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Welcome to Day 2 - Danielle Boyce

1

00:01:58.450 --> 00:02:03.379

Danielle Boyce: Welcome, everyone. We'll be getting started in about 1 minute.

2

00:02:09.070 --> 00:02:18.950

Danielle Boyce: If you are using eye gaze technology today, we will be taking question and answer in the Q&A box.

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00:02:19.130 --> 00:02:29.010

Danielle Boyce: And so, we have tested it with folks who use eye gaze, but if you would like to just drop something in the Q&A to test it, I can confirm if I saw it or not.

4

00:02:35.690 --> 00:02:42.869

Danielle Boyce: So that, on my screen, I'm seeing more, and then, Q&A. So you want to click that.

5

00:02:47.380 --> 00:02:50.690

Danielle Boyce: If you want to try it out. But it seemed to work fine.

6

00:02:51.510 --> 00:02:52.560

Danielle Boyce: Yesterday.

7

00:03:01.670 --> 00:03:02.850

Danielle Boyce: Okay.

8

00:03:04.450 --> 00:03:09.000

Danielle Boyce: Let's give it just one more minute for a few more participants to come in.

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00:03:13.540 --> 00:03:15.560

Danielle Boyce: Thank you to all the participants.

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00:03:16.730 --> 00:03:18.660

Danielle Boyce: And presenters today?

11

00:03:22.190 --> 00:03:24.870

Danielle Boyce: I'll give it to 10.01.

12

00:03:28.180 --> 00:03:31.549

Danielle Boyce: Testing, so I did receive... I'm going to...

13

00:03:33.460 --> 00:03:36.240

Danielle Boyce: Robert, I received your message.

14

00:03:41.860 --> 00:03:44.189

Danielle Boyce: And Randy, we do see your question.

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00:03:45.260 --> 00:03:47.590

Danielle Boyce: And someone will answer it.

16

00:03:48.070 --> 00:03:48.840

Danielle Boyce: Soon.

17

00:03:52.550 --> 00:03:53.680

Danielle Boyce: Okay.

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00:03:57.820 --> 00:03:59.140

Danielle Boyce: Welcome!

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00:03:59.300 --> 00:04:01.430

Danielle Boyce: Good morning, and welcome to Day 2.

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00:04:02.120 --> 00:04:07.169

Danielle Boyce: The 2026 National ALS Registry Annual Research Symposium.

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00:04:07.600 --> 00:04:12.099

Danielle Boyce: If you're new here, or if this is your first day, an extra warm welcome to you.

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00:04:12.450 --> 00:04:17.760

Danielle Boyce: And I'd like to give a brief summary of my personal reflections on day one.

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00:04:17.820 --> 00:04:35.429

Danielle Boyce: And then I'm going to talk about what we plan to share today in our presentations today. So, in case you're wondering who I am, I'm Danielle Boyce, I'm the Director of Data Science and Biomedical Informatics at ALS Therapy Development Institute.

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00:04:35.490 --> 00:04:47.380

Danielle Boyce: And I also teach at the Johns Hopkins University School of Medicine in the Biomedical Informatics and Data Science section. So, big data and electronic health records data, that's my area of specialty.

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00:04:47.460 --> 00:04:56.540

Danielle Boyce: So everything I'm going to share here comes from my own biased and specific view as a data scientist, so I welcome our panelists and other presenters.

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00:04:57.150 --> 00:05:15.009

Danielle Boyce: to weigh in and share any reflections as well. But there will be a transcript, that is released at the end of this meeting, and some select slides, Dr. Mehta slides, anything from the registry team, those slides will be shared, and select slides from our presenters, that they're able to share, you know.

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00:05:15.010 --> 00:05:18.640

Danielle Boyce: Proprietary, information that they're able to share as well.

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00:05:18.870 --> 00:05:24.839

Danielle Boyce: So, this is just kind of setting the stage for what... where we've been and where we're going. And so.

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00:05:24.850 --> 00:05:39.380

Danielle Boyce: You know, whenever I attend a scientific meeting on a topic I know really well, because I am deeply committed to working with the impacted communities, so the people who actually have the disease and their caregivers, I'm always asking myself.

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00:05:39.730 --> 00:05:43.949

Danielle Boyce: Are we addressing gaps identified by the community?

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00:05:44.760 --> 00:05:48.179

Danielle Boyce: Is what we're doing important and relevant to the community?

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00:05:48.330 --> 00:06:01.350

Danielle Boyce: These are the questions I'm often asked when I'm asked to review grants, too, like for the Patient-Centered Outcomes Research Institute, PCORI. These are the questions that we ask. Are we identifying a gap, or are we just doing something for the sake of doing it?

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00:06:01.610 --> 00:06:15.289

Danielle Boyce: And so I can tell you, after watching the talks yesterday, from my perspective, yes, many of the things I saw yesterday address gaps I know personally, because these are the things the community brings to me on a regular basis.

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00:06:16.800 --> 00:06:20.429

Danielle Boyce: So, one discussion that jumped out to me directly

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00:06:20.530 --> 00:06:24.279

Danielle Boyce: Was what the community wants, that they want,

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00:06:24.280 --> 00:06:48.050

Danielle Boyce: studies on sex-based differences. So, her ALS story, for example, was highlighted as a group that would be interested in Dr. Murdoch's work, potentially. And of course, if they're here, I'll let them speak for themselves, but that was something that a lot of young women with ALS are interested in learning more about, and that was highlighted yesterday. I also saw a lot of innovative approaches to data science, AI, big data.

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00:06:48.050 --> 00:07:03.199

Danielle Boyce: from Dr. Song, and using these computable phenotypes and approaches we could not have attempted before. And so I get asked about AI a lot from the community, and how we're using it, and so I was really heartened to see that. That was really promising to me as well.

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00:07:03.290 --> 00:07:22.110

Danielle Boyce: Another theme that stood out is the heterogeneity of the disease, and how that really translates to clinical care research from our partners' discussions. We learned all the different approaches that you sometimes have to take to meet people where they are for enrollment, for recruitment and retention.

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00:07:22.320 --> 00:07:34.729

Danielle Boyce: And we also heard a bit about the connections between neurodegenerative diseases, and we're gonna talk about that some more, today also. And finally, what was very heartening to me

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00:07:34.990 --> 00:07:43.679

Danielle Boyce: Personally, was really the open science, the sharing, the desire for everyone within this ecosystem.

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00:07:43.680 --> 00:07:59.500

Danielle Boyce: the registry, and all the scientists coming together to collaborate. So, Dr. Vieira, my colleague, talked about the collaboration between ANSWER ALS, ALS TDI, and Critical Path Institute, and making our OMOP Common Data Model work.

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00:07:59.500 --> 00:08:16.390

Danielle Boyce: But we also heard lots about collaborations with the National ALS Registry, Dr. Ostro's data core, and all of those collaborations, I think there's a great deal of material that can be shared, and that's a value that's kind of incidental to why we're here.

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00:08:16.390 --> 00:08:41.310

Danielle Boyce: But when Dr. Weiskopf gave me a really good tip on how to do something that I've been struggling with, you could really see the value of having these kinds of convenings. And so, I just wanted to highlight that. So that is a value that goes beyond any of us as individual researchers. But then we also saw patient advocates in the audience, and Pat Dolan, who said, use us. If there's something that you need as a researcher.

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00:08:41.309 --> 00:08:48.640

Danielle Boyce: please use us. And after many years of working with Pat, I can tell you that that offer is sincere, and it's also effective.

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00:08:48.670 --> 00:08:55.539

Danielle Boyce: So if there's something that researchers are finding challenging, that is how we activate our entire ecosystem, and so that's why

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00:08:55.540 --> 00:09:13.239

Danielle Boyce: It's very important for the folks in the audience to really understand what we're talking about, and use that Q&A not just to ask scientific questions, but to ask us to define terms that we're using. And that's how we're all going to be able to move forward and collaborate together, because we all need to be on the same page here.

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00:09:13.330 --> 00:09:32.640

Danielle Boyce: So, the bottom line for me was, that, that, what I saw was collaboration, teamwork, and focus on the topics that are not only important to scientists, but are important to the community. And so today, we are going to be talking, about... more about these very complex methods.

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00:09:32.640 --> 00:09:47.440

Danielle Boyce: That are being applied to understand, ALS risk factors. And so Dr. Esquireo from Harvard will talk about serological profiling. Here we go. Serological profiling of the human virome and ALS risk in military population.

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00:09:47.720 --> 00:09:57.999

Danielle Boyce: And... and then we're going to hear from Dr. Petty, forgive me if I'm pronouncing that wrong, linking long-term air pollution exposure with ALS survival and disease progression.

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00:09:58.310 --> 00:10:08.900

Danielle Boyce: Then, further talking about air pollution and risk factors. So we hear this a lot in the community. How... what are our environmental exposures, and what might they have to do

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00:10:08.900 --> 00:10:22.789

Danielle Boyce: with our ALS risk, and so we're going to be hearing, about that from Karolinska Institute. And then, Dr. Stommel and, Kevin Cornell are going to be talking about environmental toxicants in veteran CNS tissue.

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00:10:22.890 --> 00:10:37.959

Danielle Boyce: and spatial multiomics to reveal focal pathologies in ALS post-mortem cortical tissue. So that's a lot of words, so if you don't understand what that means, then please put in the Q&A. That is an appropriate question to ask also. But you will be hearing more about these.

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00:10:37.960 --> 00:10:44.929

Danielle Boyce: In, in the, in the, in the coming talk. So I just want to really make sure that you, you are encouraged to use that Q&A.

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00:10:45.180 --> 00:10:49.049

Danielle Boyce: And then we'll have a break and lunch.

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00:10:50.190 --> 00:10:53.139

Danielle Boyce: And then... Let's see, do we have a slide?

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00:10:54.550 --> 00:10:57.490

Danielle Boyce: For after lunch, There we go.

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00:10:58.100 --> 00:11:11.210

Danielle Boyce: So, so then we're going to hear from Rejma Punjani and, Patty Stanko. So, you might remember Patty from yesterday, where she talked about what the ALS Association is doing to partner with the registry to help folks get enrolled.

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00:11:11.210 --> 00:11:20.569

Danielle Boyce: I thought this was, this is a really important topic, because this is an issue that we face not only in the ALS research ecosystem, but across all diseases.

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00:11:20.570 --> 00:11:27.609

Danielle Boyce: What can we do to incentivize, to encourage people, to thank them for participating in our studies?

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00:11:27.610 --> 00:11:44.140

Danielle Boyce: And we all grapple with this, but we don't know how effective it is to put on these kinds of incentive programs. And this also ties in to me with Dr. Gautman's really brilliant presentation. So many interesting points that he brought out yesterday.

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00:11:44.140 --> 00:12:09.059

Danielle Boyce: But one was about all of the innovative approaches that his team is taking to recruit and retain their study participants, and keep them informed, and collaborate, and generate hypotheses, and learn from the people with lived experience. So, I think we're going to kind of see an application in real life as it applies to the registry today with Patty and Reshma. So, I'm really looking forward to that.

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00:12:09.340 --> 00:12:11.320

Danielle Boyce: And then, last but not least.

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00:12:11.770 --> 00:12:17.199

Danielle Boyce: I want to highlight that today at 2 Eastern, we'll be talking with 3 people.

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00:12:17.200 --> 00:12:39.620

Danielle Boyce: to caregivers of people with ALS, and then Dr. Stacey Farber, who has ALS, and they have a lot to share and a lot to teach us, about the other side, what it's like to be on the other side of this. We're all doing the research. What is it like to actually engage with this, not just clinical ecosystem, but the research ecosystem?

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00:12:39.800 --> 00:12:45.999

Danielle Boyce: what is it like to try to navigate all of this? How are we doing from their perspective?

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00:12:46.240 --> 00:12:55.539

Danielle Boyce: Going to clinic, navigating the word salad of acronyms of all the organizations, right? I did give them some prompts, but I did not censor them at all.

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00:12:55.920 --> 00:13:10.520

Danielle Boyce: So what they are going to say is the unvarnished truth from their perspective, and I encourage everyone, even though it's a long day, and you might be here

for the science part, this is the science, because this is going to help us to do a better job, so please stay.

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00:13:10.520 --> 00:13:18.989

Danielle Boyce: for the patient and caregiver talks. It's really going to be absolutely brilliant, and I, and I really can't wait to hear what we learn.

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00:13:20.130 --> 00:13:36.390

Danielle Boyce: And then we'll have some Q&A. If there's anything we miss, if you ask questions when you registered, and you feel like they were not answered, if you asked questions yesterday, and you thought you got a good answer, but maybe now you want to follow up, please put it in the Q&A.

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00:13:36.960 --> 00:13:43.839

Danielle Boyce: And we will... we will make sure that those questions get answered, and then we're gonna have a wrap-up and adjourn.

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00:13:48.420 --> 00:13:55.799

Danielle Boyce: Okay, so some housekeeping. Attendees are going to be in listen-only mode without audio or video capabilities.

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00:13:56.320 --> 00:14:00.500

Danielle Boyce: If attendees have questions, please insert them in the Q&A box.

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00:14:00.610 --> 00:14:03.019

Danielle Boyce: And if you are not sure how to do that.

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00:14:03.300 --> 00:14:16.309

Danielle Boyce: There's an email, also at cdc.gov, if you're having technical problems. One thing I noticed yesterday, and I think at least one of our panelists had this issue too, this is a somewhat new version of Zoom for me.

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00:14:16.450 --> 00:14:31.379

Danielle Boyce: So, up at the top, there is a webinar tab, and and who is sharing their screen. So, Summer right now is sharing her screen. So, if you have that, if that's what

you're seeing, and you can't see the slides, go to the tab where it says who's sharing their screen.

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00:14:31.500 --> 00:14:42.209

Danielle Boyce: And then that's where you can see the slides. So, usually in the version I use, just everything pops up all in one window, but some of us aren't seeing that today. So, if you're having problems.

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00:14:42.250 --> 00:14:52.320

Danielle Boyce: If you're having technical difficulties with your eye gaze, trying to send messages, or any other issue like that, and you can't access an email, email als at cdc.gov.

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00:14:52.600 --> 00:15:00.719

Danielle Boyce: Panelists are asked to please mute themselves when they are not presenting. That was not a problem yesterday, but we welcome your feedback during Q&A at any time.

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00:15:00.810 --> 00:15:14.229

Danielle Boyce: And the meeting is recorded to aid with the transcription, but will not be distributed. So, there will be a thorough summary of everything that happened, as well as the CDC staff slides will be made available.

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00:15:15.010 --> 00:15:19.799

Danielle Boyce: And the, and select participants of...

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00:15:19.910 --> 00:15:35.200

Danielle Boyce: presenters will offer versions of their slides. Sometimes their slides are not, like, the final science, so they're reluctant to share things that they haven't fully vetted, but they're wanting to share with this community so they can get our feedback, but they might not be ready to share

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00:15:35.360 --> 00:15:46.339

Danielle Boyce: openly, publicly. If that's the case, then we'll see if they can give us kind of an edited version of their slides, or summary, or some way of you to kind of take away what they talked about today.

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00:15:47.140 --> 00:15:48.100

Danielle Boyce: Okay?

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00:15:50.640 --> 00:15:55.109

Danielle Boyce: So, let me check. So, I work with the ALS community.

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00:15:55.410 --> 00:15:59.049

Danielle Boyce: So, that means I checked the chat.

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00:15:59.220 --> 00:16:04.590

Danielle Boyce: Because people talk in the chat, and so I'm gonna check the chat periodically.

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00:16:05.050 --> 00:16:07.499

Danielle Boyce: Here, looks... looks good.

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00:16:08.530 --> 00:16:11.500

Danielle Boyce: Let's see... oop, I don't want to share.

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00:16:12.460 --> 00:16:16.080

Danielle Boyce: And let me check the Q&A, we don't have anything open right now.

National ALS Registry Funded Research Presentations

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00:16:17.190 --> 00:16:24.869

Danielle Boyce: Well... Now we're going to start the presentations from the ALS Registry, grantees.

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00:16:27.240 --> 00:16:46.369

Danielle Boyce: And this is a treat. They're all a treat, but big treat for me. I'm, like, a fan in the audience the last few days. It's been really incredible as a researcher to be a part of this. So, we are going to be hearing from, as I mentioned, Dr. Alberto Ascherio from Harvard University.

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00:16:46.490 --> 00:16:54.290

Danielle Boyce: And his talk, as you can see, is Serological Profiling of the Human Virome and ALS Risk in a Military Population.

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00:16:55.080 --> 00:17:14.069

Danielle Boyce: So, Dr. Ascherio graduated in medicine at University of Milan in 1978 and practiced medicine and public health in Latin America and Africa for several years before moving to Boston, USA, where he became a professor of epidemiology and nutrition at the Harvard T. H. Chan School of Public Health.

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00:17:14.069 --> 00:17:17.340

Danielle Boyce: and Professor of Medicine at Harvard Medical School.

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00:17:17.339 --> 00:17:40.910

Danielle Boyce: He was awarded honorary doctoral degrees from the University of Southern Denmark and the University of Bergen, delivered the Falk Lecture in 2023, and received a 2025 Breakthrough Prize in Life Sciences for discovering that the Epstein-Barr virus causes multiple sclerosis. So when we were talking yesterday about what do these diseases have in common, and is anybody studying more than one disease.

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00:17:41.020 --> 00:17:47.679

Danielle Boyce: this is exactly what you're talking about. So, Dr. Ascherio, thank you so much, and I will... I will turn it over to you.

Serological profiling of the human virome and ALS risk in a military population

Harvard University - Alberto Ascherio, MD, DrPH

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00:17:49.010 --> 00:17:55.840

Alberto Ascherio: Thank you, Daniela, and good morning, everyone. Am I controlling my own slides from here, or...

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00:17:56.720 --> 00:17:57.550

Alberto Ascherio: I'll be...

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00:17:57.550 --> 00:18:02.440

Samer Khan (she/her): screen sharing for you, so if you can let me know when to advance, that would be great.

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00:18:02.660 --> 00:18:05.510

Alberto Ascherio: So I should screen... share my screen?

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00:18:05.570 --> 00:18:08.000

Samer Khan (she/her): I am screen sharing your slides.

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00:18:08.370 --> 00:18:09.730

Samer Khan (she/her): Are you seeing it?

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00:18:09.980 --> 00:18:14.480

Alberto Ascherio: Yeah, yeah, yeah, I'm seeing So I have to ask you when I need to move forward.

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00:18:14.480 --> 00:18:17.070

Samer Khan (she/her): If you could say next, that would be great.

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00:18:17.070 --> 00:18:18.310

Alberto Ascherio: Oh, okay.

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00:18:18.310 --> 00:18:19.020

Samer Khan (she/her): Thank you.

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00:18:19.020 --> 00:18:22.220

Alberto Ascherio: Well, good morning. Next...

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00:18:25.070 --> 00:18:43.270

Alberto Ascherio: So the topic is viral infection and ALAs, and why we thought that viral infection can be related to ALAs, in part because of the biology. One way in which cells protect themselves from viral infection is by displacing

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00:18:43.270 --> 00:19:06.450

Alberto Ascherio: TDP43 from the nuclear to the cytoplasm and causing the TDP43 aggregation. It's a defensive mechanism that shuts down the protein synthesis in case of a viral infection, so preventing the replication of the virus. And as you know, TDP43 displacement and aggregation are, you know, characteristic features of most

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00:19:06.450 --> 00:19:25.450

Alberto Ascherio: cases of ALAs. So we thought that not that the viral infection doesn't need to be a directed only cause of ALAs, but perhaps could contribute to trigger or accelerate a process that is important to the development of the pathology.

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00:19:25.740 --> 00:19:45.480

Alberto Ascherio: Now, previous studies have been relying on biological samples collected before the diagnosis that are open to many bias, and we cannot really rely on the clinical history, because many infections, even with neurotropic viruses, cause only mild symptoms or are asymptomatic.

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00:19:45.650 --> 00:19:46.730

Alberto Ascherio: Next.

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00:19:48.500 --> 00:20:05.589

Alberto Ascherio: So we conducted... to address this question, we are conducting a longitudinal study relying on repeated blood samples from a large population of healthy men and women who were followed for a long time until some of them developed ALAs.

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00:20:05.590 --> 00:20:23.740

Alberto Ascherio: This was made possible by the Department of Defense Serum Repository that archived over 80 million serum samples collected from over 11 million active duty members in the U.S. military.

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00:20:24.550 --> 00:20:35.150

Alberto Ascherio: This allows a rigorous and unbiased assessment of the possible relationship between past infection and ELS risk. Next.

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00:20:37.750 --> 00:20:49.409

Alberto Ascherio: So, there are some viruses that seem more likely than others, you know, to be related to the ELA's process. Particularly, we were focusing on enteroviruses.

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00:20:49.420 --> 00:21:06.949

Alberto Ascherio: which are known to cause acute flaccid myelitis, and neurotropic herpes viruses, you know, are potential causes of encephalitis. We use the serum level of neurofilament-like chain as a marker of neurodegeneration.

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00:21:06.950 --> 00:21:12.100

Alberto Ascherio: And we also plan... we are also planning to conduct a broad exploratory investigation

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00:21:12.100 --> 00:21:16.149

Alberto Ascherio: Of the immune response to all viral infections.

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00:21:16.620 --> 00:21:17.630

Alberto Ascherio: Next.

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00:21:19.640 --> 00:21:32.119

Alberto Ascherio: So, the military population, active duty military population, is composed mostly of young men and women. As you can see, the group under the age of 26 is the largest group here. So...

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00:21:32.640 --> 00:21:45.319

Alberto Ascherio: We are really looking at a population that is somewhat skewed, and mostly looking at early age at onset of ALS. Next.

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00:21:48.380 --> 00:22:07.400

Alberto Ascherio: So, in addition to the Department of Defense Zero Repository, through collaboration with military investigators, we've been accessing selected variables that I will show in a moment from the wealth of information collected by the Defense Medical Surveillance System. Next.

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00:22:10.220 --> 00:22:33.600

Alberto Ascherio: We had to find the balance between the scientific need of learning and research, and the protection of privacy. So the list of variables here is a best effort to

respect the privacy, but to get information important for ALA's research, and this was approved

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00:22:33.760 --> 00:22:41.960

Alberto Ascherio: Of course, by the relevant, Institutional Review Board and, Human Subjects, Committee.

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00:22:42.290 --> 00:22:52.690

Alberto Ascherio: So the reason that we don't have more details on the medical history and on deployment and other exposure is,

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00:22:53.090 --> 00:22:57.489

Alberto Ascherio: Basically, only to protect individual privacy. Next.

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00:23:01.990 --> 00:23:19.029

Alberto Ascherio: So the work started several years ago. It is a rather complex project because it requires a collaboration between multiple institutions. Our primary collaborators in this research are the

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00:23:19.030 --> 00:23:24.430

Alberto Ascherio: It uses the Uniform Service University for the Health Sciences.

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00:23:24.440 --> 00:23:35.820

Alberto Ascherio: And we needed the collaboration from the Physical Disability Agency of the Army, the Navy, and the Air Force. And through this Physical Disability Agency.

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00:23:35.820 --> 00:23:49.459

Alberto Ascherio: We obtained the medical record of individuals who were diagnosed with ALS. There is a specific code within the military that is called VA SRD code 8017.

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00:23:49.460 --> 00:24:07.810

Alberto Ascherio: And we review, you know, we had to travel to Washington because this medical record cannot leave the military facilities and review the medical record to make sure that the cases that were given to us met the research diagnostic criteria.

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00:24:07.810 --> 00:24:11.060

Alberto Ascherio: And confirmed cases were included in the study.

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00:24:11.970 --> 00:24:13.100

Alberto Ascherio: Next.

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00:24:15.650 --> 00:24:35.199

Alberto Ascherio: So where do we stand with the project? Well, the project, you know, started right in time around the COVID, just before the COVID pandemic. That created multiple difficulties and a longer time than expected to execute the agreement with the Meese Military Disability Agency.

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00:24:35.200 --> 00:24:48.020

Alberto Ascherio: So we concluded with the Army in 2022, with the Air Force in 2023, and unfortunately, the Navy, that was expected to contribute 40% of the LS

137

00:24:48.330 --> 00:25:02.079

Alberto Ascherio: cases drop out of the study because of internal logistic personal issues. So we obtained a total of 99 electronic medical records that we review, and of this next

138

00:25:06.260 --> 00:25:25.809

Alberto Ascherio: These 68 were confirmed to be genuine ALS cases meeting research criteria for inclusion in the study. You can see the exclusion there. So this was lower than what we expected at the beginning of the study. We have

139

00:25:25.870 --> 00:25:36.290

Alberto Ascherio: We had projected about 150 cases, and most of the loss is due to the missing participation from the Navy. Next.

140

00:25:39.540 --> 00:25:51.960

Alberto Ascherio: So this is the distribution by race, ethnicity. On the left of the 68 cases. 83% were men, reflecting the

141

00:25:52.030 --> 00:26:10.610

Alberto Ascherio: two factors. One, that ALS is more common in men than in women, and most importantly, that the military population is enriched with men, and the number... the proportion of women is still relatively low. So the design of the study is,

142

00:26:10.610 --> 00:26:22.299

Alberto Ascherio: It's quite straightforward, so we use what is called the risk site sampling. So for each case of ALAs, and you see an example in the diagram on the right, the red dot.

143

00:26:22.340 --> 00:26:30.030

Alberto Ascherio: We look at all the individuals who were at risk of developing ALS at that point in time, so the black line there.

144

00:26:31.210 --> 00:26:39.990

Alberto Ascherio: And then we match individuals of the same age, sex, and race ethnicity, and branch of the military.

145

00:26:40.170 --> 00:26:48.590

Alberto Ascherio: In addition, who had blood samples collected at about the same time as the ALS case, as you see.

146

00:26:48.960 --> 00:27:13.260

Alberto Ascherio: So this study design basically reproduced the results that we would get by conducting a full longitudinal study and looking at the blood sample of the entire population. And of course, you cannot look at blood samples of... analyze blood samples of 11 million people, but except for the random variation, due to the smaller sample size, the result is expected to be identical.

147

00:27:13.280 --> 00:27:15.570

Alberto Ascherio: To date of a full cohort study.

148

00:27:16.720 --> 00:27:17.790

Alberto Ascherio: Next.

149

00:27:19.810 --> 00:27:31.399

Alberto Ascherio: This is just showing that the age distribution compared to the general population, the military population is much younger, which is playing... next slide.

150

00:27:33.390 --> 00:27:50.869

Alberto Ascherio: explain that we are looking, in a very unusual population in terms of, age at onset, so the median... the mean age at onset was, 39, 39 years, with a range between 22 and 60.

151

00:27:52.000 --> 00:27:53.080

Alberto Ascherio: Next.

152

00:27:55.070 --> 00:28:04.830

Alberto Ascherio: Now, the blood sample, as you've seen in the previous diagram, we have three blood samples collected before the onset of ALAs.

153

00:28:04.990 --> 00:28:11.500

Alberto Ascherio: And the first blood sample dates back 11 years before the ALA's onset.

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00:28:12.970 --> 00:28:20.110

Alberto Ascherio: No, it's interesting, because until recently, in fact, talking about a month, or literally, you know, the...

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00:28:20.960 --> 00:28:34.930

Alberto Ascherio: there was not much evidence of a prodromal phase of ALS standing more than 5, perhaps 6 years before the onset of symptoms, based on the result of NFL elevation.

156

00:28:34.930 --> 00:28:46.140

Alberto Ascherio: But for those of you who have followed the recent literature, there is... there are papers now, based on large cohort, like APIC, the European Cancer Cohort.

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00:28:46.140 --> 00:28:54.750

Alberto Ascherio: detecting signals even up to 26 years before the onset of symptoms. So by this study, we will be able to

158

00:28:54.750 --> 00:29:14.819

Alberto Ascherio: to go back in time and explore a period that until now has been rather silent, has not been really interrogated, and see whether it is possible that there are biomarkers predicting the future risk of ALAs, even going back as long as 10 and more years before.

159

00:29:15.900 --> 00:29:17.110

Alberto Ascherio: Next stop.

160

00:29:24.330 --> 00:29:38.769

Alberto Ascherio: So, because of the delay that I've mentioned, we are still, you know, in an early phase of the data analysis. This, we have obtained, and Dr. Vjornovich, who probably is in the audience, is,

161

00:29:38.830 --> 00:29:51.869

Alberto Ascherio: is leading this analysis. This is just showing on the left the expected deviation of NFL in serum in ALS cases compared to control.

162

00:29:52.300 --> 00:30:11.260

Alberto Ascherio: On top, you have the actual NFL, and on the bo... in cases and control, in the bottom, you have the ratio between cases and measured control. As in previous study, you see a sharp elevation, and about... starting about 4 or 5 years before. On the left is a...

163

00:30:11.260 --> 00:30:17.990

Alberto Ascherio: Say, negative control, We show that there is no similar elevation in glial febrile

164

00:30:18.690 --> 00:30:25.179

Alberto Ascherio: protein, which is not being found to be consistent marker in ALS.

165

00:30:26.220 --> 00:30:27.250

Alberto Ascherio: Next.

166

00:30:30.440 --> 00:30:44.130

Alberto Ascherio: So, conserving the viral infection, the original plan was to adopt a technology that is called VirusCan, that is based on the expression of linear peptide covering all the

167

00:30:44.130 --> 00:30:52.439

Alberto Ascherio: you know, all the proteins, all the genomes, of, of known human viruses. And,

168

00:30:52.950 --> 00:31:01.740

Alberto Ascherio: for... for logistic reason, this test cannot be done. It was phased out in the laboratory with which we

169

00:31:01.850 --> 00:31:04.370

Alberto Ascherio: We're collaborating next.

170

00:31:05.860 --> 00:31:07.310

Alberto Ascherio: Next.

171

00:31:08.470 --> 00:31:26.740

Alberto Ascherio: So we have replaced the virus scan, actually, with a NSA that is, in many ways, even better, because instead of looking at linear peptide, we are looking at fully, you know, full-length protein.

172

00:31:26.840 --> 00:31:30.960

Alberto Ascherio: So these, slides that are courtesy of the...

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00:31:31.020 --> 00:31:43.490

Alberto Ascherio: Arizona State University that has a patent, and the unique provider of this... of this assay, show the technique. Basically, the

174

00:31:43.490 --> 00:32:02.860

Alberto Ascherio: it replaced the synthesis of protein and the creation of protein array with using DNA and fixing the DNA in this array, and then expressing the protein in a cell-free medium directly on the plate in situ.

175

00:32:02.860 --> 00:32:03.980

Alberto Ascherio: Next slide.

176

00:32:06.210 --> 00:32:22.089

Alberto Ascherio: So the end result is that the, as you see on the left, the protein is synthesized and is bind by an antibody that is fixed at the bottom of the wells, and dispose of the antigenic determinant

177

00:32:22.090 --> 00:32:33.189

Alberto Ascherio: to the serum of the patient, or the individual being analyzed, that is, then it's added at the top. And then the presence of the protein is detected with...

178

00:32:33.500 --> 00:32:38.970

Alberto Ascherio: with secondary antibodies, as you see in the right side. Next.

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00:32:41.670 --> 00:32:48.060

Alberto Ascherio: These are the viral species that have been included in the array. It's,

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00:32:48.060 --> 00:33:06.309

Alberto Ascherio: covering pretty much all the known human viruses, including several variants of enteroviruses, and you can see on the left the list of Kosaki's, for example, a long list of Kosaki viruses. Next.

181

00:33:09.430 --> 00:33:23.170

Alberto Ascherio: So what I have for now is some quality control and the... and results on the... not... not yet on the specific viruses related to

182

00:33:23.170 --> 00:33:41.989

Alberto Ascherio: to ALAs, but an overall look on the performance of the array. So we had a total of 527 samples that were profiled against an array of 1,889 viral, mostly viral, and a few human genes, including controls.

183

00:33:43.380 --> 00:33:58.780

Alberto Ascherio: the data are normalized. Next, I think I have an example next, I can show you. So the raw intensity that measures the binding of the antibodies to the well is normalized, and

184

00:33:58.950 --> 00:34:08.929

Alberto Ascherio: hits are considered positive. There is more than two-fold higher, signal, than, than expected next.

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00:34:11.850 --> 00:34:25.819

Alberto Ascherio: This is just the quality control run by the lab itself, showing the correlation between different runs. As you see, in most cases, we are in the 0.9, or certainly over 0.8 range.

186

00:34:26.030 --> 00:34:27.090

Alberto Ascherio: Next

187

00:34:29.000 --> 00:34:47.269

Alberto Ascherio: This is just an example of what an array looks like. So the positive responses are those in green, and that are measured quantitatively. The negative response is just the dark blue, and positive and negative controls are included in each plate. Next.

188

00:34:49.280 --> 00:35:10.249

Alberto Ascherio: These are our own blind controls, so we're a bit of sexy when we send the samples to any lab. We never reveal the case control status, and we never identify which samples are from the same subject. So the lab analyzed the samples in random order without knowing which is which.

189

00:35:10.250 --> 00:35:34.529

Alberto Ascherio: And we have a repeated sample, so the same sample in duplicate or triplicate hidden among the study sample to be able to measure the coefficient of variation. So this gives us, you know, unquestionable evidence on the, you know, on the accuracy of the, of this, that, as you see here, is pretty good with,

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00:35:34.590 --> 00:35:42.239

Alberto Ascherio: 88% with CV below 20, and 78% below 50. Next.

191

00:35:44.140 --> 00:35:56.640

Alberto Ascherio: This is just an example of raw values. Each column is one individual sample, and you see the response to different viral protein. Next.

192

00:35:59.540 --> 00:36:23.939

Alberto Ascherio: And when this is not... when this is normalized, you can see that most values will fall between, you know, below 2, between 0 and 2, and they... we have highlighted here as an example, values above 2 that are considered hit. It means this is normalized to all the protein responses in the same individual. So this means, for example, if you look individual

193

00:36:23.940 --> 00:36:35.289

Alberto Ascherio: 1, you see a 3.9 there for the human error plus viruses 1 protein. That means that that response is 3.9,

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00:36:35.290 --> 00:36:44.719

Alberto Ascherio: You know, standard deviation above the average response of this individual to all the other human proteins, viral proteins.

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00:36:45.190 --> 00:36:46.110

Alberto Ascherio: Next...

196

00:36:47.880 --> 00:36:59.950

Alberto Ascherio: And this is, you know, defined as above. This is the number of hits in each sample. This is just to show that there is diversity. Of course, there are individuals that

197

00:36:59.950 --> 00:37:10.789

Alberto Ascherio: have evidence, you know, of strong immune responses against several proteins we've marked between persons variation. Next.

198

00:37:13.080 --> 00:37:26.829

Alberto Ascherio: So the data were literally received one week ago, so I wouldn't... wasn't able to... to analyze the data in terms of the specific viral infection related to risk of ALAs.

199

00:37:26.860 --> 00:37:43.040

Alberto Ascherio: Now, we have... I want to focus on another aspect in the last few minutes. So, as I mentioned, we have a lower than expected sample size and a younger age at onset of ALAs. Next.

200

00:37:46.530 --> 00:38:02.189

Alberto Ascherio: So, over the past 3 years, and, you know, Paul, Mate, and others know how hard we've worked on this. We've been trying to extend our study to cases diagnosed after discharge from military service. Next.

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00:38:03.520 --> 00:38:12.359

Alberto Ascherio: So I am really excited to announce that very recently, we were finally able to, you know, to...

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00:38:12.360 --> 00:38:27.560

Alberto Ascherio: to achieve this goal. It took, really, 3 years of hard work, and... but now, through a collaboration with Dr. Fournier at Hemory University, we were able to identify

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00:38:27.560 --> 00:38:44.900

Alberto Ascherio: all the individuals who died, all the veterans who died with a diagnosis of ALS, and left military service after 92, and were diagnosed up to December 31, 2025.

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00:38:44.900 --> 00:38:51.630

Alberto Ascherio: So we identified 780 veterans that, have a lace according to

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00:38:52.270 --> 00:39:05.499

Alberto Ascherio: well-established criteria, and I have to thank our colleague, Dr. Mark Weiskov, that you heard yesterday for sharing his algorithm for identifying ALS cases within the VA.

206

00:39:05.620 --> 00:39:15.049

Alberto Ascherio: And we were able... the VA has transmitted the list of the cases to the Department of Defense, and the Department of Defense

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00:39:15.190 --> 00:39:30.780

Alberto Ascherio: has agreed to pull the serum of these 780 veterans, match them to controls, and provide adequate of up to 4 serum samples for research. So this is huge. Next slide.

208

00:39:32.870 --> 00:39:44.430

Alberto Ascherio: it will require more time and funding than the current grant, but, you know, I cannot overstate our level of excitement.

