

## 2024 National ALS Registry Annual Meeting September 5<sup>th</sup> - Day 2 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
9:09 AM	What proportion of total Medicare Medicaid subjects is present in the GROUSE database?	Answered on Stream	20% of the 35 million distinct EHR patients in the GROUSE database are Medicare beneficiaries
9:14 AM	Are you controlling for co-morbidities?	Answered on Stream	Yes. Yes, the 1st thing we try to control, our comorbidities and, historical medication use.
9:17 AM	Is there enough granularity of data to compare R arm L arm R leg L leg?	Answered on Stream	The short answer to that is no since in that analysis the way we identify a limb offset is primarily using diagnosis code, which oftentimes is not as specific as you would hope. Our next step is we want to harvest that random alert information out of the clinical notes from EHR so that we can further identify the subgroups.
9:20 AM	Do you know how the race/ethnicity/sex demographics of the GROUSE database compare to the US? Thanks.	Answered on Stream	The encachment area of the database is primarily the Midwest of the US, so it reflects the demographic of the Midwest, not the entirety of the US. Primarily white males.
9:20 AM	TRI Data is available at an address/lat long level	Typed in Chat	I would like to have this answered live. Can you explain TRI data, please?
9:22 AM	An ALS cluster was identified in WI in 1980s. Are there any other identified clusters in your enchachment area in the past?	Answered on Stream	No answer yet, currently at the state of identifying risk factors. The next step is to put that data back into the map of the Midwest United States and see if any clusters are found
9:26 AM	What happens in the 12,200 'ALS' cases that you say are not ALS?	Answered on Stream	Those 12,000 cases were used to see how good the model was at distinguishing ALS patients against ALS mimics (non-ALS diagnoses presenting ALS-like symptoms). Bulbar onset vs bulbar symptoms.

<b>9:26 AM</b>	Have you compared your environmental chemical exposure results to the work published by Angeline Andrews, PhD lab?	Answered on Stream	We have compared results with existing literature, but not specifically with Angeline Andrews. That is something Dr. Xing Song would like to do.
<b>9:32 AM</b>	Toxic Release Inventory is available at an address/longitudinal-latitude level. Are you aware of that and is this something you might consider.	Answered on Stream	That's exactly what we're using. For the environmental risk factor, toxic release inventory. Yes. That was one of the first sources we thought of using, they release their data on a quarterly basis. We created a multi-year TRI data and linked it to our clinical data, along with adding pesticide use estimates.
<b>9:35 AM</b>	Are patients who are 'not ALS' free of any effect on survival compared with other controls	Answered on Stream	No, we haven't done a further analysis on the survivors, but it's a very good question and we'd like to do a follow-up analysis on that.
<b>9:39 AM</b>	Thank you Dr Song and Andrea	Typed in Chat	Thank you for your question and clarification.
<b>9:52 AM</b>	Kurtzke found large bone fracture was present in more ALS cases in USA WW2 veterans. What is your data on large bone fractures in all ALS and military ALS?	Answered on Stream	I presented the results based on the MND registry at our case control study but based on the general healthcare records data we performed a study many years ago looking at fractures specifically and there is a higher prevalence of fractures among ALS patients during the year(s) before diagnosis. The military population in Sweden is quite small, so the total number of ALS patients with military experience is not high, therefore we have not looked into fractures specifically within military ALS patients in Sweden. That is something we can do in the future as the number of individuals in the military increases.

