

2024 National ALS Registry Annual Meeting September 4th - Day 1 Questions and Answers Transcript

*Note this is only a transcript of the questions asked during the webinar, questions submitted during registration were answered separately and will be provided elsewhere

Time	Question	Answer Format	Answer
9:18:00 AM	Is it possible that Vermont simply had very good self-enrollment? Or that they have a lot of people on public-payer files that you find? It seems that this report says more about participation in the Registry than actual cases that are in the state.	Typed in Chat	This analysis included self-enrollment as well as CMS and VHA/VBA data.
9:21:00 AM	This data is 6 years old. Why not more current data? 80 to 90% of the people you have data from are no longer with us, and a lot of people are alive with the disease.	Typed in Chat	Yes, you are correct. CMS data is very slow to finalize and we are looking at other alternatives to report on ALS cases in the US. Currently 70% of ALS cases in the Registry come from CMS.
9:22:00 AM	Could we have the demographic data for the biorepository samples, please?	Typed in Chat	Participants of the Biorepository comes from the consented Registry participants. Their demographic characteristics mirror the demographic distributions of the Registry. Predominantly Male, Non-Hispanic White, greater in 60-69 years of age group, and greater percentages of those with military history.
9:24:00 AM	How is the Registry leveraging AI and machine learning technologies to uncover patterns or biomarkers in ALS progression, and what potential advancements and challenges do you see in this area?	Typed in Chat	We used AI when we analyzed our open-ended survey data asking patients what do you think caused your ALS. Danielle Boyce is the lead author and Paul Mehta mentioned it in his presentation. This has been our first step using AI. We are also exploring AI looking at early symptoms of ALS.
9:36:00 AM	On page 5-17 of the NASEM report, they list four specific gaps where they say the Registry is inadequate. What are you doing specifically to address those four bullet points? Thank you.	Typed in Chat	report slides - add Dr Mehta's slide 19 from yesterday. https://www.nationalacademies.org/documents/embed/link/LF2255DA3DD1C41C0A42D3BEF0989ACAECE3053A6A9B/file/D935B2A694B6841C3D919007704A5DF4D47D7D775A0B?noSaveAs=1
9:38:00 AM	Did the (state) prevalence go down from 5.2/100K to 4.4/100K?	Typed in Chat	No, the 4.4 does not reflect the capture-recapture analysis because we were not able to add that to the state level data.
9:39:00 AM	Is the funding opportunity that was mentioned for potential international/domestic partners "RFA-TS-25-036", otherwise known as "Identify and Evaluate Potential Risk Factors for Amyotrophic Lateral Sclerosis (ALS)"?	Typed in Chat	Domestic and international, yes.

