --> 05:15:03.770

Stephen Goutman: And there are actually no clinical symptoms. We have this pre-symptomatic disease period. And then eventually there may be some early biomarker evidence of disease.

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05:15:03.860 --> 05:15:20.419

Stephen Goutman: which enters us into this pre-manifest stage, and then people may develop these possible symptoms or signs of ALS, leading to this prodromal stage, and then eventually these definitive symptoms of ALS or phenocconversion. And there's this large gap between the start of disease and this diagnosis that's at least one year.

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05:15:20.420 --> 05:15:26.419

Stephen Goutman: But we know that there's a whole number of susceptibility factors, things like the genetics, environmental exposures, and lifestyle factors.

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05:15:27.260 --> 05:15:29.039

Stephen Goutman: Another way to think about this is that

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05:15:29.180 --> 05:15:47.440

Stephen Goutman: people have a genetic risk for ALS, and there's a couple ways that we can consider this genetic risk. It may be monogenic, meaning there's a single gene that greatly increases one's likelihood of going on to develop ALS, or a polygenic risk, whereby one has a number of different modifications to the genome that collectively

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05:15:47.540 --> 05:15:51.110

Stephen Goutman: move somebody from low to higher ALS risk.

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05:15:53.110 --> 05:16:03.139

Stephen Goutman: Another way to think about this is this multi-step model of ALS, where you use both genes and exposures, or what we call the exposome, to increase somebody's likelihood of

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05:16:03.600 --> 05:16:10.749

Stephen Goutman: going on to develop ALS. If somebody has a significant ALS-associated gene, such as C9ORF72,

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05:16:11.140 --> 05:16:17.300

Stephen Goutman: fewer steps are needed to eventually go on to get ALS, and thereby perhaps fewer exposures. Whereas somebody that has

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05:16:17.540 --> 05:16:23.079

Stephen Goutman: polygenic risk of ALS, perhaps more steps or more exposures are needed to go on to develop ALS.

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05:16:23.810 --> 05:16:26.059

Stephen Goutman: We know there are a number of exposures that are...

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05:16:26.530 --> 05:16:38.530

Stephen Goutman: linked to ALS, and linked from study to study. These include factors such as lead exposure, heavy metal exposure, solvent exposure, pesticide exposure, and agricultural chemicals.

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05:16:38.710 --> 05:16:40.590

Stephen Goutman: Trauma, and even electric shock.

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05:16:41.070 --> 05:16:52.360

Stephen Goutman: And we're all aware of the elevated risk in veterans. Here's this one study looking at veterans deployed post-9-11 who received care at the VA from 2001 to 2015.

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05:16:52.810 --> 05:16:58.040

Stephen Goutman: what we see is that the risk of ALS is about 2 times that of the general population, with certain

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05:16:58.320 --> 05:17:10.909

Stephen Goutman: branches of the military experiencing even higher risk, including the Army and the Air Force, and those in the Navy and Coast Guard, and individuals serving in the occupation of tactical Operation Officers had an even higher risk.

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05:17:12.630 --> 05:17:26.390

Stephen Goutman: There's... in addition to this, there's a more recent paper by Dr. Mark Weisskopf and colleagues, really also suggesting that these risks hold, and I'm sure this is a paper he'll be discussing over the course of this meeting.

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05:17:27.100 --> 05:17:39.409

Stephen Goutman: In our own work, we've seen that self-reported occupational exposures increase ALS. These include exposures such as particulate matter, vital organic compounds, metals, and combustion and diesel exhaust.

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05:17:40.500 --> 05:17:52.270

Stephen Goutman: And when we looked in our own cohort of individuals with ALS compared to healthy controls, we found that those working, especially in production occupations, had a 1.22

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05:17:52.410 --> 05:17:58.090

Stephen Goutman: times higher risk for ALS for every 5 years of work in that industry, suggesting that there are

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05:17:58.290 --> 05:18:03.370

Stephen Goutman: Occupational exposures, as well as certain occupations that may be

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05:18:03.510 --> 05:18:07.540

Stephen Goutman: elevating one's susceptibility for going on to develop ALS.

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05:18:08.720 --> 05:18:09.550

Stephen Goutman: in our...

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05:18:10.640 --> 05:18:23.289

Stephen Goutman: ALS case and control models as well, we asked individuals about their residential risk exposures, and what we found is that certain types of exposures that people endorse in their home also associated with a higher risk of ALS.

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05:18:23.290 --> 05:18:33.150

Stephen Goutman: These included storage of chemicals, gasoline, lawn care products, and pesticides in attached garages, as well as storage of paint and solvents and woodworking supplies in the attached garage.

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05:18:33.210 --> 05:18:42.120

Stephen Goutman: And when we looked back at our case control study as well, we also asked individuals to tell us about their hobbies and avocational activities.

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05:18:42.280 --> 05:18:56.609

Stephen Goutman: Interestingly, what we found is that individuals who endorsed participation with golf, recreational dancing, gardening or yard work, hunting and shooting, woodworking, and weightlifting had an elevated risk of ALS.

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05:18:57.530 --> 05:19:00.459

Stephen Goutman: For some of these, They make sense.

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05:19:00.630 --> 05:19:10.780

Stephen Goutman: Conceptually, because of the potential chemical exposures and physical activity related to these. For some of these other ones, I'm not so sure we have an explanation for at this time.

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05:19:11.230 --> 05:19:17.120

Stephen Goutman: So when we think about one's risk of ALS, we think of the exposures, but that builds on

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05:19:17.230 --> 05:19:24.179

Stephen Goutman: somebody's underlying susceptibility to ALS, Such as their polygenic risk. So...

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05:19:24.610 --> 05:19:36.120

Stephen Goutman: One of the ways we looked into this was in our case control model, where we compared our individuals with ALS to healthy controls and performed genotyping on them with the help of my colleagues, Dr. Kelly Bukowski and Dr. John Doe.

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05:19:36.920 --> 05:19:53.310

Stephen Goutman: And what we did was we were able to build a polygenic score for thinking about somebody's underlying susceptibility to ALS. What we found is that when we considered the presence of the C9ORF72 repeat expansion, that a one standard deviation increase in

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05:19:53.320 --> 05:20:07.790

Stephen Goutman: this ALS polygenic score increase the risk of ALS by 1.28 times. So essentially what this allows us to do is think about somebody's underlying genetic susceptibility to ALS, and then how their exposures on top of that compound and

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05:20:08.030 --> 05:20:13.060

Stephen Goutman: move somebody from less likely to more likely to go on to develop ALS.

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05:20:13.240 --> 05:20:19.990

Stephen Goutman: And the reason why this is particularly important is as we think about ways and strategies of preventing ALS. And so these...

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05:20:20.330 --> 05:20:24.640

Stephen Goutman: these... these ideas about ALS prevention, these are not just...

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05:20:25.530 --> 05:20:27.929

Stephen Goutman: Thoughts that are out there, but... but real...

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05:20:28.150 --> 05:20:38.919

Stephen Goutman: I would say activities that we as a field and community are acting on. Here's a podcast that I did years ago, and I would say that Dr. Michael Benatar has really been at the forefront of really helping us to think about

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05:20:38.920 --> 05:20:53.080

Stephen Goutman: prevention and ALS prevention and really bringing together the community to really pursue how do we, as a community and collectively, pursue some of these prevention strategies for ALS? And so here's a paper that was published now a few years ago, thinking about the roadmap to ALS prevention.

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05:20:54.780 --> 05:21:07.510

Stephen Goutman: So, if we think about this in summary, what we have are this underlying susceptibility to ALS, what we call these non-modifiable risk factors. These include factors such as your polygenic risk, sex, your age.

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05:21:07.600 --> 05:21:27.030

Stephen Goutman: superimposed on these non-modifiable risk factors are these modifiable risk factors, including your occupational exposures, exposures to metals, and other hobbies. And as one has a greater exposure to some of these environmental factors, it may increase somebody's risk of eventually going on to developing ALS. And so the goal for us is really to think about

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05:21:27.160 --> 05:21:38.769

Stephen Goutman: How do we reduce the likelihood of exposure in individuals who are most susceptible to going on to get disease, so that we can really prevent people from going on to get ALS in the future?

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05:21:39.310 --> 05:21:51.200

Stephen Goutman: This led us to the proposal of what we now call the Michigan Brain Health and Environment Study, which has been funded by the CDC and ATSDR now for the past few years. We are really, really grateful

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05:21:51.370 --> 05:21:55.680

Stephen Goutman: And fortunate for this funding, for this really, really important study.

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05:21:55.880 --> 05:21:57.469

Stephen Goutman: when I think about our work.

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05:21:59.120 --> 05:22:06.490

Stephen Goutman: We have, for over a decade, been looking at individuals with ALS compared to controls, and looking retrospectively at

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05:22:06.580 --> 05:22:20.919

Stephen Goutman: different risk factors and how that may influence ALS. But in parallel, I think one of the aspects of science that's really important is for us to look prospectively. In other words, capturing individuals before they develop any type of disease.

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05:22:20.920 --> 05:22:35.730

Stephen Goutman: such as ALS, and looking prospectively at what are the factors that may be elevating their risk and susceptibility to ALS. Because a prospective study really gets us around some of the critical biases in retrospective studies.

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05:22:35.880 --> 05:22:55.060

Stephen Goutman: So, we are incredibly grateful to our colleagues at CDC for funding this study, and for their partnership over the past many, many years for allowing us to pursue this goal, and so thank you, thank you very much. You'll see at the bottom of these slides, I do include our QR code to our study website, so if you're interested in this study,

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05:22:55.060 --> 05:22:57.269

Stephen Goutman: You can find more information there.

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05:22:57.500 --> 05:23:08.400

Stephen Goutman: We have a really great study team, and so for anybody who's participated in the study, you may have seen some of these names, and so it's really an exceptional study team that allows us to carry out these studies. So.

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05:23:08.740 --> 05:23:13.020

Stephen Goutman: Our research nurse, Jaina Duell, our research coordinators, Nicole Bob.

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05:23:13.160 --> 05:23:21.690

Stephen Goutman: Carly Piqu, Alyssa Braun, our lab team, Sam Teener, Adam Patterson, Daegu Jing, and hard.

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05:23:22.080 --> 05:23:29.470

Stephen Goutman: our Managing Director, Stacey Jacoby, and my colleague, Dr. Eva Feldman. Really an exceptional study team to make all of this happen.

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05:23:29.580 --> 05:23:32.810

Stephen Goutman: The idea of this study is it has two aims.

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05:23:33.120 --> 05:23:40.669

Stephen Goutman: The aims are as follows. One is to establish a longitudinal cohort of people at risk of neurological disease. So, for example, people who

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05:23:40.900 --> 05:23:49.389

Stephen Goutman: are coming from some of these occupational, exposed backgrounds that may make them more susceptible to disease. So we want to really enrich

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05:23:49.740 --> 05:24:02.730

Stephen Goutman: Our population here for people in production occupations, and then query their exposure... exposures and symptoms to capture what's happening in real time, longitudinally, and also think about their phenoconversion risk, while also biobanking samples.

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05:24:02.870 --> 05:24:16.349

Stephen Goutman: And then, we want to take those biobank samples and develop these polygenic risk scores to think about these interactions between your polygenic score and your exposures, and how that may increase one's susceptibility to going on to get ALS.

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05:24:16.930 --> 05:24:21.619

Stephen Goutman: This is a longitudinal study, so the aims that I'm showing you today are really

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05:24:21.650 --> 05:24:39.280

Stephen Goutman: the beginnings of this study. Really, how do we get it started, build this cohort, and start this, what we believe is an important cohort, to follow now over the course of decades, to really monitor how this impact of exposures increases ALS susceptibility over time, or

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05:24:39.730 --> 05:24:44.369

Stephen Goutman: may make somebody... more or less likely to go on to develop ALS in the future.

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05:24:45.030 --> 05:24:50.570

Stephen Goutman: We have a number of strategies to recruit individuals for this... for this study.

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05:24:50.660 --> 05:25:06.860

Stephen Goutman: First is using advertisements on social media, the meta-platforms such as Facebook and Instagram. People may see these types of flyers posted on Facebook as they're scrolling about our study. We've also performed a number of community outreach activities, talking to unions and

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05:25:06.970 --> 05:25:12.690

Stephen Goutman: and other... Groups of interest in our area to try to get our recruitment materials out there.