<p><b>9:53 AM</b></p>	<p>How strong was the association between ALS and TBI in the time period AFTER ALS diagnosis?</p>	<p>Answered on Stream</p>	<p>We have not looked at but if you look at the year before diagnosis then the relative risk is more than 4-fold. That's actually a really good point and we can take a look at the year after</p>
<p><b>10:07 AM</b></p>	<p>Were clinical lab data on riluzole or before riluzole?</p>	<p>Answered on Stream</p>	<p>This is both before and after. The vast majority of our patients had riluzole and had it quite early on. The measures that were given during the diagnostic workup are pre-riluzole, and everything else is after riluzole. We haven't taken into account riluzole in the analysis, so we will adding riluzole to the analysis in subsequent projects.</p>
<p><b>10:08 AM</b></p>	<p>People with ALS often relate that their disease started after an illness, minor surgery, or injury. You have to lose a very substantial proportion of motor neurons in a muscle pool before there is clinical weakness. Some estimates are as high as 80% of MNs in a given muscle. This can mean that prior to clinical weakness, there is a loss of *functional reserves* necessary to deal with other stressors - infections, minor surgeries, etc. As an analogy, when a healthy person is bedridden for several days because of a minor surgical procedure or self-limited illness, they will feel weaker when they get up again and resume normal daily activities. If someone has lost a significant proportion of motor neurons - but not enough to notice clinical weakness... things like infections/injuries/minor surgeries can therefore *unmask* subclinical ALS. Isn't this an alternative explanation for data</p>	<p>Answered on Stream</p>	<p>You definitely, I think this is why we really want to look, you know, step-wise in time. I think this is why we really want to look step-wise in time retrospectively and see when do these things happen and what can they mean. If we were to believe there's a multi-step development of the ALS pathology you know things have to accumulate before the disease become clinically evident and precisely as you say mild trauma, TBI, an infectious event, or even a mild surgery might be the last piece that is needed to complete the pie.</p>

	suggesting increased incidence of infections prior to ALS diagnosis?		
<b>10:17 AM</b>	What about medications as steroids? My spouse started showing symptoms one month after receiving a triple dose in her left knee and another in left toe.	Answered on Stream	No direct answer to this
<b>10:25 AM</b>	What are the results of American Dental Association longitudinal study of mercury exposure and development of ALS?	Answered on Stream	Dr. Song - not familiar with that specific study but mercury exposure is one of the potential factors discovered in her aggregate level analysis
<b>10:36 AM</b>	Are you allowed to present your study data at voting centers?	Answered on Stream	We have not looked into standing outside of voting centers to recruit people.
<b>10:38 AM</b>	Can you post the URL please for the ALS study	Answered on Stream	<a href="https://www.uofmhealth.org/mi-brain">https://www.uofmhealth.org/mi-brain</a> <a href="https://www.uofmhealth.org/expose-als">https://www.uofmhealth.org/expose-als</a>
<b>10:39 AM</b>	you are enthusiastic and understand the value of this research. there probably is a major element of "survey fatigue". we have growing worries about identity theft. these have to be of concern to people	Answered on Stream	We've learned so much about these individual level data and agree that's one of the areas where we're trying to understand where that balance between capturing really important essential information and survey fatigue. Because this is a study sponsored by government entity, there is a certificate of confidentiality, but I do understand that there's a lot of concerns about who has your data and what they do with it.
<b>10:54 AM</b>	Have you tried to use Lexis-Nexis to get migration history of your cases?	Answered on Stream	I think this question is getting at are there publicly available data sources to generate somebody's residential address history. We go based off of what the participant tells us, the time and dates they lived at each individual location so we can think about timing of exposure.
<b>11:02 AM</b>	Endurance athletes have a higher rate of ALS. Do you think these group of athletes have a higher rate of ALS is do higher exposure to air pollution?	Answered on Stream	The great question -I don't know.