9:43:00 AM	so what is the official prevalence number?	Answered on Stream	So we estimate there's about 30,000 individuals living with ALS in the US at this time. That will be increasing incrementally as the population ages and ALS impacts those at a latter stage in life we estimate that 30,000 number will be increasing incrementally.
9:43:00 AM	Other countries have reported higher incidence/prevalence based on national medical record data bases. Do we have data on the criteria used to establish diagnosis of ALS in non-USA registries compared with the algorithm used for the USA ALS CDC Registry/	Answered on Stream	<p>The Registry funds a number of international institutions and work with registries around the world. We're seeing similar demographics from those other countries, predominantly white and male. In regards to prevalence, we see higher rates of ALS in Scandinavian countries, which could be due to their higher white population or the higher penetration of C9orf72 gene. There's a lot we don't know about regions like Africa and Asia, either due in part to misdiagnoses, delayed diagnoses, or underreporting.</p> <p>A number of countries have reached out to us to aid in the development of their own ALS registries. Dr. Mehta will be working with the Indian government to set up their own ALS registry, and the team was recently in Chile for a conference where they expressed interest in developing their own registry as well. The Registry has also worked closely with Dr. Orla Hardiman of Ireland with her research and efforts with a Register, as it's called in Ireland. Ireland is unique in that it is geographically smaller and thus Dr. Hardiman basically has seen everyone in the country who has ALS.</p> <p>In a recent conference we've seen difficulties in countries that have a single-payer healthcare system even have with capturing everyone who has ALS within their Registries.</p>
9:45:00 AM	That's an interesting hypothesis about the lake. It would be interesting to know if Canada have a higher rate on their side too.	Typed in Chat	Agree Kathleen. We are working on an analysis with Canada to compare their data with our US data.
9:47:00 AM	The point of the demographic question re bio-samples was to learn if the biorepository is even whiter, more male, etc. than the Registry itself.	Answered on Stream	It is a subset of the Registry itself. The samples are representative of the Registry in that they are predominantly from white sample givers.
9:48:00 AM	So many people with ALS report that they are not made aware of clinical trials or trials are not promoted by their neurologist. Can you describe what is emailed to registrants about clinical trials? Is it just a link to the trial on clinicaltrials.gov, or does the message include general information on the value of clinical trials? Thank you.	Typed in Chat	Thank you for the question. At the time of enrollment in the Registry, participants have the option to receive notification about clinical trials or other epidemiological studies that they may be eligible in. Once the registrants opt in and consent to receive emails, they will get notifications when the researchers seek patient recruitment for their study. Then, it is up to the registrants to reach out to the researchers. Of course, these notifications are

			not all inclusive. Other clinical trials can be found in clinicaltrials.gov
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9:49:00 AM	<p>In response to Andrea, following is from page 5-17 of NASEM report —</p> <p>Gaps in the National ALS Registry As it currently exists, the National ALS Registry is inadequate regarding several key pieces of information, including:</p> <ul style="list-style-type: none"> • Completeness: Several evaluations suggest that counts based on administrative databases and self-identification alone miss a significant portion of people living with ALS in the United States (Kaye et al., 2018; Nelson et al., 2021; Raymond et al., 2023). Risk factor surveys have also had low response rates (Bryan et al., 2016; Raymond et al., 2021). • Representativeness: National ALS Registry data are not representative of the United States population as a whole, particularly in terms of people of color with ALS, younger people with ALS, and people with ALS with private health insurance (Kaye et al., 2018; Nelson et al., 2021; Raymond et al., 2023). • Date of diagnosis: This is only captured based on patient recall; without knowing the true date of diagnosis, incidence data cannot be ac 	Answered on Stream	<p>Efforts are being made from multiple directions for the issues of Completeness, Representativeness, and Timeliness. These questions are also addressed with answers elsewhere in this document.</p> <p>The question of Date of Diagnosis recall was directly referenced on the stream and Dr. Mehta answered that despite it being an issue of recall bias, an ALS diagnosis is such a life altering event that rarely is it mis-remembered by the person living with ALS. The invited people living with ALS also confirmed on the stream that this was the case</p>