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05:25:13.350 --> 05:25:20.050

Stephen Goutman: Our study postings have focused on areas throughout Michigan, Northern Ohio, and northern Indiana, really areas

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05:25:20.160 --> 05:25:23.949

Stephen Goutman: right now, that are close, close to Michigan, where...

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05:25:24.210 --> 05:25:28.069

Stephen Goutman: We have good reach to our participants.

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05:25:29.160 --> 05:25:30.720

Stephen Goutman: We've also utilized

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05:25:31.910 --> 05:25:43.170

Stephen Goutman: Existing recruitment strategies within University of Michigan. These include our University of Michigan Health Research website, where people have already signed up and want to participate in research.

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05:25:43.350 --> 05:25:47.750

Stephen Goutman: And we've used this research match website, which is an NIH-supported

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05:25:48.040 --> 05:25:52.450

Stephen Goutman: research database as well, where individuals who are interested in participating

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05:25:52.560 --> 05:26:01.230

Stephen Goutman: are able to sign up, and then we're able to reach out to them. So we're really using lots of different strategies and efforts to reach potential participants.

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05:26:01.600 --> 05:26:06.620

Stephen Goutman: Combined with this, we've had some really creative social media post.

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05:26:06.800 --> 05:26:14.259

Stephen Goutman: and flyers that we can time to certain events, such as Valentine's Day, President's Day, March Madness.

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05:26:14.700 --> 05:26:23.070

Stephen Goutman: New Year's, and just so different ways of helping to make our content relevant to what's happening throughout the course of the year.

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05:26:23.330 --> 05:26:25.520

Stephen Goutman: We have different flyers here as well.

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05:26:26.170 --> 05:26:30.920

Stephen Goutman: That we can distribute and we've posted at doctors' offices and around the community.

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05:26:31.970 --> 05:26:38.230

Stephen Goutman: Pocket cards and other flyers that we have available for anyone who's interested in posting them.

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05:26:38.870 --> 05:26:43.259

Stephen Goutman: We have got shareable PDFs, we've got event postcards.

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05:26:43.590 --> 05:26:57.689

Stephen Goutman: And these ultimately lead individuals to our Michigan Brain Health and Environment Study website, where individuals can learn about the study, decide if they have questions about our study, want to learn more about our study, ask us questions, and sign up

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05:26:57.860 --> 05:27:04.139

Stephen Goutman: Which then allows us to forward them our consent form and interact with our study team to ultimately consent.

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05:27:04.430 --> 05:27:10.099

Stephen Goutman: This is a remote study, and so at this time, individuals can fully participate in their home.

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05:27:10.510 --> 05:27:18.090

Stephen Goutman: And they can consent in their home, fill out samples, and... I'm sorry, fill out surveys and submit samples, all remotely.

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05:27:18.970 --> 05:27:30.660

Stephen Goutman: Individuals, if they agree to proceed and they match our study inclusion criteria, they will be sent a study consent form, which they can look over, read, ask us questions, and ultimately sign.

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05:27:30.850 --> 05:27:32.959

Stephen Goutman: We ask individuals to fill out

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05:27:33.230 --> 05:27:46.669

Stephen Goutman: what we call our My Story Survey, our Michigan Lifestyle Information, Sports, and Hedge Trauma History, Occupations, and Residencies Since Youth study, which captures these important non-modifiable and modifiable risk factors, including

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05:27:46.690 --> 05:27:54.829

Stephen Goutman: Capturing an individual's age, biological sex, their health history, their history of exposures in the residential and occupational

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05:27:54.930 --> 05:28:03.519

Stephen Goutman: In avocational settings, their use of tobacco, their BMI, military history, and physical activity over time as well.

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05:28:04.180 --> 05:28:20.379

Stephen Goutman: We ask these questions both at baseline and then over time, so that we're able to both capture somebody's retrospective exposures, but then at the time of enrollment, really begin to look forward and understand what exposures and what activities people are participating in in real time.

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05:28:21.090 --> 05:28:29.909

Stephen Goutman: We also send people a DNA collection kit. This is a saliva kit that somebody can fill out, or I'm sorry, that somebody can collect their saliva at home, and then ship it back to us in the mail.

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05:28:30.710 --> 05:28:37.489

Stephen Goutman: These saliva kits come with instructions to help participants know how to use it, and we have our study team also able to assist and provide

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05:28:37.620 --> 05:28:39.820

Stephen Goutman: Provide instructions and support as needed.

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05:28:40.390 --> 05:28:52.159

Stephen Goutman: We also are very heavily engaged in study engagement and retention. We do newsletters, webinars, birthday cards, really to create a connection. This is a community of research, and so

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05:28:52.280 --> 05:29:09.849

Stephen Goutman: we feel that it's important for us to really have this collaborative research with the study participants and really keep them engaged with the ongoings of the study. I think the study has improved through the direct contact between our study team and the participants to capture information or really adjust the study in ways that make it more...

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05:29:09.960 --> 05:29:11.760

Stephen Goutman: Or friendly for the participants.

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05:29:12.950 --> 05:29:32.579

Stephen Goutman: As I noted earlier, we've had a lot of engagement. We've reached out to unions, we've mailed letters to neurologists in the state, we've reached out to the local ALS organization, we've provided flyers, we've worked with our communications department, we've utilized digital billboards, we've attended ALS events and encouraged guests to participate, and we've used Facebook advertising. So there's a lot that we're doing to really get the word out about this study.

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05:29:32.780 --> 05:29:43.579

Stephen Goutman: Here's an example of some of the newsletters we've put out. We really aim these newsletters to, one, connect us to participants, let the participants know who we are, who's the study team, why are we doing this research.

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05:29:43.720 --> 05:29:51.360

Stephen Goutman: Explain anything going on with the research, any upcoming activities, or explain any changes that the research may be undergoing for them to look out for.

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05:29:51.500 --> 05:29:57.629

Stephen Goutman: We have community outreach slides, so if we're invited to go speak to a group, we have these IRB-approved slides that we can

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05:29:58.220 --> 05:30:01.589

Stephen Goutman: Discuss with that particular group and answer questions about the study.

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05:30:01.870 --> 05:30:07.270

Stephen Goutman: And... I think one of the... one of the more interesting directions that this took is that

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05:30:07.490 --> 05:30:10.120

Stephen Goutman: These really fabulous individuals.

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05:30:10.330 --> 05:30:14.389

Stephen Goutman: Josh and Darla Welton, who are these welders, found our...

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05:30:14.500 --> 05:30:21.709

Stephen Goutman: found our research. And they are these individuals who run this

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05:30:22.520 --> 05:30:25.649

Stephen Goutman: This podcast and website, these are just

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05:30:25.800 --> 05:30:29.270

Stephen Goutman: Fascinating podcast, The Welder, and it's under the Fabricator website.

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05:30:29.420 --> 05:30:32.150

Stephen Goutman: These are just so interesting to listen to.

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05:30:32.350 --> 05:30:33.230

Stephen Goutman: And...

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05:30:33.340 --> 05:30:50.269

Stephen Goutman: they reached out to us and said, hey, tell us about this study that you're doing. Why are you so interested in this? And of course, we've shown in our retrospective studies this association with metal exposure and ALS, and they said, you know, we're interested in the health risk that may be out there.

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05:30:50.320 --> 05:31:02.619

Stephen Goutman: while there's a lot of personal protective equipment, maybe people don't necessarily use them, or know why they're using them, and we would really like to learn more about the study, and then they ended up actually doing an article about our study, and so this is really one of the

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05:31:02.690 --> 05:31:08.889

Stephen Goutman: interesting ways that I think that we can connect and engage with the community, and really gives me and the rest of the study team

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05:31:08.980 --> 05:31:16.489

Stephen Goutman: connections with the community. It helps me learn something new and something more, and so the Weltons are great. It was great speaking with them, and...

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05:31:16.650 --> 05:31:22.019

Stephen Goutman: And they just have some wonderful work, and really fascinating podcasts, if anyone's a podcast listener.

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05:31:22.610 --> 05:31:40.339

Stephen Goutman: We've also listened to our participants. As I said, I think it's really important that we connect with the participants, we make the study easier and better because of them, and so we've been able to simplify the surveys, make the surveys shorter, make the website and the collection system easier to navigate and less repetitive. And so we've been able to improve the study, and actually have

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05:31:40.340 --> 05:31:45.510

Stephen Goutman: Got to new ideas about questions we should be asking that we are not asking by listening to our participants.

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05:31:46.600 --> 05:32:06.460

Stephen Goutman: I'm going to show you an early look at our data, please. These are confidential, so I ask that you do not take photographs or post these. This was the last time

we really did our data poll back in May of 2026. The numbers are a little bit higher now, but you can see that we've got 1,700 females and about 600 males consented. This is the age group we're looking for, that late

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05:32:06.510 --> 05:32:16.310

Stephen Goutman: that mid to late 40s to early to mid-50s, really the decades prior to somebody, go... somebody who will likely go on to get ALS.

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05:32:16.540 --> 05:32:24.579

Stephen Goutman: We see that there's a nice mixture of ages, though, this range from 35 to 61 in females, and from 41 to 66 in males.

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05:32:24.950 --> 05:32:31.430

Stephen Goutman: We see a good distribution of educations, a good distribution of races, so what we think is a really important

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05:32:32.030 --> 05:32:36.979

Stephen Goutman: Representative population for us to really be asking these important questions about

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05:32:37.220 --> 05:32:44.050

Stephen Goutman: how exposures impact risk of ALS, as well as really other brain diseases, is what this study will allow us to accomplish.

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05:32:44.500 --> 05:32:45.240

Stephen Goutman: I've

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05:32:45.970 --> 05:32:54.370

Stephen Goutman: We're able to look at where our participants are. I've really cropped this for, study privacy, but to really... that we've got a large number of participants coming throughout Michigan.

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05:32:54.420 --> 05:33:09.410

Stephen Goutman: We're able to really look at people's SOC's, or standard occupational classification codes, by age, and what we do is we map out somebody's occupational

history. We look at their job titles and job tasks, we assign them an SOC code, and we look at how people's

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05:33:09.870 --> 05:33:22.460

Stephen Goutman: how people progress within their SOC codes over time. And you can see we go back from before 30 to some people enter their 70s, and this is the lasagna plot that really allows us to show, longitudinally, how people are in these jobs.

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05:33:22.460 --> 05:33:32.480

Stephen Goutman: I think one of the reasons why this is valuable and important is one of the questions we said is, what's the likelihood of somebody changing SOC's over time? So, in other words, if you

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05:33:32.500 --> 05:33:37.879

Stephen Goutman: are in a certain SOC code, are you always likely to stay in that SOC code, or could you have done something in the past

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05:33:38.020 --> 05:33:55.300

Stephen Goutman: but then changed to a different job classification in the future. And in fact, we did see this in some of the SOC's that are of particular interest to us, such as buildings and grounds cleaning and maintenance, construction and extraction, farming, fishing, and forestry, installation, maintenance, and repair, production occupation, protective services.

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05:33:55.300 --> 05:34:03.629

Stephen Goutman: and transportation and material moving occupations, we see that there are individuals, it's a little bit difficult to see here, but I've highlighted a few of these, but individuals who have participated

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05:34:03.720 --> 05:34:09.330

Stephen Goutman: Or worked in these particular occupations for only a short period of time, and then have gone on to have different occupations.

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05:34:09.780 --> 05:34:20.600

Stephen Goutman: So this really allows us to think about that there may be people that have a brief period of exposure, and then go on and work in a different occupation, compared to individuals who have, say, worked in that same occupation for long term.

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05:34:20.600 --> 05:34:30.359

Stephen Goutman: really, some of these important questions are, what does both short- and long-term exposure to a particular job or set of exposures do to influence one's risk of going on to develop ALS?

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05:34:30.430 --> 05:34:35.670

Stephen Goutman: Later in time. Individuals also report their... self-report their current exposures.