<b>11:03 AM</b>	PM2.5 data mapped low in upper Midwest but the rate of progression for 3 months correlated with PM2.5 Is this a methods issue can you better see relation with PM2.5 when the background geographical level is low>	Answered on Stream	Let me, hopefully answer that question. The rate of air pollution has been decreasing over time not just here in the Midwest, but all over the US. Air pollution is something that The EPA is working to decrease. We see these changes in the participants that we have followed and have provided their address information, but it's really possible that individuals who have greater gradients to the PM 2.5 may show stronger findings. So there are areas of the country that have higher PM 2.5 levels. If we're able to investigate those different gradients more thoroughly then we may see stronger results.
<b>11:31 AM</b>	Has anyone matched up Massachusetts registry data with ATSDR registry data for people from Massachusetts? Have we learned about the people the ATSDR registry misses?	Typed in Chat	Yes, we matched MA ALS Registry data with the National ALS Registry and it has been published. You can find it on our publications page.
<b>11:31 AM</b>	Has anyone matched up Massachusetts registry data with ATSDR registry data for people from Massachusetts? Have we learned about the people the ATSDR registry misses?	Typed in Chat	<a href="https://www.cdc.gov/als/researchpublications/2023/Publication_Frontotemporal.html">https://www.cdc.gov/als/researchpublications/2023/Publication_Frontotemporal.html</a>
<b>11:35 AM</b>	I have heard from a number of people that they are unwilling to share SSN digits -even just 5	Typed in Chat	Hi Anne. Thanks for your comment. I think it's important for people to know that once they enter their data into online portal for registration, this data is taken off the servers every night at midnight and then stored on a computer that's not connected to the internet, thereby, minimizing any kind of data compromises.
<b>11:38 AM</b>	Could lack of participation in the registry be to exhaustion and stress? Is there a way to engage the family to help complete surveys?	Answered on Stream	Andrea: we have a response given, which I think might go to this data issue as well, is that someone can visit the survey and enter their responses. They can save and quit rather than submitting those responses. Dr. Mehta: from start to finish, it's about our hour and a half to complete all the surveys. we want to make sure there's no reason to do it at one sitting. You can do it at numerous sittings if you want to go and complete those surveys.
<b>11:38 AM</b>	Could lack of participation in the registry be to exhaustion and stress? Is there a way to engage the family to help complete surveys?	Typed in Chat	We understand that taking each of the surveys can potentially introduce exhaustion and stress. We suggest you visit the survey, give responses, and save and quit, instead of submitting. This way you can re-log in next time and resume the same survey, as it hasn't been submitted. You can ask your family member to help, as long as you are okay with sharing your personal information.
<b>11:38 AM</b>	Could lack of participation in the registry be to exhaustion and stress? Is there a way to engage the family to help complete surveys?	Typed in Chat	To add - Make sure the surveys do get submitted when finished, as the survey will remain incomplete to us. We want your data to be counted.

<b>11:38 AM</b>	I appreciate the time that these people w ALS spent on this project. Will they have the option to continue next year, or will the registry people start over again with a brand new group? I would think that some carryover would be valuable (albeit sometimes more challenging). Thank you.	Typed in Chat	We have found that bringing new panelists on annually gives us a fresh perspective. However, we would like to give previous engagement members the opportunity to comment at subsequent years should time allow.
<b>11:38 AM</b>	I appreciate the time that these people w ALS spent on this project. Will they have the option to continue next year, or will the registry people start over again with a brand new group? I would think that some carryover would be valuable (albeit sometimes more challenging). Thank you.	Typed in Chat	Also answered live by panelists who suggested a mixture of previous and new participants might be helpful.
<b>11:41 AM</b>	Following up to Stacy's point about people living with ALS and caregivers who are involved, and how they can spread the word. How would you do this? For instance, online or on social media? And Is there anything that would be helpful to you and others in spreading the word?	Answered on Stream	Stacy: outreach needs to be multiplatform, certainly social media for its far reaching platforms. Also need to reach out to clinics and physicians directly, I will actually bring up the Registry to my next clinic appointment. Focus groups educated by the CDC and it's partners
<b>11:53 AM</b>	Given the findings that mutations in SPTLC2 lead to excess sphingolipid production, what specific therapeutic approaches are currently being explored to inhibit SPT activity or restore the regulation of sphingolipid synthesis?  Have any trials been conducted on using RNA interference or other gene-editing techniques to target the SPTLC2-related ALS mutations?	Answered on Stream	Dr. Mehta's presentation discussed the progress of amending the IRB to add juvenile ALS patients to the Registry. However, since juvenile ALS is not yet included in the scope of the Registry or its funded research and no genetic information is available in the Registry, this question was not posed to the panelists."
<b>11:54 AM</b>	With the discovery of de novo and inherited mutations in SPTLC2, how feasible is it to include this gene in broader newborn screening programs, especially for families with a history of juvenile ALS?  What are the current barriers to early genetic testing for ALS, particularly for pediatric cases where early intervention could be crucial?	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