	<p>have you looked at the distribution of neurologists in the US? perhaps the increased apparent higher prevalence of ALS in some states is a function of accessibility for diagnosis.</p> <p>Date of diagnosis: This is only captured based on patient recall; without knowing the true date of diagnosis, incidence data cannot be accurately calculated. Some researchers have opted against using date of diagnosis as an endpoint due to this recall bias (Bryan et al., 2016).</p> <ul style="list-style-type: none"> • Timeliness: Because it takes a long time to procure and process administrative claims data, the data in the National ALS Registry are not current enough to maximize their effect; recent CDC prevalence studies have been based on 5-year-old data (Mehta, 2023). Without more current data, it is impossible to track the population-level effects of advances in care, therapeutics, and access. 		
<p>9:56:00 AM</p>	<p>Pat Dolan's published maps are here: https://als-geospatial-hub-nonprofit.hub.arcgis.com/pages/the-maps</p> <p>He is brilliant.</p>	<p>Typed in Chat</p>	<p>agree with Danielle. Pat is amazing.</p>
<p>9:58:00 AM</p>	<p>I am a Survivor and previous CALS and that is very true that we do not forget diagnosis date...the day that officially changes your lives</p>	<p>Typed in Chat</p>	<p>Thank you for your comment Ashley. As you're keenly aware, ALS is a devastating disease. As such, this drives us to better understand the disease and specifically its risk factors and etiology. Thank you for all you do as a caregiver and survivor.</p>
<p>10:12:00 AM</p>	<p>Maybe if the Centers were made aware of the registry and its usefulness, you would get more people to join. We only found out by chance. THIS IS VITAL DO IT!</p>	<p>Typed in Chat</p>	<p>Hello, yes we agree 100%. Because there are a number of ALS clinics/centers around the country funded by ALSA and MDA, this is why we work directly with the national offices of ALSA and MDA so that they can provide a constant message to their care centers/clinics, chapters, and support groups to promote the registry. In reality, some of these care centers/clinics, chapters, and support groups do a better job than others in registry promotion. We're trying to get to the point we're everyone with ALS hears about the registry in a uniform way from these and other organizations. Thank you for your comment!</p>

10:15:00 AM	Thanks for the wonderful information regarding the ALSA volunteers. Could you please share how much ALSA was paid in the last year for education and outreach, and please give us some idea of the number of FTEs at ALSA dedicated to the paid education and outreach. Thank you.	Typed in Chat	Question answered in chat at 10:34 by Dr. Mehta
10:16:00 AM	Do LTF ALS patients release their EMR data to ALS CDC Registry as previously described?	Typed in Chat	The National ALS Registry is not receiving any EMR currently. We are discussing how and what it would look like in the future to enrich the Registry data for analyses.
10:34:00 AM	Similar Q for MDA - How much were they paid for registry education and outreach last year and how many FTE employees at MDA are working on registry education and outreach. Thanks again.	Typed in Chat	The National ALS Registry relies on its partner organization to get the message out on awareness for the Registry. Due to IRB (institutional review board) restrictions, we cannot ask our partners to provide specific performance metrics, such as requiring 100 new registrants each month, otherwise it would be considered coercion. The Registry is 100% voluntary. The way we actually gauge performances every month is through reports saying how many contacts reached, how many events have held, how many phone calls made, etc. We spend about 10% of our budget on outreach and learners through our partners, and are giving between \$20,000-\$100,000 a year to organizations to do what they can.
10:34:00 AM	MDA Care Centers - Do you provide service to ALS patients just like what occurs at a designated ALS Clinic certified by ALSA? Or would you refer an ALS patient to an ALS clinic?	Typed in Chat	Hi Ed - Yes, we provide the same multidisciplinary approach as ALS Clinics and many clinics across the nation are both MDA Care Centers and certified by ALSA.
10:46:00 AM	Hello everyone, we have a ALS Care home here in Winnipeg, Manitoba. The only care home in North America providing support to the people suffering from ALS. We need some support in any form to run the house and support the ALS community here in Manitoba, Canada. Thank you.	Typed in Chat	note: people in the US with ALS who are Homebound, do qualify for Medicare home health services, though there are some glitches.
11:12:00 AM	Zoom user (You): When and how are we going to address pediatric ALS? ALS onset prenatal? This question has been ignored for the last three years when ask, can this question please be acknowledged this time. Please our children are dying	Typed in Chat	We are working to add pediatric cases to our Registry. When the Registry started, patients had to be 18 years old but we have conducted a brief analysis regarding pediatric cases (<25 years) and are working to get patients less than 18 years old available to registry through self-enrollment. We are hoping to get additional funding to add pediatric cases, asymptomatic cases, and controls to the Registry.
11:33:00 AM	Melanin Children Matter Inc has been spend the last few years advocating and working to create a ALS registry In honor of her baby boy who passed from ALS. Even donated	Typed in Chat	See answer above regarding Juvenile ALS.