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05:34:36.170 --> 05:34:40.560

Stephen Goutman: And we break this down by really major and minor categories, so we see that

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05:34:41.020 --> 05:34:57.779

Stephen Goutman: A number of people, in this case 719, reported workplace exposures to welding, and we can see, we can break these down, that of these individuals reporting welding, 105 said they worked with steel, 92 worked with stainless steel, 89 alloy steel, 84 aluminum.

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05:34:57.780 --> 05:35:12.229

Stephen Goutman: We see 889 people endorsed working with chemicals, such as solvents, oils, and acids. We see a number of people endorsing metal exposures, such as aluminum, iron, nickel, lead still shows up. Different fumes, such as welding fumes.

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05:35:12.240 --> 05:35:19.440

Stephen Goutman: And so, we see That there are these workplace exposures that people are endorsing.

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05:35:20.210 --> 05:35:26.900

Stephen Goutman: And here's another way to look at this, where we can look at the particular chemicals and see which ones are most commonly endorsed.

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05:35:27.130 --> 05:35:34.899

Stephen Goutman: For chemicals, you see that the solvents, oils, acids, and, the...

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05:35:35.100 --> 05:35:49.870

Stephen Goutman: Alcohols are most common. For metals, we see aluminum and iron. For fumes, we see welding. For welding, we see steel. Fibers, we see fiberglass and radiation, we see x-ray. Just allows us to see which are the most common exposures in the participants in our cohort.

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05:35:51.310 --> 05:36:04.510

Stephen Goutman: We're also thinking about what are the particular SO... the particular self-reported exposures by SOC codes, so sometimes the SOC code may not necessarily match up to the particular exposures, so by combining both

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05:36:04.670 --> 05:36:18.280

Stephen Goutman: somebody's SOC code, their standard occupational classification code, with their self-reported exposure. It really gives us an opportunity to think about what's happening here, in terms of their occupational exposures. This is a welding block, so what we see here are in people

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05:36:18.300 --> 05:36:37.030

Stephen Goutman: who are in these different SOC codes, they report workplace exposures to welding. Some of these you would say are conceptually possible, and others you would not have considered. So, for example, there's people in SOC code architecture and engineering reporting welding, people in buildings and grounds cleaning, sale and related occupations. In fact, after

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05:36:37.110 --> 05:36:41.629

Stephen Goutman: one of our seminars, one of our participants reached out to us and said, you know, I'm in sales.

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05:36:42.050 --> 05:36:53.770

Stephen Goutman: But there were these different environments that I worked in, and in one of my manufacturing environments, I actually was working in the same building as the manufacturing, I would go to the line, and I would see how things worked, and sometimes I was actually in a different building.

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05:36:53.770 --> 05:37:04.310

Stephen Goutman: And so this really allows us to see how different SOC codes and self-reported exposures may match what we conceptually believe, or may not match, and give us more insight into the exposures that are out there.

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05:37:04.760 --> 05:37:14.130

Stephen Goutman: There's also this chemical block. This surprised me a little bit. So these were people reporting high exposure to chemicals, and when I looked at this, it was really individuals who were in these sort of.

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05:37:14.400 --> 05:37:32.149

Stephen Goutman: these personal care. And it was something that I didn't really think about, but I guess it's individuals working in salons or barbershops who are reporting these chemicals. So again, I think some really interesting insights into data that I wouldn't necessarily initially consider, but may become very important and valuable as our study goes on.

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05:37:32.530 --> 05:37:46.390

Stephen Goutman: Here's just another way to look at some of this information. I think I've discussed this already, and I'll move on for time. And we can look at the self-reported exposures by age group as well, to see if there's different exposure types by age. Just a wealth of data we have here.

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05:37:47.350 --> 05:37:51.530

Stephen Goutman: As part of our study, we also asked individuals to self-report their neurologic function.

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05:37:51.820 --> 05:37:57.010

Stephen Goutman: And we asked them to fill out these neural qual, or promise scales.

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05:37:57.080 --> 05:38:14.130

Stephen Goutman: And we standardize them by T-scores. The normal T-score is 50, and we see, for the most part, that every participant, in terms of their upper limb, lower limb, cognitive function, sleep function, is essentially in that normal range, and this gives us a baseline and a measure to compare to in the future.

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05:38:14.770 --> 05:38:17.419

Stephen Goutman: Even though these are small changes, we see that

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05:38:17.530 --> 05:38:23.259

Stephen Goutman: For all of these scores, sleep and sleep quality tends to be the poorest. I think I can agree with that.

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05:38:23.980 --> 05:38:34.929

Stephen Goutman: And we can even compare some of these patient-reported outcomes by SOC codes, although we didn't really see any significant, differences when one looks at SOC code and patient-reported outcome measure.

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05:38:35.630 --> 05:38:40.560

Stephen Goutman: So with that, I'd like to acknowledge the great group of people that I work with, both in our

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05:38:40.780 --> 05:38:53.799

Stephen Goutman: smaller lab group and our larger lab group, and our collaborators, as well as the CDC ATSDR for funding this work. Here's our funding, and I thank you so very much for your attention and your interest in this work.

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05:38:57.140 --> 05:38:59.760

Danielle Boyce: Thank you so much, Dr. Gautman.

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05:38:59.970 --> 05:39:07.510

Danielle Boyce: He is not here, right now, but I think we can all agree that that presentation was very impressive, and

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05:39:07.540 --> 05:39:27.530

Danielle Boyce: I'm... I know that there's a lot to talk about, and we're going to talk at 4 o'clock, we're going to have a Q&A, and we're... we're planning for it to go until 4.30, so you'll be able to ask all kinds of questions, and our panelists will... will be able to respond then. But first...

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05:39:27.860 --> 05:39:49.610

Danielle Boyce: I'm excited to introduce Xing Song. Dr. Song is an assistant professor in the Department of Biomedical Informatics, Biostatistics, and Medical Epidemiology, and

Associate Director of the Center for Health Policy at the University of Missouri. Her research focuses on advancing the effective and responsible use of real-world data.

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05:39:49.610 --> 05:39:57.260

Danielle Boyce: And developing data-centric computational methods to generate clinically meaningful knowledge and actionable, real-world evidence.

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05:39:57.400 --> 05:40:07.529

Danielle Boyce: Her work spans large-scale clinical data infrastructure and database architecture, machine learning and artificial intelligence, computable phenotyping.

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05:40:07.740 --> 05:40:20.849

Danielle Boyce: Causal inference and real-world evidence generation with an emphasis on translating heterogeneous health data into robust evidence that can inform clinical research, healthcare delivery, and population health.

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05:40:20.920 --> 05:40:37.640

Danielle Boyce: She also leads Data Coordinating Center and Informatics efforts for multiple NIH, CDC, and DOD-funded research initiatives. And of course, real-world evidence is one of my favorite topics, so I'm very excited to hear your presentation. Dr. Song, please take it away.

Towards Better Understanding of ALS using a Multi-Marker Discovery Approach from a Multi-Modal Database (ALS4M) National Opinion Research Center

University of Missouri-Columbia - Xing Song, PhD

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05:40:38.890 --> 05:40:53.900

Xing Song: Thank you for the introduction, and I'm very grateful, to be here to share with you, our projects, titled Towards Better Understanding of ALS Using Multimarker Discovery Approach from a Multimodal Database. Next slide, please.

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05:40:55.250 --> 05:41:09.670

Xing Song: So, this is the agenda of my talk today. I'm going to start with going over the data source, because all of the, follow sub-studies I'm going to share, will use that data source, which is, our multi-model database.

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05:41:09.670 --> 05:41:21.890

Xing Song: And I'm gonna share three, sub-studies, which corresponding to the three aims of this project. Study number one, is looking at the pre-diagnostic phase, where we're trying to build

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05:41:21.900 --> 05:41:30.649

Xing Song: a machine learning model towards an early prediction of new ALS diagnoses, leveraging, our database.

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05:41:30.650 --> 05:41:43.370

Xing Song: And then in Study 2, we are looking at the post-diagnostic phase, where we want to leverage the cultural inference techniques to quantify and then dissect the survival benefits of multidisciplinary care.

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05:41:43.410 --> 05:41:54.820

Xing Song: For ALS patients. And then study, 3 is a exploratory analysis where we try to, link environment exposures, with.

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05:41:54.820 --> 05:42:05.150

Xing Song: With individual patients living in neighborhood, and then to explore, the environmental exposing risk factors, using double machine learning algorithm.

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05:42:05.510 --> 05:42:06.830

Xing Song: Next slide, please.

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05:42:07.800 --> 05:42:16.550

Xing Song: So the data source that we are relying on, this multimodel database, is called GPC Reusable Observable Unified Study Environment.

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05:42:16.720 --> 05:42:32.449

Xing Song: So we're short for Grouse. So GPC, or the Greater Plan Collaborative, is one of the PCORnet networks, where we, multiple, health systems within our network, we have partners.

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05:42:32.450 --> 05:42:41.989

Xing Song: From 14 health... major health institutions where we, where we, put EHR data together, integrate EHR data

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05:42:41.990 --> 05:42:52.410

Xing Song: Together, to support, multi-site observational studies, and we also collaborate together to support, multi-center recruitment or trials.

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05:42:52.410 --> 05:43:03.189

Xing Song: So for this, particular, database that I'm leveraging for this project, we have collected over, 10 years' worth of EHR data across this 14,

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05:43:03.190 --> 05:43:13.059

Xing Song: partner sites, and on top of that, we integrate the EHR data with a multi-year statewide Medicare claims.

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05:43:13.060 --> 05:43:19.300

Xing Song: In order to create a more complete and comprehensive database for, for the analyses.

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05:43:19.300 --> 05:43:43.229

Xing Song: So, just to mention that the creation of GRAWS was in response to PCORI's funding announcement back in 2015, with a goal to create complete and comprehensive data sources for three longitudinal cohorts of choice. So each network choose one rare disease, one common condition, and create one cohort for obesity.

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05:43:43.340 --> 05:43:57.950

Xing Song: For GPC, given that we have, high overlapping with Center of Excellence across our EHR partners, we chose ALS to be our focus of the rare condition. Next click.

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05:43:58.630 --> 05:44:00.520

Xing Song: Maybe click 2 more times.

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05:44:00.800 --> 05:44:14.960

Xing Song: So, as you can see here, this VIN diagram showed the data composition. So, the orange circle below represent our EHR data, so we do have patients that only

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05:44:14.960 --> 05:44:31.310

Xing Song: Within our EHR database, and as you can see in the map, we have a pretty good coverage across, the... the nine states, where, the... our EHR partners reside in. And on top there are the,

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05:44:31.350 --> 05:44:48.919

Xing Song: the 100% state Medicare claims that we have purchased. So, because there is a limitation on how much Medicare claims that you can request for study, so we restricted our Medicare claims to the catchment states, as you can see.

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05:44:48.920 --> 05:44:53.630

Xing Song: highlighted on the map top there, and then we have over 10 years of Medicare

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05:44:53.630 --> 05:45:00.419

Xing Song: claims covering Part A, B, C, and D, for, for the entire catchment state.

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05:45:00.420 --> 05:45:17.740

Xing Song: And then on top of that, if you look at these two circles, the overlapping part, Part A, we've also established the linkage between Medicare claims and EHR data. So, we have over 45 million distinct lives within our EHR database.

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05:45:17.740 --> 05:45:31.219

Xing Song: over 30 million distinct, lives within our Medicare claims database, and then the over, overlapping population, which is the overlapping, cohort of A, had, over 6 million.

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05:45:31.220 --> 05:45:39.080

Xing Song: Patients where we think we have a relatively complete and comprehensive longitudinal records for them, which will be the base of our study.

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05:45:39.240 --> 05:45:40.480

Xing Song: Next slide, please.

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05:45:41.600 --> 05:45:56.110

Xing Song: So just to take a closer look at the compositions, as I said, the overlapping cohort, or we call it the crossword cohort, is what we choose based on complete case selection for supporting all of the remaining, studies.

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05:45:57.070 --> 05:45:58.420

Xing Song: Next slide, please.

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05:45:59.240 --> 05:46:17.729

Xing Song: So within this crosswalk cohort, we, leverage the CDC case ascertainment algorithm to identify confirmed ALS cases that are based on multiple diagnoses, the use of FDA-approved medications such as Riluzole and Edaravone.