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00:39:45.030 --> 00:39:46.430

Alberto Ascherio: for this project.

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00:39:47.260 --> 00:39:48.360

Alberto Ascherio: Next.

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00:39:50.350 --> 00:40:08.300

Alberto Ascherio: So, not in this slide, but first of all, I need to acknowledge and really thank the Physical Disability Agency of the Army and the Air Force, who made this study possible, and all the director and personnel of the Department of Defense Serum Repository.

212

00:40:08.740 --> 00:40:29.860

Alberto Ascherio: Listed here are only our direct scientific collaborator at Uzus, Dr. Mancuso Niebuhr, and Lindsay Lewis, our collaborator at the Harrah School of Public Health, and the Mass General Yen School for NFL Measurement at Arizona State University.

213

00:40:29.860 --> 00:40:35.600

Alberto Ascherio: For... for NAPA. And for this VA extension, we're indebted to...

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00:40:35.610 --> 00:40:47.479

Alberto Ascherio: Christina Fournier, Amir Sati, Alex Braga, who worked with Mark Weiskov, and share his diagnostic algorithm, and Mark himself. Thank you for listening. Bye.

215

00:40:52.640 --> 00:41:05.559

Danielle Boyce: Thank you very much for that talk, and I'm waiting a moment for Q&A, but meanwhile, if you have questions and you don't think of them until later, we will be covering

216

00:41:05.640 --> 00:41:15.009

Danielle Boyce: your questions, after the rest of the talks, too. Paul, you turned your camera on. Did you have something you wanted to add?

217

00:41:18.600 --> 00:41:19.820

Danielle Boyce: We can't hear you.

218

00:41:24.050 --> 00:41:25.200

Danielle Boyce: No, we can't hear you yet.

219

00:41:25.200 --> 00:41:26.169

Paul Mehta: Can you hear me now?

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00:41:26.170 --> 00:41:27.870

Danielle Boyce: There we go, yep, we can hear you.

221

00:41:27.990 --> 00:41:36.440

Paul Mehta: Great talk, Alberto. Just a quick question. Do we know how long, if someone's diagnosed with ALS in the military as an active member.

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00:41:36.440 --> 00:41:49.500

Paul Mehta: How long before they would get discharged and get into the VA system. It's always been one of those things where... where Congress is kind of, like, asking us to look at, you know, VA... I mean, cases of active military, and... and the premise is it's kind of a...

223

00:41:49.800 --> 00:42:00.859

Paul Mehta: you know, one of those questions where if you're in the military and you're showing signs and symptoms of ALS, typically you're going to be referred to a specialist, or a neurologist, or a PCP first, referred to a neurologist.

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00:42:00.860 --> 00:42:20.449

Paul Mehta: And then from there, you could potentially get discharged. Do we know how long or how often that's common, as in terms of individuals who are active military, maybe with, you know, 15, 20 years in the military, they're getting signs and symptoms of ALS, they get, you know, referred. What's the typical time course regarding, you know, discharge and getting into the VA system? Do we know that?

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00:42:21.520 --> 00:42:45.469

Alberto Ascherio: Well, I don't have the right data, but being discharged is almost certainly very quick, because, you know, the disease itself qualifies for discharge. Then, whether or

not they decide to go to the VA, I understand that it's an individual decision. I think they are eligible, you know, I imagine they're immediately eligible, whether they would

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00:42:45.610 --> 00:42:49.609

Alberto Ascherio: Join the VA may depend on the individual situation.

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00:42:49.780 --> 00:42:50.390

Paul Mehta: Great, thank you.

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00:42:50.390 --> 00:42:55.170

Alberto Ascherio: I qualify, I'm not an expert, really, so I don't really know.

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00:42:55.170 --> 00:43:18.209

Paul Mehta: Yeah, it's a question that kind of comes up sometimes, you know, what's the number of cases in the military? Well, and the question is, it's kind of nuanced, because it's not really the military, it's those who are medically discharged from the military, and they go either way into the VA system or a private care to get their care at that time, so it's kind of like, you can't have ALS and be in the military as an active member. You're going to be discharged. So, thank you.

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00:43:22.350 --> 00:43:39.979

Danielle Boyce: And I could not agree more about how exciting it is to have a data find, like you're describing, and the excitement as a scientist to have these kinds of data available, so I'm watching anxiously with what you're able to do with this in the future.

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00:43:39.980 --> 00:43:50.460

Danielle Boyce: I think we do have some questions in the chat, but I think in the interest of time, maybe we'll move on to the next, and then we'll circle back and summarize all of the questions in a bit.

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00:43:52.890 --> 00:43:54.749

Danielle Boyce: Thank you so much, that was brilliant.

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00:43:55.520 --> 00:44:08.709

Danielle Boyce: Next, we have, Dr. Meredith Pedde from the University of Michigan. So, Meredith Petty is an Assistant Research Scientist in the Department of Epidemiology at the University of Michigan School of Public Health.

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00:44:08.890 --> 00:44:20.099

Danielle Boyce: She is an environmental epidemiologist who specializes in the health effects of air pollution, with a specific interest in neurodegenerative diseases such as ALS, Alzheimer's disease, and dementia.

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00:44:20.410 --> 00:44:31.260

Danielle Boyce: She also studies air pollution interventions, including her work assessing the student health and educational consequences of national clean school bus replacement programs.

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00:44:31.770 --> 00:44:35.600

Danielle Boyce: Thank you so much, Dr. Pedde. We turn it over to you.

Linking long-term air pollution exposure with ALS survival and disease progression

University of Michigan - Meredith Pedde, PhD, MPH, MPP

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00:44:36.660 --> 00:44:45.629

Meredith Pedde: Great, thank you so much. I'm very, grateful to get to be here this morning and share our work that we've done with funding from the CDC.

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00:44:45.730 --> 00:44:56.759

Meredith Pedde: So this morning, I'm going to present our work on the associations between air pollution, and disease progression, as well as in, survival in persons with ALS.

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00:44:59.640 --> 00:45:24.599

Meredith Pedde: So my group here at, University of Michigan, oh, I'm sorry, I'll make sure to say next slide, primarily studies the relationships between air pollution and health, as motivated by decades of research that showed that higher levels of air pollution are associated with a host of, adverse health effects. And these... these outcomes range from respiratory and cardiovascular effects, to even, increased

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00:45:24.600 --> 00:45:25.600

Meredith Pedde: mortality.

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00:45:26.100 --> 00:45:27.130

Meredith Pedde: Next slide.

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00:45:29.800 --> 00:45:40.359

Meredith Pedde: But in addition to the robust literature that has linked air pollution to adverse respiratory and cardiovascular health, there's also evidence that air pollution can impact brain health.

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00:45:40.840 --> 00:45:54.369

Meredith Pedde: And this isn't actually surprising, given that the same mechanisms by which we think that air pollution adversely impacts the respiratory and cardiovascular systems, those same mechanisms can also impact the brain.

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00:45:54.620 --> 00:46:03.049

Meredith Pedde: So, for example, particle inhalation can lead to oxidative stress and inflammation, which can indirectly affect the brain.

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00:46:03.090 --> 00:46:19.179

Meredith Pedde: But particles can also directly deposit in the brain through olfactory bulb transmission, which can again lead to adverse brain effects, including neuroinflammation, neuronal damage, and increased cortisol, which are all pathways that are associated with ALS.

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00:46:19.180 --> 00:46:27.350

Meredith Pedde: Those same pathways are also associated with other, neurological outcomes, such as mental health, Parkinson's disease, and dementia.

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00:46:27.880 --> 00:46:29.140

Meredith Pedde: Next slide, please.

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00:46:31.600 --> 00:46:48.369

Meredith Pedde: And so, given these potential mechanisms, as well as the existing literature that is linked air pollution to those other neurological outcomes, in our work, we wanted to know, how does air pollution from different sources relate to disease progression, as well as survival in persons with ALS?

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00:46:48.780 --> 00:47:04.849

Meredith Pedde: And so, we were especially motivated to look at these outcomes, given that most factors currently linked to longer ALS survival are largely unmodifiable. Things such as age, age at disease onset, segment of disease onset, and genetics.

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00:47:05.130 --> 00:47:18.949

Meredith Pedde: But environmental exposures, like air pollution, may be modifiable after an ALS diagnosis at the population level, through things like stronger air quality regulations, or at the personal level, through things like air purification.

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00:47:19.520 --> 00:47:28.129

Meredith Pedde: And so, the four broad categories of pollutants that we looked at are those from agriculture, energy production, and traffic.

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00:47:28.430 --> 00:47:46.730

Meredith Pedde: Our fourth was also... that we looked at were sea salt particles, which we're using as what's called a negative control, since there's no reason that we would expect that sea salt would be associated with ALS progression or survival. So the idea of a negative control is kind of a gut check.

253

00:47:48.980 --> 00:47:50.280

Meredith Pedde: Next slide, please.

254

00:47:52.100 --> 00:48:11.799

Meredith Pedde: And to study these questions, we used air pollution data that's been estimated from highly sophisticated computational models. These models incorporate data from air quality monitors, as well as physical measures of the amount of aerosols in the atmosphere, which is data that satellites collect continuously across the globe.

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00:48:12.110 --> 00:48:22.289

Meredith Pedde: And so these computational models also incorporate atmospheric chemistry, accounts for the mixing of particles, as well as meteorology and cloud cover.

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00:48:22.830 --> 00:48:40.939

Meredith Pedde: And so, the huge benefit of using estimates generated from these types of models is that it allows us to have concentrations, so pollutant concentrations, everywhere, estimates everywhere, not just at the location, where regulatory agencies, monitor for air pollution.

257

00:48:41.530 --> 00:48:42.500

Meredith Pedde: Next slide.

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00:48:45.480 --> 00:48:57.490

Meredith Pedde: And so one of the types of air pollution that we looked at in this work, is what's called PM2.5, or fine particulate matter, which are particles with a diameter of less than 2.5 microns.

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00:48:57.590 --> 00:49:13.770

Meredith Pedde: And so if you look at the picture on the left, it puts the size into context. So it shows that PM2.5, which are the red spheres, are less than 1 tenth of the size of a human hair. So we're really talking about particles that are quite, quite small.

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00:49:14.740 --> 00:49:28.850

Meredith Pedde: On the right, the map is showing estimated levels of PM2.5 across the U.S, and you can see that these PM2.5 levels vary across the country, and how they can be, especially elevated in urban areas.

261

00:49:29.890 --> 00:49:30.890

Meredith Pedde: Next slide.

262

00:49:32.960 --> 00:49:49.829

Meredith Pedde: That said, air quality levels can also be elevated in non-urban areas, too, since pollutants are emitted from many different sources, so things like agriculture, wildfires, and energy production, as well as from mobile sources, so cars, trucks, and airplanes.

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00:49:50.340 --> 00:50:06.539

Meredith Pedde: And air pollution can be further influenced by weather conditions, so things like sunlight and wind and heat can impact, concentrations. And so air pollution really is a complex mixture of emissions, from a variety of different sources. It's not just one,

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00:50:07.050 --> 00:50:08.970

Meredith Pedde: one, factor.

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00:50:09.480 --> 00:50:10.700

Meredith Pedde: Next slide, please.

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00:50:12.470 --> 00:50:30.310

Meredith Pedde: And so that is what motivated our reason, or our desire to look at, the association of air pollution and ALS, not just by using these total fine particles, or PM2.5. We really wanted to better understand the impacts of different types of sources of pollution on ALS.

267

00:50:30.700 --> 00:50:50.109

Meredith Pedde: And so, we also studied four specific types of particles, which are the, what we call components of PM2.5. So, particles can be from anything, and we wanted to look at types of particles from different sources. So, specifically, we looked at what's called black carbon, nitrate, sulfate, and then again, sea salt.

268

00:50:50.790 --> 00:51:06.630

Meredith Pedde: And so what you can see on these maps is that since, different pollution sources emit these different types of particles, the estimated levels of these four particles types, differs regionally, just like the makeup of sources differs regionally.

269

00:51:07.110 --> 00:51:22.360

Meredith Pedde: So, for example, we see that nitrate, which is formed from ammonia, which, especially when temperatures are cold, is highest in the northern states, that have these high levels of agriculture, since agriculture is one of the leading, sources of ammonia emissions.

270

00:51:23.030 --> 00:51:38.649

Meredith Pedde: But if we look at places with warmer temperatures, there, ammonia reacts to become sulfate, which you can see has higher concentrations in the warmer

portions of the US, as well as in places with more energy production and other industrial facilities.

271

00:51:39.210 --> 00:51:47.400

Meredith Pedde: And so black carbon, on the other hand, is a sooty black material that's emitted from cars, and diesel engines, as well as from wildfires.

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00:51:48.380 --> 00:51:58.610

Meredith Pedde: And then sea salt, as you would expect, is highest on the coasts, and again, the motivation there is that we would expect there to be no association between sea salt, and ALS.

273

00:51:59.460 --> 00:52:00.709

Meredith Pedde: Next slide, please.

274

00:52:03.140 --> 00:52:13.829

Meredith Pedde: So, so far I've focused on particles, but there are also what we call gaseous pollutants, so things like ozone and NO₂, or nitrogen dioxide, which are shown here in the US.

275

00:52:13.970 --> 00:52:26.559

Meredith Pedde: And since we... our motivation here was that these are two other, what we call key criteria pollutants, which are pollutants that are regulated by the US EPA. And so we were interested in their association with ALS as well.

276

00:52:27.520 --> 00:52:28.800

Meredith Pedde: Next slide, please.

277

00:52:31.140 --> 00:52:42.590

Meredith Pedde: And so, not only are there differences in pollution levels by region, they're also differences within cities and within neighborhoods, which you can see here as we zoom into Ann Arbor, Michigan, which is where I live.

278

00:52:42.800 --> 00:52:47.589

Meredith Pedde: And so here I've highlighted 4 different points in Ann Arbor that are only 4 miles apart.

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00:52:47.640 --> 00:53:02.240

Meredith Pedde: And so the figure on the right highlights, again, this advantage of using these types of pollutant, model pollutant estimates in these types of analyses. It allows us to account for these very small-scale differences in air pollution by place.

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00:53:02.260 --> 00:53:08.390

Meredith Pedde: So that people who are living even just a few blocks apart, can be assigned different levels of air pollution.

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00:53:09.180 --> 00:53:18.109

Meredith Pedde: And so what we did, for these studies is we linked these estimated exposure concentrations to the University of Michigan,

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00:53:18.450 --> 00:53:25.210

Meredith Pedde: ALS patients using their geocoded address histories, which were collected on all of the study participants.

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00:53:25.620 --> 00:53:33.549

Meredith Pedde: And I'll pause here to say, thank you to anyone on the call who has ever provided this type of residential history information for research.

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00:53:33.550 --> 00:53:47.839

Meredith Pedde: I hope that this, you know, highlights the advantages that providing this information has. I know that it can be very hard to sometimes put together a full lifetime of residential history, but it really is what makes this type of research possible.

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00:53:48.690 --> 00:53:49.990

Meredith Pedde: Next slide, please.

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00:53:53.320 --> 00:54:02.799

Meredith Pedde: And so, even among patients seen here at the University of Michigan, which, are largely residents of Michigan and the Northern Midwest.

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00:54:02.810 --> 00:54:16.049

Meredith Pedde: You can see that there's still a wide range of levels of total PM2.5 exposure, in the 5 years before symptom onset. These values range from 4 micrograms to 16 micrograms per cubic meter.

288

00:54:16.350 --> 00:54:31.589

Meredith Pedde: And, the vertical yellow lines I've added here as a reference. So the, the line to the right represents, the US EPA's PM2.5 annual air quality standard, which is currently set at 9 micrograms per cubic meter.

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00:54:31.600 --> 00:54:40.069

Meredith Pedde: And the line to the left is the World Health Organization's guideline level, which is even lower at 5 micrograms per cubic meter.

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00:54:40.690 --> 00:54:59.990

Meredith Pedde: I will note, though, that the US EPA announced about a year ago that they're currently reconsidering that, 2024 standard, that level of 9, and so the process is currently in the courts, but if that were to be granted, that would reset the PM2.5 standard, back up to the earlier one, which was 12.

291

00:55:01.340 --> 00:55:03.010

Meredith Pedde: Next slide, please.

292

00:55:05.220 --> 00:55:22.339

Meredith Pedde: And so, the last set of plots here, we're showing the exposure variation in the study population, for those other six pollutants that we studied. And again, you can see that even in patients residing just throughout Michigan, we still have quite a lot of variation in these levels of pollution.

293

00:55:22.970 --> 00:55:24.310

Meredith Pedde: Next slide, please.

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00:55:27.200 --> 00:55:32.529

Meredith Pedde: Okay, so now the specific studies and analyses that we did with these, air pollution data.

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00:55:32.790 --> 00:55:43.910

Meredith Pedde: So first I'll talk about work that was published in the journal Environmental Research earlier this year, and this was our work looking at the role of air pollution on ALS disease progression.

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00:55:44.260 --> 00:55:59.259

Meredith Pedde: And so, really what we were interested in understanding is, do people that were exposed to more air pollution have a steeper decline in their functioning, as measured by the ALS FRSR score, than those that were exposed to less pollution?

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00:55:59.470 --> 00:56:09.859

Meredith Pedde: So, in other words, we know that physical functioning declines with ALS, but we wanted to know if that decline was more rapid in persons who had higher air pollution exposure.

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00:56:10.620 --> 00:56:12.000

Meredith Pedde: Next slide, please

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00:56:14.660 --> 00:56:30.360

Meredith Pedde: And so our outcome that I mentioned on a previous slide, was the ALS, Functional Rating Score Revised, or the ALS FRSR, which I'm sure, as most people here know, is, a validated instrument that reflects patients' overall functional status.

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00:56:30.360 --> 00:56:37.130

Meredith Pedde: Among four domains, so gross motor tasks, fine motor tasks, bulbar functions, and respiratory functions.

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00:56:37.330 --> 00:56:46.419

Meredith Pedde: So each of these domains is rated from 0 to 4, so the overall ALS FRSR score is ranging from 0 to 48.

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00:56:46.880 --> 00:56:56.739

Meredith Pedde: And in our participants, these scores were assessed in clinic approximately every 3 months, so we have these measurements throughout, a participant's disease course.

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00:56:57.170 --> 00:57:04.599

Meredith Pedde: And so, in our study, our population consisted of the 469 consenting, persons.

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00:57:04.600 --> 00:57:17.469

Meredith Pedde: seen here at the University of Michigan ALS, or Pringer ALS Clinic between 2009 and 2022. We included those who had a Gold Coast definition of ALS and had, complete data.

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00:57:18.090 --> 00:57:19.510

Meredith Pedde: Next slide, please.

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00:57:21.820 --> 00:57:34.900

Meredith Pedde: And in terms of our exposure air pollution, timing, we looked at two different time periods. So first, we focused on more recent, shorter-term, or specifically 3-month average pollutant exposures.

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00:57:34.960 --> 00:57:52.300

Meredith Pedde: To reflect potentially modifiable exposures post-ALS onset. Since our study was longitudinal, and we're assessing the outcome every 3 months, these exposures are being assessed throughout the course of disease. So again, including the time after a disease diagnosis.

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00:57:53.150 --> 00:58:03.699

Meredith Pedde: We also looked at longer-term or 5-year average pollutant exposures to reflect exposures before the onset of symptoms, to inform public health and environmental policy.

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00:58:04.300 --> 00:58:05.669

Meredith Pedde: Next slide, please.

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00:58:08.020 --> 00:58:27.610

Meredith Pedde: Okay, I do not put this slide up here to scare anyone, but just rather to show that, to answer this question, we use what's called linear mixed effects modeling, which, again, is assessing whether that rate of change in your ALS FRSSR score is a function of your air pollution exposure after we adjust for covariates.

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00:58:27.730 --> 00:58:40.179

Meredith Pedde: And just briefly, the specific things that we adjusted for were time, age at symptom onset, and other factors like sex, neighborhood socioeconomic status, race, urbanicity.

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00:58:40.180 --> 00:58:50.529

Meredith Pedde: and the distance from someone's home to the University of Michigan hospital, which we included to try and address this issue of who is seeking treatment at the University of Michigan.

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00:58:51.330 --> 00:58:55.920

Meredith Pedde: We fit what are called single pollutant models separately for each pollutant.

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00:58:55.990 --> 00:59:14.740

Meredith Pedde: But, since we know that people are actually exposed to multiple pollutants all at one, all at once, we fit what are called multi-pollutant models. So all the pollutants were in the same model, together, which is very common in our field. And again, this is another advantage of using these types of satellite, derived exposures.

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00:59:16.590 --> 00:59:17.879

Meredith Pedde: Next slide, please.

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00:59:19.550 --> 00:59:36.740

Meredith Pedde: So here I have descriptive statistics of the study population included in this progression study. So the left column is for the 469 patients overall, and then the right two columns are divided

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00:59:36.810 --> 00:59:48.180

Meredith Pedde: those people into, those with, disease progression below and above this cohort's median. So we've labeled them here as the, slow and fast disease progression rates.

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00:59:48.580 --> 01:00:00.580

Meredith Pedde: And, you can see that overall, we had 469 participants, and again, since the measures are collected every 3 months, that resulted in 3,000 observations throughout the study period.

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01:00:01.270 --> 01:00:19.440

Meredith Pedde: The patients are almost all non-Hispanic white, and somewhat more than half are male overall, but when we look at just the category of, or the column with the slow disease progression, those are more likely to be male than those in the fast disease progression column, which are those, more likely to be female.

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01:00:20.110 --> 01:00:35.910

Meredith Pedde: And then when we look at the breakdown of the onset segment, it's pretty evenly split in the population overall across bulbar, cervical, and lumbar, but it's predominantly cervical and lumbar in those with slow disease progression.

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01:00:36.510 --> 01:00:49.690

Meredith Pedde: And then if we look, at the bottom in terms of exposures, the baseline, or before disease onset, level of PM2.5 exposure were, a bit lower in the faster versus the slower progressors.

322

01:00:50.830 --> 01:00:52.150

Meredith Pedde: Next slide, please.

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01:00:53.680 --> 01:01:12.419

Meredith Pedde: And so here are the first set of results, and so here are the, findings for our shorter-term or 3-month average exposures. And just to orient you, associations to the left of the vertical line are consistent with this idea that higher levels of pollution are associated with faster disease progression.

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01:01:12.900 --> 01:01:20.809

Meredith Pedde: And if the full horizontal bar does not cross the vertical line, that would be what we call having statistically significant, results.

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01:01:21.460 --> 01:01:34.350

Meredith Pedde: And so what we found in our multipollutant models, was that only higher exposures of ozone were significantly associated with faster rate of decline in ALS FRSR scores.

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01:01:34.690 --> 01:01:52.869

Meredith Pedde: And so, specifically, we found that a 1 interquartile range increase in someone's 3-month average ozone level, over the follow-up period was associated with a 0.3 ALS FRSR points per year faster change, in the score.

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01:01:53.200 --> 01:02:07.379

Meredith Pedde: And so, if we try to put that finding into context, that magnitude of the association, so that 0.3 ALS FRS are points per year faster decline, for those with high and low ozone exposure.

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01:02:07.380 --> 01:02:24.730

Meredith Pedde: is the same as about 3% of the, annual ALS FRSR decline that across all of our study participants had in the study, which was about 11 points per year. So this is reflective of about a 3% of just the annual,

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01:02:24.760 --> 01:02:26.249

Meredith Pedde: Decline in general.

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01:02:27.210 --> 01:02:39.370

Meredith Pedde: Higher 3-month average exposures to the other pollutants were not statistically significantly associated with faster declines of the ALSFRS score in this population.

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01:02:39.380 --> 01:02:47.870

Meredith Pedde: But the association with sea salt, which again we used as a negative control, was essentially null, which was as we had hypothesized.

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01:02:48.790 --> 01:02:50.110

Meredith Pedde: Next slide, please.

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01:02:52.260 --> 01:03:09.429

Meredith Pedde: So here we're looking at the results for the 5-year average exposures. And again, having a bar to the left of the vertical line, is consistent with, levels of air pollution, higher levels of air pollution being associated with faster disease progression.

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01:03:09.770 --> 01:03:20.060

Meredith Pedde: And here, with these longer-term exposures, we found that higher black carbon and nitrate exposures were associated with faster rates of ALSFRSR decline.

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01:03:20.130 --> 01:03:33.990

Meredith Pedde: And, here, the magnitude of those associations was quite a bit larger. So for black carbon, it was 2.5, and for, nitrate, 1.2 points per year, faster declines.

336

01:03:34.370 --> 01:03:49.719

Meredith Pedde: And again, if we try to put these into context, compared to just the annual, decline overall in the population, these magnitudes of association represent 10% and 21% of that observed, annual average decline.

337

01:03:50.990 --> 01:04:04.419

Meredith Pedde: Higher, five-year average exposures to NO₂, however, were suggestively associated with, faster rates of ALS decline, while, total sea salt was not associated with faster rates of decline.

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01:04:05.160 --> 01:04:17.920

Meredith Pedde: Contrary to our hypothesis, though, we saw that lower levels of PM_{2.5} sulfate, and ozone were associated with faster rates of ALS, FRS decline.

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01:04:19.220 --> 01:04:20.580

Meredith Pedde: Next slide, please.

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01:04:22.340 --> 01:04:32.220

Meredith Pedde: And so here, if we put the two, findings together, you can see that except for sea salt, the results of each pollutant differed for the two different exposure periods.

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01:04:32.810 --> 01:04:42.160

Meredith Pedde: I will say that one particularly interesting finding may be that higher long-term nitrate exposure being associated with faster ALS progression.

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01:04:42.190 --> 01:04:51.350

Meredith Pedde: So again, given that agricultural activities and fertilized soil-related sources are now prominent contributors to nitrate pollution.

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01:04:51.350 --> 01:05:04.489

Meredith Pedde: These findings would be consistent with past research, finding that, there was higher ALS risk in people living close... in closer proximity to agriculture, and those with higher pesticide and fertilized exposure.

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01:05:05.640 --> 01:05:15.900

Meredith Pedde: I will note that these results were all consistent across of all of our different, sensitivity analyses that we did, and across different levels of, covariate adjustment.

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01:05:17.000 --> 01:05:34.280

Meredith Pedde: In terms of that inverse association for, ozone, one hypothesis we had is that, for ozone, the levels could reflect, the fact that higher, or that ozone... or sorry, the app...

346

01:05:34.330 --> 01:05:40.729

Meredith Pedde: the atmospheric conversion of ozone into other types of pollutants. So...

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01:05:41.410 --> 01:05:50.469

Meredith Pedde: And this could be consistent with other studies that have also showed weak inverse associations between ozone and ALS risk.

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01:05:51.630 --> 01:05:53.030

Meredith Pedde: Next slide, please.

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01:05:54.730 --> 01:06:09.300

Meredith Pedde: So in summary, here in our study of air pollution and ALS progression, we found evidence that shorter-term exposure to ozone and longer-term exposure to black carbon and nitrate were associated with faster ALS disease progression.

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01:06:09.500 --> 01:06:18.789

Meredith Pedde: And the magnitudes of these differences, ranged from 3 to 21% of the observed annual average decline in our study population.

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01:06:19.600 --> 01:06:31.419

Meredith Pedde: Again, counter to our hypothesis, we found that higher long-term exposures to total PM2.5 sulfate, and ozone were associated with slower declines in, disease progression.

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01:06:31.720 --> 01:06:38.200

Meredith Pedde: And this actually is not uncommon in our field to find inverse associations between ozone and health.

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01:06:38.210 --> 01:06:39.959

Meredith Pedde: And as I was...

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01:06:39.960 --> 01:07:03.449

Meredith Pedde: trying to say on the last slide, one possible explanation is that ozone is what we call highly reactive in the atmosphere. So when concentrations are low, of ozone are low, it could mean that that ozone has already converted into some different pollutant that may be more toxic, but that we're not measuring. So that could therefore induce this inverse association between ozone and health.

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01:07:03.740 --> 01:07:07.040

Meredith Pedde: So this is something that could warrant, further study.

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01:07:07.930 --> 01:07:20.429

Meredith Pedde: But overall, our findings support that reducing exposures to these pollutants, either through government regulations and technological advances, or through the use of air purification at an individual level.

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01:07:20.430 --> 01:07:29.529

Meredith Pedde: may be meaningful ways to slow ALS progression, and again, with those shorter-term, study, that would be even after, disease onset.

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01:07:30.460 --> 01:07:42.410

Meredith Pedde: And so, I'll note that we were also able to focus, on, you know, using the ALS FRSSR score, we were able to focus on an important marker of disease progression,

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01:07:42.410 --> 01:07:56.710

Meredith Pedde: Which is, I'll note, I think is an improvement over existing research, which has instead used administrative records on first hospitalizations with ALS as a kind of a surrogate for disease aggravation.

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01:07:57.310 --> 01:08:16.200

Meredith Pedde: But of course, since there are many factors, you know, that can influence someone's use of medical care, using first hospitalization could introduce what we call selection bias. And so we think that using the ALSFRSR score is, kind of a more specific way to get at, disease progression.

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01:08:17.300 --> 01:08:18.689

Meredith Pedde: Next slide, please.

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01:08:21.490 --> 01:08:29.549

Meredith Pedde: Okay, now I'll shift, and share with you their findings from our study of air pollution and survival in persons with ALS.

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01:08:29.790 --> 01:08:48.779

Meredith Pedde: I'll note first this curve, this plot here, this is not, representative of the data in our study, but it's just to conceptually show, what a survival analysis entails. So essentially, we're wondering, does higher air pollution, is it associated with, longer or shorter survival?

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01:08:49.170 --> 01:08:55.710

Meredith Pedde: And so, this study was published in the Journal of Environmental Health a couple of months ago,

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01:08:55.750 --> 01:09:10.069

Meredith Pedde: And just to give some motivation for this work, you know, in context with our last study, you know, while disease progression and survival are, of course, closely related, we wanted to look at these two things separately.

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01:09:10.069 --> 01:09:16.119

Meredith Pedde: Since we know that there is variation in that ALS FRSR score, at the time of death.

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01:09:16.160 --> 01:09:25.670

Meredith Pedde: And, not everyone, will have the minimum ALS FRSR score of zero, at the time of death.

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01:09:26.109 --> 01:09:38.399

Meredith Pedde: We also know that survival is much less susceptible to noise or, missing data than ALS FRSR, since this information on... was collected from all the participants.

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01:09:38.750 --> 01:09:47.189

Meredith Pedde: And, of course, this is also an outcome, right, that's of, probably most interest to, patients or... and loved ones.

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01:09:48.810 --> 01:09:50.100

Meredith Pedde: Next slide, please.

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01:09:51.220 --> 01:10:09.900

Meredith Pedde: And so, in this study, we... our population consisted of 477 patients, again, those seen here at University of Michigan between 2009 and 2022. We included those who met the Gold Coast definition of ALS, and who had complete information on, data across the study period.

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01:10:10.720 --> 01:10:17.300

Meredith Pedde: Here we again look at these same 7 pollutants, the same underlying data sources as we did with disease progression.

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01:10:17.400 --> 01:10:35.200

Meredith Pedde: Only this time, our exposure averaging time was 1 year. We chose this time since that's the time period most closely linked to overall, or all-cause mortality in the general population, in the existing air pollution, epidemiological literature.

374

01:10:36.930 --> 01:10:38.270

Meredith Pedde: Next slide, please.

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01:10:40.090 --> 01:10:54.530

Meredith Pedde: In this study, we used what are called Cox proportional hazards regression models. We used the number of days from diagnosis as the time axis to study whether higher levels of air pollution are associated with shorter survival.

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01:10:54.810 --> 01:11:09.990

Meredith Pedde: Here again, we were able to adjust for characteristics such as sex, race, ethnicity, time, age at diagnosis, neighborhood SES, urbanicity, and again, distance from, someone's home to the University of Michigan Hospital.

377

01:11:10.370 --> 01:11:22.269

Meredith Pedde: Our primary models also adjusted for these other pollutants, again, what I was saying, these multi-pollutant exposure models, since, again, we know that, people are exposed to more than one pollutant at a time.

378

01:11:22.830 --> 01:11:24.229

Meredith Pedde: Next slide, please.

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01:11:26.910 --> 01:11:40.909

Meredith Pedde: And so here, among the 477 participants, there were 329 of whom died during the study period, which resulted in an average follow-up period of just under 3 years per participant.

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01:11:41.270 --> 01:11:47.039

Meredith Pedde: The study population was 55% male, and again, nearly all non-Hispanic white

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01:11:47.900 --> 01:11:59.659

Meredith Pedde: In this population, the average age at symptom onset was 62 years, while the average age at diagnosis, which in this study, was our baseline period, was 64.

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01:11:59.900 --> 01:12:09.299

Meredith Pedde: And we had 92 participants that had a diagnosis of ALS, and 64% resided in an urban area at the time of their diagnosis.

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01:12:10.450 --> 01:12:11.759

Meredith Pedde: Next slide, please.

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01:12:13.960 --> 01:12:21.800

Meredith Pedde: And so here are our results for our primary models, and again, this is for one-year average exposure, and adjusted for our other pollutants.

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01:12:21.990 --> 01:12:36.029

Meredith Pedde: And here, it's actually the flip. So to orient you, the hazard ratio greater than 1, which are those to the right of the vertical line, would indicate that higher levels of air pollution are associated with decreased survival.

386

01:12:36.050 --> 01:12:48.609

Meredith Pedde: While a hazard ratio less than 1, or to the left of that vertical line, would represent the higher levels of survival for higher levels of air pollution. So the right would be consistent with our hypothesis.

387

01:12:49.200 --> 01:13:03.830

Meredith Pedde: And here you can see the confidence bands were quite wide, but we did find that a 1 interquartial range increase in PM2.5 was associated with decreased survival, in our study population.

388

01:13:03.990 --> 01:13:17.120

Meredith Pedde: And so, specifically, that one IQR increase in someone's one-year average PM was associated with a 60%... sorry, 66% increase in the hazard of death during the, study period.

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01:13:17.380 --> 01:13:30.369

Meredith Pedde: And so, again, if we try to put these findings into context, that suggests that a 2.1 microgram per cubic meter decrease in someone's one-year average PM2.5 level

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01:13:30.370 --> 01:13:39.359

Meredith Pedde: Would extend median survival by approximately 7 months, which, of course is significant given the existing treatment efficacy.

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01:13:40.370 --> 01:13:47.900

Meredith Pedde: Now, there was a suggestion that one-year average NO2 concentrations were associated with lower survival.

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01:13:48.340 --> 01:13:50.320

Meredith Pedde: And if we can go to next slide, please.

393

01:13:52.650 --> 01:14:04.160

Meredith Pedde: But those inverse results for NO₂ were null, or, zero, when we looked at 5-year average concentrations, which is what's shown here in this plot for all of the pollutants.

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01:14:04.420 --> 01:14:21.249

Meredith Pedde: That inverse NO₂ result was also, null when we looked, or when we subsetting our analyses to just those with, more than, or sorry, when we excluded, those with more than 5 years of survival, and other sensitivity analyses as well.

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01:14:22.350 --> 01:14:36.100

Meredith Pedde: But here with the longer averaging periods, we saw that higher black carbon levels, were associated with an 83% increase in the hazard of death, but that the association for all of the other pollutants, were null.

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01:14:37.350 --> 01:14:38.740

Meredith Pedde: Next slide, please.

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01:14:40.980 --> 01:14:51.440

Meredith Pedde: And so here are the two averaging periods on the same plot. I'll note that our results were unchanged when we restricted to only the time period before COVID.

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01:14:51.440 --> 01:15:02.840

Meredith Pedde: And when we looked at additional adjustment for disease characteristics, and when we restricted to, only persons meeting the revised LL scorial criteria diagnosis.

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01:15:03.780 --> 01:15:05.120

Meredith Pedde: Next slide, please.

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01:15:07.470 --> 01:15:17.640

Meredith Pedde: And so, in summary, in this work, we found evidence that higher levels of PM2.5 and black carbon were associated with shorter survival in patients with ALS,

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01:15:17.790 --> 01:15:21.310

Meredith Pedde: While higher NO2 was associated with longer survival.

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01:15:21.720 --> 01:15:31.699

Meredith Pedde: So again, similar to our findings for progression, these results suggest that reducing exposures to these pollutants may be a meaningful way to lengthen survival in patients with ALS.

403

01:15:32.390 --> 01:15:33.780

Meredith Pedde: Next slide, please.

404

01:15:35.350 --> 01:15:45.390

Meredith Pedde: And just to close, when we look at these findings from both studies, at the same time, so progression results are on the left, and survival are on the right,

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01:15:46.060 --> 01:15:52.730

Meredith Pedde: You can see that the only pollutant that has a kind of a consistent story may be the long-term exposure to black carbon.