	his samples to the NIH, grant funded to do so. Why not partner up with nonprofit to help shade awareness to pediatric ALS???		
11:49:00 AM	Would each of these patient attendees present address the initiative of signing an informed consent to directly enter their electronic medical record data directly to the USA ALS CDC Registry?	Answered on Stream	Don Zundel - I would consent given security, and could see value in that. Layne Oliff - Currently would consent and have no problem, however if younger and still had children at home, he would hesitate due to security concerns.
1:49:00 PM	How does microbiome affect riluzole levels and riluzole metabolism?	Answered on Stream	The microbiome obviously has effects on metabolism and metabolite, however the issue of its effect on riluzole has not been considered by Dr. Murdock before and will be taken into consideration in the future.
1:51:00 PM	What is effect of high dose vitamin E on microbiome?	Answered on Stream	That is also an unknown so Dr. Murdoch would have to lean on his endocrinologists for an answer to this question.
1:57:00 PM	What are your thoughts on neutrophil to lymphocyte ratios and its impact on ALS?	Answered on Stream	The higher the neutrophil-lymphocyte ratio is, the worse off you are with regards to survival and progression. There are a number of potential reasons: first is that neutrophils are bad and do damage to the central nervous system; second is that CD4 T cells, specifically T-regs are thought to be protective. As the bad-to-good ratio goes up, the worse the disease progression. Research is still looking into the underlying mechanisms of why NLR contributes to disease progression.
1:59:00 PM	See-Neutrophil-to-Lymphocyte Ratio Dynamics From Pre-diagnosis to End-Stage Amyotrophic Lateral Sclerosis (ALS): A Case Study on Association With Progression and Clinical Events Cure Us 2024	Answered on Stream	
2:08:00 PM	What are the plans for ALS epidemiology studies in the Million Veterans Program?	Answered on Stream	Dr. Weisskopf expressed high interest in getting involved with the Million Veterans Program so they can integrate genetics into the research.
2:08:00 PM	Could Coast Guard have higher risk due to water exposure (algae blooms) and could pilot. Crew, air force have higher risk due to lead in fuel?	Answered on Stream	Initial findings from Dr. Weisskopf's research needs a lot more work to be done before they can be trusted. First step is to identify the larger groups that seem to be at higher risk, then dig down deeper to find causes, Coast Guard and algae, air force and jet fuel
2:19:00 PM	do you get information as to the name of the base and years serving at that base? because you theoretically can get data on pesticide purchased annually for the base, amount of Jet A fuel, etc. as potentially environmental exposures as opposed to personal head injury, statins, etc.	Answered on Stream	Dr. Weisskopf expressed that they should have access to base information in the DMDC dataset and that it was advertised as part of the DaVinci system, however that information is currently not showing up for them. His hope is that when they ultimately get that data, they can look at whether particular bases have different risks for ALS and ascertain what may be occurring at those bases that cause the differences.
2:23:00 PM	In addition to marital status, can/are parental status collected/analyzed?	Answered on Stream	Not looking at parental status and not sure if that information would be available.