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05:46:17.780 --> 05:46:26.750

Xing Song: Multiple visits to neurologists, as well as, Medicare eligibility for disability, that are, below 65 years old.

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05:46:27.150 --> 05:46:28.450

Xing Song: Next slide, please.

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05:46:29.680 --> 05:46:40.330

Xing Song: And, so... and, over, close to 20 million distinct, Medicare beneficiaries with a full year enrollment,

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05:46:40.580 --> 05:46:58.189

Xing Song: Close to 13,000 had at least one diagnosis code for ALS, and among them, applying the CDC algorithm, we identified close to 11,000 confirmed ALS cases, and then among them, almost 50%, we also have EHR data on them.

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05:46:58.530 --> 05:47:05.309

Xing Song: And in... on the table, on the right-hand side, you can kind of see the demographic distribution. The...

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05:47:05.660 --> 05:47:18.310

Xing Song: the confirmed cases, which could include patients in the overlapping population, but could also include individuals with only Medicare claims, or individuals only within our EHR data.

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05:47:18.310 --> 05:47:32.249

Xing Song: We try to see whether, these, the linked cohort or the cross, the crosswalk cohort might have any selection bias, demographically-wise, but where we don't see significant differences.

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05:47:32.990 --> 05:47:33.960

Xing Song: Next slide.

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05:47:35.110 --> 05:47:51.580

Xing Song: So, study number one, which... where we... we tried to use these data sets, and, build a early prediction model, for... with a goal of, reduce the diagnostic delay. Next slide, please.

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05:47:52.330 --> 05:48:04.480

Xing Song: So in order to build a prediction model for the ALS, for the new ALS diagnoses, we add another, inclusion criteria, because we do need to... want to have

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05:48:04.480 --> 05:48:17.270

Xing Song: of sufficient observations that's leading up to the first ALS diagnosis. So we require, at least 2 years of full Medicare enrollment prior to their first ALS diagnosis.

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05:48:17.270 --> 05:48:24.619

Xing Song: That reduced our overall ALS cohort to close to 1,800, which is still a good amount to start.

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05:48:24.720 --> 05:48:38.270

Xing Song: And we also compared the demographic to see if we're introducing additional selection bias. It turns out we're not. It's very comparable with that, the 5,000, complete case confirmed cohort that you just saw.

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05:48:38.570 --> 05:48:39.770

Xing Song: Next slide, please.

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05:48:40.210 --> 05:48:56.670

Xing Song: And in order to build models, we collect, within that two-year, at least a two-year look-back period, we collect as many clinical information as we can from both the databases that include all the historical diagnoses.

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05:48:56.670 --> 05:49:05.340

Xing Song: And we map it to something called fecodes, which is kind of a higher level grouping of computable phenotypes for different disease or disease groups.

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05:49:05.340 --> 05:49:21.160

Xing Song: We looked at all of their medication records, both in Medicare Part D claims, as well as their EHR prescription data, that would create indicators based on generic names. And we also collect labs and vitals, which primarily come from the EHR data.

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05:49:21.160 --> 05:49:40.750

Xing Song: And we also collected their smoking status, which also comes from the EHR data. So those, are all of the covariates, or the factors that we started to look into, for building that machine learning model for predicting the new ALS diagnoses. So we... I think we, started with over 1,000 variables to look at.

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05:49:40.940 --> 05:49:42.669

Xing Song: Next slide, please.

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05:49:43.640 --> 05:50:02.679

Xing Song: So in order to, build a model to separating, new ALS diagnosis from the others, we need healthy controls. So what is one of the advantages of this database, because this database was not built, towards, a particular condition, so it's kind of a general.

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05:50:02.680 --> 05:50:17.789

Xing Song: purpose, database. So we were able to, among the 6 million, overlap cohort, we were, able to identify a variety of different types of controls, and then we were able to do this matched control sampling.

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05:50:17.880 --> 05:50:35.240

Xing Song: Within the... within the 6 million, if you, subtract the 5,000 ALS patients out of it, we still have over... well over 5 million, control pool, that we, we started to select from. But we specifically identified those comparable controls.

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05:50:35.240 --> 05:50:41.919

Xing Song: Those are patients who either had a symptomatic non-ALS sim...

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05:50:41.980 --> 05:50:55.209

Xing Song: either have similar, symptoms or representations as ALS patients with either limp or barbar symptoms, or they were diagnosed with musculoskeleton diseases or other type of neurological diseases.

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05:50:55.350 --> 05:51:09.900

Xing Song: And then we did a 1 to 5, matching, with the exact matching based on their age, at their, first diagnosis, the race, sex, and also the, availability of their Medicare data.

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05:51:11.240 --> 05:51:12.439

Xing Song: Next slide, please.

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05:51:13.620 --> 05:51:32.720

Xing Song: Since we started with a large pool of variables, just throw them into the model, you'll get a lot of spurious relationships. So we developed this, pipeline called Consensus-Based Feature Selection Pipeline, with the goal of, identifying a stable

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05:51:32.720 --> 05:51:44.920

Xing Song: parsimonious, yet also predictable feature set that can achieve, optimal performance in terms of predicting, new ALS diagnoses, even 18 months ahead of time.

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05:51:45.940 --> 05:51:47.180

Xing Song: Next slide, please.

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05:51:48.390 --> 05:52:00.869

Xing Song: Next slide. So these are just explaining... the idea of this consensus pipeline is basically we're creating different variations of feature selection, of modeling.

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05:52:00.870 --> 05:52:10.090

Xing Song: And then we want to find a feature set that all of the different variations would agree upon. Next slide, please.

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05:52:11.270 --> 05:52:12.500

Xing Song: Next slide, please.

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05:52:14.490 --> 05:52:25.850

Xing Song: So this kind of quickly go over what I just walked through as our study design, starting from, identify the eligible ALS cases, finding the matched control.

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05:52:25.850 --> 05:52:40.050

Xing Song: And then we apply 3 different layers, 3 different layers of consensus, and we want the final model that is robust against sampling perturbation, robust against the prediction task.

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05:52:40.050 --> 05:52:58.169

Xing Song: Robust against the model selection, and eventually we use the final selected features, which is a pretty sparse model feature set at the end, and then we apply that to the external holdup set for final validation.

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05:52:59.070 --> 05:53:00.220

Xing Song: Next slide, please.

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05:53:01.140 --> 05:53:19.629

Xing Song: So this is kind of show the selection process. So we have, three dimensions of consensus that we see, consensus over different samples, over different models, and over different prediction tasks. And starting from over 1,000, we ended up with 9 features that we built the final prediction model on. Next slide, please.

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05:53:20.490 --> 05:53:25.149

Xing Song: And these are the 9 features that I identified, from this pipeline.

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05:53:25.630 --> 05:53:38.789

Xing Song: Some of the features, are very interesting, as still requires additional investigation, but there are some of the features that are, reasonable, such as,

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05:53:39.100 --> 05:53:46.830

Xing Song: Something related to, musculoskeleton and pain signals, some broad systematic age-related features.

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05:53:47.890 --> 05:53:49.159

Xing Song: Next slide, please.

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05:53:50.400 --> 05:54:06.029

Xing Song: Based on these nine features, we build, the machine learning models to do, month-ahead prediction of new ALS diagnoses, and... and you see, three panels, on there that shows the area under receiver operating curve.

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05:54:06.080 --> 05:54:17.750

Xing Song: For, comparing ALS against, non-ALS patients with other neuro... neurological conditions, the model performance, reached,

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05:54:17.860 --> 05:54:23.259

Xing Song: Around 0.8, for the 18-month ahead prediction.

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05:54:23.480 --> 05:54:30.009

Xing Song: And then for patients, exhibiting, similar limb or barber,

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05:54:30.060 --> 05:54:43.950

Xing Song: either a limb symptoms or barber symptoms, the prediction model, it's even, stronger with the prediction performance or accuracy that is above .95, which is around .98.

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05:54:44.340 --> 05:54:45.590

Xing Song: Next slide, please.

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05:54:46.670 --> 05:54:55.860

Xing Song: Although there are still limitations, one thing to note is that the initial documented diagnosis is not necessarily disease onset, so...

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05:54:55.860 --> 05:55:15.370

Xing Song: As I keep saying, in my talk, we're not predicting disease onset, we're really just predicting the new ALS diagnosis, although it could resemble the disease onset, but then there's still... there's... because of the existing diagnostic delay and the differences in healthcare utilization that may still

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05:55:15.370 --> 05:55:34.120

Xing Song: affect the timing of ALS on... observing ALS onset. But we still think the model would be useful in terms of early prediction of the new ALS diagnosis, so that, to... to kind of move the policies, or the eligibility for Medicare benefits, and, early on.

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05:55:34.570 --> 05:55:53.679

Xing Song: The final high feature, or 9-item prediction model does demonstrate promising predicted performance, but there are features that are a little bit hard to explain, that we're still doing, additional investigations to really understand whether, that is, one of... whether that's the true.

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05:55:53.680 --> 05:56:07.349

Xing Song: Risk factors, or true protective factors, the word that's, that is actually, masking some other association underlying it where we were not able to observe, the underlying factors.

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05:56:08.440 --> 05:56:10.150

Xing Song: And...

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05:56:10.150 --> 05:56:28.740

Xing Song: At the moment, we're also doing external validation, because right now, the validation we're doing is still within our database, so we actually, have recently got access to the Epic Cosmos EHR database, as well as Oracle RealWorld databases, which are multi-study EHR databases where we are trying to see

1596

05:56:28.740 --> 05:56:33.059

Xing Song: Whether our model performance could persist over to the other databases.

1597

05:56:34.020 --> 05:56:35.279

Xing Song: Next slide, please.

1598

05:56:36.050 --> 05:56:55.199

Xing Song: So that's the first study, kind of corresponding to the aim 1 of the project. The second one, is, towards the aim 3 of the project, where we try to look at post, post-diagnosis phase, and we want to be able to decompose the benefit of multidisciplinary care.

1599

05:56:55.880 --> 05:56:58.520

Xing Song: Next slide, please.

1600

05:56:59.680 --> 05:57:13.100

Xing Song: So I don't think I need to, really go over this to say how important it is for ALS patients to have access to multidisciplinary therapy in a very timely fashion.

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05:57:13.200 --> 05:57:15.250

Xing Song: However,

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05:57:15.580 --> 05:57:27.790

Xing Song: Real-world evaluation can be complicated because of the dynamic and heterogeneous nature of how the multidisciplinary care is implemented at different facilities.

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05:57:27.830 --> 05:57:38.810

Xing Song: And then they think there is still, a lack of real-world evidence on which combinations of multidisciplinary services provide the greatest survival benefit.

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05:57:38.980 --> 05:57:43.469

Xing Song: And with availability of this type of large datasets.

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05:57:43.550 --> 05:58:08.060

Xing Song: that covering a more and more representative population, and also the maturity of a observational study method called target trial emulation, which is the one we're using for these analyses. We are hoping to see whether we can use our database to understand the... to compare the alternative multidisciplinary therapy strategies using our longitudinal cohort.

1606

05:58:08.910 --> 05:58:10.129

Xing Song: Next slide, please.

1607

05:58:11.800 --> 05:58:27.070

Xing Song: So, just a little bit of background on target trial emulation, or short for TTE. It is a cultural inference framework that uses observational real-world data to explicit mimic the design of a hypothetical randomized trial.

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05:58:27.470 --> 05:58:35.679

Xing Song: And one of the implementations that we're using, which we think is fitting for the study question, is called clone sensor weight.

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05:58:35.810 --> 05:58:55.269

Xing Song: So the challenge that we face with, you know, evaluating different strategies using real-world data is that patients are not randomly assigned to different multidisciplinary care strategies. In the real-world data, they receive their different combinations of care over time, and then those choices may be related to their underlying health.

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05:58:55.330 --> 05:59:03.550

Xing Song: So, the CCW clone sensor weight approach, method provided a way to adjust for that kind of potential bias.

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05:59:04.050 --> 05:59:07.800

Xing Song: So we formalized the question, and we,

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05:59:07.930 --> 05:59:20.020

Xing Song: We, designed 8, multidisciplinary care strategies, with a, increase the increased layer of complexity.