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01:15:52.730 --> 01:16:06.619

Meredith Pedde: Which in both studies was associated with faster disease progression and shorter survival in this population. But that the findings for the, other pollutants varied somewhat across studies and across averaging times.

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01:16:06.750 --> 01:16:15.190

Meredith Pedde: This perhaps suggests that, you know, additional research is needed in larger populations, and more diverse populations.

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01:16:16.490 --> 01:16:18.449

Meredith Pedde: And next slide, please.

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01:16:19.420 --> 01:16:21.749

Meredith Pedde: And with that, I will finish. I think they're...

410

01:16:22.340 --> 01:16:27.409

Meredith Pedde: Happy to take any questions now, or to, use the chat later as well.

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01:16:28.640 --> 01:16:38.169

Danielle Boyce: Thank you, so much. And, you know, as someone who does this kind of work, what really... or tries to do this kind of work, it really struck me as how

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01:16:38.170 --> 01:16:50.949

Danielle Boyce: hard it is to do this well, and all kinds of things have to align. The residential history data has to be just so. You have to have complete data on people, and all the exposures, and

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01:16:50.950 --> 01:17:15.910

Danielle Boyce: somebody in the chat, Lynn Brilmeyer, who is a brilliant advocate, happens to have ALS mentions GOALS, which is a group I'm involved with, started by Pat Dolan, who's an Esri employee, and we're doing at ALS TDI a webinar next week on just this very topic, so we'd love for you to come. But we're trying to create a repository of best practices, because we get a lot of questions, why don't you look at, you know, residential history and

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01:17:15.910 --> 01:17:25.030

Danielle Boyce: things, but it seems like it's very difficult to do this well, and it's true. So, I'm wondering if you could give some quick tips on

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01:17:25.030 --> 01:17:41.770

Danielle Boyce: If you want to do work that involves environmental exposure, like the ozone, like, where do you get the data, how do you find it, what kinds of map layers, residential history, what are best practices, you know, that kind of thing. Because I know the ALS registry, the CDC registry, is also grappling with this as well.

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01:17:42.420 --> 01:17:44.729

Meredith Pedde: Yes, thank you, and I would love to,

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01:17:44.730 --> 01:18:08.770

Meredith Pedde: be connected for that meeting next week. Yes, I really, truly want to highlight the importance and, like, the grateful... how grateful we are for those who have provided the residential history. You know, earlier generations of this type of research for other diseases and, you know, any outcome used to always rely on, someone's, you know, whatever the air pollution level was in their city, whatever it was in their zip code,

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01:18:08.770 --> 01:18:33.080

Meredith Pedde: And that would come from EPA and, air quality monitors. And not every city has one, so if you lived in the middle, of Iowa, I'm originally from Iowa, there might not be an air quality monitor anywhere near you. And so these types of data sources that we're using have really revolutionized the field. They all of a sudden allow us to give people highly accurate, both spatially and temporally.

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01:18:33.080 --> 01:18:36.140

Meredith Pedde: Expo... estimates of these exposures.

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01:18:36.140 --> 01:18:44.080

Meredith Pedde: But again, that's only possible because we have someone's residential history. We cannot do that linkage without that, so it's so imperative.

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01:18:44.080 --> 01:18:59.990

Meredith Pedde: In terms of where to find these things, there are the fields kind of exploding and the different options that are available. I'm happy to share specific, sources with folks, after any time. But really, it all hinges on having that residential history, which we are so grateful for.

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01:19:01.410 --> 01:19:20.330

Danielle Boyce: Thank you so much, and thanks for highlighting that, because, you know, so much, like you said, so much depends on data quality. There's only so much you can do to investigate these questions with thorough and high-quality methods, which is what you use. There's only so much you can do if you don't have the right data. So, thank you so much. And we'll take some Q&A after this.

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01:19:20.650 --> 01:19:27.269

Danielle Boyce: And... and now, without further ado, we have, Fang Fang and Xing Wu.

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01:19:27.580 --> 01:19:51.730

Danielle Boyce: Fang Fang is a professor in epidemiology at the Karolinska Institute, Stockholm, Sweden, focusing on studying the risk and prognostic factors of ALS, so continuing on with the air pollution theme. And Xing Wu is a postdoc in neuroepidemiology at the Karolinska Institute in Stockholm, Sweden, focusing on studying the impact of environmental exposures, especially air pollution.

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01:19:51.750 --> 01:20:01.359

Danielle Boyce: on neurodegenerative diseases such as ALS, multiple sclerosis, Parkinson's disease, and dementia. Thank you very much. I'll turn it over to you.

Ambient Air Pollution as a Potential Risk Factor for ALS Using a Multiomics Approach in a High-Quality Epidemiologic Study Karolinska Institute - Fang Fang, PhD, Jing Wu, PhD

426

01:20:02.670 --> 01:20:19.070

Fang Fang: Thank you, Danielle, for the kind introduction. I would also like to thank the ALS Registry, the CDC, and the ATSDR for their support of some of our research on ALS in Sweden, and of course for the possibility to present some of our findings today.

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01:20:19.070 --> 01:20:43.189

Fang Fang: So I will start by briefly introducing the specific aims of our ongoing ALS registry-funded project, air pollution as a potential risk factor for ALS, and then Jing, as I said, will give us a more detailed presentation of some of the findings we have obtained so far. So the basic idea of this project is to see whether air pollution

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01:20:43.640 --> 01:20:55.179

Fang Fang: is related or can be indicative of a different risk and prognosis of ALS. And the second part of this project is to understand what are the potential

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01:20:55.300 --> 01:21:10.860

Fang Fang: underlying mechanisms. So the project is divided into three specific aims. The first aim will leverage the Swedish Motor Neuron Disease Registry, which was established in 2015, and has been

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01:21:10.860 --> 01:21:23.249

Fang Fang: Collecting data from more than 85% of all motor neuron disease patients here in Sweden, with complete follow-up on clinical measures, quality of life, biomarkers, etc.

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01:21:23.260 --> 01:21:39.609

Fang Fang: So, in this aim, we will try to assess so-called associations and see if air pollution is associated with a different risk of ALS, and also associated with a different clinical of ALS patients.

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01:21:40.210 --> 01:21:57.160

Fang Fang: So AIM2 and Aim 3 will be trying to understand any associations we observe in AIM1, what kind of biological mechanisms might explain such associations. So these two aims will leverage a case control study we

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01:21:57.160 --> 01:22:02.119

Fang Fang: started together with the ALS Clinical Care Center here in Karolinska.

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01:22:02.120 --> 01:22:11.899

Fang Fang: from 2016 onward, where we have today included more than 700 newly diagnosed ALS patients and 500 controls.

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01:22:11.910 --> 01:22:16.939

Fang Fang: So in Aim 2, we will be addressing several...

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01:22:17.560 --> 01:22:32.699

Fang Fang: biological pathways that have been proposed to be involved in ALS etiopathology or biology, including oxidative stress, inflammation, and as Dr. Murdoch was talking about, the gut microbiome.

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01:22:32.700 --> 01:22:45.779

Fang Fang: And we will be measuring different proteins in the blood and the cerebrospinal fluid samples to understand protein expressions in pathways relevant for oxidative stress and inflammation.

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01:22:46.040 --> 01:22:50.080

Fang Fang: And then we will be studying patient-donated,

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01:22:50.110 --> 01:23:01.979

Fang Fang: fecal samples to understand the composition as well as the function of gut microbiome, and see whether these measures will be different among patients

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01:23:01.980 --> 01:23:13.490

Fang Fang: with different exposure histories for, to air pollution. In the final aim, we will be studying 50 ALS patients with very detailed

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01:23:13.490 --> 01:23:16.919

Fang Fang: Profiling of immune cells, and immune cell

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01:23:16.980 --> 01:23:26.389

Fang Fang: immune cell functions in both the blood and cerebrospinal fluid sample using a technology called single-cell RNA sequencing data.

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01:23:26.390 --> 01:23:41.560

Fang Fang: to see if the immune cells in the periphery, the blood, and the intracranial compartment, which is reflected by the CSF sample, whether the air pollution experience of the patients will be

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01:23:41.620 --> 01:23:44.260

Fang Fang: Influencing how the immune cells work.

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01:23:45.110 --> 01:23:47.680

Fang Fang: And today, Jin will be...

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01:23:47.680 --> 01:24:10.340

Fang Fang: telling us some findings we obtained from AIM1, and we are currently working on the research questions we propose in AIM 2 and 3. So we hope... hopefully next year, we will meet again, and we will update you with the findings from the next two AIMS. Of course, our... our ultimate goal of our ALS research project is always to improve

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01:24:10.340 --> 01:24:15.170

Fang Fang: understanding of the disease etiology of ALS, and to

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01:24:15.330 --> 01:24:23.969

Fang Fang: get new knowledge on potential... potential preventive and therapeutic targets for this disease. Now, I leave the floor to Jean.

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01:24:27.350 --> 01:24:30.160

Jing Wu: Thank you, Fong, for the introduction.

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01:24:30.550 --> 01:24:32.019

Jing Wu: Next slide, please.

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01:24:34.390 --> 01:24:46.000

Jing Wu: So, as we know that, there are emerging, evidence, looking at the association between air pollution and ALS risk.

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01:24:46.070 --> 01:24:55.570

Jing Wu: During the dec- decades ago, but as you see, these, studies,

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01:24:55.990 --> 01:25:01.779

Jing Wu: Well, quite small, with... can you click, 3 more times, please?

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01:25:04.220 --> 01:25:17.830

Jing Wu: Yes. So as you can see, these studies, were mostly with small sample sizes and mixed with, prevalent and incident, ALS, patients.

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01:25:17.850 --> 01:25:27.049

Jing Wu: And, these results were not really consistent, across studies. And also.

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01:25:27.050 --> 01:25:41.029

Jing Wu: previously, there's no, studies exploring the association between air pollution and disease progression. And so, with these, research gaps, we conducted,

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01:25:41.230 --> 01:25:44.999

Jing Wu: our, studies. Next slide, please.

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01:25:46.590 --> 01:25:59.570

Jing Wu: Called Long-Term Exposure to Air Pollution Risk and Prognosis of Motor Neuron Disease, which has been published early this year. And next slide, please.

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01:26:01.140 --> 01:26:18.970

Jing Wu: So in this study, we aim to assess the impact of long-term exposure to air pollution and MND risk, and to further explore whether long-term exposure to air pollution is associated with MND progression and mortality.

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01:26:19.910 --> 01:26:21.330

Jing Wu: Next, please.

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01:26:21.920 --> 01:26:38.770

Jing Wu: So as Faun introduced, so, we used the data from the Swedish Modern Neuron Disease Registry, which included 1,463 newly diagnosed MND patients

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01:26:38.770 --> 01:26:48.859

Jing Wu: from 2015 to 2023. So, in the first aim, we conducted, two case control studies.

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01:26:48.860 --> 01:26:52.440

Jing Wu: First one, include... we included

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01:26:52.800 --> 01:27:07.030

Jing Wu: randomly selected, population controls based on the age and sex matched to the MND patients from the total population register in Sweden.

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01:27:07.110 --> 01:27:17.519

Jing Wu: And then we matched the patients to their siblings to serve as sibling controls from the multi-generation register.

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01:27:18.460 --> 01:27:34.060

Jing Wu: With the second aim, regarding mortality and disease progression, we only included the patient, of MND and conducted a patient cohort study. Next, please.

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01:27:34.890 --> 01:27:37.079

Jing Wu: Can you click 4 more times?

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01:27:40.160 --> 01:27:43.340

Jing Wu: Yes, thank you. So...

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01:27:43.550 --> 01:27:58.139

Jing Wu: you can see here, in the middle, these are the, study population I, I introduced. So, based on their, residential history, we,

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01:27:58.250 --> 01:28:05.680

Jing Wu: collected from the tax agency in Sweden, we are able to identify,

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01:28:05.680 --> 01:28:18.419

Jing Wu: Their yearly air pollution exposure at residential addresses that are assessed by the spatial temporal models from 2005 to 2018,

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01:28:18.610 --> 01:28:27.710

Jing Wu: And this including, PM2.5, PM10, PM2.5 to 10, and NO2.

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01:28:27.830 --> 01:28:36.239

Jing Wu: And with a resolution of 1 by 1 kilometer across the whole Sweden. And...

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01:28:36.720 --> 01:28:45.809

Jing Wu: Because the exposure windows, were not so clear in, environmental, epidemiology regarding the,

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01:28:46.020 --> 01:29:01.080

Jing Wu: MND risk, so we explored 4 exposure windows, 1, 3, 5 to 10 years before the disease diagnosis, and with 1 year time buffer to,

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01:29:01.470 --> 01:29:04.930

Jing Wu: To, reduce the reverse causation.

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01:29:05.580 --> 01:29:17.879

Jing Wu: And all these, patients in the MND register were usually followed up every 6 months, and the clinicians, carefully assessed

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01:29:17.880 --> 01:29:25.999

Jing Wu: Their function, regarding bulbar, fine motor, gross motor, and respiratory, functions.

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01:29:26.000 --> 01:29:30.780

Jing Wu: using the ALSFRS are,

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01:29:31.040 --> 01:29:39.339

Jing Wu: score. So we, using this data, we are able to monitor how fast

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01:29:39.340 --> 01:29:53.340

Jing Wu: their disease progress over time. So, with this data, we used, linear mixed effect models, to, to calculate the functional decline over time.

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01:29:53.340 --> 01:30:12.380

Jing Wu: And based on the rate, we classified these patients into two groups. Fast progression group, which is the upper 55% of the rate of the decline, and then slow progression group, the rest of the lower

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01:30:12.380 --> 01:30:15.620

Jing Wu: 75% of the patient.

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01:30:16.420 --> 01:30:24.079

Jing Wu: And then we assess... we will assess the mortality risk, next slide, please.

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01:30:25.750 --> 01:30:44.570

Jing Wu: So, here comes the result, of the long-term exposure to alcohol and the risk of MND. To the left, panel, this is the result showing the population comparison, as I mentioned before. So, the...

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01:30:44.570 --> 01:30:50.820

Jing Wu: If you look at the middle, there's a dashed line,

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01:30:50.820 --> 01:31:04.740

Jing Wu: that represent the odds ratio of 1. If the odds ratio is over, 1, that means there's a higher risk. So, you can see clearly,

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01:31:04.980 --> 01:31:22.629

Jing Wu: the, the, all these four air pollutants were associated with higher risk of MND onset. And, longer exposure windows show, is, is associated with, highest,

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01:31:22.780 --> 01:31:24.430

Jing Wu: risk.

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01:31:24.610 --> 01:31:44.249

Jing Wu: And then, to the right panel, you can see the sibling comparisons. These results show similar patterns at the population comparison. However, you can see these lines was slightly wider, that means the statistical power

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01:31:44.250 --> 01:31:49.679

Jing Wu: Well, were reduced because of, the reduction of the sample size.

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01:31:50.230 --> 01:31:51.769

Jing Wu: Next slide, please.

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01:31:53.280 --> 01:32:08.130

Jing Wu: And then we explored whether, all these four air pollutants were associated with the mortality after the MND diagnosis. And you can see, we, we found, the PM...

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01:32:08.130 --> 01:32:24.540

Jing Wu: 10 and 02 were associated with increased risk of, mortality. The highest, association was, one year before the, before, the disease diagnosis.

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01:32:25.420 --> 01:32:32.540

Jing Wu: But we did not observe a significant association for PM2.5 and PM2.5 to 10.

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01:32:33.260 --> 01:32:34.559

Jing Wu: Next, please.

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01:32:37.030 --> 01:32:46.429

Jing Wu: And then we looked at the association between air pollution and the risk of fast progression, and you can see,

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01:32:46.710 --> 01:33:05.199

Jing Wu: this, these bubbles across this table. For the total score, you can see, all this, all particular matters were associated with the overall fast pro... Progression, but not NO2.

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01:33:05.280 --> 01:33:20.809

Jing Wu: Well, fine motor function were, were influenced by all these, pollutants. Pm2.5 to 10, tend to associate it with, fast progression of growth

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01:33:20.850 --> 01:33:28.919

Jing Wu: motor function, and PM2.5 associated with, respiratory, function.

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01:33:30.040 --> 01:33:31.620

Jing Wu: And next, please.

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01:33:32.720 --> 01:33:45.370

Jing Wu: So, in summary, we found a very consistent association between increased risk of MND and higher level of air pollution in different exposure windows

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01:33:45.370 --> 01:34:01.000

Jing Wu: And up to 10 years before, diagnosis. And, further, we found, air pollution was associated with increased risk of mortality after the disease diagnosis.

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01:34:01.030 --> 01:34:09.379

Jing Wu: And a faster loss of motor and respiratory functions, but not bulbar function, was,

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01:34:09.600 --> 01:34:17.310

Jing Wu: However, evident among patients with MND with a higher average exposure to PMs, Next, please.

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01:34:19.310 --> 01:34:28.019

Jing Wu: So, after this, study, we want to know whether this association,

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01:34:28.060 --> 01:34:40.839

Jing Wu: like, like, what kind of mechanism was underlying this, air pollution and M&D risk association? So, one, could,

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01:34:40.960 --> 01:34:54.290

Jing Wu: one could think that, infection, might play a role in this association. So, in this study, we explored, the role of infection,

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01:34:54.600 --> 01:35:00.399

Jing Wu: Specifically for air pollution, M&D risk, and prognosis.

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01:35:00.510 --> 01:35:01.660

Jing Wu: Next, please.

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01:35:03.110 --> 01:35:19.479

Jing Wu: And to assess, the infection, we, used the Swedish patient register and identified all the infections in inpatient hospital and, and outpatient hospital treated.

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01:35:19.480 --> 01:35:30.899

Jing Wu: patients. And then we, identified, use of anti-infective medications from the prescribed drug register.

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01:35:31.360 --> 01:35:32.560

Jing Wu: Next, please.

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01:35:34.360 --> 01:35:50.019

Jing Wu: So... so this study, we used the same study population, but, with slightly complicated, designs, because we want to ensure the temporality of,

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01:35:50.120 --> 01:36:07.019

Jing Wu: the exposures, that means we want to make sure that the exposures, happen before the, outcomes, which is the, which are the, diagnosis and mortality in this study. So...

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01:36:07.280 --> 01:36:13.890

Jing Wu: Firstly, we want to see if air pollution, will interact

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01:36:13.890 --> 01:36:28.249

Jing Wu: with infection, on, disease diagnosis. And then we want to see whether, infection is mediating this association. And so first.

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01:36:28.250 --> 01:36:39.669

Jing Wu: We explored, air pollution, 10 years before, air pollution and any infection, 10 years before the disease diagnosis.

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01:36:39.670 --> 01:36:52.500

Jing Wu: And, for the infection analysis. And then, for the mediation analysis, we assessed, air pollution, 10 to 5 years before the diagnosis, and

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01:36:52.500 --> 01:37:03.170

Jing Wu: any infection 5 to 1 year before the diagnosis. And, we excluded the infection one year before diagnosis.

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01:37:03.970 --> 01:37:09.830

Jing Wu: And then, for the mortality, we want to include,

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01:37:10.020 --> 01:37:22.900

Jing Wu: the infection that, after disease diagnosis to... to make sure the temporality. So for the air pollution, we use the 10 years before the disease diagnosis.

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01:37:23.920 --> 01:37:25.549

Jing Wu: Next, please.

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01:37:26.680 --> 01:37:44.560

Jing Wu: And so... so in, air pollution, epidemiological research, one issue of, multi-pollutant model is that most of the, air pollutants, were highly correlated to each other.

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01:37:44.860 --> 01:38:06.210

Jing Wu: To, to model them in the same, model, it's, we might increase the problem of, collinearity. So to tackle this problem, we used a group-based multi-trajectory modeling for air pollution.

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01:38:06.210 --> 01:38:14.849

Jing Wu: To identify the trajectory... the trajectories of, air pollution across different, air pollutants.

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01:38:15.200 --> 01:38:20.010

Jing Wu: So, the best model fit found,

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01:38:20.010 --> 01:38:43.899

Jing Wu: two distinctive, trajectories. One, if you look at the right-hand side of, the slide, you can see, air pollution levels were decreasing over time, in general, and then, we found, one group with low-level exposure to air pollution and

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01:38:43.980 --> 01:38:50.910

Jing Wu: Another group, high-level, exposure to air pollution.

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01:38:51.030 --> 01:38:54.139

Jing Wu: Over time, next, please.

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01:38:56.680 --> 01:39:05.080

Jing Wu: And then, to, to look at the air pollution, Together.

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01:39:05.520 --> 01:39:15.679

Jing Wu: We calculated an air pollution score based on the 10-year average air pollution levels for air pollutants.

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01:39:15.700 --> 01:39:34.990

Jing Wu: Firstly, we standardized these air pollutants into a Z score, and then we used the principal component, analysis, to sort of downgrade all the complexity of the air pollution.

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01:39:34.990 --> 01:39:38.089

Jing Wu: Into one, air pollution score.

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01:39:38.310 --> 01:39:59.359

Jing Wu: So, we found, only, the first principal component already explains 80% of the variance for all four pollutants, so we, we, we will use that, as our air pollution score in, the next, in the, rest of the, analysis.

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01:40:00.300 --> 01:40:13.179

Jing Wu: So, you can see, to the right side of the slide, this air pollution score were quite, fitting the air pollution, levels for, for air pollutants.

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01:40:13.810 --> 01:40:15.060

Jing Wu: Next, please.

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01:40:16.760 --> 01:40:32.650

Jing Wu: And then here you can see the distribution of air pollution levels by the air pollution trajectory we identified in the previous model. You can see clearly that the low level and decreasing group

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01:40:32.650 --> 01:40:40.560

Jing Wu: Have the air pollution levels, lower than the high level and decreasing group.

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01:40:41.230 --> 01:40:42.430

Jing Wu: Next, please.

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01:40:46.030 --> 01:40:59.930

Jing Wu: to come, to, assess the role of infection, between air pollution and MND risk or prognosis, we used, a causal inference framework called.

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01:40:59.930 --> 01:41:13.199

Jing Wu: Four-way effect decomposition, to see if infection is, interaction or is a modifier or mediator in this association.

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01:41:13.670 --> 01:41:24.070

Jing Wu: So here, we decompose the effect into four parts. First one, is the control direct effect.

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01:41:24.070 --> 01:41:43.850

Jing Wu: So if you look at this, red line here, so that means this association was, not explained by, infection or the interaction between infection and air pollution. It's purely, from... directly from air pollution to MND risk for prognosis.

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01:41:44.690 --> 01:41:46.530

Jing Wu: And then,

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01:41:46.660 --> 01:42:02.209

Jing Wu: And then the reference interaction, that's... that's the... the path from air pollution to infection and air pollution interaction, and then to MND risk or prognosis.

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01:42:02.210 --> 01:42:07.009

Jing Wu: So that means this effect is due to infection only.

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01:42:07.390 --> 01:42:11.100

Jing Wu: And then mediated interaction,

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01:42:11.290 --> 01:42:26.009

Jing Wu: So, if you look at the red line here, the pass, goes from air pollution to infection, and then to the infection, the rest, and the last to, MND risk or prognosis.

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01:42:26.010 --> 01:42:32.700

Jing Wu: So it can be explained as disassociation is due to mediation and infection.

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01:42:33.290 --> 01:42:47.939

Jing Wu: So the, the last one is the pure indirect effect. That means air pollution, goes through, infection and then cause, or, linked to, MND risk or prognosis.

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01:42:48.870 --> 01:42:50.050

Jing Wu: Next, please.

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01:42:51.740 --> 01:43:05.339

Jing Wu: So, here comes the results. So, firstly, we investigated the interaction between L. Fusion and any infection, 10 years before the diagnosis on MND risk.

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01:43:06.060 --> 01:43:27.489

Jing Wu: Within the population comparison, so the shaded pink area, you can see that for the air pollution trajectory we identified using the group-based trajectory model, we found that the highest risk of the association was

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01:43:27.490 --> 01:43:32.360

Jing Wu: Among high-level and decreasing group, and with infection.

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01:43:33.190 --> 01:43:46.000

Jing Wu: And, but we did not, find, any, statistical significant, interaction, for this association.

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01:43:46.580 --> 01:43:54.789

Jing Wu: And, for the rest, air pollution score, PM, PM2.5, PM 2.5 to 10, PM...

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01:43:54.790 --> 01:44:08.430

Jing Wu: 10 and NO2, we all find, significant association, regardless, if the patient... if the, participant experienced infection or not.

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01:44:08.680 --> 01:44:16.769

Jing Wu: And similarly, we see these results within the sibling comparison. If you look at the

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01:44:16.930 --> 01:44:27.680

Jing Wu: the last two, columns here. But as, as before, because the reduction of the sample size.

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01:44:27.680 --> 01:44:40.559

Jing Wu: the confidence interval become, became, wider. So, but the, the magnitude of the association was similar to the population comparison.

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01:44:40.620 --> 01:44:41.810

Jing Wu: Next, please.

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01:44:43.930 --> 01:44:52.129

Jing Wu: And then we explored the interaction and mediation roles of infection on PM2.5 and MND risk.

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01:44:52.460 --> 01:45:00.579

Jing Wu: As I explained previously about this, decomposition, you can see,

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01:45:00.580 --> 01:45:13.250

Jing Wu: the first control direct effect of PM2.5 to MND diagnosis was about 86%.

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01:45:13.250 --> 01:45:24.390

Jing Wu: So that means the majority of the, association, was, directly from PM2.5 to M&D, risk.

567

01:45:25.220 --> 01:45:38.790

Jing Wu: And then, and then the, the interaction and mediated interaction only, had a very small proportion in this association.

568

01:45:38.790 --> 01:45:47.140

Jing Wu: But, infection, the mediation role of infection was around, 12%.

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01:45:47.140 --> 01:46:06.669

Jing Wu: So overall, if you look at the, percentage of mediated effect was around, 13% for infection, and the interaction was, very, little. The emulated risk due to,

570

01:46:06.920 --> 01:46:16.510

Jing Wu: The risk of infection can be eliminated was about, 14% in this association.

571

01:46:16.900 --> 01:46:18.039

Jing Wu: Next, please.

572

01:46:20.830 --> 01:46:22.420

Jing Wu: Next slide, please.

573

01:46:23.240 --> 01:46:30.730

Jing Wu: Here. So for PM to... PM10, we see, like,

574

01:46:30.740 --> 01:46:50.189

Jing Wu: 12% of the association, were due to the, the mediation of infection, but... and, the interaction role is very minor. The overall, risk can be eliminated was about, 14%.

575

01:46:50.850 --> 01:46:59.249

Jing Wu: If we, if we ex... if we eliminate the infection risk, 10 years before the disease diagnosis.

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01:46:59.740 --> 01:47:00.859

Jing Wu: Next, please.

577

01:47:02.350 --> 01:47:16.320

Jing Wu: And for NO2, we only see, like, 4% of the association was emitted, by, infection, but there's no, interaction in this association.

578

01:47:16.640 --> 01:47:17.770

Jing Wu: Next, please.

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01:47:19.010 --> 01:47:29.119

Jing Wu: And, for the overall air pollution trajectory, the midday, the, the overall association was,

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01:47:29.120 --> 01:47:40.110

Jing Wu: directly from air pollution trajectory to MND diagnosis, we did not see any mediation or interaction role for infection here.

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01:47:40.570 --> 01:47:41.720

Jing Wu: Next, please.

582

01:47:43.000 --> 01:47:50.669

Jing Wu: And also for the air pollution score, we did not see any mediation or interaction.

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01:47:51.200 --> 01:47:52.270

Jing Wu: Next, please.

584

01:47:54.170 --> 01:48:07.979

Jing Wu: And then, for the next aim, we, explore the interaction between air pollution and infection on mortality after the disease diagnosis. You can see,

585

01:48:08.270 --> 01:48:22.629

Jing Wu: The result showing that the high level and decreasing group end with infection showed significant elevated risk of mortality after disease diagnosis.

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01:48:23.380 --> 01:48:25.839

Jing Wu: And also,

587

01:48:25.880 --> 01:48:41.389

Jing Wu: Those, those people who, who had severe infection after disease diagnosis, had, elevated risk, of, air pollution.

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01:48:41.390 --> 01:48:50.549

Jing Wu: For mortality, across all exposure, exposure to different air pollutants.

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01:48:51.470 --> 01:48:52.630

Jing Wu: Next, please.

590

01:48:54.280 --> 01:49:08.220

Jing Wu: And then, similarly, we explored the, interaction and mediation roles of infection, and for PM2.5, we found, this is,

591

01:49:08.340 --> 01:49:21.700

Jing Wu: This, mediation, mediating and, interaction role of infection was, stronger compared to, to, risk.

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01:49:21.700 --> 01:49:38.669

Jing Wu: You can see that, for the, PM to pi... No, sorry, infection was associated with, 20% of the, can be explained the 20% of the risk.

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01:49:40.390 --> 01:49:47.299

Jing Wu: And though overall risk can be eliminated was around 40%, next, please.

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01:49:48.780 --> 01:49:54.110

Jing Wu: And, but PM2.5 to 10 was not,

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01:49:54.150 --> 01:50:14.129

Jing Wu: the infection in the, in the association between PM2.5 to, 10, and mortality was not, majorityly, mediated, from interaction, of infection, but mostly interaction.

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01:50:14.510 --> 01:50:15.660

Jing Wu: Next, please.

597

01:50:16.770 --> 01:50:21.629

Jing Wu: And for, PM10 exposure,

598

01:50:22.050 --> 01:50:32.810

Jing Wu: And only 3% of the association, were mediated by the infection. Next, please.

599

01:50:34.450 --> 01:50:49.740

Jing Wu: Similarly for the NO2, the majority of the association, were direct, were due to the direct effect, but not, through the infection pathway. Next, please.

600

01:50:51.480 --> 01:51:00.920

Jing Wu: And, however, if you look at the air pollution trajectory, about 12% of the association were mediated.

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01:51:01.230 --> 01:51:03.060

Jing Wu: Through infection.

602

01:51:03.490 --> 01:51:04.609

Jing Wu: Next, please.

603

01:51:06.660 --> 01:51:14.370

Jing Wu: And, the mediating role of infection for air pollution score was quite minor.

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01:51:14.690 --> 01:51:15.870

Jing Wu: Next, please.

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01:51:17.890 --> 01:51:31.300

Jing Wu: So, in conclusion, we... in this study, we found that infection may be partially mediates the association between air pollution and M&D risk.

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01:51:31.300 --> 01:51:40.350

Jing Wu: Well, infection can, may also, modify the association between high-level air pollution exposure and post

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01:51:40.350 --> 01:51:52.449

Jing Wu: diagnosis mortality. However, we found, this, studies, not powered, for sample sizes because

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01:51:52.450 --> 01:52:02.379

Jing Wu: We only identified infections, like, severe infections from, hospital... inpatient hospital, and outpatient hospital,

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01:52:02.380 --> 01:52:26.129

Jing Wu: treated patients, but not, but we did not include those people who, like, with minor infections. So, we think future studies, with more, power sample sizes are needed to confirm, our, studies, results and, clarify the underlying residual mechanisms.

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01:52:27.630 --> 01:52:28.740

Jing Wu: Next, please.

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01:52:29.680 --> 01:52:32.059

Jing Wu: Fan, do you want to take over?

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01:52:34.680 --> 01:52:45.019

Fang Fang: Yeah, I just want to thank very much all the family, patients, and their families who participate in this study in Sweden, the Swedish ALS care teams.

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01:52:45.020 --> 01:52:57.750

Fang Fang: the Kalolinska ALS research team, very many faces are on these pictures, and of course, the kind funding support from the ALS registry, CDC, and ATSDR. Thanks a lot.

614

01:53:00.480 --> 01:53:13.859

Danielle Boyce: Thank you very much, and we're starting to get some questions in the Q&A, so presenters, feel free to answer directly in the Q&A, and we will circle back, before lunch, and or after lunch, if there is other questions come in.

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01:53:15.370 --> 01:53:27.860

Danielle Boyce: And it is my pleasure to introduce the Dartmouth team today, who are going to be working together and presenting. First, Dr. Elijah Stummel, and then Kevin Cornell.

616

01:53:28.500 --> 01:53:42.410

Danielle Boyce: Dr. Stammel is a professor of neurology at Dartmouth's Geisel School of Medicine and a neurologist at Dartmouth-Hick Medical Center. He received a PhD and MD from the Boston University School of Medicine.

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01:53:42.440 --> 01:53:47.380

Danielle Boyce: He has worked with ALS patients for the last 30 years or more.

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01:53:47.390 --> 01:53:57.930

Danielle Boyce: And his main research interests have focused on potential environmental risk factors related to ALS. So if you've been to this meeting before, you've probably seen him present in all of his amazing work.

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01:53:57.930 --> 01:54:22.689

Danielle Boyce: He has run several investigator-initiated clinical trials for ALS, established the Northern New England Neurological Biorepository, and has made scientific contributions to understanding the role of environmental toxins in ALS, particularly cyanobacterial toxins, pesticides, and toxic metals. His research continues to explore the relationships and dynamics between environmental toxins and ALS,

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01:54:22.720 --> 01:54:42.369

Danielle Boyce: and through a multidisciplinary approach, bridge the gap between basic and translational science. By doing so, he hopes to deepen our understanding of ALS and its causes, to develop new diagnostic tools and therapeutics. And while I'm here, I'm going to introduce both of our speakers. They'll flow one into the other.

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01:54:42.370 --> 01:55:06.940

Danielle Boyce: Kevin Cornell, I had the pleasure of meeting at the ALSMND meeting last year. Hi! Kevin Cornell is a staff scientist and clinical research coordinator in Dr. Stommel's lab at Dartmouth Health, where he manages the lab and neurology department biorepositories and works on a variety of research projects with students and colleagues, involving neuropathology, metallomics, transcriptomics, clinical biomarkers.

622

01:55:06.940 --> 01:55:14.469

Danielle Boyce: In addition to neuroscience, he has an academic and professional background in environmental science and disease ecology.

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01:55:14.560 --> 01:55:18.739

Danielle Boyce: Where he is interested in bridging public health with conservation.

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01:55:19.000 --> 01:55:23.940

Danielle Boyce: And I will turn it over to this team. Thank you so much for being here today.

Persistent Environmental Toxicants in Veteran CNS Tissue: Identifying Exposures Determining Higher ALS Risk

Geisel School of Medicine at Dartmouth - Elijah Stommel, MD

625

01:55:25.560 --> 01:55:27.899

Elijah W. Stommel: Good morning. Oh, soon to be afternoon.

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01:55:28.110 --> 01:55:31.379

Elijah W. Stommel: I guess I'll go to the next slide.

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01:55:32.120 --> 01:55:36.650

Elijah W. Stommel: Are you going to the next slide? There we go.

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01:55:36.820 --> 01:55:39.919

Elijah W. Stommel: I'm Elijah Stommel,

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01:55:40.360 --> 01:55:59.880

Elijah W. Stommel: I'm sure that, Kevin Cornell will have something more interesting to talk about than I, but we'll... we'll find out. This is a multidisciplinary team. We couldn't do this research without, all these people listed here. Next slide.

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01:56:04.210 --> 01:56:08.280

Elijah W. Stommel: I think you went... okay, so... next slide.

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01:56:09.640 --> 01:56:19.140

Elijah W. Stommel: This is, just to stress that this is work in progress, and we have a lot more to do, but an update nevertheless.

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01:56:19.290 --> 01:56:30.709

Elijah W. Stommel: So what are the putative exposures or risks to veterans that have about a two-fold higher rate of ALS, as been talked about yesterday?

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01:56:31.070 --> 01:56:37.250

Elijah W. Stommel: Undoubtedly, diesel exhaust, jet exhaust, burn pits, pesticides.

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01:56:37.490 --> 01:56:45.209

Elijah W. Stommel: A variety of heavy metals and elements, Persistent organic pollutants, Possibly even microplastics.

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01:56:45.580 --> 01:56:54.280

Elijah W. Stommel: are all involved. And then, on top of that, there are probably premorbid behaviors, such as head trauma, smoking, stress.

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01:56:54.860 --> 01:56:59.330

Elijah W. Stommel: Dietary issues and metabolic issues.

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01:56:59.780 --> 01:57:04.629

Elijah W. Stommel: Athleticism, and one of my pet peeves, cyanotoxins.

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01:57:05.840 --> 01:57:09.569

Elijah W. Stommel: So, next slide.

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01:57:12.390 --> 01:57:20.010

Elijah W. Stommel: So what we have set out to do here is to look for exposures to veterans by examining brain tissue.

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01:57:20.430 --> 01:57:26.600

Elijah W. Stommel: And to look for exposures that can be measured in retrospect, that hang around for a long time.