2:24:00 PM	Adjusted by marital status. Interesting. Why?	Answered on Stream	The suspicion is that marital status, as seen in the Danish registry, may effect how quickly someone is seen by healthcare professionals with regards to their ALS. It's not being looked at as a risk factor, but the impact of marital status on the speed at which people go in to get seen effects the epi-analysis that is done
2:30:00 PM	Could you please provide information on the specific efforts and strategies the ALS National Registry is implementing to ensure effective outreach and engagement with military personnel of color? I'm particularly interested in understanding how the registry is addressing the unique needs and challenges faced by this group	Answered on Stream	The Registry is always looking for ways to reach out to minority populations. We work with our partners in any capacity to boost minority enrollment and are open to any ideas and suggestions to help. Specifically for minorities in the military, we are looking to work with the Paralyzed Veterans of America (PVA), which has an ALS research arm that could potentially link the Registry with a population of minorities in the military. An underlying factor with underrepresentation of minority communities is the large gap in healthcare access that come from racial disparities and socioeconomic issues.
2:42:00 PM	What proportion of familial ALS patients do not have an identified gene or variant of unknown significance?	Answered on Stream	In almost all cases, if you have familial ALS, then there is typically one of the identified genes present. In rare cases from the ARC study, people with ALS have reported parents and grandparents who have had ALS, but nobody has identified a gene associated with their ALS.
2:43:00 PM	What progression data ALSFRS-R Vital Capacity is available to be entered into USA ALS CDC Registry?	Typed in Chat	ALSFRS-R data can be captured longitudinally every 3 months. The Biorepository team also asks participants to complete the ALSFRS when they are consenting to provide samples to the Biorepository. This helps provide ALSFRS scores close to the date of sample collection. If the participant has time, we help administer and go through the questions with the participant.
2:44:00 PM	How to request access to the ARC Data commons?	Answered on Stream	https://www.als.net/arc/data-commons/
2:51:00 PM	Paralytic polio was more common in higher education and higher socioeconomic class, Is young ALS infectious compared with old ALS?	Answered on Stream	Dr. Avi Nath at NIH has looked into HERV-K retroviral infections, showing certain strains of HERV-K are more prominent in ALS patients, however it's still early on and there isn't conclusive evidence of HERV-K involvement in ALS Progression Regarding Juvenile ALS, we've typically seen FUS mutations in younger patients and Neil Snyder from Columbia University is working on this area.

3:01:00 PM	How can a family member whose PALS has passed on contribute to research? My PALS's was a fast-progressing disease, 3 months, and was unable to contribute to research during the limited time between diagnosis and death.	Answered on Stream	3rd parties entering data on behalf of others posthumously is frowned upon due to recall bias, but the Registry acknowledges that a portion of the data that is collected is likely in that category. Additionally the Registry recognizes that fast progressors may be unrepresented in the database because of the speed at which the disease progresses, and these people would only be able to be entered posthumously. The Registry is looking into having some sort of indicator that could be selected so that entries can be identified as self completed or completed on behalf of someone else.
3:08:00 PM	Paul Mehta -- If we were to write someone at CMS to better understand what is the actual holdup for data beyond 2018 to be provided as input to the ALS National Repository, who would that name be at CMS?	Typed in Chat	CMS Data is obtained through a data use agreement with CMS.
3:14:00 PM	How often are you running the death index against the Registry data?	Answered on Stream	Twice a year
3:15:00 PM	When you say younger people diagnosed with ALS, live longer. Do you account for people who have been trach-ed? Because it might be a false positive because the individual took medical procedure to extend their life. Thanks	Answered on Stream	It is unknown if tracheostomy are taken into account for the survival rate of younger people diagnosed with ALS. ALSFRS slopes have found to be less steep for those diagnosed in a younger person than those diagnosed in older people, their progression rate is slower.
3:24:00 PM	Forgive me if you covered this while I was in meetings. Do you have data on those taking the continuing ed? Numbers? Do you know the demographics of the healthcare professionals taking the continuing ed?	Answered on Stream	We can reach out to the team that manages data of the CE module. I believe general demographic information can be obtained, but we need to check. I'll take note of that.
3:26:00 PM	A few years back I saw a presentation by the Million Veterans project folks. Smoking by a large percentage of participants was a consideration in health outcomes they were seeing. Is this a concern in vets' ALS data?	Answered on Stream	Smoking has been linked to ALS in many different ways and is suspected to be related to the disease. As long as MVP collects smoking behavior, then that data point can be used. The Registry's Risk factor surveys also collect data on smoking behavior. The Registry is analyzing military risk factors and have seen that smoking is significantly higher in veterans with ALS than non-veterans with ALS in our data.
3:28:00 PM	Melanin Children Matter Inc would love to partner up, not sure how to obtain her email address though?	Typed in Chat	They can email us at als@cdc.gov. Thanks