1613

05:59:20.320 --> 05:59:34.919

Xing Song: The question that we're trying to answer here is, does earlier completion of increasingly comprehensive, multidisciplinary care really improve overall survival after ALC index diagnoses? So the eight strategies, as you can see.

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05:59:34.920 --> 05:59:44.640

Xing Song: In the figure there, Strategy A is with only neurologists involved. Strategy B, C, and D is neurologist adding another specialty.

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05:59:44.640 --> 06:00:02.070

Xing Song: Rehab, which include PTOT functional care and mobility device use. C, include, speech and communication therapy, and, a speech-language pathologist involvement. D is neurology plus respiratory care.

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06:00:02.090 --> 06:00:16.129

Xing Song: And then, the strategy E and F is where, on top of these two specialties, we're adding another one, with three specialties, and then the, strategy G and H are, with four specialties.

1617

06:00:16.860 --> 06:00:18.069

Xing Song: Next slide, please.

1618

06:00:19.090 --> 06:00:27.920

Xing Song: So this is to give you, a idea of what the clone sensor width is really doing. The basic idea is actually fairly intuitive.

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06:00:27.920 --> 06:00:45.179

Xing Song: At the time of the ALS index diagnoses, we actually create virtual copies, or clones, that's what a clone stands for, for each individual patient, and we basically use their clones and then assign them to all these different aid strategies.

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06:00:45.220 --> 06:00:58.689

Xing Song: to compare. And then we follow each colon forward in time with a allowed grace period to observe their exposure, or to observe their, their, treatment.

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06:00:58.720 --> 06:01:07.740

Xing Song: And then if the patient's actual care becomes inconsistent with their assigned, strategy, they are censored.

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06:01:08.320 --> 06:01:12.709

Xing Song: So the, the, where we stop following them.

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06:01:13.210 --> 06:01:32.710

Xing Song: So... so the only thing that would remain to be solved is, these... the sensor may not be non-informative, which is different from the general survival analysis, so we just need to adjust for the bias, the informative censoring, by using inverse probability of censoring weight.

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06:01:33.600 --> 06:01:52.999

Xing Song: So, in simple terms, the clone sensor weight approach is using clone to create comparable starting groups, using sensor to keep each group consistent with their care strategy we're trying to evaluate, and using the weight to correct for the selection bias introducing by the informative sensory.

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06:01:53.690 --> 06:01:54.849

Xing Song: Next slide, please.

1626

06:01:55.890 --> 06:02:12.419

Xing Song: So here to see, because we want everyone to start with having a neurologist involvement, we require an additional, inclusion criteria, which is, their ALS index diagnosis needs to be assigned by a neurologist.

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06:02:12.420 --> 06:02:19.269

Xing Song: Or... and then... and that's been confirmed by our data. That reduced our cohort slightly to 4,448.

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06:02:19.270 --> 06:02:28.409

Xing Song: And as you can see, on the right table over there, one-third of the group had,

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06:02:28.600 --> 06:02:36.819

Xing Song: And then the grace period that we chose is 180 days to give enough time to observe, the different specialty involvement.

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06:02:36.820 --> 06:02:49.929

Xing Song: And, over one-third of our base cohort had rehab, involved, rehabilitation care, involves OT or PT or functional care, within the first 6 months.

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06:02:49.930 --> 06:03:07.719

Xing Song: Over a quarter had speech-language pathologists involved. A little bit over, 12% has respiratory specialists involved, and as you can see, the more complexity they were adding to the MDT strategy, the smaller, the percentage become.

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06:03:08.000 --> 06:03:09.109

Xing Song: Next slide, please.

1633

06:03:10.020 --> 06:03:21.080

Xing Song: So here is the results. The big takeaway is, early involvement of STT is definitely benefit, and as you can see on the right-hand side, which shows the hazard ratio.

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06:03:21.220 --> 06:03:33.660

Xing Song: The vertical dotted line is the reference point, which is 1. Anything on the left hand of it shows a lower hazard ratio, or better survival benefit. And among...

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06:03:33.660 --> 06:03:44.239

Xing Song: Although, for all of the other seven strategies that we compare, they are not statistically significant from each other, but numerically, the one with the best,

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06:03:44.240 --> 06:03:54.839

Xing Song: Survival benefit or lowest, the hazard ratio is the... is strategy B, neurologist, with the rehab, within the first, within the first, 6 months.

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06:03:56.560 --> 06:03:57.750

Xing Song: Next slide, please.

1638

06:03:59.510 --> 06:04:15.640

Xing Song: So, the conclusion, is, so the, at least based on this study setting, all, MTT strategies that we, compare were associated with improved survival, with the largest estimated benefit observed for neurology and the rehab.

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06:04:15.900 --> 06:04:22.740

Xing Song: That include, you know, PT, OT, functional, and mobility device prescription.

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06:04:22.990 --> 06:04:25.640

Xing Song: Some,

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06:04:25.640 --> 06:04:45.030

Xing Song: Some multidisciplinary care components could be reliably evaluated because... could not be reliably evaluated because of the sparse capture, such as we wanted to include social work, but we were not able to capture a lot of the data from our database, probably because of the coding issues or some other potential reasons.

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06:04:45.230 --> 06:04:55.689

Xing Song: Residual confounding by disease severity would still be possible. One thing I want to note is, for this kind of large EHR network.

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06:04:55.770 --> 06:05:14.219

Xing Song: The data are usually more consistent and made available, or what we call structured data, or tabulated data, or discrete data. But there are a lot of important, valuable information that can suggest disease severity, or use it as important confounders that are still residing in the unstructured nodes.

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06:05:14.220 --> 06:05:19.779

Xing Song: which are in EHR, but it does take some informatics effort to extract that out, which we're also working on.

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06:05:20.880 --> 06:05:39.040

Xing Song: So overall, the findings support the potential survival benefit of coordinated and multidisciplinary care, while also highlighting the need for visual clinical data to better distinguish the contribution of individual MDT components, and also, we're thinking about a way to find not just evaluating the specialty involvement.

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06:05:39.040 --> 06:05:43.899

Xing Song: But other type of coordination strategies that the different centers are doing.

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06:05:44.850 --> 06:05:46.079

Xing Song: Next slide, please.

1648

06:05:46.980 --> 06:06:06.059

Xing Song: The last but not least, we are, trying to integrate a new data... relatively new data source, that we obtained from EPA, Environment Protection Agency, and then we're trying to investigate, environmental, exposure, risk factors.

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06:06:06.060 --> 06:06:08.950

Xing Song: Using something called double motion learning. Next slide, please.

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06:06:10.570 --> 06:06:27.120

Xing Song: So, we have come across, and then many of the great studies also been mentioned, by previous speakers on, ecological studies, that's suggesting strong environmental exposures, that may contribute to geographical variation in ALS risk.

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06:06:27.410 --> 06:06:42.049

Xing Song: but individual-level evidence linking specific toxic exposure to ALS, I mean, patient-level evidence, that linking specific toxic exposure to ALS risk remains limited.

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06:06:42.290 --> 06:06:58.969

Xing Song: So one strategy we're thinking about trying out is to link the longitudinal residential history that we do have, collected from Medicare and EHR data with something called the EPA Race Exposure Estimate, which we're gonna talk about in a little bit.

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06:06:58.970 --> 06:07:06.000

Xing Song: Where we can enable the attribution of environment exposure to patient level.

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06:07:06.340 --> 06:07:15.530

Xing Song: And then we can leverage other patient-level characteristics to where adjust for the association estimation.

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06:07:15.770 --> 06:07:29.939

Xing Song: One of the approach, that has been popular recently is called double motion learning that combines flexible motion learning based confounding adjustment with interpretable estimate of exposure, ALS associations.

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06:07:30.440 --> 06:07:31.670

Xing Song: Next slide, please.

1657

06:07:32.890 --> 06:07:38.500

Xing Song: So the data sets that we, we, we, learn about,

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06:07:38.700 --> 06:07:49.690

Xing Song: the EPA TRI, everyone... most of the people from the team probably have heard about TRI, which is the toxic release inventory.

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06:07:49.690 --> 06:07:59.550

Xing Song: That is a national database that tracks the releases and the management of over 650 toxic chemicals reported by industry facilities across the United States.

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06:07:59.550 --> 06:08:09.479

Xing Song: So it tells us what chemicals those facilities are releasing out into the environment, where they were released, and how much was released, I believe, on a quarterly basis.

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06:08:09.650 --> 06:08:16.840

Xing Song: However, the amount released alone does not necessarily translate into their potential health impact.

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06:08:16.950 --> 06:08:29.040

Xing Song: So later on, we learned about this new, this, new database called Risk Screening Environmental Indicator, which is a, a feature developed by EPA.

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06:08:29.140 --> 06:08:39.739

Xing Song: That combines the raw TRI release information with factors such as chemical toxicity, environmental fate, and transport.

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06:08:39.780 --> 06:08:51.989

Xing Song: and potential human exposure, and then I create these weighted, scores, that could be directly used, you know, to understand this association with health.

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06:08:52.300 --> 06:09:04.230

Xing Song: And it's more importantly for our study, this RACI database also provides a model toxicity-weighted concentration at a much finer geographic resolution.

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06:09:04.580 --> 06:09:05.949

Xing Song: Next slide, please.

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06:09:08.600 --> 06:09:15.899

Xing Song: So if you see the... the panel 2, the RACI database is actually provided,

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06:09:16.100 --> 06:09:31.479

Xing Song: on this raster is a raster database that basically cut the United States continent into, all of this little, geographic unit that are... each of the units are 810 meters by 810 meter grid cells.

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06:09:31.480 --> 06:09:38.530

Xing Song: And then the RACI scores are actually calculated and attributed to each one of the squid cells.

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06:09:38.700 --> 06:09:51.790

Xing Song: And using that, together with some area-to-area mapping strategy, we were able to, link the RACI score, the exposure, at individual residence level.

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06:09:53.350 --> 06:09:54.440

Xing Song: Next slide, please.

1672

06:09:55.090 --> 06:10:08.100

Xing Song: And of course, since we do have, longitudinal records of their residential histories, we will also be able to calculate their exposure, their exposure kind of over time.

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06:10:08.690 --> 06:10:10.989

Xing Song: So, the...

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06:10:11.690 --> 06:10:28.269

Xing Song: We resorted to a double-motion learning model, it's because when it comes to modeling risk factors against an outcome, we always need to consider confounders. And when it comes to what might cause ALS, there are so many other possible reasons that need to be well controlled.

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06:10:28.440 --> 06:10:42.429

Xing Song: And since we are able to create this individual-level risk exposure, we were also able to use that alongside other individual-level clinical variables, which I showed in the previous slides.

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06:10:42.490 --> 06:11:00.359

Xing Song: And then because of all of these variables are kind of highly collinear related with each other, one of the, robust approaches is this double machine learning approach. In simple terms, double machine learning, or DML, basically they use machine learning twice.

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06:11:00.420 --> 06:11:14.520

Xing Song: So they first used machine learning model to build an exposure, model, basically modeling the exposure in here. It's the environment exposure of interest, the T, against all the other confounders.

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06:11:14.590 --> 06:11:24.469

Xing Song: And then build a second model, modeling the outcome, which is the why, against all the other confounders, and then using residual under residual to really find...

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06:11:24.670 --> 06:11:36.079

Xing Song: what, what remaining differences after controlling for all the confounders in the exposure still predict ALS? So that's kind of the idea. I know I'm running out of time. Next slide.

1680

06:11:36.990 --> 06:11:56.659

Xing Song: So this is, the finding we have. So we built this on all the four... over 400, chemicals that we... with sufficient sample, and we built it over 2 years cumulative exposure, or 3 years cumulative exposure, and we found these 3 interesting ones that are sticking out.

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06:11:56.770 --> 06:11:59.889

Xing Song: That are show... showing sustain...

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06:12:00.070 --> 06:12:04.760

Xing Song: Sustainably, highly association with risk.

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06:12:04.970 --> 06:12:12.240

Xing Song: They, they are lead, atrazang, and the other one, very hard to pronounce, diacyanids.

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06:12:12.350 --> 06:12:27.829

Xing Song: So I know lead has been shown, in multiple literatures, and we're glad we find this confirmation, which is the top important risk factor. But HSA, which is a widely used herbicide, particularly for controlling weeds in crops such as corn.