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01:57:26.750 --> 01:57:31.460

Elijah W. Stommel: And those would include dioxins, PAHs, PCBs.

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01:57:31.590 --> 01:57:36.610

Elijah W. Stommel: Metals and nanoparticles, all of which can be measured in brain.

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01:57:36.870 --> 01:57:44.390

Elijah W. Stommel: And... what part of the brain you want to look at depends on the toxin.

644

01:57:44.620 --> 01:57:47.689

Elijah W. Stommel: And then, of course, there are synergies between toxins.

645

01:57:48.400 --> 01:57:49.890

Elijah W. Stommel: And,

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01:57:50.210 --> 01:57:56.929

Elijah W. Stommel: We also have to consider what genes are turned on or off, which Kevin will talk about in a little more detail.

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01:57:59.220 --> 01:58:12.089

Elijah W. Stommel: And should the veteran ALS patients be stratified? Dr. Weiskopf talked about this yesterday. I was interested to hear that the Coast Guard seemed to have the highest rate of ALS,

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01:58:12.460 --> 01:58:17.010

Elijah W. Stommel: So, they do spend a lot of time in helicopters and boats.

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01:58:18.170 --> 01:58:21.899

Elijah W. Stommel: So, practicalities... next slide.

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01:58:24.130 --> 01:58:28.750

Elijah W. Stommel: Getting brain tissue is not necessarily as easy as it looks.

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01:58:28.880 --> 01:58:33.090

Elijah W. Stommel: And, it's especially hard to get control of brain tissue.

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01:58:33.250 --> 01:58:41.270

Elijah W. Stommel: Some of the toxins can be missing. Their half-lives may not be long enough to be actually measured.

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01:58:41.520 --> 01:58:46.950

Elijah W. Stommel: And different exposures between individuals, may be missing.

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01:58:47.240 --> 01:58:50.310

Elijah W. Stommel: The timing of exposures is important.

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01:58:50.580 --> 01:58:55.290

Elijah W. Stommel: Other potential risk factors that I mentioned previously might be things like head trauma.

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01:58:55.290 --> 01:58:56.050

Fang Fang: I promise.

657

01:58:56.410 --> 01:58:58.640

Elijah W. Stommel: family history.

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01:58:59.140 --> 01:59:07.979

Elijah W. Stommel: metabolic issues, athleticism, smoking, and maybe even vaccinations. The, veterans do get a lot of vaccinations.

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01:59:08.440 --> 01:59:17.720

Elijah W. Stommel: And even where you've been, residing, which military base you're on, could have an effect as well.

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01:59:18.420 --> 01:59:22.309

Elijah W. Stommel: So, you want to ask... oh, next slide.

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01:59:23.220 --> 01:59:33.500

Elijah W. Stommel: You want to ask early for tissues, as early as you possibly can. There may be deficiencies in demographic information.

662

01:59:34.100 --> 01:59:37.320

Elijah W. Stommel: And getting controls is particularly difficult.

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01:59:37.420 --> 01:59:38.600

Elijah W. Stommel: Next slide.

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01:59:41.380 --> 01:59:52.090

Elijah W. Stommel: So, we've... Approached and received, brain tissues from the following brain banks,

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01:59:52.510 --> 01:59:55.160

Elijah W. Stommel: And it's been a process,

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01:59:55.340 --> 01:59:59.820

Elijah W. Stommel: But our program officer, our program,

667

02:00:01.310 --> 02:00:07.380

Elijah W. Stommel: operational person, Kay Sullivan, has been very important in getting these samples.

668

02:00:07.740 --> 02:00:14.180

Elijah W. Stommel: This is just to mention some of the brain banks that we've gone to.

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02:00:15.200 --> 02:00:19.460

Elijah W. Stommel: Our specific aims include a bulk analysis.

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02:00:19.570 --> 02:00:24.660

Elijah W. Stommel: Of brain tissue, looking at lipophilic organic compounds that don't go away.

671

02:00:25.240 --> 02:00:28.470

Elijah W. Stommel: Persistent organic pollutants.

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02:00:28.790 --> 02:00:34.610

Elijah W. Stommel: And our second, Specific game is to look at metals and elements.

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02:00:35.000 --> 02:00:39.000

Elijah W. Stommel: On a spatial level, Oh, this is the next slide, I'm sorry.

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02:00:40.100 --> 02:00:41.309

Elijah W. Stommel: Two slides.

675

02:00:43.530 --> 02:00:48.129

Elijah W. Stommel: And our third, specific aim is to,

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02:00:49.150 --> 02:00:56.170

Elijah W. Stommel: Look at the ultrastructure of nanoparticles, That are certainly, abundant.

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02:00:56.310 --> 02:00:58.680

Elijah W. Stommel: in military operations.

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02:00:58.850 --> 02:01:05.999

Elijah W. Stommel: And I'll go into that in a little more detail. And then our fourth specific game, Kevin is going to talk about.

679

02:01:06.960 --> 02:01:10.110

Elijah W. Stommel: I think I'll skip the next slide.

680

02:01:10.850 --> 02:01:12.530

Elijah W. Stommel: Skip... yeah, there we go.

681

02:01:13.010 --> 02:01:23.909

Elijah W. Stommel: So the highlights... of this study are that the research is uniquely focused on the U.S. population of

682

02:01:24.090 --> 02:01:28.520

Elijah W. Stommel: veterans who are at higher risk of developing ALS

683

02:01:28.870 --> 02:01:40.579

Elijah W. Stommel: It's a multidisciplinary form of research, so, where one person may be deficient in knowledge, somebody else will have quite a bit of knowledge, and we can work together.

684

02:01:41.150 --> 02:01:52.680

Elijah W. Stommel: And we're... we aim to evaluate the in-situ location, concentration, and potential synergy of a variety of long-term toxins.

685

02:01:53.100 --> 02:02:01.879

Elijah W. Stommel: And we're able to look at nanoparticle characteristics at the subcellular level with EM.

686

02:02:02.120 --> 02:02:07.980

Elijah W. Stommel: And with EDX, And look at associated ultrastructural damage.

687

02:02:08.310 --> 02:02:10.270

Elijah W. Stommel: Next slide.

688

02:02:12.770 --> 02:02:18.100

Elijah W. Stommel: When does ALS start? There was a recent paper

689

02:02:19.110 --> 02:02:36.110

Elijah W. Stommel: done in Great Britain, where they showed that colonic polyps from patients who eventually developed ALS showed the pathology of TDP43 25 years before the diagnosis was made. It's an extraordinary paper.

690

02:02:36.260 --> 02:02:42.429

Elijah W. Stommel: There's a genetic predisposition, which certainly plays a role.

691

02:02:42.890 --> 02:02:49.350

Elijah W. Stommel: And, in veterans, In general, they developed ALS about 10 years after deployment.

692

02:02:49.640 --> 02:02:55.589

Elijah W. Stommel: And at an earlier age, because they're, by definition, young when they go into the military.

693

02:02:56.000 --> 02:03:01.259

Elijah W. Stommel: When patients show up in our clinics with ALS,

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02:03:01.670 --> 02:03:04.439

Elijah W. Stommel: About half the motor neurons are already gone.

695

02:03:05.080 --> 02:03:09.750

Elijah W. Stommel: It makes it easier to make a diagnosis, but it makes it much harder to treat.

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02:03:10.140 --> 02:03:17.129

Elijah W. Stommel: So, early biomarkers and risk profiles, are very, important.

697

02:03:17.290 --> 02:03:18.740

Elijah W. Stommel: Next slide.

698

02:03:19.730 --> 02:03:29.960

Elijah W. Stommel: So our specific aim number one, looking at persistent organic pollutants in brain tissue, is being done by Dr. Bijan Yan's lab at Columbia.

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02:03:30.500 --> 02:03:33.560

Elijah W. Stommel: And we're looking at dioxins and PAHs.

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02:03:33.690 --> 02:03:41.330

Elijah W. Stommel: The dioxins are looked at with gas chromatography, and the PAHs are looked at with liquid chromatography.

701

02:03:44.780 --> 02:03:57.559

Elijah W. Stommel: We expect that about greater than 90% of the dioxins and PAHs can be measured in a 0.75 gram, piece of tissue.

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02:03:57.940 --> 02:04:10.059

Elijah W. Stommel: We did do a pilot study because this tissue is very valuable, and we found that the PAHs and dioxins are pretty well distributed throughout the brain.

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02:04:10.210 --> 02:04:20.360

Elijah W. Stommel: And I won't go into the details of this, because we're so pressed for time, but we were able to show that the anatomical location, to measure these

704

02:04:20.600 --> 02:04:27.740

Elijah W. Stommel: Substances is not particularly necessary. All right, so next slide.

705

02:04:28.920 --> 02:04:30.359

Elijah W. Stommel: And then the next slide.

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02:04:33.760 --> 02:04:40.290

Elijah W. Stommel: So... Polycyclic aromatic hydrocarbons,

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02:04:41.060 --> 02:04:45.579

Elijah W. Stommel: Actually activate the aryl hydrocarbon receptor.

708

02:04:45.820 --> 02:04:57.489

Elijah W. Stommel: and impair TDP43 degradation, and can lead to accumulation of TDP43 in cells, can lead to DNA damage, mitochondrial dysfunction.

709

02:04:57.750 --> 02:05:03.960

Elijah W. Stommel: reactive oxygen species, and even apoptosis. So that's important. Next slide.

710

02:05:04.880 --> 02:05:17.400

Elijah W. Stommel: And I already mentioned this, different, methods are used to measure the PAHs versus The, dioxins.

711

02:05:17.830 --> 02:05:18.990

Elijah W. Stommel: Next slide.

712

02:05:19.480 --> 02:05:29.290

Elijah W. Stommel: And there have been measurements near burn pits in the military where various PAHs and dioxins have been, measured and quantified.

713

02:05:29.500 --> 02:05:31.070

Elijah W. Stommel: Next slide.

714

02:05:32.660 --> 02:05:41.880

Elijah W. Stommel: Dr. Beijan Yan's lab also, is interested in nanoplastics, and he actually made, the news

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02:05:42.090 --> 02:05:51.100

Elijah W. Stommel: He made the news, I heard about him on NPR once, where he came up with a method to measure nanoplastics.

716

02:05:51.280 --> 02:05:57.970

Elijah W. Stommel: in, in tissues. And in liquids as well.

717

02:05:58.140 --> 02:06:00.240

Elijah W. Stommel: Next slide.

718

02:06:01.630 --> 02:06:11.490

Elijah W. Stommel: He uses pyrolysis and simulated Ramond scattering to measure microplastics.

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02:06:11.690 --> 02:06:14.949

Elijah W. Stommel: And microplastics are really quite common.

720

02:06:15.210 --> 02:06:20.980

Elijah W. Stommel: In the military, environment, Boat...

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02:06:21.420 --> 02:06:32.820

Elijah W. Stommel: 5-6% of what's burned in pits, are plastics, and about 50-65% of military uniforms are made of plastics.

722

02:06:33.260 --> 02:06:36.739

Elijah W. Stommel: And these microplastics have been shown

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02:06:37.020 --> 02:06:47.179

Elijah W. Stommel: To cause oxidative stress, neuroinflammation, and they also carry the ability to carry toxins, other toxins, into the central nervous system.

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02:06:48.960 --> 02:06:51.809

Elijah W. Stommel: I think you can go to the next slide.

725

02:06:51.980 --> 02:06:54.890

Elijah W. Stommel: So this is where Dr. Young

726

02:06:55.160 --> 02:07:01.319

Elijah W. Stommel: Had quite a bit of publicity with his... Roman spectroscopic method.

727

02:07:01.750 --> 02:07:03.010

Elijah W. Stommel: Next slide.

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02:07:03.310 --> 02:07:06.530

Elijah W. Stommel: This is a really interesting fact,

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02:07:07.350 --> 02:07:19.669

Elijah W. Stommel: And I'm gonna run out of time here, I'm sure. A typical bottle of plastic... a plastic bottle of water, drinking water, contains a thousand times less

730

02:07:20.140 --> 02:07:25.500

Elijah W. Stommel: microplastics than the CSF in a typical adult patient.

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02:07:25.830 --> 02:07:30.069

Elijah W. Stommel: And the microplastics tend to increase with time.

732

02:07:31.340 --> 02:07:37.379

Elijah W. Stommel: So when you get to be 70, you have quite a bit more than when you were in your 30s.

733

02:07:38.060 --> 02:07:45.389

Elijah W. Stommel: So, the next specific game is directed by Brian Jackson, who has a core facility at Dartmouth.

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02:07:45.750 --> 02:07:55.569

Elijah W. Stommel: And we've set about to evaluate the concentrations of a variety of toxic metals and ailments in CNS samples.

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02:07:55.910 --> 02:08:07.140

Elijah W. Stommel: And we hypothesize that metal elements, concentrations, spatial localization, and synergistic effects will differ between the VA population

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02:08:07.520 --> 02:08:15.729

Elijah W. Stommel: Who deployed an... Control groups, both VA and non-VA control groups.

737

02:08:16.730 --> 02:08:19.070

Elijah W. Stommel: Next slide.

738

02:08:19.330 --> 02:08:21.790

Elijah W. Stommel: Sorry, you'll have to go to the next slide.

739

02:08:23.110 --> 02:08:30.270

Elijah W. Stommel: These are just some representative images, from Dr. Jackson's lab. These are axial cuts.

740

02:08:30.460 --> 02:08:38.900

Elijah W. Stommel: through spinal cord, and you can see the various metals, being measured. Next slide.

741

02:08:41.060 --> 02:08:45.230

Elijah W. Stommel: And this is a... Higher resolution picture of,

742

02:08:45.340 --> 02:08:55.389

Elijah W. Stommel: 3 different, metals in spinal cord. And this is such a, A granular system

743

02:08:55.500 --> 02:09:00.869

Elijah W. Stommel: That you can get down to a single cell level and see what metals are prevalent.

744

02:09:01.050 --> 02:09:03.529

Elijah W. Stommel: What elements are present?

745

02:09:05.450 --> 02:09:09.090

Elijah W. Stommel: That'll be important for, what...

746

02:09:09.200 --> 02:09:12.690

Elijah W. Stommel: Kevin Cornell's going to talk about. Next slide.

747

02:09:13.800 --> 02:09:17.759

Elijah W. Stommel: These are just some other images. On the left is cadmium.

748

02:09:18.140 --> 02:09:22.900

Elijah W. Stommel: And on the right is, I believe that's iron.

749

02:09:23.850 --> 02:09:27.340

Elijah W. Stommel: And here's some showing Mercury.

750

02:09:28.640 --> 02:09:35.080

Elijah W. Stommel: So, I'm not a statistician, but logistic regression results

751

02:09:36.070 --> 02:09:43.300

Elijah W. Stommel: show that ALS metal analysis adjusting for age, sex, and batch In the regression.

752

02:09:44.070 --> 02:09:50.629

Elijah W. Stommel: out of a total of 276 participants, 122 of which were ALS cases.

753

02:09:50.910 --> 02:09:55.399

Elijah W. Stommel: Veteran ALS cases, and 154 being controls.

754

02:09:55.500 --> 02:10:09.470

Elijah W. Stommel: That there... our, certain... Odds that are higher Or lower, sodium Being the highest,

755

02:10:10.010 --> 02:10:14.620

Elijah W. Stommel: And then cobalt, iron, zinc, Magnesium and sulfur.

756

02:10:14.970 --> 02:10:18.050

Elijah W. Stommel: And lower odds are there on the right.

757

02:10:18.540 --> 02:10:20.740

Elijah W. Stommel: Next slide.

758

02:10:21.990 --> 02:10:27.749

Elijah W. Stommel: And when you use a joint metal mixture associated with higher ALS odds.

759

02:10:27.940 --> 02:10:36.410

Elijah W. Stommel: Using a quantile G computation on 26... 27 metals adjusted for age, sex, and batch.

760

02:10:36.540 --> 02:10:46.109

Elijah W. Stommel: You can see, a... Simultaneous one quartile increase in every mixture component.

761

02:10:46.340 --> 02:10:52.300

Elijah W. Stommel: Associated with approximately 9.9-fold higher odds of ALS.

762

02:10:52.720 --> 02:11:00.839

Elijah W. Stommel: And if there's time later on, Zhang Gui, our statistician, can go into that in more detail.

763

02:11:01.350 --> 02:11:05.170

Elijah W. Stommel: And then...

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02:11:06.060 --> 02:11:14.910

Elijah W. Stommel: positive direction. I thought it was interesting that sulfur is high in the list, especially after listening to Dr. Petty's lecture.

765

02:11:15.400 --> 02:11:19.810

Elijah W. Stommel: And, thallium, was a negative direction.

766

02:11:20.000 --> 02:11:23.949

Elijah W. Stommel: So, these risks can be categorized in that, in that manner.

767

02:11:26.580 --> 02:11:37.450

Elijah W. Stommel: And lastly, I'll just briefly talk about Lillian, Calderin's work. She's, Neuropathologists.

768

02:11:37.740 --> 02:11:46.009

Elijah W. Stommel: And a toxicologist who spends some of her time in Mexico City and has looked at the population there because of the air pollution there.

769

02:11:46.410 --> 02:11:54.249

Elijah W. Stommel: We'd like to characterize the composition, size, shape, and location of nanoparticles

770

02:11:54.680 --> 02:11:57.989

Elijah W. Stommel: And their association with ultrastructural damage

771

02:11:58.260 --> 02:12:02.340

Elijah W. Stommel: In our veteran population versus controls.

772

02:12:02.480 --> 02:12:10.039

Elijah W. Stommel: And we still haven't really started this. We do have the tissues, and we're planning to start using them soon.

773

02:12:10.670 --> 02:12:12.760

Elijah W. Stommel: Next slide.

774

02:12:13.690 --> 02:12:27.039

Elijah W. Stommel: The sources of nanoparticles have been talked about, quite a bit today and yesterday, but, combustion engines, burning fossil fuels, motor vehicle, use, jet exhaust, diesel exhaust.

775

02:12:27.350 --> 02:12:32.550

Elijah W. Stommel: Burn pits, waste incinerators, and electronic waste are all important.

776

02:12:32.780 --> 02:12:34.449

Elijah W. Stommel: Especially in this setting.

777

02:12:34.780 --> 02:12:36.260

Elijah W. Stommel: Next slide.

778

02:12:36.690 --> 02:12:40.239

Elijah W. Stommel: These nanoparticles can lead to oxidative stress.

779

02:12:40.550 --> 02:12:44.499

Elijah W. Stommel: They can directly damage membranes, cell membranes.

780

02:12:45.210 --> 02:12:50.459

Elijah W. Stommel: They can lead to apoptosis, a dysregulation of autophagy.

781

02:12:50.770 --> 02:12:57.119

Elijah W. Stommel: And they can create immune responses and neuroinflammation, and also break down the blood-brain barrier.

782

02:12:57.390 --> 02:12:59.409

Elijah W. Stommel: And some of them are magnetic.

783

02:12:59.530 --> 02:13:02.190

Elijah W. Stommel: Next slide.

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02:13:03.090 --> 02:13:11.430

Elijah W. Stommel: Metal nanoparticles are quite common, especially in the setting of combustion engines and diesel exhaust and jet exhaust.

785

02:13:11.570 --> 02:13:19.829

Elijah W. Stommel: And, when you go under power lines, or when you're using your cell phone with its 5G capabilities.

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02:13:19.980 --> 02:13:24.699

Elijah W. Stommel: You may very well be moving these particles around inside your brain.

787

02:13:25.080 --> 02:13:26.909

Elijah W. Stommel: Next slide.

788

02:13:27.770 --> 02:13:37.630

Elijah W. Stommel: So we need trans-electron microscopy To, properly evaluate the nanoparticles, And,

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02:13:37.850 --> 02:13:45.239

Elijah W. Stommel: It can target things like mitochondria, Golgi apparatus, lysosomes, and nuclei.

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02:13:45.450 --> 02:13:52.580

Elijah W. Stommel: And they can break down the nuclear membranes, break down heterochromatin, and the nucleoli.

791

02:13:54.870 --> 02:14:03.369

Elijah W. Stommel: So the properties, the material properties of these nanoparticles are very important, and they have a very high surface area to volume ratio.

792

02:14:03.930 --> 02:14:12.429

Elijah W. Stommel: And the particle number concentrations are certainly very important. Next slide.

793

02:14:13.820 --> 02:14:15.310

Elijah W. Stommel: You can go to the next slide.

794

02:14:18.140 --> 02:14:20.260

Elijah W. Stommel: So...

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02:14:20.570 --> 02:14:32.229

Elijah W. Stommel: with this technique, we can use energy dispersive X-ray spectroscopy and actually identify what metals we're looking at in the nanoparticles.

796

02:14:32.370 --> 02:14:44.630

Elijah W. Stommel: And iron is by far the most common intracellular heavy magnetic metal, and it can associate with any number of other elements and metals.

797

02:14:44.750 --> 02:14:45.920

Elijah W. Stommel: Next slide.

798

02:14:47.240 --> 02:14:53.279

Elijah W. Stommel: This is a, transient picture on the...

799

02:14:53.590 --> 02:15:03.170

Elijah W. Stommel: left, and the EDX on the right. These are iron nanoparticles with a superimposed gold grid.

800

02:15:03.720 --> 02:15:06.370

Elijah W. Stommel: So there is evidence of gold there as well.

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02:15:07.730 --> 02:15:12.280

Elijah W. Stommel: Lastly, on the left.

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02:15:12.550 --> 02:15:22.539

Elijah W. Stommel: Is a red blood cell in a healthy control, full of nanoparticles that's making contact with the endothelial cells

803

02:15:22.710 --> 02:15:28.550

Elijah W. Stommel: And those in the lower left, those endothelial cells can absorb

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02:15:28.720 --> 02:15:34.629

Elijah W. Stommel: The nanoparticles then can get across the blood-brain barrier and get into the brain.

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02:15:35.040 --> 02:15:37.260

Elijah W. Stommel: On the right is an ALS case.

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02:15:37.830 --> 02:15:53.460

Elijah W. Stommel: Where the nanoparticles Are, breaking down The, nuclear pores, And, also affecting the the... various...

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02:15:54.290 --> 02:15:57.819

Elijah W. Stommel: Chromatin inside the cells, inside the nuclei.

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02:15:58.050 --> 02:16:05.119

Elijah W. Stommel: So, thank you, for this very short, rushed presentation.

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02:16:05.270 --> 02:16:09.929

Elijah W. Stommel: I want to thank the CDC for their,

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02:16:10.880 --> 02:16:21.180

Elijah W. Stommel: funding me, and I want to thank my extensive collaborators and their help with this research project. Thank you.

Spatial multiomics to reveal focal pathologies in ALS postmortem cortical tissue

Geisel School of Medicine at Dartmouth - Kevin Cornell

811

02:16:35.080 --> 02:16:36.010

Kevin Cornell: Alright.

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02:16:36.830 --> 02:16:51.400

Kevin Cornell: Thank you, Dr. Stommel, for giving me a part of your talk. I think we're a little pressed for time, so I'll try to be brief. I might skip over a few sections here to get over to what probably matters most of this part of the presentation, but...

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02:16:51.559 --> 02:17:07.199

Kevin Cornell: And, you know, thank you for the CDC group for letting me present as well. So, you know, Dr. Stommel has talked a lot about our bulk testing of toxicants, but, you know, he mentioned earlier what we really want to understand and learn is, you know, what are some of these toxicants actually doing?

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02:17:07.200 --> 02:17:15.629

Kevin Cornell: To our patients here, to start trying to really dissect which one, which, you know, toxins and metals might matter the most.

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02:17:15.629 --> 02:17:22.549

Kevin Cornell: And one of these methods that we have developed for the CDC grant is to use some methods in spatial biology. So instead of

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02:17:22.549 --> 02:17:41.250

Kevin Cornell: You know, mashing up tissue and putting it in a machine and getting quantitative results for some of these things, we actually retain some of the anatomical components of the cortex samples and spinal cord, and actually compare some of these toxicants where they are to specific genes, cell populations, and proteins.

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02:17:42.150 --> 02:17:53.970

Kevin Cornell: And, you know, the hope is here to, you know, really try to understand between all these risk factors, you know, which ones truly matter the most, and maybe even start looking into patient-specific biomarkers. Next slide, please.

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02:17:57.980 --> 02:18:13.990

Kevin Cornell: Yeah, so really quickly, you know, we're all so familiar with all of this work. Regarding environmental risk factors, there's a handful of them, and, you know, how they potentially cause this devastating disease. We can kind of skip along this section. Next slide.

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02:18:14.250 --> 02:18:25.930

Kevin Cornell: But the main takeaway I just really wanted to, you know, show here that, you know, we need to really untangle all these complex risk factors that contribute to some of the mechanisms that'll lead to disease over time.

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02:18:25.930 --> 02:18:46.510

Kevin Cornell: you know, I really kind of subscribe to this idea, this multi-step hypothesis, where it's not necessarily, you know, one cause for the disease, but, you know, multiple causes over the course of someone's life, that eventually lead to, you know, cascade into the tipping point of disease onset and rapid progression for many of our patients. Next slide, please.

821

02:18:49.430 --> 02:19:08.259

Kevin Cornell: And so the main point here is, you know, there's so many different potential risk factors, exposure routes, dose timing, all these things likely influence different, pathways and pathological hallmarks, which in turn can maybe explain some of the patient heterogeneity, differences in patient side of onset, upper versus lower motor neuron.

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02:19:08.260 --> 02:19:13.769

Kevin Cornell: dominance, progression rates, age of diagnosis, survival, etc, etc.

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02:19:14.020 --> 02:19:34.680

Kevin Cornell: And so, you know, there's also evidence that some of these toxicants, you know, may induce subtle changes over time that might be statistically overlooked by a lot of the incredible work that, you know, everyone else is doing right now, whether it's bulk sampling or epidemiologically. And so, you know, our hope is here to maybe develop another method that can kind of untangle some of these,

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02:19:34.680 --> 02:19:36.739

Kevin Cornell: cofactors here. Next slide.

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02:19:38.250 --> 02:19:45.810

Kevin Cornell: So here, this sub-aim, I'm looking at, you know, why metals, are a specific environmental risk factor. You know, metals are very interesting, where...

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02:19:45.850 --> 02:20:00.949

Kevin Cornell: It's kind of twofold. One, you have essential metals. There's about 20 essential to human life that are tightly regulated through cell signaling, transportation, sequestration, and other mechanisms. And, you know, subtle changes to these metals may,

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02:20:00.950 --> 02:20:20.569

Kevin Cornell: cause vulnerability to metal dyshomeostasis, where, you know, these minor changes in abundance can actually have cascading effects, larger effects, copper being one of note in the literature due to its low abundance, sensitivity to change, and role as a cofactor in the SOD1 protein.

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02:20:20.740 --> 02:20:43.059

Kevin Cornell: On the other end of this, there's also elements that are toxic. Some of the leading ones we know, arsenic, lead, and mercury. And so, you know, elements interact very interesting in what I call the metallomic profile, where we have all these elements that are interacting with each other, interacting with our biology, competing for binding sites, transport disruption, oxidative stress, things like that.

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02:20:43.060 --> 02:20:46.749

Kevin Cornell: So it's really, really important to be looking at all these metals all together.

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02:20:47.040 --> 02:20:48.270

Kevin Cornell: Next slide, please.

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02:20:48.420 --> 02:20:49.839

Kevin Cornell: Next slide, please, again.

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02:20:51.990 --> 02:21:06.150

Kevin Cornell: You know, so this is from our CDC colleagues who aggregated all these, you know, all this data on metal, on metals and ALS risk, and, you know, the take-home

question is, we see so many that are associated, some with conflicting results, some unresolved.

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02:21:06.150 --> 02:21:13.139

Kevin Cornell: Which metals truly matter? And do metals, which tend to aggregate differently in different components of

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02:21:13.140 --> 02:21:16.939

Kevin Cornell: of tissue, where do they matter the most?

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02:21:17.160 --> 02:21:28.390

Kevin Cornell: And are we missing certain risk factors because of this kind of masking effect from bulk tissue measurements? And how do we establish more of a causal role with metals and ALS pathology? Next slide, please.

836

02:21:30.590 --> 02:21:45.090

Kevin Cornell: So the experimental overview is... so this is the fourth aim for the CDC grant. You know, in concept, it's... it's fairly... fairly simple. We have these... we have a piece of brain tissue, and we are able to, with proper handling.

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02:21:45.090 --> 02:21:50.910

Kevin Cornell: Techniques and preparation techniques, creates slides of these tissues to do different assays.

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02:21:50.910 --> 02:22:09.779

Kevin Cornell: In this experiment, we did elemental imaging, which Dr. Stommel showed earlier with the metal maps. We did neuropathological annotations of cortical layers, using HNE staining, and then spatial transcriptomics using 10X Genomics Visium of cytosist, and I'll get into more of these in a second. Next slide, please.

839

02:22:13.200 --> 02:22:37.239

Kevin Cornell: So, elemental imaging, as Dr. Sommel showed, essentially we can put a tissue slide on... a piece of tissue onto a slide and do laser-ablated ICPMS, which creates these beautiful metal maps of all the tissue, of up to 40 elements. These things vary in sensitivity and specificity, depending on what metals we want to look at and how confidently we know and want to know those metals.

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02:22:37.240 --> 02:22:39.030

Kevin Cornell: are there and want to quantify them.

841

02:22:39.030 --> 02:22:40.080

Kevin Cornell: Next slide.

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02:22:40.390 --> 02:22:46.639

Kevin Cornell: And here's, like, a much more detailed version of one of the samples from this pilot experiment I'm about to show you.

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02:22:46.990 --> 02:22:52.260

Kevin Cornell: And, you know, this is a look at iron and a nice piece of motor cortex. Next slide, please.

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02:22:54.220 --> 02:23:07.249

Kevin Cornell: And what we can do, we can take those metal imaging matrices or maps of all the metals that we've scanned for using that machine, and overlay them with whole slide imaging information. And this can range for anything from

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02:23:07.250 --> 02:23:15.840

Kevin Cornell: neuropathological annotations, such as shown here of the cortical layers. Myself and the neuropathologist did.

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02:23:16.120 --> 02:23:23.110

Kevin Cornell: And... but it also could be, certain proteins that we want to look for, such as TDP43, whatever it might be.

847

02:23:23.430 --> 02:23:39.000

Kevin Cornell: And we've done quite a bit of work over the last couple years basically verifying this work, that these disparate serial section and tissue sections are actually overlaying properly. It's a mix of manual methods and machine learning that do it, and we're actively publishing these methods right now.

848

02:23:39.800 --> 02:23:41.049

Kevin Cornell: Next slide, please.

849

02:23:42.260 --> 02:23:52.549

Kevin Cornell: And what we get are these really kind of comprehensive spatial analyses of where metals are aggregating within cortical tissue. You know, to really... to really summarize,

850

02:23:52.980 --> 02:23:59.920

Kevin Cornell: these, you know, results. We're comparing right now a SOD in one case who did not have any

851

02:23:59.920 --> 02:24:20.170

Kevin Cornell: ALS diagnosis, and a sporadic ALS case on the bottom for case number 2, who had a very aggressive, was a young patient, case of ALS, and was confirmed sporadic. And what we can do, we can compare metal aggregations within these layers between, different groups at the donor level, or even within a single donor

852

02:24:20.170 --> 02:24:25.129

Kevin Cornell: And what we see is that we see certain metals aggregate at certain layers,

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02:24:25.290 --> 02:24:42.820

Kevin Cornell: for example, we see iron and manganese peak in cortical layer 5, which is a really important layer that houses a lot of our motor neurons, and tends to be heavily affected with people with ALS, and we see a decrease in zinc in that layer. And we see these more, we see basically a higher,

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02:24:42.990 --> 02:24:50.560

Kevin Cornell: a much higher level of these differences in our sporadic case compared to our familial cases in this experiment.

855

02:24:50.810 --> 02:24:53.689

Kevin Cornell: For basically all the intensities of the metals that we looked at.

856

02:24:55.160 --> 02:24:56.370

Kevin Cornell: Next slide, please.

857

02:24:58.330 --> 02:25:06.349

Kevin Cornell: And next, we do this thing called spatial transcriptomics. I'm sorry, it looks at my slides, got a little, obscured when I transferred it over.

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02:25:06.720 --> 02:25:14.220

Kevin Cornell: But to briefly touch on what transcriptomics are, you know, it's the central dogma biology. DNA makes RNA, which makes

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02:25:14.230 --> 02:25:37.600

Kevin Cornell: proteins, and we're looking at this RNA part, where genes are basically expressing certain things based off the biology that is happening. And so, you know, transcriptomics are a really nice snapshot to understand, you know, what types of cells are occurring at that spot, spatially, in the case of spatial transcriptomics, what type of genes are being upregulated or down-regulated, and what pathologies are specific to that region.

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02:25:37.600 --> 02:25:42.489

Kevin Cornell: Which is being overlaid with these elemental maps, as I showed before.

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02:25:42.860 --> 02:26:00.770

Kevin Cornell: And so, just a brief look at kind of how it works. You know, these slides are quite expensive, and so we can... for this experiment, we took just regions of interest, where I try to capture all the cortical layers, as well as white matter, into the transcriptomics pipeline, and then we can overlay the metals

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02:26:00.770 --> 02:26:12.409

Kevin Cornell: and do a pretty standard transcriptomics workflow, which I'm not going to get into now, which basically estimate the up-regulated genes in those spots that are most differentially expressed.

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02:26:12.620 --> 02:26:25.860

Kevin Cornell: As well as the estimated cell types in those regions as well. And so, just down here, you can kind of see very similar spatial patterns for where zinc and manganese are, compared to some really important genes, involving

864

02:26:25.890 --> 02:26:34.959

Kevin Cornell: Involving neuronal synapses, as well as astrocytes, and also the cell types that are most associated with those metals as well.

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02:26:35.040 --> 02:26:36.309

Kevin Cornell: Next slide, please.

866

02:26:38.710 --> 02:26:53.530

Kevin Cornell: And, you know, there's so many things and analyses that we've done, there's pilot experiments that we've done to basically wrinkle out some of the things we're going to be doing for our CDC grant, but, you know, for this, over... some interesting things that really stand out, first of all, only iron and zinc were

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02:26:53.530 --> 02:27:04.080

Kevin Cornell: correlated to sporadic ALS cases, our two sporadic compared to our two familial, as differently expressed genes, and this kind of goes true with the pathway analyses, as well as the cell types.

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02:27:04.080 --> 02:27:23.289

Kevin Cornell: And then manganese and zinc were correlated with, all the familial, differently expressed genes, and metals were mostly correlated with glial or normal cell signaling. You know, all this slide is really basically show you, when we look at the whole tissue, you know, unbiased, whole tissue, we see pretty standard

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02:27:23.290 --> 02:27:30.969

Kevin Cornell: Gene upregulations and cells that are associated in, essentially, healthy tissue, essentially healthy, healthy,

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02:27:31.270 --> 02:27:49.490

Kevin Cornell: cells and biology. But... next slide, please. But when we start to dissect this more regionally, so when we actually incorporate those cortical layers, and we can compare cortical layers within either a single group of donors, or even with a single donor itself, to compare what's going on between these layers, we see something really interesting.

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02:27:49.490 --> 02:28:12.560

Kevin Cornell: And the one thing that really stands out here is that iron is heavily associated with this vulnerable layer, layer 5 of the motor cortex. Essentially, iron is associated, when you look at the whole tissue, with neurons. But when you just look at this

one layer, it switches to being more associated with reactive astrocytes. And essentially, these cells are kind of telling us, hey, iron is here.

872

02:28:12.560 --> 02:28:19.190

Kevin Cornell: These astrocytes are doing something in response to neuronal death or other pathologies.

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02:28:19.330 --> 02:28:28.769

Kevin Cornell: And is also correlated with, you know, most correlated with this gene, FTL, ferritin light chain, which basically is an iron sequestration gene. And so.

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02:28:29.080 --> 02:28:39.009

Kevin Cornell: We found that really, really interesting, that because when we look at this more granular level of cortical layers, we see pretty drastic shifts in these gene expressions associated with these metals.

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02:28:39.110 --> 02:28:40.979

Kevin Cornell: Next slide, please.

876

02:28:45.070 --> 02:28:52.850

Kevin Cornell: And then the last thing we can do, we can do some focus pathway analyses based on metal concentrations. And so, one thing we did for this kind of last

877

02:28:52.850 --> 02:29:17.100

Kevin Cornell: aim here of this pilot experiment is we took a curated version... curated library of all known pathologies associated with ALS, and all those genes responsible for those pathologies. And we basically wanted to see, okay, which ones are most differentially expressed in areas of high, amounts of these elements based off these spatial overlays. And what we found with iron is that iron is most associated with

878

02:29:17.450 --> 02:29:33.909

Kevin Cornell: High iron is most different. The genes and pathways, associated with high levels of iron are oxidative phosphorylation and aberrant TDP43 to electron transfer and complex I. You know, very, very cool, that we are seeing some things that,

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02:29:33.990 --> 02:29:40.530

Kevin Cornell: may or may be associated with ALS pathology and high iron concentrations, and

880

02:29:40.650 --> 02:29:45.609

Kevin Cornell: And, it kind of helps us proof of concept, show that some of these methods might be working.