<p><b>11:55 AM</b></p>	<p>Are there any ongoing clinical trials specifically focusing on ALS caused by SPTLC2 or related sphingolipid metabolic dysfunctions? If so, what are the preliminary results?</p> <p>How are current ALS research and treatments for adult-onset ALS being adapted to target pediatric-onset forms related to SPTLC2 mutations?</p>	<p>Answered on Stream</p>	<p>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.</p> <p>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.</p> <p>An underlying factor with underrepresentation of minority communities is the large gap in healthcare access that come from racial disparities and socioeconomic issues.</p>
<p><b>11:56 AM</b></p>	<p>What opportunities are available for collaboration between ALS researchers and advocacy organizations like Melanin Children Matter to raise awareness and funding for research into rare pediatric ALS cases?"</p> <p>What role can patient registries play in advancing research for SPTLC2-linked ALS and other rare genetic forms of the disease?</p>	<p>Answered on Stream</p>	<p>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.</p>
<p><b>11:57 AM</b></p>	<p>How do symptom progression and management strategies differ between juvenile ALS caused by SPTLC2 mutations and adult-onset ALS, and are there specialized treatments for pediatric cases?</p>	<p>Typed in Chat</p>	<p>ALSFERS-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.</p>
<p><b>11:58 AM</b></p>	<p>Dear Dr. Song your current technique may not be statistically valid if you are using two different granularities of data, e.g. census tract level emissions data with address level residential history</p>	<p>Typed in Chat</p>	<p>Thank you very much for the comment, Bart! There are actually very sophisticated GIS methods (a bit beyond my expertise) area that can disaggregate area-level exposure values to more granular geographical regions. In addition to that, there are environmental exposure data reported using the "point of the emission", which can be linked with the "point of residential address" to create that point-level estimate. However, you are correct about neither of these estimates would be perfect, but the hope is to at least provide a secondary source of truth that we can use to generate more robust findings (and at some level, reduce the burden and stress of data entering for patients)</p>

<b>1:57 PM</b>	How does a pALS volunteer to work with the registry?	Answered on Stream	Federal laws prevent people from volunteering directly with the Registry. Therefore we recommend any people living with ALS interested in volunteering to reach out to the partner organizations (ALSA, Team Gleason, Les Turner, MDA) to see if they can participate on a more local level
<b>1:59 PM</b>	Re raising awareness in the community. Yesterday we talked of the funds spent with “partners.” Those funds are not chopped liver, and we should be measuring results and setting performance standards. If we’re going to contract with partners, those contracts should have measurable results and expectations. Thank you.	Answered on Stream	Dr Mehta responded that the partners' contracts spell out specific outreach and awareness activities planned for each year of the contract and then report monthly to the Registry on the specific results achieved.
<b>2:00 PM</b>	Should we be encouraging people with ALS to prioritize certain forms? I believe I was told recently that the form which captures critical information about aspects important to diversity and equity is one of the very last forms, and people may give up before they get that far.	Answered on Stream	Priority really depends on what the Registry is actively looking into for research. Survey 1, which is demographic data is always relevant and needed; meanwhile we are currently looking at symptom onset and interventions that the patients are going through, so survey 17 data is needed right now.  We are also working on changing the way the surveys are laid out so that they are easier to digest.
<b>2:02 PM</b>	What about having local advocates/people with lived experience available IN clinic to help people fill out the forms? i.e., a grass roots version of what we heard about yesterday with the pilot program helping people to do the forms in some communities.	Answered on Stream	It is a lot more challenging and complicated to have this work. People living with ALS will find it extremely difficult either to dedicate the time or the energy needed to go to a clinic on a regular basis
<b>2:07 PM</b>	The outrage efforts in Kentucky is almost nonexistent. How can we bring funding and awareness and connections to Kentucky?	Answered on Stream	There is an ALSA clinic in Lexington, KY. The panelists were unsure which part of KY this question is in reference to. Patti Stanco of ALSA has offered her contact info to follow up on this question
<b>2:08 PM</b>	When is this ALSA focus group/feedback collection happening?	Answered on Stream	It's a pilot program in a single clinic right now. We're looking to get feedback from 40-50 clinic patients, with the intent to repeat it in other clinics



<b>2:10 PM</b>	I'll be more direct. Why are we paying ALSA c\$400K per year, MDA c\$350K per year?	Answered on Stream	Question answered in # 41
<b>2:19 PM</b>	My question was not silly. What are the measurables in the contracts? What are those goals? How do you measure results, success? Thank you.	Answered on Stream	Question answered in # 41
<b>2:23 PM</b>	What is your call to action for the pALS and cALS community?	Answered on Stream	Get the word out Tell 2 people in your circle about the Registry today
<b>2:52 PM</b>	We also maintain a database with lots of links on the CDMRP ALS Research Program Website: <a href="https://cdmrp.health.mil/alsrp/resources/FY24%20ALSRP%20Research%20Resource%20database%2020240410.pdf">https://cdmrp.health.mil/alsrp/resources/FY24%20ALSRP%20Research%20Resource%20database%2020240410.pdf</a>	Typed in Chat	Thanks, we will add to the notes.