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06:12:27.970 --> 06:12:36.860

Xing Song: We've seen some sparse evidence on their potential neurotoxicity, but there's no established evidence for association with ALS.

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06:12:37.000 --> 06:12:50.999

Xing Song: The other, diasocyanamates are a group of industrial chemicals used primarily to make polyurethane products, including foams, insulation, coating, adhesive, and paints. So kind of,

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06:12:51.120 --> 06:12:56.039

Xing Song: Related to... and usually those exposures related to manufacturing and construction.

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06:12:56.350 --> 06:13:11.619

Xing Song: So I think there might be some interest in... also reflecting on the previous speaker's, finding, Dr. Gottman's finding on production occupation, that are associations. I think there's some interesting, correlations over there that we need to further investigate.

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06:13:11.840 --> 06:13:25.190

Xing Song: So that's pretty much the end of it, and I... the last slide is to, limitation and discussion. I'm gonna skip that one. The last one to... really, grateful for CDC and ATSDR for sponsoring the work.

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06:13:25.190 --> 06:13:32.050

Xing Song: as well as my, collaborators across the GPC network for making this happen.

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06:13:32.060 --> 06:13:32.840

Xing Song: Thank you.

End of Day Discussion

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06:13:34.460 --> 06:13:44.859

Danielle Boyce: Thank you very much, and of course, I had so many thoughts and questions, and I was very inspired with, you know, with our work. It's so interesting because, you know, we have electronic health records in the...

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06:13:44.860 --> 06:14:09.169

Danielle Boyce: ALS TDI database, but a much smaller amount. But on the other hand, I do a lot of work with the OMOP Common Data Model, you know, and I'm thinking, and maybe a question for us separately from this, but I'm thinking about how we might adapt some of this work to do network studies across, you know, the Odyssey community, which would be basically free, and not require data sharing. But I really, I just...

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06:14:09.170 --> 06:14:19.189

Danielle Boyce: I just am very fascinated by what you're doing and appreciate it. While I have you here, since we're going into the Q&A, and we have some questions just for you, let's start, if you don't mind, with you.

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06:14:19.190 --> 06:14:19.860

Xing Song: Absolutely.

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06:14:20.050 --> 06:14:37.449

Danielle Boyce: Okay, wonderful. So the first question is, I think it would be interesting and possibly valuable to run such a prediction model on people who were never diagnosed with ALS and who died with other causes of death. We might find some people who may well have died from ALS, but were never diagnosed.

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06:14:37.860 --> 06:14:46.980

Xing Song: That's a very, very interesting thought. Yes, we do have the potential to do that, although the cost of death information,

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06:14:46.990 --> 06:15:03.759

Xing Song: probably you can... you have the same experience, Dr. Boyce, and EHR is a little tricky. You do need to integrate other data sources, such as the National Death Index data, where the cough of death would be available, but I think that's a very interesting direction.

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06:15:03.760 --> 06:15:09.249

Danielle Boyce: Yeah, yeah, yeah, that's one of the challenges with these multimodal data sets, you know, and I...

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06:15:09.250 --> 06:15:34.219

Danielle Boyce: Dr. Weisskopf kind of alluded to it, too, I thought, is, you know, you can get a data set up to a certain point, and then this piece is missing, and then... and it's hard when you're working with big data, because the whole point, often, why it's collected, is that it's not consented, right? And so, it's very difficult to go back and rejoin people, but yeah, I think that's a great question, too. Also, okay, Dr. Song, I'm very surprised that respiratory intervention and MDT

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06:15:34.220 --> 06:15:36.069

Danielle Boyce: Care did not improve survival.

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06:15:36.290 --> 06:15:38.380

Xing Song: It did student-proof Survival. It did.

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06:15:38.380 --> 06:15:39.030

Danielle Boyce: Oh, I did.

1704

06:15:39.030 --> 06:15:49.450

Xing Song: It did. So it's just not as strong as, the, the other MDT strategy. If you go back to the slide, can we still do that?

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06:15:49.620 --> 06:15:50.359

Xing Song: All of that.

1706

06:15:50.360 --> 06:15:51.140

Danielle Boyce: Can we...

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06:15:51.140 --> 06:15:51.600

Xing Song: Yes.

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06:15:51.600 --> 06:15:57.180

Danielle Boyce: Yeah, sorry, go ahead. Can we go back to this slide showing the multidisciplinary, care?

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06:15:57.180 --> 06:16:00.259

Xing Song: Maybe 4 more?

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06:16:00.540 --> 06:16:10.479

Xing Song: One more, one more, one more, one more... there. There, there we go. All of the strategies improve survival.

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06:16:10.740 --> 06:16:19.400

Xing Song: The... the... and there's no statistically difference across these different strategies. It's just a slight numerical difference with a point...

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06:16:19.550 --> 06:16:22.450

Xing Song: With a... with a degree of 0.01.

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06:16:22.630 --> 06:16:27.979

Xing Song: So, with the respiratory, it does improve survival for up to 30%.

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06:16:30.050 --> 06:16:37.620

Danielle Boyce: Very good, very good. Now, let me see if any other questions came in. Let's see, trying to pull up the chat here.

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06:16:37.860 --> 06:16:40.490

Danielle Boyce: slightly different Zoom version for me than I'm...

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06:16:40.650 --> 06:16:42.550

Danielle Boyce: Used to here, but I'm doing it.

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06:16:42.920 --> 06:16:48.779

Danielle Boyce: Okay, so... What I'm gonna do now is, we have a number of questions.

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06:16:48.870 --> 06:16:56.390

Danielle Boyce: In the chat and in Q&A that have been answered, but there were also a few that kind of,

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06:16:56.420 --> 06:17:09.850

Danielle Boyce: that have kind of broad... a broad inter... might be interesting to actually have the conversation, now. So I'm gonna have the hosts and panelists, or the panelists, if you're available still, and you can come on. I'm just gonna see who's here.

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06:17:09.950 --> 06:17:15.059

Danielle Boyce: And... So I'm not asking questions to folks who aren't here.

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06:17:15.370 --> 06:17:18.109

Danielle Boyce: Alright, so we have a question...

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06:17:18.360 --> 06:17:26.449

Danielle Boyce: Which I thought was really a good one. What do you make of POPs tested in blood versus brain?

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06:17:27.200 --> 06:17:36.680

Danielle Boyce: And that might be, for Dr. Weisskopf, maybe Dr. Murdoch, but definitely Dr. Weisskopf, we're talking about POPs.

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06:17:37.000 --> 06:17:50.770

Marc Weisskopf: Yeah, so, well, I guess I have a few thoughts on that. I mean, obviously, from the perspective of where we think the damage is occurring, if we knew pops in brain, that would be ideal.

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06:17:50.950 --> 06:17:59.400

Marc Weisskopf: The tricky part is, we can't really get that, with one... Potential minor,

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06:17:59.780 --> 06:18:06.689

Marc Weisskopf: caveat to that, it's very hard, if not impossible, to get that from living people, so...

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06:18:06.730 --> 06:18:25.830

Marc Weisskopf: you're looking at the levels in brain necessarily post-ALS, and so one has to worry about how all the changes related to having ALS may affect distribution of POPs in different tissues, and redistribution with things like weight loss, or even just

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06:18:25.910 --> 06:18:40.710

Marc Weisskopf: behavioral phenomena about what you are and aren't exposed to, so that raises that extra concern. The blood... the blood allows us, you know, I mean, it's not... still not easy, quote-unquote, but it... but if there are scenarios where you can get it prior to ALS, it allows you to...

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06:18:40.710 --> 06:18:47.279

Marc Weisskopf: have that temporality better. If we're... if the interest is in... in, you know, is it related to the incidence of...

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06:18:50.680 --> 06:18:54.920

Danielle Boyce: Okay, anybody else want to comment on that? Because I have another one for you. Dr. Ostro.

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06:18:55.310 --> 06:19:01.710

Lyle W. Ostrow MD PhD, Temple LKSOM: Yeah, this might be a dumb question, but wouldn't... aren't the levels in blood going to depend on what you eat because of the lipid content?

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06:19:03.750 --> 06:19:09.010

Lyle W. Ostrow MD PhD, Temple LKSOM: If I eat a different meal in a day, or if I'm on, like, tube feeds that have a lot of lipid, isn't that gonna change stuff?

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06:19:09.240 --> 06:19:09.810

Lyle W. Ostrow MD PhD, Temple LKSOM: Yeah.

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06:19:09.810 --> 06:19:16.819

Marc Weisskopf: So typically, you will adjust for... you will try and adjust for the lipids, so that... so that you remove that effect, but it's certainly...

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06:19:16.980 --> 06:19:28.979

Marc Weisskopf: possible. and I'm not sure whether, you know, a very high lipid meal or something, and then you take that blood draw will change it. That's certainly a possibility. I guess the,

1736

06:19:29.200 --> 06:19:34.879

Marc Weisskopf: Right, I mean, there is the adjusting for the lipid level when you do the analysis for that, but the...

1737

06:19:35.410 --> 06:19:36.840

Marc Weisskopf: the...

1738

06:19:37.340 --> 06:19:54.280

Marc Weisskopf: Right, I mean, that would be something... I guess there's different concerns that come in different places, but you... you know, unless you're... if you're getting it prior to the diagnosis of ALS, then as long as it's early enough before that, then, you know, whether or not you ate that meal

1739

06:19:54.290 --> 06:20:07.060

Marc Weisskopf: may be unrelated to ALS. I mean, you do have to worry about whether certain types of diets are related to ultimately developing ALS, and that's what you're seeing, but it is less likely that it is sort of changes in your diet because of ALS that are now going to affect what you're.

1740

06:20:07.060 --> 06:20:14.459

Lyle W. Ostrow MD PhD, Temple LKSOM: I guess I meant, like, actually meal-to-meal, right? Like, if I have a fatty meal for... if I had a hamburger for lunch versus a salad, doesn't that change.

1741

06:20:15.100 --> 06:20:18.180

Marc Weisskopf: Oh, I don't think that will change the measurement that you wind up getting.

1742

06:20:18.180 --> 06:20:20.230

Lyle W. Ostrow MD PhD, Temple LKSOM: Acutely? Okay. Huh. Okay.

1743

06:20:23.060 --> 06:20:25.990

Danielle Boyce: Okay. Anyone else on that one?

1744

06:20:27.470 --> 06:20:29.790

Danielle Boyce: Okay, so here's another question.

1745

06:20:30.100 --> 06:20:35.430

Danielle Boyce: Is the diversity of the bacteria of the microbiome in part related to diet?

1746

06:20:35.820 --> 06:20:41.050

Danielle Boyce: Another diet question. As ALS progresses, the patient's diets change.

1747

06:20:41.790 --> 06:20:54.630

Ben Murdock: Yeah, so that's... that's a great question. I think I answered one of it kind of on a personal note to, I think... I believe it was Elijah, but the answer is... is yes, it's possible.

1748

06:20:54.630 --> 06:21:12.019

Ben Murdock: So, at least in our initial studies, we tended to use people who were, early on in disease, and so that was kind of their more normal diet. With some of the new samples that we're doing, we're doing some longitudinal things, and so we'll be looking at stuff over time, so that is something that can be a factor.

1749

06:21:12.020 --> 06:21:20.800

Ben Murdock: One of the things we have done with, that we have in the data set now, and I didn't have time to go into this in our talk, is we've started enrolling at-risk patients.

1750

06:21:20.800 --> 06:21:34.250

Ben Murdock: And these are people who are typically family members, so they shouldn't share genetic makeup, and most of the time, they are the caregivers for the, you know, for people with ALS, or, you know, so they are in kind of a similar environment.

1751

06:21:34.250 --> 06:21:54.669

Ben Murdock: And so, one of the ways we're trying to get around that question is to enroll people and use as controls people that are... come from a very similar environment. Now, that being said, you know, you can control for it a little bit, but that's always going to be a bit of an issue. So it's definitely something we need to take into account, but we do... do try to control for that as much as possible.

1752

06:22:00.190 --> 06:22:06.000

Danielle Boyce: So keep putting your question... if you have any outstanding questions, let me look at... sorry, see what's...