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02:29:46.230 --> 02:29:47.509

Kevin Cornell: Next slide, please.

882

02:29:49.620 --> 02:29:59.439

Kevin Cornell: So, just a quick overview, you know, this is... this is very early work, this is not published yet, we're in the process of publishing it right now, and kind of wrinkling at some irons and doing more key seat.

883

02:29:59.440 --> 02:30:15.470

Kevin Cornell: QC stuff, you know, metals accumulate heterogeneously throughout cortical layers, which is very important if we want to do metal sampling. They seem to appear to be higher in sporadic ALS compared to familial, and we're doing another study right now on a different cohort, examining this a little bit closer.

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02:30:15.770 --> 02:30:36.409

Kevin Cornell: Iron and manganese increase in cortical layer 5, while zinc decreases, and iron becomes associated with reactive astrocytes in layer 5, suggesting potential involvement in motor neuron pathology. And then finally, targeted gene expression and pathways in specific tissue regions associated with metals can kind of help unravel some of this complexity that we're seeing with toxicants and risk.

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02:30:36.410 --> 02:30:40.270

Kevin Cornell: And help understand ALS pathobiology a little bit better.

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02:30:40.830 --> 02:30:42.020

Kevin Cornell: Next slide, please.

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02:30:42.480 --> 02:30:56.699

Kevin Cornell: And just a few things, you know, we're improving tissue processing methods, getting larger data sets, tighter QCs, looking at proteomics, and also implementing, you know, higher resolution assays. These are all... all these methods are using pretty...

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02:30:56.700 --> 02:31:03.420

Kevin Cornell: pretty novel, newer technologies that are improving almost, by the month. So we're keeping up a fold of that as we go.

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02:31:03.640 --> 02:31:04.610

Kevin Cornell: Next slide.

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02:31:05.770 --> 02:31:17.610

Kevin Cornell: Yeah, and thank you. There's... there's so many people involved, but, you know, here's a group that was heavily involved in this pilot experiment, and will be involved in the spatial biology aspects of some of this work. So, yeah, with that, thank you so much.

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02:31:19.340 --> 02:31:28.089

Danielle Boyce: Thank you so much, Dr. Stammel and Kevin. That was really, really fascinating, and I'm sure folks will have some

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02:31:28.090 --> 02:31:44.689

Danielle Boyce: questions, and we'll take some time to digest those while we're eating, our lunch. And if you have any questions for the panelists, or if you are a panelist and you want to answer questions, please do that during the break, and we'll continue to answer your questions directly, but I think.

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02:31:44.690 --> 02:31:47.410

Fang Fang: directly, but I think we should break...

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02:31:47.970 --> 02:31:52.499

Danielle Boyce: Whoops, we should break for lunch, and come back at 1.30. Thank you so much.

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02:57:16.440 --> 02:57:22.899

Danielle Boyce: So... Now, we're going to have a presentation, about

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02:57:22.990 --> 02:57:45.810

Danielle Boyce: the National ALS Registry and ALS Association Incentives Pilot Project. And so, as Patty mentioned yesterday, this was a collaborative effort between the ALS Association and the CDC. And so, for those of you who weren't here yesterday, I'm going to give you an introduction to Patty, and also Rajma Punjani from the CDC.

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02:57:46.450 --> 02:58:00.899

Danielle Boyce: So, Patty Stango is Associate Director of Mission Engagement at the ALS Association. 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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02:58:01.150 --> 02:58:19.200

Danielle Boyce: 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 associated with ALS at multidisciplinary clinics, support groups, and on the Hill in Washington, D.C.

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02:58:19.420 --> 02:58:32.049

Danielle Boyce: Patty brings a strong commitment to advancing the mission of ALS Association and the National ALS Registry, and obviously has a wealth of experience in many areas related to what we're talking about over the last few days.

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02:58:32.630 --> 02:58:55.590

Danielle Boyce: And then, the co-presenter today is Rishma Punjani, is a health scientist with the National ALS Registry. So, Rishma works with the registry. She joined the registry team in 2016 after earning a Master's of Public Health degree in epidemiology. Over the last decade, she has contributed to numerous peer-reviewed research papers focusing on ALS incidence and prevalence.

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02:58:55.590 --> 02:59:07.080

Danielle Boyce: Geographic access to multidisciplinary ALS care, ALS survival, and differences in ALS across populations and regions. Patty and Rishma,

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02:59:07.080 --> 02:59:08.429

Danielle Boyce: Please take it away.

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02:59:08.670 --> 02:59:12.100

Danielle Boyce: I'll get your slides loaded up if they're not already. Yep, there we go.

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02:59:14.280 --> 02:59:16.120

Danielle Boyce: Go ahead, Patty and Reshma.

National ALS Registry and ALS Association Incentives Pilot Project - Reshma Punjani, MPH – National ALS Registry, Patricia Stanco, MHS – ALS Association

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02:59:17.930 --> 02:59:34.259

Reshma Punjani: I will get started. Good afternoon, everyone, and thank you, Danielle, for the introduction. So my name is Reshma Punjani, and today I'm going to be discussing the Incentive Pilot Project, which was a collaboration between the National ALS Registry and the ALS Association.

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02:59:34.550 --> 02:59:44.279

Reshma Punjani: I'm especially excited to share this project because I've had the opportunity to lead it from initial concept through research, development, implementation, and evaluation.

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02:59:44.290 --> 03:00:06.130

Reshma Punjani: This has been a collaboration, and it's required significant work, persistence to bring this pilot to life, but it's also given us the opportunity to address a clear gap in registry participation, and to test a practical, evidence-based solution. So today, I'm going to walk you through the rationale for this pilot, how it was implemented, and the results we achieved.

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03:00:06.170 --> 03:00:07.419

Reshma Punjani: Next slide, please.

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03:00:09.100 --> 03:00:12.700

Reshma Punjani: So, I have no disclosures to report. Next slide, please.

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03:00:14.160 --> 03:00:26.799

Reshma Punjani: So, to provide some background, at the time the pilot was developed, enrollment among individuals self-enrolling in the registry and completing risk factor surveys was lower than expected based on our data estimates.

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03:00:27.090 --> 03:00:40.990

Reshma Punjani: Historically, Texas had consistently been among the states with lower enrollment compared with the national average, which highlighted an opportunity to identify strategies to increase participation in this state.

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03:00:41.520 --> 03:00:48.960

Reshma Punjani: We looked to other programs that had successfully used monetary incentives to encourage participation and engagement.

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03:00:49.320 --> 03:01:00.469

Reshma Punjani: And these previous programs had demonstrated a higher response and retention rate among participants who received a monetary incentive compared to those who did not.

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03:01:00.890 --> 03:01:13.220

Reshma Punjani: So based on this evidence, we propose to implement a small incentive pilot to assess whether providing an incentive could increase registry enrollment and participation in the risk factor surveys.

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03:01:13.730 --> 03:01:20.410

Reshma Punjani: This pilot was intended to provide practical evidence whether this approach could be feasible for the registry.

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03:01:20.620 --> 03:01:21.949

Reshma Punjani: Next slide, please.

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03:01:24.580 --> 03:01:35.450

Reshma Punjani: So this pilot had two primary goals. First was to increase participation in the registry, and second was to improve the completion rates of our 18 risk factor surveys.

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03:01:35.770 --> 03:01:49.529

Reshma Punjani: In addition to improving enrollment and survey completion percentages, we set a specific target for the pilot, enrolling at least 100 people living with ALS in the state of Texas over the 6-month period.

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03:01:50.030 --> 03:01:57.919

Reshma Punjani: Our target audience were individuals with a current ALS diagnosis who were eligible for the registry but had not yet enrolled.

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03:01:58.350 --> 03:02:06.610

Reshma Punjani: Participants also needed to be U.S. citizens or legal residents with a ALS diagnosis that reside in the state of Texas.

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03:02:07.260 --> 03:02:15.699

Reshma Punjani: Finally, the pilot focused on ALS patients residing in Texas who had enrolled with the Texas ALS Association.

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03:02:17.450 --> 03:02:18.840

Reshma Punjani: Next slide, please.

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03:02:25.060 --> 03:02:42.779

Reshma Punjani: So after establishing the goals and the target audience, we next established the inclusion and exclusion criteria that were used to determine eligibility for this pilot. For inclusion, participants needed to be registered with the Texas ALS Association and have a diagnosis of ALS.

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03:02:43.050 --> 03:02:56.240

Reshma Punjani: They could already be enrolled in the National ALS Registry, but could not have completed all of the risk factor surveys. This really provided an opportunity for those who had already registered to still be a part of the pilot.

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03:02:57.020 --> 03:03:05.840

Reshma Punjani: Participants were U.S. citizens or legal residents living in Texas, and they needed to elect to participate during the designated pilot period.

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03:03:06.410 --> 03:03:16.170

Reshma Punjani: There were also several exclusion criteria. Individuals with a non-ALS diagnosis, such as PLS, were excluded, as well as deceased individuals.

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03:03:16.490 --> 03:03:27.430

Reshma Punjani: Participants who were already enrolled in the registry and had already completed all of the risk factor surveys were also excluded because they no longer had any outstanding surveys to complete.

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03:03:28.380 --> 03:03:35.829

Reshma Punjani: In addition, individuals who were not willing to provide an email address or consent to register enrollment were excluded.

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03:03:36.160 --> 03:03:43.160

Reshma Punjani: Finally, anyone who expressed interest in participating after the pilot period had ended was also not eligible.

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03:03:43.840 --> 03:03:56.679

Reshma Punjani: So these criteria really helped us ensure that the pilot focused on our intended population, which were individuals with ALS who had not yet enrolled in the registry and still had the opportunity to do the risk factor surveys.

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03:03:57.160 --> 03:03:58.519

Reshma Punjani: Next slide, please.

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03:04:02.240 --> 03:04:14.070

Reshma Punjani: So once we had established the data justification and parameters for this project, we submitted this request to the Office of Management and Budget, and finally received the OMB approval to launch our project.

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03:04:14.330 --> 03:04:25.710

Reshma Punjani: The project was then launched statewide across Texas, and ran for a 6-month period from April 1st through October 31st, 2025, with a follow-up period.

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03:04:26.310 --> 03:04:28.819

Reshma Punjani: The incentive was structured in two parts.

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03:04:29.060 --> 03:04:34.370

Reshma Punjani: New registry enrollees received \$50 for enrolling in the registry.

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03:04:34.540 --> 03:04:41.569

Reshma Punjani: This provided that initial incentive to encourage individuals who were eligible but had not enrolled to participate.

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03:04:42.080 --> 03:04:51.089

Reshma Punjani: Then there was an additional \$100 available for both new and existing registrants who completed all the 17 risk factor surveys.

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03:04:51.460 --> 03:04:58.450

Reshma Punjani: Because there were 17 risk factor surveys, we made sure to reflect the monetary incentive to match the time burden.

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03:04:58.970 --> 03:05:09.509

Reshma Punjani: So, for a participant who was new to the registry and completed all of the required surveys, the maximum total incentive they were eligible to receive was \$150.

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03:05:09.910 --> 03:05:21.550

Reshma Punjani: And this two-step approach was designed to encourage both initial enrollment and completion of the risk factor surveys, rather than just focusing on getting individuals into the registry.

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03:05:22.040 --> 03:05:23.339

Reshma Punjani: Next slide, please.

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03:05:26.250 --> 03:05:32.830

Reshma Punjani: So this flowchart summarizes some of the eligibility and enrollment process that was used for our pilot.

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03:05:33.060 --> 03:05:41.159

Reshma Punjani: So the process truly begins when a person living with ALS learns about the pilot from the ALS Association Care Services staff.

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03:05:41.380 --> 03:05:46.670

Reshma Punjani: The first step was determining whether the individual was eligible to participate.

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03:05:47.270 --> 03:05:58.959

Reshma Punjani: So for those who were eligible, there were several possible starting points. For example, someone who had not yet enrolled in the registry, or someone who was already enrolled but hadn't completed the risk factor surveys.

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03:05:59.190 --> 03:06:02.520

Reshma Punjani: These individuals were directed to complete the enrollment form.

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03:06:03.180 --> 03:06:16.499

Reshma Punjani: So the enrollment form collected basic contact information and included consent to receive communications. The care services staff could assist with completing and submitting this form on the participant's behalf.

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03:06:17.420 --> 03:06:23.349

Reshma Punjani: So once enrolled, participants were given a defined period to complete the required risk factor surveys.

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03:06:23.630 --> 03:06:34.159

Reshma Punjani: CDC and the ALS Association communicated regularly to confirm enrollment, survey completion, and the email address associated with the registry account.

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03:06:34.950 --> 03:06:49.509

Reshma Punjani: So after the required activities were completed, ALS Association sent these participants an email gift card through Tremendous, which was the online gift card platform that was used, with instructions for redeeming their gift card.

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03:06:50.160 --> 03:06:56.190

Reshma Punjani: In addition, to reduce fraud, the gift cards were linked with the email that was used to enroll in the registry.

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03:06:56.700 --> 03:07:11.330

Reshma Punjani: Now, if you look on the right-hand side, the red pathways show situations where individuals were not eligible. For example, if they had already completed all of the risk factor surveys, or if the enrollment was completed outside of the program timeframe.

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03:07:11.780 --> 03:07:21.399

Reshma Punjani: So, as this was a collaboration with the ALS Association, Patty will speak on more details at the Texas level for enrollment, eligibility, and outreach.

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03:07:21.640 --> 03:07:23.029

Reshma Punjani: Next slide, please.

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03:07:25.330 --> 03:07:34.779

Reshma Punjani: So this slide presents our important preliminary findings. If you look on the left, Figure 1 summarizes the distribution of the gift card incentives.

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03:07:34.780 --> 03:07:49.760

Reshma Punjani: Among the participants. So if you see the largest proportion, which was 51%, or 34 participants, received the full \$150 for the incentive, which means that they created a new account and completed all risk factor surveys.

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03:07:50.430 --> 03:08:00.739

Reshma Punjani: An additional 30 participants, or 45%, received the \$50 for creating a new account. But these individuals did not go on to complete the risk factor surveys.

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03:08:01.160 --> 03:08:14.249

Reshma Punjani: And there were 4%, or 3 participants, who received the \$100, which was associated with an existing registry account. So these individuals had an account already, and then went on to complete all the risk factor surveys.

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03:08:14.670 --> 03:08:29.920

Reshma Punjani: So, also not pictured on Figure 1 is there were 39 additional individuals who completed the enrollment form with the ALS Association, but did not receive any incentives because they did not take the action to enroll in the registry.

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03:08:30.080 --> 03:08:37.329

Reshma Punjani: This could have been due to the nature and challenges of the disease, as the ALS Association did provide several methods of follow-up.

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03:08:38.170 --> 03:08:46.540

Reshma Punjani: Now, if you look on the right, Figure 2 provides a longitudinal comparison of registry enrollment before and during the pilot.

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03:08:46.580 --> 03:09:00.660

Reshma Punjani: So if you see during April through October, enrollment stayed pretty consistent. An increase from 21 new accounts in 2022 to 30 in 2023, and then followed by 25 in 2024.

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03:09:00.820 --> 03:09:13.490

Reshma Punjani: However, if you look at 2025, we observed there were 90 new registry accounts, which included the 26 non-incentivized, but then you see the jump to the 64 incentivized accounts.

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03:09:13.860 --> 03:09:20.889

Reshma Punjani: So overall, enrollment increased by approximately 260% compared with the 2024 period.

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03:09:21.160 --> 03:09:29.980

Reshma Punjani: So while these are preliminary results, the findings do suggest that the incentive approach was associated with a meaningful increase in participation.

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03:09:30.510 --> 03:09:39.009

Reshma Punjani: We can say that the incentive pilot was successful, as it demonstrated a substantial increase in registry participation during the pilot.

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03:09:39.220 --> 03:09:51.389

Reshma Punjani: The magnitude of the increase and the strong association with the incentive intervention really supports our hypothesis and the continued use of monetary incentives in the future.

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03:09:51.910 --> 03:10:09.570

Reshma Punjani: So now, currently, we are, continuing to analyze the data and really evaluate the effects of this incentive structure in greater detail. So a manuscript describing the study methodology, the full results, and a statistical analysis is currently in preparation and will be published soon.

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03:10:09.790 --> 03:10:24.790

Reshma Punjani: Finally, as Paul mentioned yesterday, we're also aiming to replicate and launch this incentive project across other under-enrolled states, such as California, Florida, or New York, pending OMB approval. Next slide, please.

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03:10:27.010 --> 03:10:40.049

Reshma Punjani: So before we go into comments and questions, I will now pass it on to Patty Stanko with the ALS Association to discuss the project implementation at the local level with the Texas Care Services staff. Thank you.

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03:10:42.620 --> 03:10:44.110

Patricia Stanco, MHS: Thanks, Freshmoths!

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03:10:45.750 --> 03:10:54.970

Patricia Stanco, MHS: So... So the afternoon on day two, but come on, we just gotta take a minute and say, wow!

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03:10:55.080 --> 03:11:01.329

Patricia Stanco, MHS: I mean, it's just... we've been wanting to try this for so long, and we have been so excited to share these results.

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03:11:01.540 --> 03:11:09.080

Patricia Stanco, MHS: And, I mean, this is very doable, so we're really, really excited about the possibilities.

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03:11:09.280 --> 03:11:13.590

Patricia Stanco, MHS: So thank you for indulging me to just...

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03:11:13.690 --> 03:11:15.859

Patricia Stanco, MHS: Gotta just do a little happy dance here.

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03:11:16.250 --> 03:11:32.059

Patricia Stanco, MHS: But I'm gonna go ahead, if we can go to the next slide, as Reshma mentioned, this is a collaboration, and we just wanted to go over some of the details about implementation, because it's never been done before, and it's like, how... how do you do this? How do you get gift cards from

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03:11:32.200 --> 03:11:45.030

Patricia Stanco, MHS: somewhere to people who do this, and what are the processes, and how does it work, and how do we make sure everything's going to flow the way we expect? So, starting with a little few details about Texas.

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03:11:45.890 --> 03:11:49.290

Patricia Stanco, MHS: The ALS Association's Texas team includes six

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03:11:49.310 --> 03:11:55.879

Patricia Stanco, MHS: care services staff, who support approximately 1,200 people living with ALS across the state.

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03:11:55.880 --> 03:12:17.079

Patricia Stanco, MHS: Texas is also home to 14 multidisciplinary clinics and 8 support groups, giving us several important touchpoints where people living with ALS and their families receive support, learn about available resources, and hear about opportunities like the National ALS Registry and the Incentive Pilot Program. These existing relationships and service networks

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03:12:17.080 --> 03:12:24.289

Patricia Stanco, MHS: helped us to create a strong foundation for introducing the Registry Incentive Pilot Program across the state. Next slide.

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03:12:26.690 --> 03:12:39.809

Patricia Stanco, MHS: And as I've said, this was truly a collaborative effort. It brought together the National ALS Registry, the ALS Association, and our Texas Care Services team, with each partner playing an important role.

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03:12:39.820 --> 03:12:52.369

Patricia Stanco, MHS: The registry provided the infrastructure of the registry itself, and taking time to confirm the participation, making sure that all of our T's were crossed and I's were dotted.

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03:12:52.900 --> 03:13:02.110

Patricia Stanco, MHS: And the ALS Association helped to design and support the outreach strategy and the process. So this included, you know, we had a kickoff webinar, we...

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03:13:03.210 --> 03:13:10.439

Patricia Stanco, MHS: Daniel, your mosquito has flown into my space, so pardon me.

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03:13:10.920 --> 03:13:29.460

Patricia Stanco, MHS: We had, flyers that we distributed both electronically and in hard copy. We had an electronic sign-up form, we had reminder emails, setting up with the gift card vendor, tracking the progress of each participant, confirming status with the CDC, and sending out those gift cards by email.

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03:13:29.460 --> 03:13:36.470

Patricia Stanco, MHS: And then our Texas Care Services team, they brought the trusted relationships that they had with the community

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03:13:36.470 --> 03:13:46.349

Patricia Stanco, MHS: that we needed for people to, be able to learn about this unique opportunity. They were able to answer questions and provide follow-up as needed.

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03:13:46.510 --> 03:13:56.659

Patricia Stanco, MHS: That partnership was critical, because this type of program relies not only on information, but also on trust, timing, and repeated communications. Next slide.

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03:13:58.450 --> 03:14:20.249

Patricia Stanco, MHS: This is what the program flyer looked like. So, to introduce the program, we created one that was in English and another in Spanish, and the sign-up form was also available in both languages. The goal was to make the opportunity clear, approachable, and easy to understand what the registry is, what exactly participants were being asked to do.

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03:14:20.250 --> 03:14:35.549

Patricia Stanco, MHS: and what incentives would be available. We wanted the flyer to feel like an invitation, rather than another complicated research request, especially because people living with ALS and their families are often managing many competing priorities, as we know.

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03:14:35.870 --> 03:14:53.599

Patricia Stanco, MHS: The flyer also helped to create consistency across outreach, so that whether someone heard about the program from a care services staff member, from an email, or through follow-up communication, the messaging was the same. So this was an important first step in making the program easy for staff to explain.

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03:14:53.600 --> 03:14:56.400

Patricia Stanco, MHS: And easy for participants to consider.

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03:14:56.740 --> 03:14:57.730

Patricia Stanco, MHS: Next slide.

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03:14:59.220 --> 03:15:13.340

Patricia Stanco, MHS: And a few additional components of implementation were that participants were asked to complete the required activities within 60 days, although additional time was granted when needed to account for the realities of living with ALS.

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03:15:13.410 --> 03:15:25.889

Patricia Stanco, MHS: Email reminders were sent throughout the process to keep the opportunity visible, answer questions, and encourage participants to take the next step. We also made volunteers available to provide virtual assistance.

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03:15:26.080 --> 03:15:33.080

Patricia Stanco, MHS: So that participants who needed help navigating the registry process had that additional support by video chat or by phone.

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03:15:33.770 --> 03:15:34.860

Patricia Stanco, MHS: Next slide.

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03:15:36.670 --> 03:15:48.339

Patricia Stanco, MHS: And then, as Reshma mentioned, you know, we had \$50 for creating the account, which typically takes 10 to 15 minutes on average, and then \$100 to complete the surveys. That can take 1-2 hours on average.

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03:15:48.350 --> 03:15:58.119

Patricia Stanco, MHS: And then after everything was confirmed, this is the email that went out. So it was branded by the registry. It was the registry that was sending this out, not the ALS Association, not the CDC.

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03:15:58.300 --> 03:16:05.889

Patricia Stanco, MHS: And to, as Reshma mentioned, this only went to the email of the confirmed email that was associated with the valid account.

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03:16:06.140 --> 03:16:07.220

Patricia Stanco, MHS: Next slide.

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03:16:09.430 --> 03:16:27.709

Patricia Stanco, MHS: This graph shows the trend in signups and new registry accounts during the pilot period, so it just helps us to see that participation definitely increased after the pilot was introduced, which suggests that the program did help to move people from awareness to follow-through.

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03:16:27.890 --> 03:16:44.140

Patricia Stanco, MHS: Just as importantly, this graph reminds us that engagement often takes more than one touchpoint. So some people may respond right away, but others may need reminders, more time, or additional support before they're ready to be open to volunteering for this process.

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03:16:44.480 --> 03:16:58.890

Patricia Stanco, MHS: And the increase in new accounts reinforce that when registry participation is presented in a clear, supportive, and accessible way, and when a person's time, energy, and effort is acknowledged, more people may be willing to participate.

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03:16:59.120 --> 03:17:00.270

Patricia Stanco, MHS: Next slide.

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03:17:01.720 --> 03:17:15.699

Patricia Stanco, MHS: So this is... these are kind of just the data chart for the, for the graph that Reshma shared. You can just... it just compares the 6 months in the year before to the 6 months of the,

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03:17:17.120 --> 03:17:30.019

Patricia Stanco, MHS: Pilot program, and again, just reinforces that incentives may be an effective tool to help move people from awareness to action, and especially when they're part of a broader engagement strategy.

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03:17:33.380 --> 03:17:34.520

Patricia Stanco, MHS: Next slide.

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03:17:36.010 --> 03:17:49.760

Patricia Stanco, MHS: Reshma also mentioned the limitations, and I want to touch on that as well, because it's important to be transparent about that. Some participants may have faced challenges, as Reshma mentioned, having to do with disease progression, fatigue.

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03:17:50.070 --> 03:17:53.789

Patricia Stanco, MHS: Caregiver availability, or just other competing demands.

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03:17:53.890 --> 03:18:11.889

Patricia Stanco, MHS: It's also possible that the incentive amount was just not enough for some people, but these limitations are helpful as we think about future engagements, including how to set realistic goals, provide additional support, and continue to try and reduce barriers to registry participation.

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03:18:12.440 --> 03:18:13.410

Patricia Stanco, MHS: Next slide.

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03:18:15.190 --> 03:18:16.809

Patricia Stanco, MHS: So, in conclusion.

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03:18:17.310 --> 03:18:25.549

Patricia Stanco, MHS: We feel that the Texas Incentive Pilot showed that a structured, collaborative effort can increase participation in the National ALS Registry.

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03:18:26.600 --> 03:18:32.700

Patricia Stanco, MHS: Incentives can be an effective engagement tool, especially when paired with trusted outreach.

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03:18:33.500 --> 03:18:42.649

Patricia Stanco, MHS: This pilot also reinforces the importance of recognizing that participation in research or survey activities does take time, energy, and effort.

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03:18:42.840 --> 03:18:53.909

Patricia Stanco, MHS: And while there are still barriers to over... to be overcome, for sure, the success of this program does point to the potential for similar strategies to be scaled or adapted in other areas.

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03:18:54.160 --> 03:19:03.260

Patricia Stanco, MHS: Ultimately, increasing this participation strengthens ALS data, supports research, and helps to ensure, and this is...

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03:19:03.450 --> 03:19:16.580

Patricia Stanco, MHS: This is my personal favorite. This is the biggest thing. It helps to ensure that the experiences of more people who are living with ALS are reflected in the National ALS Registry, so that everyone's story is told.

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03:19:18.060 --> 03:19:27.850

Patricia Stanco, MHS: We are collaborating on a manuscript to share these findings more broadly, and as I mentioned yesterday, we do have a poster that will be at the upcoming NEXUS meeting.

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03:19:27.870 --> 03:19:38.379

Patricia Stanco, MHS: So, next slide, yeah, what am I gonna do, you guys? The meeting's next week, I have to plug it, so come join us and check it out. And, we... I think we have time for a few questions.

1024

03:19:39.860 --> 03:19:55.419

Danielle Boyce: Thanks so much to both of you. You know, there's always this debate, like, does it matter? Will it make a difference if you offer money? But what... what I thought was interesting, what you said, and I can relate, because I personally am a caregiver, not an ALS, but in a different disease.

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03:19:55.420 --> 03:20:19.879

Danielle Boyce: is... it's an engagement tool, is what I'm reading. So I... my attention, I might light up to see \$100, \$150, but it would be the one-to-one support and feeling like I'm not overwhelmed. I mean, that's just from my perspective. It seems like that would be the case, and also interesting to me is the fact that these might otherwise be people who we are overlooking. We're always talking about missing folks.

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03:20:20.020 --> 03:20:33.550

Danielle Boyce: in our research studies, and maybe it's because they don't have that one-to-one support. So, I wonder if you can comment on that, like, maybe it's less about the money than it is about, like, now being a part of this network, and then just the funds are what caught the attention?

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03:20:35.020 --> 03:20:56.360

Patricia Stanco, MHS: I completely agree with you, Danielle, and I mean, I think that's what Reshma and I found as we went through this process, is we're... we wanted to test the incentive, but then it's just hard to tease it out from the other components. You can't just offer the incentive, because we wanted to... we found... we wanted to send out more email reminders and make more phone calls to remind people, and then it's... at a certain point, it's like, wait.

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03:20:56.550 --> 03:21:06.109

Patricia Stanco, MHS: are we testing the incentive, or are we testing the reminders? You know, you gotta be careful there. So, but ultimately, it was a joint package. We weren't going to do one without the other.

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03:21:06.110 --> 03:21:06.730

Danielle Boyce: Right.

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03:21:06.730 --> 03:21:10.610

Patricia Stanco, MHS: But we did... it did spark some of those Reflections.

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03:21:10.940 --> 03:21:35.069

Danielle Boyce: Yeah, and I'm wondering, you know, since this is a pilot, and, you know, using Texas, and it's, like, I saw that you translated it, and, you know, kind of culturally sensitive, do you think it is, it is smart to kind of... I don't know, I don't know the answer to this, but, like, to really customize with the local team? You know, you said this is a trusted community locally, and so, instead of just having one, this is how we do it across all

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03:21:35.370 --> 03:21:46.550

Danielle Boyce: you know, every domain, but, like, kind of go from region to region and try to customize with those teams? Do you think... I wonder, do you think that would make it more effective as you unroll it nationally?

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03:21:46.550 --> 03:22:05.449

Patricia Stanco, MHS: Oh, absolutely. Much in the same way that, as a community, you know, nothing about ALS without someone who's living with ALS, I heard those sentiments repeated often yesterday, and I couldn't agree more. And likewise, you know, we went to our Texas team, and we're like, we're not taking the next step until we...

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03:22:05.450 --> 03:22:13.499

Patricia Stanco, MHS: Work with, you know, we had a working group, we talked about the process, we talked about the materials, we asked them what would be most helpful for you.

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03:22:13.530 --> 03:22:15.660

Patricia Stanco, MHS: To have and to share, so...

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03:22:15.750 --> 03:22:17.570

Patricia Stanco, MHS: Yeah, I can see it, you know, there could be.

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03:22:17.570 --> 03:22:18.100

Danielle Boyce: Definitely.

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03:22:18.100 --> 03:22:20.650

Patricia Stanco, MHS: Each tweaks and differences in other regions.

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03:22:21.210 --> 03:22:29.979

Danielle Boyce: And we have a question. Did you ask Visa, Walmart, or Amazon if they would donate the gift cards, or is that something that would be of interest?

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03:22:30.340 --> 03:22:44.130

Patricia Stanco, MHS: Well, we went through a vendor, and we chose the vendor because of a couple of things. They... the vendor did not charge any fees to people living with it, you know, they wouldn't charge any fees to the users, they didn't charge any fees to us either.

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03:22:44.130 --> 03:22:44.620

Danielle Boyce: So...

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03:22:44.620 --> 03:23:02.520

Patricia Stanco, MHS: All we paid was for the cash value of the card, and then anything that wasn't used did get returned. I mean, ultimately, these are taxpayer dollars, so we want to be good stewards of that. So no, we didn't... we didn't reach out through Visa, Amazon, and Walmart directly. We went through the

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03:23:03.100 --> 03:23:21.219

Patricia Stanco, MHS: And I did, you know, I did ask... I'm like, you know, how do you guys make money, and how do you... how does this work, and how are you not able to charge fees, and to make sure everything was above board? But you could choose from over... I mean, they had hundreds of vendors that you could choose from, we just wanted to keep it simple.

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03:23:22.820 --> 03:23:35.190

Danielle Boyce: And I see a question, congratulations on the huge increase in enrollment for the registry. What was different besides the incentive, or the same in the process compared to before or after the pilot?

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03:23:37.780 --> 03:23:43.220

Patricia Stanco, MHS: Well, I'll... yeah, Rushma, I was gonna say, why don't... because we didn't just go back one year, we went back a couple years.

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03:23:43.460 --> 03:23:57.660

Reshma Punjani: Yes, so we really looked at the data coming in, that's what was in my slide of what was enrollment looking like. And when we looked at Texas, it was historically under-enrolled, so we knew that this would be a good measure of the monetary incentive.

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03:23:57.660 --> 03:24:11.300

Reshma Punjani: So like we mentioned, of course they're gonna go hand-in-hand, the monetary incentive, as well as the support, but with everything else remaining the same, the incentive was the primary thing that changed.

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03:24:11.320 --> 03:24:18.079

Reshma Punjani: While we could say it was all the incentive, it could have been some of the support they were receiving from the Texas staff.

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03:24:18.760 --> 03:24:26.590

Reshma Punjani: was pretty consistent over time. You know, these individuals that go to clinic, they're seeing their same friendly faces, and the staff members.

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03:24:26.920 --> 03:24:43.999

Reshma Punjani: nothing has changed with the care they're providing. I think it was just something, the novelty of it, too, is seeing that there's \$150, and I know during the planning process, we had a lot of discussions on what would the number be. What would kind of, you know.

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03:24:44.160 --> 03:25:06.530

Reshma Punjani: make someone go over the threshold of an incentive that would be worth their time. And especially if you know our risk factor surveys are quite detailed. You know, there's 17 risk factor surveys looking at numerous risk factors, and we wanted to really compensate individuals for their time, and we thought that the \$150 provided that compensation.

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03:25:09.130 --> 03:25:14.559

Danielle Boyce: I mean, it makes sense to me. You know, all things... it sounds to me like...

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03:25:14.630 --> 03:25:28.720

Danielle Boyce: If they had wanted to participate in the registry before, the team would have been all in the same exact way. It's just that what sparked their interest was this incentive, potentially. Nothing else had really changed other than

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03:25:28.720 --> 03:25:38.229

Danielle Boyce: Other than the fact that they were willing to try to walk through that door, overcome what might have been overwhelming to them, and give it a shot, because it...

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03:25:38.540 --> 03:25:41.750

Danielle Boyce: It caught their eye that there was that incentive.

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03:25:41.850 --> 03:25:42.939

Danielle Boyce: I mean, I, I...

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03:25:43.210 --> 03:25:58.560

Danielle Boyce: I think that's terrific, and so somebody said, Ashley, followed up. I saw the slide, but what I was referring to was the outreach, marketing, improved clinic process, etc. Sounds like nothing else changed, which would assume the incentive was the difference, yeah, so...

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03:25:59.380 --> 03:26:15.679

Danielle Boyce: Well, thank you so much for that, and I'm looking forward to the paper, and I hope others in the field read it and learn something from it, especially in these diseases that are so hard to enroll, and the data, as we have seen, is so precious, and so, you know, we really...

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03:26:15.680 --> 03:26:28.000

Danielle Boyce: owe it to the community to try our best to support them, and if we are already supporting them, to get them through the door so that they can find the support. And, you know, I'm thinking, who knows what other supports they might have

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03:26:28.010 --> 03:26:40.850

Danielle Boyce: experienced or been offered as a result of that increased interaction with the ALS Association Clinic as well, right? So... so there could have been a whole bunch of things that they got out of this, other than participation in the study, so...

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03:26:41.400 --> 03:26:43.229

Danielle Boyce: Thank you very, very much for that.

Living with ALS: Testimonies from Patients and Caregivers - Doug Butchart, Stacy Farber, Mara Dolan

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03:26:44.190 --> 03:26:50.280

Danielle Boyce: And I think it's a perfect tie-in to our... Our last, panel.

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03:26:50.460 --> 03:26:52.919

Danielle Boyce: I'm gonna give everyone a chance to...

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03:26:54.710 --> 03:27:04.909

Danielle Boyce: all of our panelists to come on. And if you asked a question and it hasn't been answered yet, the registry team is working on answering your Q&A.

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03:27:05.680 --> 03:27:10.580

Danielle Boyce: And we will have a Q&A section at the end, and we'll try to wrap everything up.

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03:27:19.460 --> 03:27:30.739

Danielle Boyce: Okay, let's see, there's... I see Mara, I... See, Stacy... And... there's Doug. Alright.

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03:27:32.660 --> 03:27:47.050

Danielle Boyce: Okay, welcome. I... no pressure to the panel, but I've been touting this as the best... as the best and most exciting panel, and I'm suggesting everybody stays. And... and I... I... this is really a panel that means a lot to me.

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03:27:47.180 --> 03:27:52.379

Danielle Boyce: As well, welcome to our lived experience panel discussion, Living with ALS.

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03:27:52.880 --> 03:28:08.549

Danielle Boyce: And... and today, you are going to meet 3 exceptional, advocates and humans, Doug Bichardt, Mary Dolan, or sorry, sorry, Mara Dolan, and Stacey... Dr. Stacey Lewin-Farber.

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03:28:08.650 --> 03:28:10.900

Danielle Boyce: I've had the privilege to get to know

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03:28:11.690 --> 03:28:28.050

Danielle Boyce: these folks, over the last, several months, and I've known, full disclosure, I've known, Mara Dolan, for quite some time, because, Mara and I worked together, through her husband Pat's organization, or her and her husband Pat.

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03:28:28.050 --> 03:28:36.900

Danielle Boyce: Pat Dolan's organization, GOALS, and I've just known Mara to be such a fierce advocate and articulate

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03:28:36.900 --> 03:28:50.730

Danielle Boyce: person expressing the challenges of being in this community. So... so in this panel, the way we're going to do this is we're going to go in two rounds, but we also encourage question and answer. And...

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03:28:50.920 --> 03:29:10.590

Danielle Boyce: there were some listening sessions that I did not participate in before coming on as moderator, but then we had our own conversations after that. And what happened... reading the notes from the listening sessions, and then also my own conversations with this group, a lot of really

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03:29:10.590 --> 03:29:30.249

Danielle Boyce: relevant points to the things that we've been talking about over the last two days, and this team is going to, I'm sure, share with you their insights on this. A lot of things have come up, you know, but on the other side, so we've been talking about all of what we can do with the data, right? But not talking about what it's like.

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03:29:30.350 --> 03:29:39.669

Danielle Boyce: To participate, or want to participate and not be able to navigate the system, or not know what happens when you do participate.

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03:29:39.670 --> 03:29:53.210

Danielle Boyce: whatever happened with that, you know, when you've spent your hard work and your effort to navigate. And some of these stories that I heard, it's just the people trying so hard to participate and finding challenges.

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03:29:53.210 --> 03:30:08.459

Danielle Boyce: At clinic, in the research ecosystem, and these are really smart and motivated people, and they're having trouble. And so, it really goes to show you that we have a ways to go, and so I...

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03:30:08.510 --> 03:30:18.069

Danielle Boyce: I presented to this team, and I'm going to introduce them one at a time as they speak, but I presented them with some prompts, but I didn't censor them at all.

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03:30:18.070 --> 03:30:30.069

Danielle Boyce: And so the first round is going to be... so Kamara's thinking, careful what you wish for, Danielle. But good, right? That's what we want to hear. What's the point of doing this if we tell people what to say?

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03:30:30.070 --> 03:30:43.910

Danielle Boyce: But the first round is going to be your advocacy origin story. So, you know, yes, your journey, if you want to share that with ALS or caring for someone with ALS,

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03:30:44.560 --> 03:31:04.490

Danielle Boyce: But then, prompts like, the experience has made me... that has made me want to speak up is... or I became involved with ALS advocacy because... or one challenge that shaped my perspective was, right? And then, we're going to do another round where we talk about what I wish I had known.

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03:31:04.490 --> 03:31:19.239

Danielle Boyce: and what I want decision makers to know. And now is your chance, if you are leading projects in research, in advocacy, in clinics around ALS, now's your chance to hear from people who not only speak for themselves.

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03:31:19.420 --> 03:31:35.659

Danielle Boyce: But they also hear the stories of thousands of other people with the disease and their families. So, this is, like, the focus group you wish you could have, right? And we're giving it to you here, because we really want you to take this home with you.

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03:31:35.660 --> 03:31:44.140

Danielle Boyce: And not only take the science, which I certainly have taken the science that I've learned about today, but also take the lived experience. So.

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03:31:44.320 --> 03:31:50.199

Danielle Boyce: without further ado, we're going to start with Dr. Farber, who I have just been

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03:31:50.380 --> 03:32:03.330

Danielle Boyce: So impressed and grateful to be able to get to know Dr. Farber. Dr. Stacey Lewin-Farber was diagnosed with limb onset sporadic ALS in February 2021.

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03:32:03.450 --> 03:32:10.710

Danielle Boyce: Prior to her diagnosis, She practiced obstetric anesthesiology for over 20 years.

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03:32:11.310 --> 03:32:25.279

Danielle Boyce: Determined to not let her diagnosis be for nothing, Stacy, along with her husband Dan and sons Zachary and Ethan, have become fierce advocates in the hope to see positive changes in the world of ALS.

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03:32:26.230 --> 03:32:35.150

Danielle Boyce: So, thank you so much, Dr. Farber, for joining us, and I know that you have, prepared a statement with

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03:32:35.420 --> 03:32:39.620

Danielle Boyce: your, technology, and so I'm gonna pass it over to you.

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03:32:47.340 --> 03:32:50.580

Stacy Farber: Good afternoon. It is a pleasure and an honor

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03:32:53.150 --> 03:33:04.200

Stacy Farber: To be speaking to you today, along with the other panelists, ALS, is known to be a very heterogeneous disease. No two patients present in the same manner, and every one of us progresses differently.

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03:33:04.200 --> 03:33:15.160

Stacy Farber: However, I can guarantee that there is one thing we all have in common, and that is a vivid memory of when and where we were when we first learned that our lives would be tragically altered.

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03:33:15.960 --> 03:33:28.259

Stacy Farber: February 2021, seated in our basement in front of my laptop, because COVID was still raging, I officially heard the news that confirmed what I had suspected. The statement was.

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03:33:28.260 --> 03:33:36.469

Stacy Farber: I am sorry, you have ALS, and it felt like the floor dropped out from under me. What started as difficulty cracking open glass

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03:33:36.520 --> 03:33:53.080

Stacy Farber: medication vials in the operating room 7 months earlier was now a terminal diagnosis with a 2-5 year life expectancy. My husband Dan and I spent the next month crying and trying to figure out how to tell our sons, Ethan and Zach.

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03:33:53.080 --> 03:34:13.530

Stacy Farber: Then ages 17 and 21, my diagnosis. They knew something was wrong. Unbeknownst to me, in a role reversal, Zach was slooping on social media and tracking all of my ALS searches. We sat the boys down when school was done in May, telling them what we were facing was one of the hardest days of my life, ALS.

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03:34:13.530 --> 03:34:35.550

Stacy Farber: does not just affect me, it affects my entire family. We all had a good cry, and decided as a family that we would fight to live, both for ourselves and for others in the ALS community. This was a pivotal moment for me. With family and friends behind us, we began our advocacy journey. I realized that I was fortunate. Compared to most ALS patients.

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03:34:35.550 --> 03:34:47.030

Stacy Farber: I was diagnosed relatively quickly after my first symptom. I had medical knowledge and knew how to navigate the medical system, and I was still overwhelmed. I live in an urban area with

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03:34:47.030 --> 03:34:55.200

Stacy Farber: multiple top-notch ALS treatment centers nearby. If I was overwhelmed, what must patients who could not advocate for themselves be feeling?

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03:34:55.200 --> 03:35:11.090

Stacy Farber: I wanted to combine my science background and my experience as a patient to help make a difference. I started with IMALS and gained a mentor from their peer mentor program. My mentor, who is now a close friend, educated me on research and advocacy. He explained...

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03:35:13.560 --> 03:35:37.159

Stacy Farber: The value of participating in observational studies and contributing data to the CDC National Registry. My care team at the ALS Hope Foundation guided me to become a Niels Research Ambassador. This opened up a multitude of opportunities. Raising awareness, education, and research became driving principles for me. I am passionate about the importance of including the patient voice in topics such as research study design. I sit on the scientific research and home care services

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03:35:37.160 --> 03:35:50.989

Stacy Farber: committees for ALS United Mid-Atlantic, and I'm a patient board member and peer mentor for the Hope Foundation. I am an active member of the IMALS Tim Lowry educational panels, which are delivered to students in medical, PT, OT,

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03:35:50.990 --> 03:36:15.900

Stacy Farber: speech, dietary and nursing programs, and much more. This is so valuable to raise awareness for practitioners at the beginning of their careers. As a member of many pharmaceutical patient advisory boards and a consumer reviewer for the CDMARPI, I'm grateful for the opportunity to be a patient voice. I appreciate all of you hearing and listening to our voices today. ALS, exhausts me, but this work fuels me. I cannot emphasize enough the

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03:36:15.900 --> 03:36:19.760

Stacy Farber: importance of raising awareness, education, and collaboration. Thank you.

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03:36:22.710 --> 03:36:29.040

Danielle Boyce: Thank you so much. You know, what strikes me whenever I chat with,

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03:36:29.540 --> 03:36:38.880

Danielle Boyce: Dr. Farber, is just, how busy you are, right, doing free things, you know, basically, you know, volunteering.

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03:36:38.980 --> 03:36:47.860

Danielle Boyce: skilled labor, and this is just something that I've noticed across the ALS community at large. We have such a

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03:36:48.090 --> 03:36:49.399

Danielle Boyce: talent pool.

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03:36:49.690 --> 03:37:02.329

Danielle Boyce: such... and, you know, all of you here are perfect examples, but so many talented people in the ALS community, and it makes me wonder if it were any of us, would we...

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03:37:02.750 --> 03:37:12.270

Danielle Boyce: spend that much time and effort, you know, trying to help and inform, and so it... to Pat Dolan's point yesterday, you know, we're here

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03:37:12.310 --> 03:37:28.320

Danielle Boyce: the advocates are here and ready and willing to serve, and as you can see here, I mean, it is... it is a driving, sentiment that... from... from this community that they want to help and make it easier for others, but we don't always make it easy for them.

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03:37:28.790 --> 03:37:33.229

Danielle Boyce: So next, I'm going, to go to Doug.

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03:37:33.640 --> 03:37:43.289

Danielle Boyce: Bachart, and he is a retired automotive and truck technician with more than 40 years of experience, so again, all of this experience.

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03:37:43.570 --> 03:37:53.170

Danielle Boyce: to learn from. He is now a full-time caregiver to his wife, Shadine, who is... who was diagnosed with limb-onset ALS in 2017.

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03:37:53.680 --> 03:38:03.400

Danielle Boyce: Since her diagnosis, Doug has become deeply involved in ALS research and clinical trials, helping coordinate her participation in expanded access programs.

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03:38:03.530 --> 03:38:05.570

Danielle Boyce: And numerous research studies.

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03:38:06.150 --> 03:38:18.479

Danielle Boyce: Which I'm sure you can tell us, Doug, there's a lot, a lot to do getting into an EAP. He is also an active ALS and rare disease advocate, working with organizations including IMALS,

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03:38:18.690 --> 03:38:23.359

Danielle Boyce: The Muscular Dystrophy Association, the ALS Association.

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03:38:23.580 --> 03:38:40.579

Danielle Boyce: and the Les Turner ALS Association. Doug is passionate about using his experience as a caregiver and a research partner to ensure that patients and caregivers have a stronger voice in research, healthcare, and public policy. And Doug, I'm going to pass it to you for round one.

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03:38:44.280 --> 03:38:44.990

Doug Butchart: Thank you.

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03:38:45.570 --> 03:38:52.129

Doug Butchart: Thank you for letting me speak today. My name is Doug Beauchart, and I am the full-time caregiver for my wife, Shadine.

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03:38:52.380 --> 03:38:58.850

Doug Butchart: Shadine was diagnosed with limb onset ALS in 2017.

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03:38:59.060 --> 03:39:07.290

Doug Butchart: I decided to retire early so I could care for her full-time. It was the right choice for our family, but it came at a real cost.

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03:39:07.940 --> 03:39:12.140

Doug Butchart: Shadine doesn't qualify for SSDI, Medicare.

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03:39:12.260 --> 03:39:22.299

Doug Butchart: her government assistance to help with her care. So we've had to carry the financial, medical, and caregiving weight of ALS largely on our own.

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03:39:22.890 --> 03:39:27.879

Doug Butchart: All while watching a progressive and devastating disease take its course.

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03:39:28.150 --> 03:39:33.770

Doug Butchart: This journey has taught me one thing. No two ALS experiences are the same.

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03:39:34.630 --> 03:39:41.240

Doug Butchart: The disease moves differently in every person, and every family's financial situation is different, too.

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03:39:41.780 --> 03:39:49.540

Doug Butchart: Some families have insurance, disability benefits, savings, and other resources to lean on, but...

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03:39:50.350 --> 03:39:54.769

Doug Butchart: But you can't truly understand what ALS does to a family.

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03:39:54.950 --> 03:39:57.659

Doug Butchart: Until you live with it every single day.

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03:39:59.150 --> 03:40:05.359

Doug Butchart: Because ALS doesn't just touch The person diagnosed that touches everyone who loves them.

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03:40:08.220 --> 03:40:10.819

Doug Butchart: The experience gives me

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03:40:11.610 --> 03:40:19.080

Doug Butchart: a deeply personal reason to care about whether we truly know how many people are living with ALS and where they are.

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03:40:19.250 --> 03:40:20.380

Doug Butchart: Where they are.

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03:40:20.800 --> 03:40:30.749

Doug Butchart: The registry matters to me because as a caregiver and advocate, I've come to understand that our current system doesn't give us the complete picture.

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03:40:31.400 --> 03:40:44.409

Doug Butchart: The CDC's ALH registry relies in part on people identifying themselves and choosing to participate, rather than healthcare systems automatically reporting every diagnosis.

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03:40:45.180 --> 03:40:55.329

Doug Butchart: That's why I was so encouraged to hear the speakers yesterday talk about training their care coordinators to get the ALS patients registered right in clinic.

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03:40:56.370 --> 03:41:01.570

Doug Butchart: Care coordinators already have regular contact with ALS patients.

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03:41:07.400 --> 03:41:10.129

Doug Butchart: They're in a unique position to help

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03:41:10.410 --> 03:41:14.359

Doug Butchart: People sign up and make sure that patients know the registry exists.

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03:41:14.490 --> 03:41:22.090

Doug Butchart: That kind of on-the-ground, one-on-one support is exactly what we need to reach families that...

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03:41:22.340 --> 03:41:24.609

Doug Butchart: Who might otherwise never hear about it.

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03:41:27.210 --> 03:41:36.179

Doug Butchart: And it's why I've been advocating Illinois, in Illinois, to make ALS a reportable condition. Better information about who

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03:41:36.680 --> 03:41:41.740

Doug Butchart: Has ALS is essential to understanding the disease and to planning for

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03:41:42.210 --> 03:41:45.179

Doug Butchart: For the people and families it affects.

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03:41:46.040 --> 03:41:47.270

Doug Butchart: I also...

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03:41:47.560 --> 03:41:56.399

Doug Butchart: know the consequences of gaps in the system firsthand. I know how hard it is for an ALS family to navigate care.

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03:41:56.670 --> 03:42:00.489

Doug Butchart: Benefits... Research and support.

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03:42:00.590 --> 03:42:03.970

Doug Butchart: When the safety nets other families depend on.

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03:42:04.140 --> 03:42:08.590

Doug Butchart: aren't available to you. The burden can be... become overwhelming.

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03:42:09.970 --> 03:42:20.669

Doug Butchart: So my advocacy for ALS data isn't really about collecting numbers, it's about making sure people with ALS are seen, counted, and understood.

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03:42:21.390 --> 03:42:28.279

Doug Butchart: It's about having the information we need to know who... Affected where they are.

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03:42:29.980 --> 03:42:39.920

Doug Butchart: what they're up against, and what resources they need. And ultimately, it's about making sure decisions about ALS research

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03:42:40.510 --> 03:42:46.910

Doug Butchart: Services, benefits, and resources are grounded In the best information possible.

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03:42:47.300 --> 03:42:49.139

Doug Butchart: Shitting has taught me

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03:42:49.750 --> 03:42:58.599

Doug Butchart: that behind every number in the ALS registry is a person, a family, and a story. Every journey is different.

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03:42:58.860 --> 03:43:04.400

Doug Butchart: But every family affected by ALS deserves to be seen, counted, and supported.

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03:43:05.000 --> 03:43:13.080

Doug Butchart: Thank you. I'd also like... to mention Brian Wilson, who was scheduled to be a presu...

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03:43:13.610 --> 03:43:16.530

Doug Butchart: On the panel, but passed away over the weekend.

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03:43:17.360 --> 03:43:18.190

Doug Butchart: Thank you.

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03:43:22.210 --> 03:43:32.850

Danielle Boyce: Sorry, thank you, Doug. I... I... we did hear that, yesterday. I mean, and... and you had made this point, Doug, when we were talking about this before the meeting.

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03:43:32.970 --> 03:43:44.669

Danielle Boyce: That... that just in the time where there was a delay, you know, in... in the... in the meeting, and in that time, we lost a panel member, to, you know, to... who died, from...

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03:43:44.800 --> 03:44:00.150

Danielle Boyce: ALS, and I was saying that the last time that we did... I hosted this meeting, was the moderator, we had... well, we had a number of panelists, who were on that lived experience panel, and,

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03:44:00.150 --> 03:44:06.829

Danielle Boyce: Becky Mowry, Sandy Morris, Glenn Rouse, and they're all gone. And... and they were...

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03:44:06.830 --> 03:44:26.779

Danielle Boyce: and some of them were gone before the next meeting, you know, and, you know, so... so it gives you that sense of urgency, but it's really hard to explain, unless you're in the community, what that's like, and how that impacts the people who are still living through it, and...

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03:44:26.780 --> 03:44:39.770

Danielle Boyce: trying to advocate, and how devastating that is when you're in a community and watching that, it's very hard to express that, and so I was so glad that you brought that up, Doug, because I think that that's just something that

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03:44:40.020 --> 03:44:47.700

Danielle Boyce: People need to hear, and need to understand that when you're... when someone is critiquing your research project.

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03:44:47.910 --> 03:44:51.359

Danielle Boyce: Or complaining that things aren't moving fast enough.

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03:44:51.570 --> 03:44:57.279

Danielle Boyce: That's why they're saying it. That's why they're doing it. When there seems to be a bureaucratic issue.

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03:44:57.350 --> 03:45:16.300

Danielle Boyce: and you're spending all your time around and around, it's just... that's how... why it's so infuriating. And that's why you see the response that you get sometimes from advocates, because that's what... that's... it's life and death, and that's what you're seeing every day. And so that... that is what I have learned being in this community. And I think someone who can speak to that

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03:45:16.700 --> 03:45:22.369

Danielle Boyce: very eloquently is, Mara Dolan, who is our next, presenter.

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03:45:22.410 --> 03:45:36.379

Danielle Boyce: So Mara is a caregiver, advocate, and co-founder of GEOALS, a nonprofit created to improve access to ALS care and accelerate ALS research. Full disclosure, I'm on the board of directors of GEO ALS.

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03:45:36.400 --> 03:45:52.300

Danielle Boyce: And as you might have learned, I'm a map nerd, so I get a lot out of, all the way around being a part of that group. Her husband, Mara's husband, Pat Dolan, who has joined us here and had some very insightful comments over the last few days.

1177

03:45:52.300 --> 03:45:58.860

Danielle Boyce: Has been living with ALS for 10 years, and is recognized by many in the ALS community for his work mapping ALS data.

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03:45:58.860 --> 03:46:18.770

Danielle Boyce: Including the CDC data. So, we had a big project where we mapped all the data and looked at it all kinds of ways and, brought in experts from ESRI, and so that is where Mara works as well. So, through GEOLS and their lived experience navigating ALS care, Mara and Pat focus on supporting patients and families

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03:46:18.770 --> 03:46:36.129

Danielle Boyce: And helping researchers, clinicians, and advocates better understand where care gaps are, and how data can help close them. It's amazing what you can do with a map, right? Amara also serves as a developer relations coordinator at Esri. Esri is the software company that makes the

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03:46:36.290 --> 03:46:46.130

Danielle Boyce: best software in the game, you know, in mapping. She brings a candid caregiver perspective on the real-world consequences of delayed recognition.

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03:46:46.170 --> 03:46:58.469

Danielle Boyce: Fragmented care, limited ALS knowledge across healthcare settings, so not just your neurologist, but when you go to the hospital for an inpatient visit, where is the... where is the information lost?

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03:46:58.550 --> 03:47:10.349

Danielle Boyce: and healthcare and research system that has not changed fast enough for people with ALS. And so, Mara, I'm going to ask you, what is your advocacy origin story? Please, please tell, tell us

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03:47:10.450 --> 03:47:11.920

Danielle Boyce: And share your insights.

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03:47:12.610 --> 03:47:30.929

Mara Dolan: Thank you so much, Danielle, and just thank you so much for letting me speak today. I just have all these heroes that I'm seeing here. Over the past 10 years, I've gotten to know some of the folks who spoke, and they're my heroes, so it's actually a thrill for me to be in the same day, in the same seminar as them.

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03:47:31.040 --> 03:47:34.060

Mara Dolan: Not seminar, it's a symposium.

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03:47:34.710 --> 03:47:36.519

Mara Dolan: But yeah, so thank you,

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03:47:36.660 --> 03:47:48.299

Mara Dolan: And I have to say, like, every time someone gives a story, like Doug did, and Stacy, I just... it's just, like, it's a spear through the heart. It's just so hard to hear it.

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03:47:48.440 --> 03:48:02.999

Mara Dolan: I'm glad... so glad you're saying it, but it just takes me back to our origins and... and how hard it is. Like, you all said it. I'm gonna repeat a lot, but you all said it, like, you just cannot imagine the rawness and how everything's broken into bits.

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03:48:04.330 --> 03:48:22.370

Mara Dolan: And there's no hope, you know? It's just really hard. It's... and to hear those guys say it, and just know... just, like, flashing back to what we went through, and how hard it is to be told, like, you have this terrible thing that you barely even ever heard of. I had heard of Lou Gehrig's, but to be told, like, you have this horrible thing, and...

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03:48:22.780 --> 03:48:32.260

Mara Dolan: Basically, science hasn't really advanced. This is how we heard it. Science has let you down for, like, 30, 40, 50 years. We have nothing to offer you.

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03:48:32.450 --> 03:48:40.010

Mara Dolan: we have... nothing... no idea what... what causes it. Absolutely none. And,

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03:48:40.600 --> 03:48:44.190

Mara Dolan: we have, like, one interventional trial for you.

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03:48:44.890 --> 03:48:51.980

Mara Dolan: But you don't qualify for it, basically, is what happened to us. So anyway, that is, like, in a nutshell, kind of our... our,

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03:48:52.230 --> 03:49:01.989

Mara Dolan: trajectory, but just to go back to our story, so I'm a caregiver... my name's Mara, and I'm a caregiver for Pat, and he... I've been a caregiver for him for 10 years.

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03:49:02.340 --> 03:49:07.290

Mara Dolan: And he was diagnosed in, 2016 with limb onset.

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03:49:07.650 --> 03:49:09.740

Mara Dolan: And, he...

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03:49:09.930 --> 03:49:18.489

Mara Dolan: Basically got trached in 2019, had a lot of struggles up till then, and got trached, and then a whole... a set of different struggles began.

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03:49:19.080 --> 03:49:26.339

Mara Dolan: But, our biggest, the biggest thing we learned through this whole process was it's just really hard to...

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03:49:26.480 --> 03:49:35.120

Mara Dolan: get in a trial. We tried to get into several trials. Neuron was the biggest one that took the most, effort, took many trips.

1200

03:49:35.640 --> 03:49:47.089

Mara Dolan: And, it just seemed like... I don't want to cast shade on that group, but it just seemed like there wasn't a sense of urgency, because we signed up, he met all the criteria, that was in April.

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03:49:47.260 --> 03:50:05.960

Mara Dolan: and every month I would call, like, so, are we in? Can we start getting the stuff? He's dying, you know, can we start getting the meds? He's dying, and it's working on people, so let's go. And not to make light of it, but it's just like, what are you guys... what's going on? And I'd get, like, oh, we're still reviewing, we're still reviewing. I think he's in, he meets all the criteria, but...

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03:50:05.960 --> 03:50:10.840

Mara Dolan: Then another month would pass, and another month would pass. We'd go back and get some more...

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03:50:10.860 --> 03:50:13.629

Mara Dolan: FVC's values done.

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03:50:13.740 --> 03:50:29.129

Mara Dolan: And they're going down pretty... I called June. He's not gonna keep passing, you know? What are we waiting for? Let's get him signed up, let's get this stuff pumping through him. What are we waiting for? And then, like, early July, we got the... well, I called, and they said, oh yeah, he's not...

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03:50:29.340 --> 03:50:34.910

Mara Dolan: he's, like, 2 points off, and I said, what points? You know, he's been on, and they said, oh, well...

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03:50:35.340 --> 03:50:45.620

Mara Dolan: I don't know, I honestly don't know if it was a typo or my misunderstanding, but I thought as long as he was, at 62, he was good, and I thought they had told me that several times, honestly, but...

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03:50:45.810 --> 03:50:52.099

Mara Dolan: That July day, they said, no, he, it's now 65% FVC, so he's out.

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03:50:52.510 --> 03:50:59.510

Mara Dolan: And that was his only thing. Like, he met every other criteria we went down faithfully, you know? So...

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03:50:59.870 --> 03:51:16.540

Mara Dolan: I just imagine, and he... and we have resources, like, we have, like Stacy was saying, how can you do this if you don't have a medical background? I don't have a medical background, but we have friends galore. I shouldn't say resources, we have friends and family just piling on, because Pat is very beloved.

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03:51:16.620 --> 03:51:20.029

Mara Dolan: So, that was a... that was an eye-opener to how, like.

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03:51:20.360 --> 03:51:32.140

Mara Dolan: Oh, and then, like, later we heard basically that group saying, like, they couldn't find recruit... they couldn't find patients, and I was like, what? So, I can just imagine this is so frustrating for folks, like.

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03:51:32.590 --> 03:51:48.659

Mara Dolan: seeing that, and not being able to, like... at least I can speak out about it and talk about it, and I have, and I have just said, like, this just seems backwards to me from... from day one. Everything seemed backwards. And that's what got me to be an advocate. Like, in 2018, I,

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03:51:49.450 --> 03:52:04.419

Mara Dolan: had just, like, read enough, talked to enough neurologists. We had two different clinics with different... many different neurologists, and I hammered them all on, like, what? Like, wait, what? There's nothing? Like, what about B12? What about that GM Genova thing? It was...

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03:52:04.480 --> 03:52:09.669

Mara Dolan: Jenner Von. I don't know if you guys remember that. I was, like, hammering that because it looked so good at the time.

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03:52:10.750 --> 03:52:16.940

Mara Dolan: Neurone was another one, and that there's just a bunch of closed doors, like, no, there's nothing we can do.

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03:52:17.480 --> 03:52:32.479

Mara Dolan: And it just was, like, unfathomable to me. So that's what spurred me to, like... it just seemed like something was broken. And I didn't have a lot of understanding of the whole process at the time. It just seemed like, you know, well, how did HIV get it? How did cancer knock it out? Like...

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03:52:32.570 --> 03:52:41.490

Mara Dolan: later COVID came? Like, what... why is ALS taking so long? And I didn't realize then, it's a very... it is a very complicated disease, but I do still feel like

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03:52:42.010 --> 03:52:46.140

Mara Dolan: I still feel today that there are creative things we could do to,

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03:52:46.240 --> 03:52:53.349

Mara Dolan: move the research along a little faster. We need that slow... the slow, methodical stuff, but I feel like we need this fast track.

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03:52:53.520 --> 03:52:55.980

Mara Dolan: going on at the same time, which I feel is missing.

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03:52:56.440 --> 03:52:58.249

Mara Dolan: For patients today.

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03:52:58.630 --> 03:53:08.379

Mara Dolan: But anyway, so my... my... into the... into the advocacy story is I then got connected with Sandy Morris. I wish I could remember how. I cannot remember how. I think it was Phil Green.

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03:53:08.660 --> 03:53:16.890

Mara Dolan: But anyway, so I started attending their meetings, the IMALS, legislative... what became the legislative group meetings, and

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03:53:17.030 --> 03:53:19.109

Mara Dolan: That's how I started my advocacy.

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03:53:19.360 --> 03:53:23.299

Mara Dolan: I'm trying to think if I missed anything that I wanted to touch on there.

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03:53:26.250 --> 03:53:29.059

Mara Dolan: Yeah, that is... that's pretty much it.

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03:53:29.550 --> 03:53:36.130

Mara Dolan: Oh, yeah. Maybe just a quick mention that in that... in those beginning days, the MDA and,

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03:53:36.340 --> 03:53:49.250

Mara Dolan: also helped us very much, and they did push very perfectly. Like, they weren't pushy, but they got the point across, like, you have to join the registry, you have to get in there. And we kept putting it off, and putting it off because of

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03:53:49.610 --> 03:53:51.779

Mara Dolan: The life that we were trying to deal with.

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03:53:51.790 --> 03:54:02.060

Mara Dolan: But we finally did it. Pat finally filled it out and did it, and was glad he did it. But we wouldn't have done it without, I absolutely know, without all ALS Association and MDA.

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03:54:02.060 --> 03:54:14.159

Mara Dolan: and their materials, and the... and the gentle nudges back then. And we're data people, we were like, let's get all of our data out there. We're... so the fact that we hesitated or didn't do it immediately tells you how, like.

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03:54:14.620 --> 03:54:25.490

Mara Dolan: completely snowed under we were. We were just struggling so much. It's so hard. Just... I guess that's the takeaway, like, it's... it's just a very hard disease in the beginning, and it's hard to...

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03:54:26.190 --> 03:54:29.819

Mara Dolan: Enroll, it's hard to be an advocate, it's hard to...

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03:54:30.570 --> 03:54:33.310

Mara Dolan: You know, add your data to the registry.

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03:54:35.160 --> 03:54:53.169

Danielle Boyce: Thanks, Mara. And you mentioned Phil Green, and also Lane Olaf. Like, I'm thinking of all of these people who we worked with, and I mean, it's tremendous advocates who were working... and what's lost, the knowledge that they accumulated

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03:54:53.420 --> 03:55:03.609

Danielle Boyce: and lost. I feel like that is such a challenge in this disease, compared to other diseases, so I come from rare epilepsy community, and these are parents.

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03:55:03.860 --> 03:55:28.489

Danielle Boyce: Right, and so they have this longevity, you know, and the children do not have exactly the same timeline that you have, and sometimes they do, but oftentimes we have more time. And so, the difference that it makes to have that longevity in advocacy and knowledge really makes a difference, because you're starting all over from scratch, you know, each time, and we lose all of this, these

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03:55:28.870 --> 03:55:38.100

Danielle Boyce: Great thinkers. The other thing I'm thinking about, just hearing you all, and just from before, a couple of things. One is, I don't think we realize in clinic

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03:55:38.540 --> 03:55:54.110

Danielle Boyce: junior clinic research staff, we don't realize how it comes across when we say, not yet, or give it a few weeks, or something. Like, I hear that a lot, and it wasn't until I worked in Duchenne muscular Dystrophy.

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03:55:54.180 --> 03:56:09.399

Danielle Boyce: where, I would have mothers calling, just like you, it reminds me so much of that story, is they would call and say, he has to have a certain 6-minute walk in order to qualify, and he's losing that 6-minute walk. What's taking so long? Like, what is going on? And it was often something

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03:56:09.430 --> 03:56:24.869

Danielle Boyce: stupid, like... like a contract or something, you know, something that, to me, as a mother, just seems like just an outrageous excuse, and so... I don't know how to solve that, because those problems are real on the clinic side, but I... just to say that

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03:56:24.940 --> 03:56:34.090

Danielle Boyce: When you're dealing with those types of issues for clinical trials that might actually benefit you, the individual, in this life or death situation.

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03:56:34.410 --> 03:56:36.219

Danielle Boyce: It has to be...

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03:56:36.450 --> 03:56:55.280

Danielle Boyce: far out of your mind to participate in an observational research study that might not benefit you directly, right? So, if we made it easier all around, maybe we would have more bandwidth to do more, you know, research and participate. Yeah, I'm hearing that too.

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03:56:56.400 --> 03:57:03.599

Danielle Boyce: And we have a lot of questions and comments, so... so this is going to be great after, afterwards when we have some discussion.

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03:57:03.930 --> 03:57:14.060

Danielle Boyce: So... Round 2... I thought, now's your chance. You have the best and the brightest research, advocacy.

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03:57:14.350 --> 03:57:18.900

Danielle Boyce: policy makers, you name it, we have it in your audience. So now's your chance.

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03:57:19.260 --> 03:57:26.569

Danielle Boyce: What do you wish you had known? And this could be your clinical experiences, this could be your research experiences.

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03:57:26.840 --> 03:57:31.869

Danielle Boyce: What... what do you wish you had known? And I'm gonna start with Dr. Farber.

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03:57:38.760 --> 03:57:42.249

Stacy Farber: I believe that the visit at which the official diagnosis is

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03:57:42.330 --> 03:58:01.479

Stacy Farber: given should be just about delivery of the news. The diagnosis is so overwhelming that not much other information can be absorbed. A subsequent visit should be scheduled shortly after. It is crucial that we be made to feel like partners in our care and in all decisions affecting us. There are so many acronyms, organizations.

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03:58:01.480 --> 03:58:24.039

Stacy Farber: studies, insurance policies, and accessibility options to consider. My head spins just remembering that period of my disease. I think it's important to break down the topics simply at first. If I were to pick one topic to elaborate upon now, it would be research, because there is a limited time for eligibility in clinical trials.

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03:58:24.040 --> 03:58:39.619

Stacy Farber: I would have appreciated knowing that there was a time limit, and also a brief overview of how to learn about available trials that were appropriate for me. I didn't understand the difference between open label extension and expanded access programs.

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03:58:39.670 --> 03:58:43.270

Stacy Farber: Observational studies were not explained to me initially.

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03:58:43.270 --> 03:59:00.100

Stacy Farber: Questions I had were, if I could, I participate in observational studies concurrent with drug trials? And what was the difference between various registries? How would my data be protected and my information not duplicated? Eventually, I found these answers out.

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03:59:00.100 --> 03:59:06.719

Stacy Farber: However, it took research and asking a lot of questions. I wish it would have been an easier process.

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03:59:06.720 --> 03:59:29.180

Stacy Farber: The clinic I attended then is not the same one that I go to now. To date, I have participated in a drug trial, I'm currently in an EAP, and have taken part in many, many observational programs. I would like all patients to have these opportunities. The CDC National Registry Listening Sessions are a step in the right direction. Equally, if not more important.

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03:59:29.180 --> 03:59:32.769

Stacy Farber: We'll be implementing the changes discussed. Thank you.

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03:59:38.390 --> 03:59:44.820

Danielle Boyce: Thank you, Stacy. And you know, I'm thinking, here we have... a physician.

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03:59:45.990 --> 03:59:54.740

Danielle Boyce: Right? We have a physician. Think of how knowledgeable and plugged in, and... and if she's struggling with this, with all of this, and I...

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03:59:54.910 --> 04:00:12.120

Danielle Boyce: It's totally relatable, I can totally relate to this. If she's having trouble navigating and figuring out who is doing what and who are all these different groups, I mean, anyone who comes in as an employee, you know, new to the field, even if they're not personally impacted by ALS, I'm sure we all know what she's talking about, right?

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04:00:12.410 --> 04:00:22.949

Danielle Boyce: what is this study of that study? Who is this? Why don't these people work together? Isn't that the same study? What is going on? So imagine if you have the overlay

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04:00:23.160 --> 04:00:28.400

Danielle Boyce: of... you've just been given this diagnosis. The financial...

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04:00:28.700 --> 04:00:43.300

Danielle Boyce: that Doug described, right? All the financial challenges, and you're trying to pick the thing that could help you directly, and could make the largest impact globally. You're trying to do all of this while managing this new diagnosis.

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04:00:43.300 --> 04:00:55.270

Danielle Boyce: I definitely think that, you know, we think we have tools, but clearly they're not getting to the people, right? Because we're hearing this again and again, the same kinds of questions that you're having.

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04:00:55.460 --> 04:00:58.880

Danielle Boyce: Doug, would you like to comment on that?

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04:00:59.040 --> 04:01:00.640

Danielle Boyce: Next section.

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04:01:03.240 --> 04:01:04.290

Doug Butchart: Sure.

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04:01:05.810 --> 04:01:08.919

Doug Butchart: The... When my wife was first diagnosed.

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04:01:11.530 --> 04:01:15.890

Doug Butchart: She was diagnosed at... at Rush... University Hospital.

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04:01:16.030 --> 04:01:17.170

Doug Butchart: In Chicago.

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04:01:17.930 --> 04:01:24.460

Doug Butchart: But... They wouldn't take her insurance, so we ended up... At a different clinic.

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04:01:24.640 --> 04:01:29.070

Doug Butchart: We went to... Mercy Health in... in... In Rockford.

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04:01:29.450 --> 04:01:33.179

Doug Butchart: And I... I tried to get her into...

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04:01:33.310 --> 04:01:38.569

Doug Butchart: Clinical trials and all that stuff, and... And there was nothing available.

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04:01:38.950 --> 04:01:39.990

Doug Butchart: And...

1277

04:01:43.020 --> 04:01:47.829

Doug Butchart: I'm not a doctor, I don't know anything about medical stuff, so...