1753

06:22:06.870 --> 06:22:13.490

Danielle Boyce: It's open. Any NFL levels studied in veterans with ALS?

1754

06:22:17.300 --> 06:22:28.759

Marc Weisskopf: I... I don't... know of anything specifically targeting veterans? I could be wrong about that.

1755

06:22:29.100 --> 06:22:32.939

Marc Weisskopf: Not that they're not in some other populations, but I'm.

1756

06:22:32.940 --> 06:22:33.780

Danielle Boyce: Give me.

1757

06:22:34.070 --> 06:22:36.460

Marc Weisskopf: So I'm not 100% sure, but I don't...

1758

06:22:36.600 --> 06:22:40.419

Marc Weisskopf: Noah, off the top of my head, anything particularly targeting the veterans for NFL?

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06:22:41.210 --> 06:22:46.889

Danielle Boyce: I can say that at ALSTDI, with the AHRQ study, because we do have veterans, right, and we do

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06:22:46.980 --> 06:23:03.949

Danielle Boyce: you know, test for that, then we do have some. And the Champion Insights study that is... was recently launched, will do that as well. So, we'll do all kinds of, you know, blood tests on... on those participants. So I think that potentially could be a valuable source of those types of data.

1761

06:23:05.200 --> 06:23:16.769

Danielle Boyce: Okay, so... let me... oh, I have another question, let's see. Dr. Murdock, have you reached out to the young woman in her ALS story to study neutrophils in these women diagnosed before 35?

1762

06:23:19.360 --> 06:23:22.409

Ben Murdock: So, have I reached out to the young women in Hurston?

1763

06:23:22.870 --> 06:23:27.069

Danielle Boyce: Her ALS story is the group of women who were diagnosed before 35.

1764

06:23:27.530 --> 06:23:30.189

Ben Murdock: We have not.

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06:23:32.470 --> 06:23:46.490

Ben Murdock: I think that's actually a good suggestion to getting enrollment up in younger women. That's actually... so I've answered a few questions, both in the question and answer and also directly in the chat, and that is actually one of the problems we do run into, is that there's so few women

1766

06:23:46.490 --> 06:24:03.610

Ben Murdock: who are younger in these studies, in terms of demographics, you know, women tend to have very low rates of ALS until around menopause. That's actually one of the reasons we started looking at hormones and things like that. And then it tends to jump up and be very similar to men. So that's actually a really good suggestion. We have not.

1767

06:24:03.610 --> 06:24:22.029

Ben Murdock: In terms of analysis, one of the things we are currently doing is we've switched over from traditional flow cytometry to spectral flow cytometry, which gives more

granular data. And one of the things we're currently working on, actually, is trying, and this is through the CDC, is trying to

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06:24:22.030 --> 06:24:33.140

Ben Murdock: establish a way that we can do a multi-center analysis using flow cytometry. So, flow, one of the downsides of it, and as much as I love flow, and as much as I've built a huge chunk of my career on it.

1769

06:24:33.170 --> 06:24:47.600

Ben Murdock: One of the downsides is it tends to require fresh samples. It doesn't really play nice with frozen samples. So one of the things we're doing now is we're doing a series of tests and an initial analysis, I think, on around 50 patients.

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06:24:47.610 --> 06:25:03.340

Ben Murdock: to see whether or not we can get reliable data from frozen samples using spectral flow. And so if that's the case, then we actually could potentially use, you know, that source of patients.

1771

06:25:03.340 --> 06:25:09.119

Ben Murdock: But right now, you know, we could use it maybe for the microbiome, if you want to convince a bunch of young women to...

1772

06:25:09.190 --> 06:25:26.750

Ben Murdock: defecate into a bag. That can potentially be arranged, and we might be able to do that. However, except we're, like, flow cytometry and a lot of these other analyses, it can be kind of tricky with frozen samples. So we're working on it, but I actually think that's a wonderful idea, so thank you for throwing that out there.

1773

06:25:29.980 --> 06:25:32.419

Danielle Boyce: Anyone else on that... on that question?

1774

06:25:33.850 --> 06:25:47.060

Danielle Boyce: Okay, here's... so here's a question from Mr. Pat Dolan, who is my longtime collaborator and mapping expert, so I always know where he's coming from. And he asked the question I was actually about to ask, so great minds, Pat.

1775

06:25:47.060 --> 06:26:03.390

Danielle Boyce: This question is for all the researchers. What are the top 3 datasets you wish you had? For example, a complete ALS census. I was thinking more, like, what linkages do you wish you could get that are frustrating that you can't get? But what are some data sets that you wish we could have?

1776

06:26:04.590 --> 06:26:12.419

Ben Murdock: I can go first, and I mentioned this in my talk a little bit during the question, but, patients before they get ALS.

1777

06:26:12.450 --> 06:26:30.580

Ben Murdock: I think for me, that's the big one. I mean, we have lots of patients that we, you know, you can get cerebral spinal fluid, you know, from the CNS, you can get blood, but one of the hard things is because ALS is so rare, getting people before the disease happens and seeing what they look like

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06:26:30.580 --> 06:26:34.689

Ben Murdock: you know, someone asked about, you know, NLR as a biomarker, and it's like.

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06:26:34.690 --> 06:26:45.369

Ben Murdock: well, we don't know, like, before people get... we don't do testing on people before they get the disease, and so if I could have a data set of just people who get ALS and they're...

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06:26:45.740 --> 06:26:55.280

Ben Murdock: inflammatory profile, microbiome, etc, before disease onset. I think that would be absolutely huge, but that's very, very difficult to come by.

1781

06:26:55.520 --> 06:27:10.299

Danielle Boyce: Well, I could... I can tell you that the project that Dr. Vierra mentioned at his last slide with Kaiser, that's exactly what we're doing, and we would love to collaborate. Anyone who wants to chat about that, we'd be very glad to do it. We are...

1782

06:27:10.300 --> 06:27:20.169

Danielle Boyce: we're looking at a number of things, but I... just the same thing. Boy, wouldn't it be nice if I could see what happened before they were diagnosed, because all of our data is afterward.

1783

06:27:20.240 --> 06:27:41.599

Danielle Boyce: And it can only do so much, and of course, Dr. Benatar's study, was so, you know, wonderful, looking at the prediction, with proteomics, but those are people he'd been following so closely, because they were asymptomatic carriers. And so, Kaiser... I happened to hear that Kaiser had, such a data set, and I... but I didn't know if they had anybody with ALS, and they do.

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06:27:41.600 --> 06:27:47.980

Danielle Boyce: And so... so that's the work that we're doing. We're just in the early stages, but would love to collaborate with anyone who's...

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06:27:47.980 --> 06:27:57.620

Danielle Boyce: who's listening and wants to learn more about that, and be a part of that, we would love to chat with you. We could use all the brains on this as we can get, so...

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06:27:57.620 --> 06:28:03.159

Marc Weisskopf: Danielle, is that... can I ask on that one, is that with their, the research biobank at.

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06:28:03.160 --> 06:28:03.870

Danielle Boyce: Yes.

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06:28:03.870 --> 06:28:28.720

Danielle Boyce: Yeah. Yes, sir. So, yeah, so they ask questions, so the way that that works is when you come into their health system, they give you the option of participating in research, and so, which is such a brilliant idea, and so they take your blood, if you consent, you take your blood. They ask you a very thorough questionnaire, very, very thorough, lifestyle and risk factors and all kinds of... not with ALS in mind, just very broadly, and then

1789

06:28:28.720 --> 06:28:53.680

Danielle Boyce: They do blood samples, sometimes they do longitudinal blood samples, so we, we, we're trying... we don't know what we're gonna end up getting, but we're gonna try to get everything we can. And their electronic health records. And so, like, like, Dr. Song

was saying, some of the challenges are, you know, with the unstructured data. A lot of what we want is data of symptom onset, and, and not just

1790

06:28:53.680 --> 06:29:06.469

Danielle Boyce: the diagnosis with the symptoms, and that is often in a note, and so it remains to be seen if we're going to have to do a proxy measure for that or not. I think that's going to be really important if we're doing, like, proteomics and

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06:29:06.470 --> 06:29:31.249

Danielle Boyce: you know, we're trying to do the same type of work that Dr. Benatar did in that population, and he had the date of symptom onset, and so... and it was quite precise, right? And so, we might not have that, so we'll see, because it's real-world evidence, but yeah, it's... I'm really excited about the possibility, and just really have my fingers crossed that it... we can get a lot of good data out of it. There's at least 100, people that

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06:29:31.250 --> 06:29:37.740

Danielle Boyce: that we'll be able to get. And then, of course, we're trying to get as many age and sex match controls

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06:29:37.740 --> 06:29:53.029

Danielle Boyce: As well, and, you know, with certain inclusion criteria, so... but I just wanted to throw that out there, because that's something that ALSTDI is actively doing, and we would love to collaborate and share. And then, of course, we'll share the data back to Kaiser so that they can make it open as well.

1794

06:29:53.170 --> 06:30:17.070

Marc Weisskopf: But I could also add to this, because it actually rips off a question that I responded to, somebody asked in the Q&A, but another data set, I think they were asking about, you know, trying to find out what's going on with military recruits when they come into the military. And Alberto Scario, who's talking tomorrow, is doing work with this very large military biorepository, where they have all sorts of serum samples from people.

1795

06:30:17.340 --> 06:30:19.989

Marc Weisskopf: And I'm working with the VA data.

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06:30:20.080 --> 06:30:38.529

Marc Weisskopf: he even wanted... he wanted to just say, could I tell him, like, which of those folks had ALS? And... and it was virtually impossible to make the DOD and the VA talk to each other that way, and the hoops to go through. We have still not managed to figure out how to do this, and so if anybody

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06:30:38.540 --> 06:30:42.050

Marc Weisskopf: I mean, that would be a great merging of data sets, where we have all this.

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06:30:42.050 --> 06:30:42.490

Danielle Boyce: Yes.

1799

06:30:42.490 --> 06:30:55.729

Marc Weisskopf: repository information on the recruits, and it just needs to be linked up with the VA health data to find out who got ALS, but... but I don't know who... we need people with connections that can push the VA to work together better on this.

1800

06:30:55.730 --> 06:31:18.290

Danielle Boyce: Well, I did see some of my friends from the Veterans Affairs advocacy teams, throughout the various patient advocacy groups who have connections and work with these groups regularly, and I think that would be a terrific advocacy topic, right, for them to help pursue while they have those, you know, direct connections, because it's, you know, obviously it's a hindrance, and it's...

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06:31:18.350 --> 06:31:19.400

Danielle Boyce: Silly.

1802

06:31:19.400 --> 06:31:39.200

Danielle Boyce: And, you know, this is the ALS clock, right? And bureaucracy shouldn't... that's why I studied bureaucracy, that's why I have my DPA and not anything else, because I wanted to figure out how we could navigate this bureaucracy and data. And so, yeah, I will follow up personally on that, because I think that's really terrific, because

1803

06:31:39.200 --> 06:32:02.930

Danielle Boyce: you know, that's very... as we know, it's very difficult to enroll people in the military in one of these studies, that it doesn't involve the military data sets themselves, you know, the clinics, you know, if you're not associated with the clinic, it's very difficult for

us to acquire EHR data, for example, directed from the participants who are in veterans' clinics. You know, it's much easier to get data from EPIC, you know, for example, for them to self-direct it.

1804

06:32:02.930 --> 06:32:18.719

Danielle Boyce: But most of these linkages that we have don't even, you know, work with VA or, you know, the medical... the military medical centers, which is why we were doing this Champion Insights at ALSTDI, just to kind of oversample it, because it is so difficult. But if we could get data at that level.

1805

06:32:18.830 --> 06:32:37.319

Danielle Boyce: and get that linkage, that would be huge. And we wouldn't even have to necessarily, you know, violate any privacy, or there's all kinds of things that can be done to do that. It's, it's not about an IRB or privacy issue, really. It seems like a bureaucratic challenge to me. My two cents.

1806

06:32:38.020 --> 06:32:46.320

Danielle Boyce: Okay, Pat, I hope we answered your question. Pat, anyone else, though? Anyone else have a linkage that they would like to have, a data set that they would like to see?