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04:01:48.290 --> 04:01:52.499

Doug Butchart: So it was a very large learning curve.

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04:01:52.890 --> 04:01:59.010

Doug Butchart: And... We went... that clinic closed.

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04:01:59.260 --> 04:02:04.120

Doug Butchart: And then we went to another clinic, And then that clinic closed.

1281

04:02:04.570 --> 04:02:11.089

Doug Butchart: And then she ended up... that, clinic in Chicago.

1282

04:02:11.590 --> 04:02:21.220

Doug Butchart: And we had the opportunity to get wrote, bolivial.

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04:02:22.760 --> 04:02:26.549

Doug Butchart: And... But we had... she had to be seen at Northwestern.

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04:02:27.230 --> 04:02:29.610

Doug Butchart: So we had to go to another clinic.

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04:02:30.560 --> 04:02:36.340

Doug Butchart: So, right now, she's still at Northwestern, And...

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04:02:36.950 --> 04:02:46.850

Doug Butchart: And obviously, she's not on Relivrio anymore, because... She's, taking, CNM AU8.

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04:02:47.000 --> 04:02:47.830

Doug Butchart: Which...

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04:02:51.170 --> 04:03:01.310

Doug Butchart: She's still alive. She was diagnosed 9 years ago, so... That's... That's one big thing.

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04:03:04.660 --> 04:03:08.010

Doug Butchart: 9 years of, of... Of not knowing

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04:03:08.840 --> 04:03:13.510

Doug Butchart: What's going on? How... what the outcome will be.

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04:03:14.450 --> 04:03:16.850

Doug Butchart: It is... It's pretty tough.

1292

04:03:19.480 --> 04:03:21.129

Doug Butchart: There's... there's a...

1293

04:03:23.320 --> 04:03:28.720

Doug Butchart: If I... there's a lot of things that I wish I had known 9 years ago, that I know now.

1294

04:03:29.350 --> 04:03:33.529

Doug Butchart: Because there's a lot of things that we would have done differently, but...

1295

04:03:34.590 --> 04:03:37.160

Doug Butchart: My wife, she can still walk.

1296

04:03:37.310 --> 04:03:38.180

Doug Butchart: Burp.

1297

04:03:38.820 --> 04:03:43.130

Doug Butchart: With assistance. She's not trached. She doesn't have a feeding tube.

1298

04:03:43.250 --> 04:03:47.210

Doug Butchart: And that... so, I mean, that... for those things, I'm grateful.

1299

04:03:48.260 --> 04:03:55.970

Doug Butchart: But... there's... Like I said, I wish there was... there was a lot of things I wish I hadn't.

1300

04:03:59.150 --> 04:04:00.330

Doug Butchart: I don't know.

1301

04:04:00.680 --> 04:04:02.989

Doug Butchart: That's all I can think of saying no. Thank you.

1302

04:04:05.430 --> 04:04:07.789

Danielle Boyce: I think you said a lot, Doug.

1303

04:04:08.380 --> 04:04:09.780

Danielle Boyce: The...

1304

04:04:10.260 --> 04:04:24.420

Danielle Boyce: the 9 years of not knowing what's going to happen has got to take such a toll, and I think that we almost just take for granted that people with ALS and their families are all dealing with that. We don't even talk about that part.

1305

04:04:24.650 --> 04:04:29.220

Danielle Boyce: Of how... what that must do to you, and how that might... might impact you.

1306

04:04:29.440 --> 04:04:30.889

Danielle Boyce: In your dealings.

1307

04:04:31.000 --> 04:04:34.460

Doug Butchart: Most people's journey is... It's very fast.

1308

04:04:34.670 --> 04:04:35.780

Doug Butchart: I'm very short.

1309

04:04:36.890 --> 04:04:39.529

Doug Butchart: So, you know, I'm grateful that my wife.

1310

04:04:40.660 --> 04:04:41.240

Danielle Boyce: Yeah.

1311

04:04:41.240 --> 04:04:42.719

Doug Butchart: It's still with me.

1312

04:04:43.700 --> 04:04:44.620

Doug Butchart: review.

1313

04:04:46.050 --> 04:04:46.890

Danielle Boyce: first.

1314

04:04:47.990 --> 04:04:49.230

Danielle Boyce: So, Mara...

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04:04:49.760 --> 04:05:09.569

Danielle Boyce: I know, just from knowing you well. And one of the reasons why I was really glad that you came, because I know you're very wise and willing to share what you wish you had known with Newly Diagnosed, and have a real passion for mentoring people new to the community. And so, would you like to comment on that?

1316

04:05:10.530 --> 04:05:13.300

Mara Dolan: I was thinking about that because I...

1317

04:05:13.530 --> 04:05:21.370

Mara Dolan: There is so much, like Doug said, there's just so much I wish I would have known. I was... I'm not medical still, I'm not medical. I feel a bit medical now.

1318

04:05:21.630 --> 04:05:29.390

Mara Dolan: But yeah, I think it's just, it's not really related to research as much, but it lets you ultimately get to research. Just...

1319

04:05:30.850 --> 04:05:33.729

Mara Dolan: Get over not wanting to ask for help. Get over it.

1320

04:05:33.880 --> 04:05:45.440

Mara Dolan: just be a... be begging all the time, it's all I do. It's... it's fine. Like, we... luckily, we're surrounded by extremely generous, beautiful people who love Pat, so... but before I asked.

1321

04:05:45.850 --> 04:05:50.979

Mara Dolan: it was really hard. It was me. It was me, and Pat didn't want to tell anybody for a while.

1322

04:05:51.180 --> 04:06:05.590

Mara Dolan: And I don't blame him one bit. So, I was, like, carrying this, like, crazy thing, like, your husband's gonna die very soon, could be 6 months, could be 2 years. At the very least, he's gonna have some choking incidents, gonna be real unpleasant.

1323

04:06:06.520 --> 04:06:16.310

Mara Dolan: And, he's gonna have a lot of goodbyes, goodbye to walking, goodbye to talking, goodbye to breathing on his own, you know? And we had to, like, hold that in for a couple months.

1324

04:06:16.410 --> 04:06:20.689

Mara Dolan: And I get it, I mean, I get it. It was very hard, I think, for him and me, but...

1325

04:06:21.580 --> 04:06:25.250

Mara Dolan: But I would say, like, try to get over that...

1326

04:06:25.420 --> 04:06:35.699

Mara Dolan: trying to go through it all yourself. I see that with so many people. I get... I'm so grateful. I get sent people who are just diagnosed a lot by our, people around us, and... and...

1327

04:06:35.860 --> 04:06:47.390

Mara Dolan: some of our ALS Association folks, and I'm so happy that I can, you know, with everybody's permission, like, they... they're like, can anybody help? And, you know, and I'm right here near them, so...

1328

04:06:47.420 --> 04:06:54.329

Mara Dolan: But they all... it's always the same thing, like, we don't want to ask for help every single time, like, I just want... we want to handle this ourselves.

1329

04:06:54.360 --> 04:07:13.419

Mara Dolan: And I would say, just get over that, because you need help, like, you... it's just... we do know people who have one caregiver, their spouse, like, we actually know two

people, but everybody else has an army of people to survive this thing. And that's what I would say, just make sure you reach out,

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04:07:13.830 --> 04:07:17.819

Mara Dolan: Because you need resources, you need to figure out money, you need to figure out...

1331

04:07:18.310 --> 04:07:24.989

Mara Dolan: trials, you know, you might want to... you want to... you want to help the science, you want to get an interventional trial, that's the goal.

1332

04:07:25.350 --> 04:07:26.420

Mara Dolan: But,

1333

04:07:26.570 --> 04:07:38.260

Mara Dolan: you can't do it with just you and someone who's, like, losing function and trying to get their affairs in order and trying to get their bucket list checked off. You got, like, 6 months, maybe, to do all that, in most cases.

1334

04:07:38.380 --> 04:07:40.240

Mara Dolan: So, it's really brutal.

1335

04:07:40.910 --> 04:07:45.240

Mara Dolan: yeah, just reach out for help. That's what I would say, but it doesn't really,

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04:07:45.700 --> 04:07:51.820

Mara Dolan: Really, to research so much, but... Yeah, I think...

1337

04:07:52.000 --> 04:07:57.660

Mara Dolan: the... the big... the big ta... the big thing I learned, I, I would... I would like to say this in my Round 2, is that

1338

04:07:57.780 --> 04:07:59.410

Mara Dolan: We really need...

1339

04:07:59.850 --> 04:08:14.039

Mara Dolan: I mean, all this research I listened to today was so great, I can't wait to sink my teeth into it today and yesterday. I mostly listened yesterday, but I heard bits from today, and I was like, oh my goodness, they're doing... it's so close to what we're doing. Like, it would help us, we could maybe help them. But,

1340

04:08:14.210 --> 04:08:17.820

Mara Dolan: you know, at the end of the day, I feel like there's still this missing piece that...

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04:08:18.260 --> 04:08:33.830

Mara Dolan: if we all got together as researchers, we could, like, make... make this thing happen where we have a central body, like a steward, like cancer has, like a Center for Excellence for neuro... neuro... Sorry, Neurosciences. Cancer has that.

1342

04:08:33.940 --> 04:08:37.679

Mara Dolan: HIV had a big upwelling, and that's how they got it done.

1343

04:08:38.120 --> 04:08:45.060

Mara Dolan: cystic fibrosis just has a really, really strong association solely focused on

1344

04:08:45.290 --> 04:08:48.209

Mara Dolan: their people today. They want to get something to their...

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04:08:48.460 --> 04:08:51.620

Mara Dolan: the people living with CF today, and they did it.

1346

04:08:51.940 --> 04:08:52.930

Mara Dolan: They did it.

1347

04:08:53.060 --> 04:09:10.440

Mara Dolan: So, that's what I feel is missing in this... this... in our world. It just feels like we're... we're doing these really important long-term studies. We gotta keep doing those, but I feel like at the same time, we have to have this fast track. Like, maybe it's crowdsourcing, maybe it's open label galore, maybe it's,

1348

04:09:10.440 --> 04:09:22.469

Mara Dolan: just a bunch of EAPs. By the way, we couldn't... we tried... we could get into an EAP, but we'd have to drive 9 hours in our... in our condition, like, you know, vent-dependent, needing suction all the time.

1349

04:09:22.570 --> 04:09:29.899

Mara Dolan: to breathe. Like, not just needing suction for comfort, like, to breathe, you need to have a suction go down that has to be sterile, you know?

1350

04:09:30.750 --> 04:09:42.370

Mara Dolan: it's just... I feel like there's... there's a better way to do this. It's gonna be... have to be radical. We're not... no one's gonna like it in research, I'm afraid. Like, it's gonna be hard. But I just feel like...

1351

04:09:42.920 --> 04:09:51.850

Mara Dolan: that's how we get out of this pattern of just, like, oh, we're still just not there, we still don't have... we have Toforsen, but we still don't have a treatment. We really still don't have a treatment.

1352

04:09:52.410 --> 04:09:58.510

Mara Dolan: So that's what... that's what my takeaway is from my whole 10 years' experience caring for my husband, like.

1353

04:09:59.110 --> 04:10:06.859

Mara Dolan: there's a... there's gotta be a different way. This is... this way, I love all this research, I'm a part of it, I... I... I support it.

1354

04:10:07.050 --> 04:10:08.850

Mara Dolan: But, like.

1355

04:10:08.970 --> 04:10:18.690

Mara Dolan: it's... and it's not the CDC's fault that the RIFs happened, but, like, the biorepository getting smushed down to nothing, basically, and...

1356

04:10:18.810 --> 04:10:22.010

Mara Dolan: Air pollution controls, like.

1357

04:10:22.120 --> 04:10:37.600

Mara Dolan: like, now we're... now the standard is even gonna be worse. It sounds like that's proposed, and it's gonna... so we're gonna have even less control over the crap that we're breathing, and... I mean, that's... this is all, like... this is all things that this gov... this steward could do. This body of...

1358

04:10:38.630 --> 04:10:58.119

Mara Dolan: this central thing could do. They could push to get the right stuff done for this disease, because we cannot speak. Like, we cannot... we literally are just hamstrung as patients and caregivers. It's not until afterward, and I see so many caregivers want to help, but they're like, I have to... I have... I've been in trauma for, like, 10 years. I need...

1359

04:10:58.500 --> 04:11:03.139

Mara Dolan: I cannot be in this for a couple years. And then sometimes they come back, sometimes they don't.

1360

04:11:03.460 --> 04:11:14.189

Mara Dolan: So yeah, we need... we just need that spokesman for us, and I know we're so close. These groups that have been talked today are, like, so close to being that, or helping to form that with other groups, but...

1361

04:11:14.310 --> 04:11:26.569

Mara Dolan: we're not... I feel like we're not there, and that's, like, the missing piece that has just got to happen somehow. I don't have an answer. I just know what the problem... I think that's the problem. That's one of the problems. And it's a complex disease. It's a complex disease.

1362

04:11:27.380 --> 04:11:31.940

Mara Dolan: But... Doug had a... I wrote it down, what did I say?

1363

04:11:32.420 --> 04:11:34.140

Mara Dolan: Mandatory reporting.

1364

04:11:34.270 --> 04:11:38.690

Mara Dolan: what a great first step, I believe. I've been advocating for that forever.

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04:11:38.850 --> 04:11:39.639

Mara Dolan: I just think...

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04:11:39.640 --> 04:11:40.039

Danielle Boyce: Oh my god.

1367

04:11:40.120 --> 04:11:41.400

Mara Dolan: That's gotta happen.

1368

04:11:41.850 --> 04:11:42.779

Mara Dolan: That's one of the radical.

1369

04:11:42.780 --> 04:11:43.130

Danielle Boyce: Oh, things.

1370

04:11:43.130 --> 04:11:50.900

Mara Dolan: I think has to happen. It's happening in some states. Let's make it all states and get the data we need. If we're seeing we can't get the data.

1371

04:11:51.470 --> 04:11:53.270

Mara Dolan: Do what we gotta do to get the data.

1372

04:11:54.030 --> 04:11:55.080

Mara Dolan: Do... do it...

1373

04:11:55.080 --> 04:11:55.410

Danielle Boyce: Yeah.

1374

04:11:55.410 --> 04:11:59.180

Mara Dolan: COVID-style, brute force, like, get what we gotta get done, let's do it.

1375

04:11:59.930 --> 04:12:00.710

Mara Dolan: Easy to say.

1376

04:12:00.710 --> 04:12:02.200

Danielle Boyce: Yeah, it's promising.

1377

04:12:02.330 --> 04:12:03.160

Danielle Boyce: Sorry.

1378

04:12:03.550 --> 04:12:28.480

Danielle Boyce: as promising as the big data and electronic health record work that I do, you know, is. You don't get everyone with that. Even if I were to get everyone who has their data in OMOP, common data model format, every hospital, I'm not going to get everyone, because those are generally the larger centers where I'm more likely to get the information anyway, you know, or more likely to be collaborating and doing the research. And so, to your point, like, I feel like we're

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04:12:28.480 --> 04:12:33.979

Danielle Boyce: yeah, I think that is still a gap, so it's, like, really exciting, like you said, but, like, then there's still...

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04:12:33.980 --> 04:12:49.659

Danielle Boyce: pieces that we all know are there, and have these limitations, and it's super frustrating, but it's almost like sometimes we've just accepted it as the reality of doing research in ALS, and, you know, I guess we're just gonna have to work around it. But from your perspective, you know, looking at it through your eyes.

1381

04:12:49.890 --> 04:12:57.720

Danielle Boyce: that's not good enough, right? And the other thing that you mentioned, when we were talking, a few days ago was

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04:12:57.780 --> 04:13:13.779

Danielle Boyce: not knowing what happens with drugs in the pipeline. And I don't think that everyone in the audience who works in research, who doesn't work with people with ALS, really understands they're keeping track of this. When somebody says they're going to start a study and it's really exciting.

1383

04:13:13.820 --> 04:13:28.800

Danielle Boyce: you're watching that. And so, to not... like, you had told me that, like, there are different, different, studies, and you're like, whatever happened to that? And... and we might know it because we all work in research, and we all talk to each other and go to the meetings, but, like.

1384

04:13:28.800 --> 04:13:36.140

Danielle Boyce: it was really an eye-opener when you were trying to track down a few things, and I'm like, you know what? There really aren't good websites that

1385

04:13:36.140 --> 04:13:47.100

Danielle Boyce: tell us what happened to that, and where it is, and was that promising or not? I mean, why... why are you adding that to your plate that you all described to try to figure that out, right?

1386

04:13:47.310 --> 04:13:53.739

Mara Dolan: Right, I have a database of 75 promising treatments that I've been tracking, and one of them is that H... it might have been the H...

1387

04:13:53.880 --> 04:13:55.820

Mara Dolan: 411 or 144, it's a, it's a...

1388

04:13:56.260 --> 04:13:58.270

Mara Dolan: Probiotic that showed

1389

04:13:58.390 --> 04:14:09.250

Mara Dolan: it... massive neuroprotection, like, I'm not... I'm not a meta... I'm gonna use the word massive, but it was significant, changes in different animal models, and

1390

04:14:09.440 --> 04:14:17.809

Mara Dolan: everybody was all excited about it. A Phase 1 trial was planned, or I guess it was pre-clinical, whatever the very first thing was, was planned, and

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04:14:17.990 --> 04:14:21.850

Mara Dolan: Yeah, it was... There's a lot of excitement, it got funded.

1392

04:14:21.960 --> 04:14:25.760

Mara Dolan: It also had... I have it here, it had... it showed,

1393

04:14:27.110 --> 04:14:30.569

Mara Dolan: Activation, or I don't know what the correct word is, but...

1394

04:14:30.990 --> 04:14:34.050

Mara Dolan: in... I'm not gonna find it, but it was, like.

1395

04:14:34.170 --> 04:14:51.309

Mara Dolan: not only in SOD1, but two different models, like TDP or something, I don't know. I'm so sorry, I can't get to it quickly. But anyway, it, it looked really good, and then just gone. Like, it just went off the face of the earth. Okay, TDP43 and few space models, as well as SOD1.

1396

04:14:51.810 --> 04:14:53.860

Mara Dolan: I wrote, funded, concrete.

1397

04:14:54.170 --> 04:14:57.670

Mara Dolan: Safe for humans, definitely safe. People have taken it before.

1398

04:14:58.500 --> 04:15:03.059

Mara Dolan: gone. And I can't even try it, like, you can't even go buy it. It's just a freaking probiotic.

1399

04:15:03.060 --> 04:15:03.600

Danielle Boyce: I mean...

1400

04:15:03.600 --> 04:15:04.330

Mara Dolan: I was like.

1401

04:15:04.330 --> 04:15:05.000

Danielle Boyce: Yeah.

1402

04:15:06.010 --> 04:15:12.199

Danielle Boyce: And, I mean, think about that. You have a database. She made a database, right? You know what I mean?

1403

04:15:12.200 --> 04:15:14.749

Mara Dolan: Happy for anybody to be added.

1404

04:15:14.750 --> 04:15:26.850

Danielle Boyce: And so many other people I've spoken to who don't have data background. That's why I love working with the community, though, because they're people like you, and it's, like, there's no boundary there, you know, what you won't do, right?

1405

04:15:26.850 --> 04:15:27.260

Mara Dolan: You're loving.

1406

04:15:27.260 --> 04:15:31.600

Danielle Boyce: You know, what do you do for your loved one? You do... you lift a car up over it, you'll do anything.

1407

04:15:31.600 --> 04:15:32.020

Mara Dolan: You will.

1408

04:15:32.020 --> 04:15:40.310

Danielle Boyce: You'll do anything for them. And the details and the data, and so that's also something that I've learned working in the community, is that, like.

1409

04:15:40.410 --> 04:15:41.189

Danielle Boyce: I, I...

1410

04:15:41.190 --> 04:16:03.730

Danielle Boyce: I often go to my colleagues in the advocacy community, people living with ALS, for advice, like, actual research advice. Like, have you heard about this, or do you know this? Because I heard about it, but I can't find anything, and you probably know the

person sat on the panel, like Stacy, you know, you probably sat on the panel, advised the group, helped them design the study, and so... so it's not,

1411

04:16:03.730 --> 04:16:26.829

Danielle Boyce: It's not something to do to be nice to the community, it's something to be nice to yourself as the researcher, is what I'm trying to get across. I'm looking at some comments, and I just want to highlight a few from folks who put in questions, and you know, Lynn Brillmeyer, of course, we all know Lynn, who is a really fantastic, terrific advocate.

1412

04:16:26.830 --> 04:16:34.780

Danielle Boyce: For people, with ALS, and he himself happens to have ALS, and he wrote, I chased an EAP for 10 months.

1413

04:16:35.180 --> 04:16:38.219

Danielle Boyce: In the 6th month, they changed the criteria.

1414

04:16:38.450 --> 04:16:40.789

Danielle Boyce: Yeah, he changed the word to chase loans.

1415

04:16:40.790 --> 04:16:41.630

Mara Dolan: Oh, I'm sorry, I'm sorry.

1416

04:16:41.630 --> 04:16:51.860

Danielle Boyce: I changed it below. That's okay. I chased an EAP for 10 months. In the 6th month, they changed the criteria. However, they didn't tell me until the 10th month that I no longer qualified.

1417

04:16:52.350 --> 04:16:57.530

Danielle Boyce: To back up, EAPs are only for those who don't qualify for clinical trials.

1418

04:16:57.690 --> 04:17:02.430

Danielle Boyce: I found out I was too far gone for an EAP after being in.

1419

04:17:02.600 --> 04:17:05.249

Danielle Boyce: Two years later, I'm still here.

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04:17:05.400 --> 04:17:12.240

Danielle Boyce: And I'm so glad you are, Lynn. It goes to show that we still have a poor understanding of disease progression.

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04:17:12.520 --> 04:17:17.110

Danielle Boyce: A better understanding is crucial to better trial outcomes analysis.

1422

04:17:17.940 --> 04:17:35.890

Danielle Boyce: And just thinking about that, like, chasing an EAP for 10 months, like, what that means. Research, conversations, phone calls, you know, and not necessarily being able to do those things yourself or with the physical tools that you had before your diagnosis, and so that's what really...

1423

04:17:36.250 --> 04:18:00.899

Danielle Boyce: stresses me out when I'm talking to the community, just feeling that burden of all the work they have to do just to enroll, and then here we are saying, why won't people enroll, you know? And that's what's like this cognitive dissonance that I have all the time when we're having these conversations, because most of the people I know are begging to participate in research. They want to, but they're dealing with, you know, all of these different

1424

04:18:00.930 --> 04:18:16.479

Danielle Boyce: obstacles, and I, you know, of course, working at ALSTDI, I know that we have, you know, an online study, we try to make it as easy as possible, we send a phlebotomist to your home, but that's... that's not always the case, right? And that's... and that is not a clinical trial.

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04:18:16.480 --> 04:18:25.310

Danielle Boyce: And so, in the registry, same thing. I mean, we're incentivizing participation, and we're doing outreach, but... but if you're...

1426

04:18:25.310 --> 04:18:48.200

Danielle Boyce: if you're trying to chase down an EAP because you think that drug might help you prolong your life, then probably the last thing on your mind is what I'm hearing from these listening sessions, the last thing on your mind is participating in a long-term

natural history study where there's no drug that you're going to take, and that is just an added thing. So it sounds like from talking to you

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04:18:48.200 --> 04:18:50.360

Danielle Boyce: Mara, is that changing

1428

04:18:50.910 --> 04:19:01.450

Danielle Boyce: something over here might help something over here, you know? It's not necessarily a, you know, just fix the research, fix the clinical stuff too, right? Like, fix all of it.

1429

04:19:01.770 --> 04:19:15.210

Mara Dolan: Yeah, there's just... but there's no ombudsman, or no, like, person who can... or group, not single person, probably can't do it. Maybe you, Danielle, and Pat Dolan. But, no, I just... yeah, we need that voice, I feel.

1430

04:19:15.550 --> 04:19:23.030

Mara Dolan: and they can... and something else that Doug said, I just thought of, to me, too, is, like, he's having to find a clinic and go all around, they keep closing.

1431

04:19:23.170 --> 04:19:24.979

Mara Dolan: It just reminded me, too, like.

1432

04:19:25.560 --> 04:19:33.310

Mara Dolan: there's such a thing as home health. Why couldn't we get creative there and just have, like, the blood draws... have a home health nurse come? You know, we have that now.

1433

04:19:33.310 --> 04:19:33.830

Danielle Boyce: because...

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04:19:33.830 --> 04:19:35.230

Mara Dolan: Pat is bed-bound.

1435

04:19:35.510 --> 04:19:42.389

Mara Dolan: So... so why not... like, why... like, why do we have to drive 9 hours You know, to...

1436

04:19:42.560 --> 04:19:46.030

Mara Dolan: To get our blood drawn and meet someone for 5 minutes, basically.

1437

04:19:46.030 --> 04:19:46.470

Danielle Boyce: Yeah.

1438

04:19:46.470 --> 04:19:55.090

Mara Dolan: I'm sure there's, like, they'll, like, push in his hands and stuff, but basically, that's my impression, like, it would be something like that, which his doctor could do, who is down the street here, or...

1439

04:19:55.450 --> 04:20:06.510

Mara Dolan: you know, some... you can get a doctor to make a house call, it's expensive, but, like, for something like that... I don't know, I just... I feel like there's... there's not the thing that's saying, like, we gotta be creative, we gotta, like.

1440

04:20:07.210 --> 04:20:16.140

Mara Dolan: we're doing all these very smart studies, we are, and I think they have to get done. They're the right things to do, but I also feel like we have to be a little...

1441

04:20:16.250 --> 04:20:19.229

Mara Dolan: Rogue over here, and just do some other stuff.

1442

04:20:20.930 --> 04:20:22.090

Danielle Boyce: Yeah, no.

1443

04:20:22.090 --> 04:20:47.079

Danielle Boyce: I mean, that's what I've kind of heard the theme over the last few days. It's a heterogeneous disease, and Doug said you meet one person with ALS, you've met one person with ALS, basically. So, right? And so... and it impacts people different ways. It causes hardship that you can't possibly imagine. I know there's often an assumption that you have some devastating disease, and you'll all of a sudden get all of these services.

1444

04:20:47.080 --> 04:21:00.950

Danielle Boyce: That's a huge, huge misconception, right? Doug is saying this, like, she didn't have enough credits to get SSI, like, and people do not understand it. They also think that it's easy to get home health, and it's not, right? And it's not worth...

1445

04:21:00.950 --> 04:21:01.440

Mara Dolan: Not paid for.

1446

04:21:01.440 --> 04:21:17.569

Danielle Boyce: Or you have to be the human resources department to manage all the home health. To me, even reaching out to a support community can be daunting, right? Like, just waiting for that phone call, making sure you're free, making sure you're not doing trach care, you know, respiratory stuff or whatever.

1447

04:21:17.570 --> 04:21:18.599

Mara Dolan: Good job.

1448

04:21:18.600 --> 04:21:38.320

Danielle Boyce: Right, or hope, yeah, and one person working, so... Yeah, so somebody else meant, Christy Taddy, I want to say, so I'm also a physician, and I told my primary neurologist that I had, ALS 4 months before my genetic testing confirmed it. I have been told by both University of Michigan and, Mayo Clinic that I don't qualify for trials.

1449

04:21:38.320 --> 04:21:42.829

Danielle Boyce: There are a number of questions related to

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04:21:42.830 --> 04:22:06.289

Danielle Boyce: who is eligible to participate in trials, in trial eligibility, and I wonder if we have, clinicians on our panel, if they, if they would, you know, maybe jump in and answer some of these Q&As that have come through. Questions about whether you're diagnosed with bulb or ALS, why are you excluded from trials, for example? I think that's got to be really, hard to... first, you've never worked in this field.

1451

04:22:06.290 --> 04:22:10.740

Danielle Boyce: Now, all of a sudden, you're trying to read a clinicaltrials.gov inclusion criteria statement.

1452

04:22:10.790 --> 04:22:26.440

Danielle Boyce: That's really hard. And of course, we have lots of organizations, ALSTDI, we have clinical trial, navigation resources, and lots of groups have that, but it's kind of like getting to those resources that I know is always the...

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04:22:26.440 --> 04:22:32.150

Danielle Boyce: the challenge. Once you find them, then it's easier, but it could be a long time before you get

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04:22:32.180 --> 04:22:48.450

Danielle Boyce: you get that. Before you even get your diagnosis, also, right? And that also delays your ability to... that delay can affect your ability to participate in a clinical trial as well. I see the CDC registry team has... a couple of you have joined,

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04:22:48.730 --> 04:22:51.929

Danielle Boyce: Paul, do you have anything that you wanted to share?

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04:22:55.390 --> 04:22:57.320

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

1457

04:22:58.890 --> 04:23:00.109

Paul Mehta: Sorry, can you hear me now?

1458

04:23:00.380 --> 04:23:01.090

Danielle Boyce: Yes,

1459

04:23:01.090 --> 04:23:02.720

Paul Mehta: Just want to simply, you know.

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04:23:03.040 --> 04:23:16.309

Paul Mehta: the perspectives of those living with ALS and their caregivers, I mean, this is really, really heartbreaking stuff, and I mean, you know, we're not in your shoes. You know, we've not gone through what you've gone through, but I mean, you know, this is so...

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04:23:16.540 --> 04:23:33.600

Paul Mehta: you know, as researchers, you know, we're kind of, like, sometimes outside the realm, you know, sitting on a different altitude, but the perspective really hits home when Doug and Stacy and Mara, you know, tell everybody about their stories. I mean, this is really, really heartbreaking, you know, and...

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04:23:33.790 --> 04:23:49.929

Paul Mehta: you know, we have the ALS Association, we have MDA, we have Team Gleason, we have Les Turner, you know, and in the future, we'll probably have ALS United as well on these calls. So, I mean, you know, this is a way for them to hear these stories and potentially, you know, push back to those individuals who make these decisions. You know, we...

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04:23:49.930 --> 04:23:55.070

Paul Mehta: You know, we're sitting here at the register, we don't have that influence to do that, but certainly.

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04:23:55.070 --> 04:24:06.860

Paul Mehta: you know, the ALS Association, like, like Kevin Horton once told me a long time ago when I first started, he goes, the ALS Association is kind of like the NRA without the guns. You know, they show up with their wheelchairs, and they're very...

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04:24:06.870 --> 04:24:25.790

Paul Mehta: they push things through, and so, you know, it's certainly a very, you know, a noble thing what they've done, you know, to reduce the disability requirements and this and this, but what Doug was saying about his wife not being covered, that certainly is extremely, you know, heartbreaking, and it's... I'm so sorry to hear that, Doug, about what you're going through.

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04:24:26.190 --> 04:24:42.330

Paul Mehta: And so forth, but I mean, it's... but certainly, I mean, I think, you know, the voices that you guys have and your perspectives are being heard by, you know, by the advocacy groups here who are sitting here, and who are also listening to this stuff, and simply saying, hey, you know, you know, we hear you, and so forth.

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04:24:43.330 --> 04:25:00.209

Paul Mehta: The question from Eric Johnson, and I'll defer to my neurologist colleagues here, Fernando, Lyle, as well as Stephen Goutman, to kind of answer that question. I mean, I know what the answer is, but I think they could probably do it in a much more subtle way.

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04:25:00.210 --> 04:25:08.070

Paul Mehta: Regarding why the qualification may not be there for those trials. Lyle, Fernando, Steven, if you guys could potentially answer that question?

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04:25:12.530 --> 04:25:13.260

Paul Mehta: Yup.

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04:25:13.260 --> 04:25:26.560

Lyle W. Ostrow MD PhD, Temple Univ.: Sure, I'm a little bit blurry-eyed because you guys made me cry, but that's okay. You know, we all need to do better at this. The specific question, which one? Because I see a lot of them in the chat that are on this topic.

1471

04:25:26.560 --> 04:25:31.099

Paul Mehta: Lyle, it's a question. Why are those diagnosed with diagnosed with bulb or ALS?

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04:25:31.100 --> 04:25:31.420

Lyle W. Ostrow MD PhD, Temple Univ.: Yeah.

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04:25:31.420 --> 04:25:32.420

Paul Mehta: for many trials.

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04:25:32.420 --> 04:25:40.079

Lyle W. Ostrow MD PhD, Temple Univ.: Right, and by the way, you guys, not that... I mean, there's a lot of places doing this, but, you know, Terry Hammond-Patterson and I do this monthly Zoom.

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04:25:40.260 --> 04:25:51.560

Lyle W. Ostrow MD PhD, Temple Univ.: That's co-sponsored by the Hope Foundation and, everything ALS, and it's called Citizen Research, and they're all recorded. and this is exactly what we do. It's just like a...

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04:25:51.560 --> 04:26:06.689

Lyle W. Ostrow MD PhD, Temple Univ.: you know, talk about these things whenever people want to talk about, open kind of session, but we also talk about, like, how to digest information, how to read a press release, how to, you know, how we can all help each other in this data-heavy world that we live in, be responsible consumers of information, and...

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04:26:06.790 --> 04:26:22.160

Lyle W. Ostrow MD PhD, Temple Univ.: and, you know, understand what's going on, and understand why certain things get into trials, and how the trials are designed, and the why. So, join us if you want. Also, email me anytime, and I'm happy to talk about anything. I work for you, right? This is my job. So,

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04:26:22.270 --> 04:26:30.340

Lyle W. Ostrow MD PhD, Temple Univ.: I'm always happy to talk. There also are several organizations that do similar things that are, like everything ALS,

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04:26:30.500 --> 04:26:44.230

Lyle W. Ostrow MD PhD, Temple Univ.: has one that's called Fireside Chats. Most of the organizations do, which are meant to be kind of safe spaces for you guys to talk about this stuff. And I joined a bunch of them, and I originally joined because I thought it was going to be, like, people

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04:26:44.240 --> 04:26:52.999

Lyle W. Ostrow MD PhD, Temple Univ.: talking about goofy snake oil, you know, and I wanted to make sure that wasn't going on, but that wasn't what it was at all, and in fact, I've learned so much from those sessions, and they're...

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04:26:54.410 --> 04:27:02.049

Lyle W. Ostrow MD PhD, Temple Univ.: and the topics you guys are bringing up right now are the things that are always discussed. There also are... there's a push in a lot of clinics right now to start, like,

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04:27:02.270 --> 04:27:08.940

Lyle W. Ostrow MD PhD, Temple Univ.: Men's groups, and this kind of thing, and groups of, you know, caregivers groups, groups of people who have these shared experiences.

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04:27:09.150 --> 04:27:17.040

Lyle W. Ostrow MD PhD, Temple Univ.: To the specific question about clinical trial design, you know, clinical trials are designed a certain way for a couple reasons, and

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04:27:17.260 --> 04:27:30.619

Lyle W. Ostrow MD PhD, Temple Univ.: And one of them is, you want to not have... you want to be able to see a change in the length of the trial, right? If somebody has slowly progressing disease over 8 or 9 years, well, how long of a trial do you need to tell if the drug helps them?

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04:27:31.450 --> 04:27:48.140

Lyle W. Ostrow MD PhD, Temple Univ.: bulbar symptoms, you know, breathing in particular, what happens is that as somebody's disease progresses, like, if you're in a trial and you have to drop out because you stopped coming to clinic because your breathing has gotten so bad, like, the trial can't replace you. It's lost data. And,

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04:27:48.500 --> 04:27:55.370

Lyle W. Ostrow MD PhD, Temple Univ.: And so a lot of the requirements about things like that are about, you know, getting people who are going to see a change over time.

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04:27:55.840 --> 04:28:10.670

Lyle W. Ostrow MD PhD, Temple Univ.: getting people who will more likely to stay in the trial. That being said, you know, we need broader inclusion, and we need, you know, to let everybody be in all the trials. And the answer to that, the way we're going to get at that, is something I spoke about yesterday, which is

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04:28:10.670 --> 04:28:16.959

Lyle W. Ostrow MD PhD, Temple Univ.: Having these biomarkers that are specific to a particular drug that tell us

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04:28:16.990 --> 04:28:30.850

Lyle W. Ostrow MD PhD, Temple Univ.: you know, like the example I used, you know, in diabetes, I can measure somebody's sugar, right? So, if there's a clinical trial of a drug that's supposed to affect a particular thing about your cells and your body, you know, if I had a way to measure that particular thing.

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04:28:30.870 --> 04:28:40.139

Lyle W. Ostrow MD PhD, Temple Univ.: specifically, maybe I could tell, and I wouldn't... and I wouldn't have to be so strict about fast progress or slow progress, or whatever it is, I could tell if the drug was working, but

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04:28:40.630 --> 04:28:42.530

Lyle W. Ostrow MD PhD, Temple Univ.: We are kind of a long way from that.

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04:28:43.260 --> 04:28:53.579

Lyle W. Ostrow MD PhD, Temple Univ.: I will say this, too. You know, if you asked me 3 years ago, like, what's the best I could hope for for an ALS patient, you know, I thought maybe we could slow down the disease.

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04:28:53.640 --> 04:29:08.679

Lyle W. Ostrow MD PhD, Temple Univ.: I now know that we can make people better, right? Because we've done it with some of these genetic forms. We... some people who are, you know, with the SOD mutation, more recently, people who are taking these medicines for the bus mutation and a few others, some people have actually gotten better, and...

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04:29:09.070 --> 04:29:12.569

Lyle W. Ostrow MD PhD, Temple Univ.: And I didn't know that that was possible before, and now I do.

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04:29:13.160 --> 04:29:19.399

Lyle W. Ostrow MD PhD, Temple Univ.: And I know that the reason we were able to do it was in those specific people, we were able to figure out

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04:29:20.100 --> 04:29:25.520

Lyle W. Ostrow MD PhD, Temple Univ.: what's the problem, right? What's their underlying problem that caused their disease? And we were able to target it.

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04:29:25.670 --> 04:29:35.980

Lyle W. Ostrow MD PhD, Temple Univ.: And, you know, for these trials in sporadic ALS, we don't do that. We know that there's different people that cluster with different biological abnormalities, but

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04:29:36.290 --> 04:29:49.100

Lyle W. Ostrow MD PhD, Temple Univ.: But, you know, what we basically do would be like enrolling everybody in a trial of a medicine for one particular gene mutation, whether they had the mutation or not. That's what we do. And so it's not surprising that these trials fail, and we need to get better at that.

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04:29:49.550 --> 04:29:55.359

Lyle W. Ostrow MD PhD, Temple Univ.: As far as where you can look to find information on these trials, there are some newer tools, so there's a

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04:29:55.550 --> 04:29:59.360

Lyle W. Ostrow MD PhD, Temple Univ.: I mean, you guys know about all the trial searches. Honestly.

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04:29:59.510 --> 04:30:11.930

Lyle W. Ostrow MD PhD, Temple Univ.: you know, some of the, like, Claude and ChatGPT are not bad. You also can just call your doc, or call me, or email, you know, there's a bunch of us who are always happy to talk and tell you what we know. We don't know anything magic. We don't have any...

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04:30:11.940 --> 04:30:31.779

Lyle W. Ostrow MD PhD, Temple Univ.: you know, information about what's going to work or what's not going to work, but we can tell you what's going on with different trials. There's an AI-enabled chatbot that's on the Everything ALS app that just talks to you in plain English. You can ask it questions about, like, you know, just... and it'll talk to you like a conversation. It's, you know, and it's trained on specific reliable data.

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04:30:32.550 --> 04:30:47.720

Lyle W. Ostrow MD PhD, Temple Univ.: I talk to it and try and screw it up, like, I ask it, like, who's the tallest ALS doctor, and it gets mad at me. But it will answer questions when you have questions about the status of different trials. But the reason that the trial criteria exist are to get an answer, right? And...

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04:30:47.830 --> 04:30:49.979

Lyle W. Ostrow MD PhD, Temple Univ.: And the last thing I'll say,

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04:30:50.780 --> 04:31:01.250

Lyle W. Ostrow MD PhD, Temple Univ.: you know, when you are in a trial, there's one of three things that can happen. You can get better, you can get worse, you can stay the same, right? And if you look historically, not many people have gotten better, and... and so...

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04:31:01.350 --> 04:31:19.860

Lyle W. Ostrow MD PhD, Temple Univ.: The reason for being in a trial is to help figure out an answer, and help get, you know, find out if a drug works, and they're designed to do that. And then, if a drug is working, like, if there's a signal, and if there's an obvious signal early, the trials get stopped early, right? If a trial is clearly working, they stop the trial, and they give people, you know, and...

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04:31:19.920 --> 04:31:25.100

Lyle W. Ostrow MD PhD, Temple Univ.: And that's always going to be the case. And so, all... the thing that I would say that I'm...

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04:31:25.100 --> 04:31:40.259

Lyle W. Ostrow MD PhD, Temple Univ.: so optimistic and excited about right now is how many different things there are. I mean, I... it's impossible to keep track of. You said you had a database of how many, Mara? It was... right? Like, do you realize how much... how different that is than just a few years ago? I mean, it's insane. And so.

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04:31:40.260 --> 04:31:41.810

Lyle W. Ostrow MD PhD, Temple Univ.: You know,

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04:31:42.440 --> 04:31:53.219

Lyle W. Ostrow MD PhD, Temple Univ.: it really is incredible, and because we live in this interconnected, data-heavy world, we're all going to find out about them. But, but if you have specific questions about a specific trial or trial design, you know.

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04:31:53.260 --> 04:32:07.900

Lyle W. Ostrow MD PhD, Temple Univ.: reach out, there are some videos online, too, I can email you guys some stuff, but just understand that the trials are specifically designed so that you can detect a change over a certain period of time, so that, you know, your groups are matched, and so that people aren't going to drop out halfway through.

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04:32:16.130 --> 04:32:26.999

Danielle Boyce: So, kind of wrapping up the session, and I know we're going to have some more Q&A, so we can continue this, kind of the Q&A around various things after this, but...

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04:32:27.310 --> 04:32:31.220

Danielle Boyce: I'm wondering if any of our panelists have

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04:32:31.820 --> 04:32:36.099

Danielle Boyce: Any closing thoughts? Like, Doug, I mean, do you...

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04:32:38.130 --> 04:32:48.450

Danielle Boyce: If you could ask the community, or tell the community one thing, and this is for any of you, if you could... if you could share one thing with the community that

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04:32:48.870 --> 04:33:01.749

Danielle Boyce: you want them to know to... this is the research community, to inspire their work, and to, you know, keep your loved one in their thoughts. Do you have any additional thoughts, any of you?

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04:33:05.480 --> 04:33:06.330

Doug Butchart: Yes.

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04:33:08.380 --> 04:33:16.250

Doug Butchart: I appreciate the important work that the National Register... ALS Registry is doing the data pro...

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04:33:16.619 --> 04:33:24.229

Doug Butchart: it provides the ALS community. At the same time, it's difficult for families and advocates to rely on a national

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04:33:24.380 --> 04:33:31.969

Doug Butchart: prevalence report based on 2018 data, when the ALS landscape treatment options

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04:33:32.119 --> 04:33:47.109

Doug Butchart: and needs of families continue to change. I hope the CDC, ATSDR can find ways to provide more timely, clearly labeled annual estimates while continuing to carefully work

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04:33:47.759 --> 04:33:48.810

Doug Butchart: Needed.

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04:33:50.990 --> 04:34:00.510

Doug Butchart: finalized reports, better connection with ALS clinics, electronic health records, state registries, and mortality data could help

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04:34:00.619 --> 04:34:04.700

Doug Butchart: Give families, researchers, and policy makers a more current.

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04:34:05.400 --> 04:34:17.039

Doug Butchart: picture of who is living with ALS and what supports are needed. ALS moves quickly, and the information that guides research, care, and policy should move

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04:34:17.310 --> 04:34:18.470

Doug Butchart: Quickly, too.

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04:34:21.230 --> 04:34:22.300

Danielle Boyce: Thank you, Doug.

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04:34:24.860 --> 04:34:38.200

Danielle Boyce: Stacy, if you wanted to communicate anything to the group, if you wanted to put anything in the chat, I would follow up if you have anything else that you'd like to add, and we'll be sure to keep it in the follow-up discussions as well.

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04:34:39.439 --> 04:34:47.649

Danielle Boyce: Thank you, everyone. Thank you, all three of you. I know that it wasn't easy to come and do this, and all the planning, and all the emails.

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04:34:47.869 --> 04:35:07.899

Danielle Boyce: That we had, and it really, it really means a lot, and from the activity that I'm seeing in the chat, in the Q&A, you really hit a nerve with a number of people, and I think there's probably a lot of people in the audience who'll go away not being the same, because they met you, and that was the goal, and you certainly achieved that.

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04:35:07.900 --> 04:35:09.799

Danielle Boyce: So, thank you very, very much.

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04:35:10.099 --> 04:35:14.779

Mara Dolan: Thank you so much, Danielle, and everybody, for doing what you do. You're amazing humans.

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04:35:14.949 --> 04:35:15.799

Doug Butchart: Thank you.

End of the Day Wrap-up/Questions/Open Discussion

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04:35:18.130 --> 04:35:21.520

Danielle Boyce: I think we're gonna turn, to, a...

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04:35:21.720 --> 04:35:26.779

Danielle Boyce: question and answer and kind of wrap up some of the questions. I don't know how

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04:35:26.869 --> 04:35:41.130

Danielle Boyce: you all want to, the panelists want to proceed. There are questions in the Q&A that you might want to answer directly, so if you are a panelist and you see something that you might want to answer, go ahead, but meanwhile.

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04:35:41.130 --> 04:35:48.260

Danielle Boyce: I can kind of go through some of them and, that are still outstanding, for the people who are still here.

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04:35:49.610 --> 04:35:50.930

Danielle Boyce: Let's see...

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04:35:53.529 --> 04:36:06.380

Danielle Boyce: Pat Dolan says, did you find any differences based on military campaigns veterans served in? For example, was there a higher rate of ALS for veterans who served post-9-11 wars? Thanks.

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04:36:10.710 --> 04:36:35.669

Paul Mehta: So, I know Mark published some work on that just recently, and it was, let me see if I can find the article, but they went by different various branches as well. I think that's what he presented partly yesterday as well, but, we do know that there are certain branches of the military which are more effective than others, Air Force, Coast Guard, and so forth, but I'm not sure why, you know, I think some of the hypotheses are the fact that maybe there's exposures to

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04:36:36.200 --> 04:36:43.569

Paul Mehta: UV rays, as well as certain toxicants, which are off-gassing for pilots and so forth. There is an article that just came out

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04:36:43.570 --> 04:36:56.440

Paul Mehta: which showed pilots and flight attendants have a higher rate of cancers, these skin cancers and so forth, just core cancers in general, and so I think that's because of the exposures of UV rays on a constant basis.

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04:36:56.580 --> 04:36:58.969

Paul Mehta: But as in terms of, you know, what's happening

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04:36:58.970 --> 04:37:23.779

Paul Mehta: before 9-11 or after 9-11. I think, you know, there are some research being done. I think Mark certainly is doing that, as well as Alberto, as well. The data that we have, we're looking more on the instance and the prevalence, and it's more, it's pretty much past, 2001, so it's not, before that right now. But if we can get access to earlier data, we certainly could go ahead and look at and compare and contrast the number of cases coming in before 9-11.

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04:37:23.779 --> 04:37:29.829

Paul Mehta: and after 9-11 as well, and that's where we partner with the VA to kind of make that happen.

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04:37:31.029 --> 04:37:45.579

Paul Mehta: one of our VA collaborators, Ileana Howard, Dr. Howard, she's not... I think she's on leave right now, but normally she's one of our co-authors in a lot of the papers. She's out of, Puget Sound, and so forth, and so she's very, very good, very knowledgeable about the VA community and the care.

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04:37:49.450 --> 04:37:52.150

Danielle Boyce: Thanks. I have another one.

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04:37:52.349 --> 04:38:11.320

Danielle Boyce: Has anyone looked at ALS cases by proximity to coal-fired power plants versus gas-fired? I went into my little mini knowledge graph that I use at work, and I did not see this particular one, but that doesn't mean it's not out there, it just means it's not in my database. Does anyone

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04:38:11.540 --> 04:38:16.429

Danielle Boyce: Does anyone know of this? Otherwise, we'll mark that down as something for follow-up.

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04:38:17.009 --> 04:38:21.560

Danielle Boyce: I mean, it's... and collecting it is different from publishing on it, right? So...

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04:38:21.689 --> 04:38:25.540

Danielle Boyce: There might be... it might be in data somewhere, but has anybody

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04:38:25.960 --> 04:38:29.249

Danielle Boyce: leveraged the data and looked at it. I am not aware of this.

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04:38:30.060 --> 04:38:44.420

Paul Mehta: Yeah, I'm not aware of it either. I think one of the things is, I think it's generally, as in terms of you could map the number of cases and where they're at, and then go ahead and map out the actual coal-fired plants and their gas-fired plants, but you also have to look at prevailing wind patterns as well.

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04:38:44.419 --> 04:39:09.390

Paul Mehta: and so forth, and how those potentially impact those living downstream. And so there's a lot of factors and variables involved when it comes to possible exposures. I mean, it's certainly a very, very good question, because we want to see exactly if those people living closer to these particular plants, are they at higher risk of getting ALS than those who are not? So it's certainly a very, very interesting question. It's the one that University of Michigan also presented. I think Meredith was the one who presented it earlier today.

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04:39:09.390 --> 04:39:26.089

Paul Mehta: about the fact that looking at, PMO2... PM2.5 and seeing exactly how far it is from certain geographic areas as well, and looking at the exposures and so forth. So University of Michigan is doing a lot of work on that, pollution areas as well, so, which is really interesting, so...

1556

04:39:26.090 --> 04:39:28.239

Paul Mehta: But that's a very, very interesting question.

1557

04:39:31.849 --> 04:39:32.899

Danielle Boyce: Here's one.

1558

04:39:33.009 --> 04:39:39.279

Danielle Boyce: Good question here. So, WHO has indicated that all forms of tobacco nicotine use is not safe.

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04:39:39.529 --> 04:39:57.719

Danielle Boyce: Is there research looking at risk-impact of vape devices, nicotine versus nicotine-free, on ALS or neurodegenerative conditions? And it's interesting, because we asked, like, ever smoker in the AHRQ study, but I... I don't know that we... I don't... we... we do not specify by vapor or not, and it...

1560

04:39:58.209 --> 04:40:11.119

Danielle Boyce: does make you wonder if there are things that are being left out. That's one thing I think of, is maybe people skip that. Nope, I vape, you know? And that doesn't count, because it's not a cigarette or tobacco. Well, it is... it is, but, you know, they don't think of it that way.

1561

04:40:11.269 --> 04:40:20.339

Danielle Boyce: Has anybody looked at vaping? Is there a date... what kind of data do we have on vaping? I don't think the registry collects it that way either, does it, Paul?

1562

04:40:20.660 --> 04:40:34.779

Paul Mehta: Yeah, I'll defer to Jamie, but I don't believe we're asking... we're asking ever or... or never smokers, right, Jamie? I don't believe we're asking specifically on vaping itself. Vaping, I mean, obviously, it's been around for a while, but it's also, it's somewhat new as well. I mean, I think there's other...

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04:40:35.560 --> 04:40:42.159

Paul Mehta: Considerations regarding vaping as in terms of lung issues down the road, and so forth, and possible complications down the road.

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04:40:42.800 --> 04:40:49.819

Paul Mehta: That's a question we certainly could go ahead and ask in the registry itself. It would be an adjustment of the surveys themselves. Jamie?

1565

04:40:51.100 --> 04:41:04.700

Jaime Raymond: Yeah, I was just gonna say, yeah, it is not... we don't specifically ask about smoking, we do not ask about vaping, current or former, smoker or a never-smoker, and then we look at packs a day, packs a year, that kind of thing.

1566

04:41:04.700 --> 04:41:21.040

Jaime Raymond: I would say probably vaping is probably a little bit newer to the population that's in our registry, so we probably wouldn't see that yet, but it is something to think about moving forward as the populations change, that we need to start thinking about other

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04:41:21.040 --> 04:41:25.819

Jaime Raymond: Other potential risk factors that were not originally picked up.

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04:41:28.900 --> 04:41:31.769

Danielle Boyce: Yeah, I'm thinking about that too, like, and as...

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04:41:31.980 --> 04:41:36.840

Danielle Boyce: The world changes, sometimes we need to change our instruments,

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04:41:37.100 --> 04:41:47.860

Danielle Boyce: Yeah, so we'll... I'll definitely bring that back to... to Alan from Asiri, who does our... is our Director of Clinical Operations, like all the other things I... poor guy, I ask him on a daily basis.

1571

04:41:47.860 --> 04:41:52.739

Paul Mehta: So, Daniel, is ASTDI collecting that information regarding vaping or not, or...

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04:41:52.740 --> 04:42:09.870

Danielle Boyce: No, we have... we have smoking, tobacco use. In fact, I think we modeled those questions after the registry, right? But... and... and I'm wondering, because we do have... so a couple of things. We have electronic health records, and we can easily mine them, and so I, you know, that could be a place where people might mention it, because it's contemporary, you know, to their physician.

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04:42:09.870 --> 04:42:16.779

Danielle Boyce: But it's not consistent, as far as I know, consistently captured. I think most people ask the cigarette

1574

04:42:16.780 --> 04:42:23.170

Danielle Boyce: question, you know, and the tobacco use, the pipe tobacco use, you know, kind of question. Most people don't ask the...

1575

04:42:23.570 --> 04:42:41.970

Danielle Boyce: the vaping question. So, yeah, and like you said, Paul, that does... that introduces new risk factors, too, because vaping is different than... than cigarette or tobacco smoke. So, good question. Here's one. Are World Trade Center autopsy specimens available to CDC to compare with military specimens?

1576

04:42:44.080 --> 04:42:48.250

Paul Mehta: So, I'm not very familiar with the World Trade Center program,

1577

04:42:48.760 --> 04:43:06.750

Paul Mehta: Kevin, do you have ex... do you have... I think that program was at ATSDR many years ago. Whether they did autopsies or not, I'm not exactly sure if that was the case or not, but if there are, as in terms of specimens available, I mean, there's no reason why we could not compare, you know, both of those specimens, you know, with us. I mean, certainly, that's certainly a possibility.

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04:43:09.060 --> 04:43:15.709

Kevin Horton: Yeah, we've never really explored trying to get those types of data, but it's not to say we can't.

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04:43:18.890 --> 04:43:21.759

Danielle Boyce: Okay, so let's see...

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04:43:21.780 --> 04:43:37.610

Danielle Boyce: Oh, so, the original question of Becky Wong says, I'm asking about vaping since the younger generation have preference for this. Also, is there interest in juvenile ALS? This might be of interest. Somebody asked the question about juvenile ALS, yesterday as well.

1581

04:43:37.610 --> 04:43:44.210

Danielle Boyce: And I think we answered it in line, but... but while we're here, and somebody brought it up, what, you know, what...

1582

04:43:44.210 --> 04:43:54.600

Danielle Boyce: what can we say about people under the age of 18? Which, I just like to say, as a researcher, I know is a whole can of worms from an IRB perspective, which, again, is one of those things, Mara.

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04:43:54.700 --> 04:44:06.050

Danielle Boyce: that is not your problem, you know, it shouldn't be anybody's problem, but from a bureaucratic perspective, it does add a layer of complexity, in my experience. So, Jamie, what is going on there with you?

1584

04:44:06.050 --> 04:44:12.169

Jaime Raymond: Yeah, so juvenile ALS is actually diagnosed as symptom onset before age 25.

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04:44:12.380 --> 04:44:21.830

Jaime Raymond: So we... we did do a brief report on anyone who was, 18 to 24 who was in our registry, and I put that link up yesterday.

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04:44:21.830 --> 04:44:42.050

Jaime Raymond: Yes, we currently cannot collect any data from patients that are under 18, which is why... so we limited that, and of course, our analysis wasn't symptom onset, it was diagnosed before age 25, because we don't have symptom onset information from all of our patients, so we didn't want to limit it to just those.

1587

04:44:42.070 --> 04:44:58.960

Jaime Raymond: But it is something we are interested in. It is something that comes up. Obviously, it would be a big undertaking, so additional funds would have to be available if we were to, you know, change our database and change our structure to include patients, under 18.

1588

04:45:00.540 --> 04:45:19.379

Paul Mehta: Yeah, I mean, typically, Jamie's right, we would have to make a change, because we'd have to get consent from the, the parent, since someone's under the age of 18 to go ahead and register. We... once... on occasion, we do get these queries coming in, and typically I'll refer them to, Dr. Neil Schneider over at, Columbia, because he's done a lot of the work.

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04:45:19.380 --> 04:45:26.980

Paul Mehta: on FUST mutations in the juvenile cohort and so forth. But, I mean, it is very rare, but it does happen, though.

1590

04:45:28.310 --> 04:45:44.609

Danielle Boyce: And I just wanted... I'm reading the chat, because Sandy Moore has taught me well. And Dr. Farber says, please collaborate and continue to hear the patient voice. Thank you. I just want to make sure that her parting words weren't shared. And Lauren Webb from Les Turner, who presented.

1591

04:45:44.610 --> 04:45:53.199

Danielle Boyce: for us yesterday, says, if someone is interested in juvenile ALS, there will be a meeting in September. I'm just waiting for all the details, but she provides her email there.

1592

04:45:53.200 --> 04:46:06.810

Danielle Boyce: So you can email her and keep... and keep up with that project. That's probably going to be a wonderful way to plug into everyone who's interested in that, right? Lyle, you had... Dr. Oster, you had a question.

1593

04:46:09.310 --> 04:46:18.860

Lyle W. Ostrow MD PhD, Temple Univ.: Yeah, so first of all, please do call me Lyle. I always say on these Zooms, I'm Lyle. I'm not anybody's doctor here, so I'm Lyle. But, you know, I saw a couple comments about, like, you know.

1594

04:46:19.010 --> 04:46:27.969

Lyle W. Ostrow MD PhD, Temple Univ.: advocating for staffing, up the registry in different ways. And I know, Paul, one thing I've said, like, over and over, over the years, is that, you know.

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04:46:28.590 --> 04:46:43.289

Lyle W. Ostrow MD PhD, Temple Univ.: there's all this amazing research going on, all these people all over the place that we all know about, and we have such a problem sharing data, right? And we all do, because all of our institutions interpret all the rules differently, and it's a moving target, and international, and, you know, and... and...

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04:46:43.290 --> 04:46:50.930

Lyle W. Ostrow MD PhD, Temple Univ.: The best scientists I know, and the best researchers I know, not so good at, like, the admin regulatory stuff, and we hate it, because it's not what we're trained to do.

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04:46:50.930 --> 04:46:54.839

Lyle W. Ostrow MD PhD, Temple Univ.: And in my mind, like, if I had a wish list of what I thought, you know.

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04:46:54.840 --> 04:47:14.070

Lyle W. Ostrow MD PhD, Temple Univ.: really, the registry could really make an instant difference that would just really, really move the needle for everyone. It's if advocates were to convince Congress to put in language that says, you know, to give you funding specifically to staff up and administer a true global unique identifier, right? So we all have these ways that we

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04:47:14.210 --> 04:47:17.680

Lyle W. Ostrow MD PhD, Temple Univ.: We de-identify patient data so that, you know.

1600

04:47:17.720 --> 04:47:37.080

Lyle W. Ostrow MD PhD, Temple Univ.: So that we can share it, but the problem is there's, like, 6 different ones, and the rules are different, and... and how people interpret them are different. And if there was a governmental organization that was, oh, by the way, the National Registry of the Disease, who was administering a truly global, you know, unique identifier.

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04:47:37.280 --> 04:48:02.140

Lyle W. Ostrow MD PhD, Temple Univ.: all our institutions would leave us alone, and not only would we be able to share data, but if somebody was in a trial somewhere, and we're in a registry somewhere else, and in a research study somewhere else, and we're in ALSTDI, and we're blah blah blah blah, you know, all that stuff would be instantly linked, and instantly linked in a de-identified and regulatory compliant way. And so advocates, if you're, you know, on this call, like, that's easy language to put one

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04:48:02.140 --> 04:48:05.910

Lyle W. Ostrow MD PhD, Temple Univ.: or two sentences into a, you know, dear Congress letter.

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04:48:05.910 --> 04:48:09.050

Lyle W. Ostrow MD PhD, Temple Univ.: With a specific ask and a specific, you know.

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04:48:09.050 --> 04:48:19.999

Lyle W. Ostrow MD PhD, Temple Univ.: line item budget attached to it, and it really should live in the place that is the National Disease Registry. So that's my soapbox, I've said it before, but I think it would make a huge difference.

1605

04:48:23.340 --> 04:48:24.630

Paul Mehta: So, we do have a GP.

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04:48:24.630 --> 04:48:25.350

Danielle Boyce: Yeah.

1607

04:48:25.350 --> 04:48:26.500

Paul Mehta: Obviously, we don't...

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04:48:26.500 --> 04:48:26.880

Danielle Boyce: Bye.

1609

04:48:26.880 --> 04:48:42.550

Paul Mehta: We do have a GOID, which is both through the NIH as well as the neural stamp through, Mass General, and so forth, but we, we are not, like, Dr. Lyle said, we're not the actual, group that actually,

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04:48:42.800 --> 04:48:47.119

Paul Mehta: yes, in terms of gets them out, or actually issues them, there's no.

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04:48:47.120 --> 04:49:01.930

Lyle W. Ostrow MD PhD, Temple Univ.: Paul, as you know, there's the NeuroGuit, there's the NeuroStamp, there's the GUID, there's the... I mean, and again, and each of our institutions doesn't know what to do with this stuff, and it really... it would make our life so much easier. And if you put the information in wrong, you get a different, you know, middle initial wrong, I mean.

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04:49:01.930 --> 04:49:07.709

Lyle W. Ostrow MD PhD, Temple Univ.: there's so much room here to just very quickly make it so that we all... we all want to share, and I know you guys.

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04:49:07.710 --> 04:49:10.029

Lyle W. Ostrow MD PhD, Temple Univ.: Like, every time I talk to a person with ALS, they're like.

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04:49:10.310 --> 04:49:16.440

Lyle W. Ostrow MD PhD, Temple Univ.: share my data, what are you talking about? I don't care, I've got ALS, you know? And, it would just...

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04:49:16.560 --> 04:49:31.619

Lyle W. Ostrow MD PhD, Temple Univ.: so much, like you just mentioned right now, you said, oh, if I hear about Jubina, like, talk to Neil Schneider. That's what I do too, right? Because he's, like, my go-to for fuss. And the point is, if we all had the ability to just share that data easier, faster, instantaneously, even, it would really make a difference.

1616

04:49:31.620 --> 04:49:50.149

Paul Mehta: I mean, you know, I think having that conversation with the NIH, with Amelie, and so forth, and Amy over at the NIH, because, I mean, they have their own, NIH GUID, and there's no reason why, potentially, maybe if they want to, you know, we have the access to technology and so forth, to kind of maybe have some sort of registered GUID, which would be a global one for everybody.

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04:49:50.150 --> 04:49:55.709

Paul Mehta: You know, and if everybody can kind of be on board, and so forth. Hopefully we're not stepping on any toes with the NeuralStat people.

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04:49:55.710 --> 04:50:00.560

Paul Mehta: And so forth, but, but certainly, you know, we do have the capabilities of doing that if we have to.

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04:50:01.490 --> 04:50:07.940

Danielle Boyce: Yeah, and just backing up one... just one step for the folks in the audience, because I think this is confusing a little bit,

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04:50:07.940 --> 04:50:22.009

Danielle Boyce: Because everyone says, share data, right? And so, ALSTDI, we have... we share our data freely, openly on this Looker platform with a data use agreement, and so... so what's the problem? Well, the problem, what you're talking about with this GUID,

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04:50:22.060 --> 04:50:27.579

Danielle Boyce: Is that... so, it's one thing to share, so we can put all of our data in one big...

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04:50:27.680 --> 04:50:33.310

Danielle Boyce: pool, and we can even standardize it all with, like, the OMOP Common Data Model, which is what we did.

1623

04:50:33.450 --> 04:50:50.470

Danielle Boyce: But if I don't know if my person... person ID 12345 is your person 99994, then we might be accidentally conflating their contribution to the... into the database, because they're counted twice.

1624

04:50:50.650 --> 04:51:05.130

Danielle Boyce: And also, we're not able to look, so let's say one group has incredible omics data, or the other group has incredible environmental risk factor data. It's very hard to know, to combine them and have one big.

1625

04:51:05.170 --> 04:51:19.160

Danielle Boyce: you know, data set. It's very hard to do that. And our institutions, because of laws protecting patient privacy, which are there for a reason, those institutions will not let us just share your name and date of birth.

1626

04:51:19.210 --> 04:51:32.099

Danielle Boyce: You're usually not allowed to do that, and we usually, on your consent form, say, I promise, you know, we say, I promise we will not share your name or date of birth with anyone else. So that puts us in a pickle, because then we can't... we want to share.

1627

04:51:32.100 --> 04:51:43.599

Danielle Boyce: But even if we do share, we can't... we can't tell who's who and who's connected, and so that's... that's what they're talking about, and so there's a way of issuing these global unique identifiers

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04:51:43.750 --> 04:51:47.830

Danielle Boyce: So that we... we are able to assign these numbers without...

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04:51:47.850 --> 04:52:06.339

Danielle Boyce: violating any privacy, especially when important genetic data, let's say, or information that could be very, you know, damaging if it got out, so you don't... you don't want people to know it's your name and social security number and so on. But there have been challenges in administering them, and so what... what Dr. Ostro was talking about is having a

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04:52:07.250 --> 04:52:11.049

Danielle Boyce: central, you know, source of those IDs.

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04:52:11.050 --> 04:52:15.910

Lyle W. Ostrow MD PhD, Temple Univ.: Yeah, Danielle, just as a real quick example, I mean, right now, so, you know, so my...

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04:52:16.140 --> 04:52:31.740

Lyle W. Ostrow MD PhD, Temple Univ.: Autopsy Corps is funded by a collaboration with the CDC Registry. And, we went through and did the manual work and figured out that we... I mean, because we have GUIDs on people, that there's people who are... who are in the registry, and who also, just by chance, we have their autopsies, right?

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04:52:31.740 --> 04:52:40.739

Lyle W. Ostrow MD PhD, Temple Univ.: And we could link those, because we have the GUIDs. And that's incredibly useful, because suddenly the tissues that I have, if somebody has a hypothesis.

1634

04:52:40.740 --> 04:52:55.699

Lyle W. Ostrow MD PhD, Temple Univ.: that has something to do with data that the registry collects, well, they can make that data request from the registry, and they can make the request from us, and it's de-identified. But here's the rub. I'm pretty certain that I've got a lot more autopsies on other people that may also be in the registry, and I don't have a way to figure that out.

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04:52:55.700 --> 04:53:04.630

Lyle W. Ostrow MD PhD, Temple Univ.: And if I did, you know, those tissues and that information could be used the same way. And one of the talks today, you know, talking about

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04:53:05.150 --> 04:53:21.199

Lyle W. Ostrow MD PhD, Temple Univ.: veterans and analysis on brain tissue, like, we tried desperately to figure that out for them, and it's not... it's not part of a standard academic medical record who's a veteran, but it's a perfect example where just having this stuff done globally and done the same way

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04:53:21.250 --> 04:53:25.590

Lyle W. Ostrow MD PhD, Temple Univ.: The data is instantly bigger and better, and more rigorous for everyone.

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04:53:27.430 --> 04:53:28.390

Danielle Boyce: Well said.

1639

04:53:28.770 --> 04:53:50.110

Danielle Boyce: And so, I think, I think we're gonna probably wrap it up for today. If you have, unanswered questions, we're gonna try to get them answered in the chat and the Q&A, and if not, there... there will be publishing a transcript with Q&A and all that, and following up with people as appropriate.

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04:53:51.040 --> 04:54:05.309

Danielle Boyce: Right, and some... Lynn says Europe also has different privacy standards. That's a good point, Lynn, too. Yes. And so, just when you think you're ready to share or do something, oh, you know, then there's a whole other, what is it, G...

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04:54:05.310 --> 04:54:16.079

Danielle Boyce: GDPR, or is it GRDP? Yeah, it's one of those. Yeah, it's kind of like a HIPAA, but for a different community. Yeah. So, so,

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04:54:16.080 --> 04:54:26.850

Danielle Boyce: I just want to say thanks to Ross Strategic, to the CDC team, to Hite Consulting, to, of course, to, Dr. Farber, Doug, and Mara.

1643

04:54:26.850 --> 04:54:37.150

Danielle Boyce: And all of the panelists who really showed up and gave some great science in a short period of time, some really incredible scientific presentations.

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04:54:37.360 --> 04:55:02.309

Danielle Boyce: I am excited about what I heard. I have follow-up to do. I have emails out to my team, you know, with things that I want them to see, and approaches that I want them to look into. So it has been very meaningful for me as a scientist, and I hope it has been exciting and thought-provoking, and for people in the community to see how many different people

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04:55:02.310 --> 04:55:04.030

Danielle Boyce: Have been working on this.

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04:55:04.030 --> 04:55:29.009

Danielle Boyce: And I hope that gives you some hope, and know that we are all available to you. You can email me anytime, just like, Dr. Ostro, just like, Palmetto, like, we're all here to support this community, and we all believe in this ecosystem, and want to share and collaborate. And sometimes with... sometimes people think that we don't, you know, and I hear that a lot from the community. Why don't you work together? And I just only wish they knew how

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04:55:29.010 --> 04:55:48.360

Danielle Boyce: how much warmth and affection there is between all of us who are all facing these wicked problems together, and struggling and trying to share. I mean, just, when I hear something, sometimes I'll think of a scientist, you know, I'll see something at a meeting, I think, oh, I have to send that to Dr. Gautman, you know? So that happens all the time.

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04:55:48.460 --> 04:55:52.800

Danielle Boyce: And so, I hope that came across, too, because it's true.

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04:55:53.590 --> 04:55:55.639

Danielle Boyce: Alright, Paul, I'm gonna send it to you.

Closing Remarks - Paul Mehta, MD

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04:55:56.000 --> 04:56:07.410

Paul Mehta: Thanks, Daniel. And, you know, these past couple days have been very, very hopefully helpful for everybody here on the call to kind of learn exactly what we are doing, and so forth, and all the various facets of the registry itself.

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04:56:07.410 --> 04:56:20.990

Paul Mehta: But first and foremost, I want to thank, those living with ALS, Stacy and Pat, and everybody else on the call, as well as the caregivers, Doug and Mara. You know, your support and your input is extremely, extremely valuable.

1652

04:56:20.990 --> 04:56:41.950

Paul Mehta: And thank you for sharing your heartfelt, stories. I mean, this is your registry. We are caretakers of it, and, you know, we're always striving to improve the registry, and so forth. Just want to also thank the A-list team members. I want to thank Kevin Horton, he's our brand chief, and his leadership, and always going to bat for us. That's really, really important. I think we probably don't tell Kevin

1653

04:56:41.950 --> 04:56:42.920

Paul Mehta: that much.

1654

04:56:42.920 --> 04:56:50.719

Paul Mehta: We don't tell Kevin that too often, but we appreciate Kevin and everything he's done for us, for the program, and always going to bat for us. Thank you, Kevin.

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04:56:50.950 --> 04:57:15.860

Paul Mehta: I want to thank Ted for support and providing feedback to the team. Jamie, our lead epidemiologist, pushing all the data analyses, along. I mean, she's very, very, very good in what she does, and she's always working on something. Rob, our deputy director, for all the support. Moon, for taking care of the biorepository, she's kind of like the biorepository shepherd, and so forth, for Rashma, for overseeing our IRB and OMB

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04:57:15.860 --> 04:57:17.000

Paul Mehta: processes.

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04:57:17.000 --> 04:57:40.910

Paul Mehta: For Audrey, who's our contracts officer, I'm always bugging her to figure out exactly, you know, where the contracts are, and where we are, and so forth, and appreciate her patience. For Tim Copeland, for our IT approvals for the registry, as well as our contractors, Song, Essie, Courtney, Cy, Calvin, and Rick. These are people you may not know, but they work in the background. Song, obviously, you guys know, because he's been here

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04:57:41.250 --> 04:58:05.210

Paul Mehta: working with Ross Strategic, our partners, Patty from the AL Association, Lauren from Les Turner, MDA, Peyton and Meredith, Adina from Team Gleason, Temple, Lyle and his team, our funded grantees who presented these past couple days, Fernando,

Steven, Feng Feng, Sheng, Shing Tsong, Ben, and Elijah, and so forth. And I also want to thank Danielle for her,

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04:58:05.210 --> 04:58:30.120

Paul Mehta: moderating for this, register. I mean, you did a great job, Daniel, and we appreciate everything you've done and all the valuable input that you've provided to the community, and we know you're very close to the community, and that certainly is extremely, extremely important. That's pretty much it. Like I said, I mean, you know, we want to thank everyone for participating, sorry, and, you know, providing feedback, and, any questions you guys have, please send us an email or give us a call.

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04:58:30.120 --> 04:58:32.509

Paul Mehta: We are here for you. Thank you so much.

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04:58:35.500 --> 04:58:36.390

Danielle Boyce: Thank y'all.

1662

04:58:36.540 --> 04:58:37.180

Paul Mehta: Thanks.