1807

06:32:49.910 --> 06:32:57.139

Danielle Boyce: I can think of a million things that I... so we wish, and Pat, I'm talking to you, Pat, but we wish we had very detailed residential history.

1808

06:32:57.750 --> 06:33:13.009

Danielle Boyce: On... on everyone. That would be incredible. Oftentimes, we get, you know, Denver, you know, is where we lived, and that doesn't... that is not enough, right? We need more, and so we do offer those surveys, the registry offers them, we, you know, we offer them, but just...

1809

06:33:13.010 --> 06:33:25.210

Danielle Boyce: It's... it's a lot of work to come up with that, you know, to answer those questions for someone who has ALS. It's a long questionnaire. I've often said that it would be nice for people who want to help.

1810

06:33:25.370 --> 06:33:30.159

Danielle Boyce: That is a good thing that a helper can do, is help you to catalog

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06:33:30.190 --> 06:33:45.460

Danielle Boyce: your risk factors, your exposures, your residential history, and help you fill those things out. If a caregiver is looking for something specific to do, not just let me know if you need help, this is how you could help, and help ALS broadly.

1812

06:33:46.030 --> 06:33:58.270

Marc Weisskopf: Related to that, and I agree with that, and I've been thinking about things where... so I would add to that that, you know, these registries, I mean, ideally, like, Massachusetts or Michigan, as was talked about, that have full state ones, are very valuable, but

1813

06:33:58.270 --> 06:34:09.360

Marc Weisskopf: being able to link to that residential history would be even more valuable. One thing to consider for those scenarios is that there have been some attempts to look at trying to create past, you know, get

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06:34:09.540 --> 06:34:19.529

Marc Weisskopf: other data to fill in past residential history, and NIH even did a whole series of testing, different approaches. And LexisNexis, in that context, turned out to be.

1815

06:34:19.530 --> 06:34:19.900

Danielle Boyce: Clue.

1816

06:34:19.900 --> 06:34:27.849

Marc Weisskopf: If you start with a current address and information, feed it to them, they can... they were extremely good at getting a full residential history.

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06:34:27.850 --> 06:34:28.250

Danielle Boyce: Bye!

1818

06:34:28.250 --> 06:34:41.810

Marc Weisskopf: I don't know how far back, necessarily. They could go pretty far back, I don't remember how far, but it worked pretty well. So that's a way, if you want to try and

either alleviate burden on the person, or if you don't have the person, of potentially trying to get that history.

1819

06:34:42.720 --> 06:35:00.079

Danielle Boyce: Excellent. Pat, I'm putting you in charge of following up with that one. Thank you so much. Alright, let's move on to the next one in the interest of time. So, is there any genetic data on neutrophil-lymphocyte ratio response to various toxic infection autoimmune exposures?

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06:35:01.020 --> 06:35:06.949

Ben Murdock: That's a great question. We're still processing some of those data, so, we didn't make it

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06:35:06.960 --> 06:35:17.209

Ben Murdock: Into today's talk, but one of the things our group has been doing is it's the transformative grant that we've been working on for a number of years, which basically combines giant data sets

1822

06:35:17.210 --> 06:35:36.070

Ben Murdock: From various people who are working on ALS. So, you know, you heard Stevens talk about, environmental exposures and toxins and pollution, and then, you know, I have the microbiome, but especially my immune work. And so we haven't gotten down to really drill down into those just yet, because we've been basically, like, we have these

1823

06:35:36.110 --> 06:35:41.580

Ben Murdock: I want to say, like, 5 or 6 massive data sets that we're kind of, like, seeing how they all interact.

1824

06:35:41.580 --> 06:35:56.760

Ben Murdock: But that is something that we do plan on looking at, is, you know, does someone who has a high level of exposure, do they tend to have, you know, a higher NLR? We do collect genetic data on them as well, and so...

1825

06:35:56.820 --> 06:36:11.759

Ben Murdock: Right now, the two questions we have to... or issues we have to deal with are, one, just time, just because these are very large data sets, and there's just so many

different ways you can kind of combine them, you know, do you want to associate this with this, or that with that, that sort of thing.

1826

06:36:11.910 --> 06:36:31.349

Ben Murdock: And then the other issue, too, is that, you know, based on when we get funding or, you know, how we collect the data, that they might not be perfectly overlapping data sets. So a lot of times, maybe I'll do, you know, 400, 500 patients, you know, in our most recent paper, looking at immune profiles, and then of those patients.

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06:36:31.400 --> 06:36:40.330

Ben Murdock: say 200 of them, maybe, will have had an analysis of blood, you know, POPS levels and other factors.

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06:36:40.460 --> 06:36:54.310

Ben Murdock: So, it's something that we're looking at, but it's very complicated, and it's kind of a lot of moving parts, so it's something we're definitely looking into, but there are some issues getting to that point, both in terms of, you know, both time and actual overlap between these data sets.

1829

06:36:57.140 --> 06:37:10.559

Danielle Boyce: We have one more in here. If we look at the list of environmental exposures for ALS, remove military history, what overlap is there for, I believe, Alzheimer's, Parkinson's, LBD, FTD, etc?

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06:37:13.490 --> 06:37:20.380

Danielle Boyce: fluid body dementia, I assume, and... What is the overlap?

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06:37:20.640 --> 06:37:25.409

Danielle Boyce: Environmental... if we look at the list of environmental exposures.

1832

06:37:29.300 --> 06:37:32.089

Ben Murdock: I think Mark might have stepped away, and I... Steven's still in.

1833

06:37:32.090 --> 06:37:32.450

Danielle Boyce: Absolutely.

1834

06:37:32.450 --> 06:37:37.749

Ben Murdock: If you were... if you were here... if he were here, I could say that he could probably answer this a little bit, but,

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06:37:38.270 --> 06:37:45.980

Danielle Boyce: We can circle back to that one. We... we can, we can bring that back tomorrow, and, and, and yeah, that's what we'll do.

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06:37:46.600 --> 06:38:06.230

Lyle W. Ostrow MD PhD, Temple LKSOM: We should bring it back tomorrow, but to be honest, I think that the data is that everything overlaps, right? There's very few that don't overlap. I think the pesticides, the metals, solvents, air pollution is found in all of these diseases, because we actually, embarrassingly, I don't know how to say this, but we did this as a drinking game, where, anyway, we were googling PubMed about what,

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06:38:06.460 --> 06:38:14.650

Lyle W. Ostrow MD PhD, Temple LKSOM: Classes of... of toxic... could we find neurodegenerative diseases that were not... did not have an implicated one of these classes of toxins?

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06:38:15.180 --> 06:38:21.700

Lyle W. Ostrow MD PhD, Temple LKSOM: So I'd love to hear what they say tomorrow, but I think virtually all of them overlap. I don't think there's any that really don't.

1839

06:38:21.970 --> 06:38:35.240

Danielle Boyce: Yeah, I'm thinking of this knowledge graph that we've been working on, with my team, with... it's, the PubMed, just what you're saying. PubMed and all of the different neurodegenerative diseases, it's the same thing, it's just kind of like all the colors kind of...

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06:38:35.240 --> 06:38:46.310

Danielle Boyce: smushed together over all the targets and all the exposures, and I thought, maybe I'm just not smart enough to understand this, or maybe, like you said, they're all just implicated. Dr. Weisskopf, do you have any thoughts about that?

1841

06:38:46.520 --> 06:39:01.869

Marc Weisskopf: Yeah, I should say, I apologize, because I do have to run, but I sort of second what Lyle was saying. I think that's generally correct, although I would say it's probably an interesting analysis, if it could be done, to see if you could actually try and do direct comparisons and fingerprint something, but there's a lot of overlap.

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06:39:02.290 --> 06:39:05.159

Lyle W. Ostrow MD PhD, Temple LKSOM: Not in my wheelhouse at all, but from, you know, from what I remember, like.

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06:39:05.450 --> 06:39:15.949

Lyle W. Ostrow MD PhD, Temple LKSOM: there are some that are stronger, right? Like, pesticides and Parkinson's are stronger, right? I think that that's, you know, Alzheimer's and air pollutants, I think, is stronger, but, you know, not my wheelhouse. But yeah, I think,

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06:39:16.050 --> 06:39:21.940

Lyle W. Ostrow MD PhD, Temple LKSOM: It's one of the frustrating things, right, is the selective vulnerability. We still don't understand how all these diverse

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06:39:21.960 --> 06:39:37.200

Lyle W. Ostrow MD PhD, Temple LKSOM: you know, environmental, genetic... I mean, it's the same genes, too, right? And a lot of these diseases can cause these very specific selected diseases. And, you know, I talked briefly about what happened in Guam. Like, whatever happened in Guam, why did some people get PD, and some people get dementia, and some people get ALS?

1846

06:39:37.200 --> 06:39:43.789

Lyle W. Ostrow MD PhD, Temple LKSOM: And it's frustrating, because we don't understand that. Why do some people with C9 or expansions get FTD and some get ALS?

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06:39:43.830 --> 06:39:47.369

Lyle W. Ostrow MD PhD, Temple LKSOM: And, you know, that is really a missing piece in all of this.

1848

06:39:47.550 --> 06:39:48.030

Danielle Boyce: Nope.

1849

06:39:48.030 --> 06:39:48.410

Xing Song: And,

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06:39:48.410 --> 06:39:50.429

Danielle Boyce: Well, thank you very much. Thank you, everybody.

1851

06:39:50.430 --> 06:39:51.010

Marc Weisskopf: I gotta run.

1852

06:39:51.010 --> 06:39:53.659

Danielle Boyce: Thank you, Dr. Weiscott. See you next time.

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06:39:53.660 --> 06:40:12.190

Xing Song: On that topic of toxicity, I wanted to just throw in, and there are a couple of available data sources published by EPA on neurotoxicity evidences, showing different chemicals, and then there's established evidence relating to different kind of neural conditions, not just the neuromuscular, but other type of neurological conditions.

1854

06:40:12.190 --> 06:40:21.050

Xing Song: could be useful. That's usually what I'm going to when I want to see whether my finding directly driven from data had some foundation. So, yeah.

1855

06:40:21.470 --> 06:40:33.550

Danielle Boyce: That's great. I'm gonna have to connect with you, because we're putting together a little GitHub repo with, like, links to all of these, so you'll have to tell us what we're missing. That's great. So I personally, I've gotten a lot out of this today, so...

1856

06:40:33.550 --> 06:40:57.689

Danielle Boyce: I really appreciate this. I made all kinds of great connections on different projects. We have one more question, and then we're... I guess it's adjourned. We have one more question, and then I'm just gonna make sure that the CDC registry team doesn't have anything else that they want to add before we go to tomorrow. But Pat just wanted... Pat Dolan just wanted to remind us that to all researchers, you have an army of patients

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06:40:57.760 --> 06:41:22.750

Danielle Boyce: and caregivers and advocates who will be, will do anything to advance the science of ALS, so put us to work. If you need data, tell us what you need and the barriers to getting it. If you need organizations to do something, tell us who they are and what the issues are. If there are any other questions that we didn't cover today, we will be sure to document them and try to get you the answer tomorrow. I do hope you come to the presentation

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06:41:22.750 --> 06:41:30.040

Danielle Boyce: tomorrow. There's going to be more kinds of presentations, like we had today on the science and on the registry itself.

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06:41:30.040 --> 06:41:46.210

Danielle Boyce: And then at the... toward the end of the day, we're going to have a really great conversation with people living with ALS and their caregivers, who are going to give us, really, such insight and information about... from their perspective, as to what we need to be doing as a research community.

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06:41:46.210 --> 06:41:51.269

Danielle Boyce: Dr. Mehta, or Horton, do you have anything else you'd like to add before we adjourn?

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06:41:51.430 --> 06:41:59.520

Paul Mehta: No, no, thank you for a great day, and thank you for all the researchers, for all their findings and input. That'd be very, very helpful for everybody.

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06:42:01.690 --> 06:42:03.750

Danielle Boyce: Thank you, hope to see you tomorrow at 10.

1863

06:42:03.820 --> 06:42:05.170

Xing Song: See you tomorrow. Bye.

1864

06:42:05.170 --> 06:42:05.900

Danielle Boyce: Bye.