

2019 National ALS Registry Annual Meeting Executive Summary

The National ALS Registry meeting was held in Atlanta on July 23-24, 2019.

National ALS Registry Update: Goals, Methodology, and Achievements

The goals of the National Amyotrophic Lateral Sclerosis (ALS) Registry are to determine the incidence, prevalence, demographics, and risk factors for ALS in the United States (US). Because ALS is a non-notifiable condition in the US, Agency for Toxic Substances Disease Registry (ATSDR) uses a two-pronged approach to ascertaining ALS cases including (1) online registration by ALS patients via the web portal and (2) identifying ALS cases from large national databases (i.e. Medicare and the Veterans Administration). Persons with ALS can also provide information about risk factors for ALS by completing one or more of the Registry's 17 online surveys.

The Registry does more than just count cases, it is also:

- Funding investigator-initiated research for ALS epidemiological studies and clinical trials,
- Collecting biospecimens including tissue, hair, nails, and blood and post-mortem samples (brains, spinal cords, and other specimens), through the National ALS Biorepository,
- Connecting patients with researchers recruiting for ALS clinical trials or epidemiological studies,
- Gathering etiologic data from Registry enrollees via online risk factor modules such as, occupational history, military history, residential history and history of traumatic brain injury (TBI),
- Providing data and biospecimens to scientists to further ALS research.

Registry accomplishments since the last meeting include:

- ATSDR funded 16 research studies to date, with three new studies funded in Fall 2018 and another to be funded in Fall 2019.
- Assisted over 45 institutions (e.g., pharmaceutical companies and academia) with their clinical trials and epidemiological studies resulting in over 1000 patients recruited to date.
- The National ALS Biorepository has received blood and saliva samples from over 800 participants and over 40 post-mortem collections.
- The fourth *Morbidity and Mortality Weekly Report (MMWR)* report on the Prevalence of ALS in the US was published on November 23, 2018, covering calendar year 2015.
- ATSDR held its first-ever Registry webinar for partners that was attended by 123 people.
- ATSDR is in the process of launching a new user-friendly Registry website.
- A new Spanish Registry website was launched on July 22, 2019.
- New social media, graphics, and other digital assets have been created to enhance the Registry communications and outreach efforts.
- Over 60 peer-reviewed publications/abstracts from Registry staff and research partners (over ½ dozen more since last year) have been published.
- A State Outreach Project was conducted jointly with the ALS Association, MDA, and the Les Turner ALS Foundation to increase Registry enrollment in health districts that were currently under-enrolled.
- Targeted 56 percent of Registry funding to supporting ALS research.

Research Update

The most recent findings from the Registry indicate that in 2015, there were 16,583 persons identified in the US as definite ALS cases through the national databases and the Registry portal. This equates to

a prevalence estimate of 5.2 cases of ALS per 100,000 persons, representing a slight increase since 2014. ALS continues to be more common in whites, males, and persons aged from 60-69 years of age.

Persons with ALS can complete 17 risk factor surveys on the Registry portal, which has created a rich source of risk factor information for ALS. Data requests are being submitted from researchers for the risk factor surveys and releases have begun. Some of the institutions conducting analyses of the data include the Mayo Clinic, Rutgers University, and Columbia University.

The Research Notification System is connecting ALS patients to researchers who are recruiting for participants in their new studies and clinical trials. Approximately 95% of Registry enrollees opt in to receive notifications about opportunities to participate in these research efforts. As of the meeting date, 45 institutions have used the notification system.

ATSDR is also supporting ALS research with 56% of the Registry's funding being allocated to external research.

National ALS Biorepository

Persons with ALS who are enrolled in the National ALS Registry may also take part in the National ALS Biorepository. The Biorepository sends a phlebotomist to the patient's home to collect the biospecimens, including blood, urine, and saliva, at no charge to the patient. Postmortem specimens are also collected including brain, spinal cord, cerebral spinal fluid (CSF), bone, muscle, and skin. Biorepository participation from January 2017 – June 2019 resulted in the collection of 678 in-home blood and urine samples, 154 saliva only samples, and 20 postmortem samples. Researchers can request samples for their ALS research projects. Samples can also be paired with demographic and risk factor data from the Registry. The types of specimens most likely to be requested are blood and postmortem tissue. To date, over 5,000 samples have been provided to researchers.

Research Notification System

This past year the Registry used its Research Notification System to assist academia and pharmaceutical manufacturers to help them recruit for their [clinical studies](#). The system was used by Brainstorm Cell Therapeutics, Orphazyme, Orion Pharma, Amylyx Pharmaceuticals, The ALS Association, Columbia University, and the University of Sydney.

Enrollment in the Registry

In 2018, the Registry began collecting data on how participants are being referred to the Registry. The findings indicate most referrals were made by the ALS Association and doctors/neurologists. Regarding the risk factor surveys, there are now 17 surveys available on the Registry for enrollees to complete. The survey that has the highest rate of completion is the demographics survey, with nearly 60% of enrollees completing the survey in 2017. Currently, on average, enrollees are completing about six of the 17 surveys. Comparing registration date to date of diagnosis, those registering in 2017 were diagnosed just under a year earlier. The findings also show that states that are registering the highest percentage of persons with ALS have a slightly higher percentage of survey completion than states with the lowest percentage of registered patients.

Under-Enrolled States Outreach Project

The Under-Enrolled States Outreach Project was a six-month study conducted jointly by ATSDR, the ALS Association, MDA, and the Les Turner ALS Foundation during July - December 2018. The goal was to determine if increased specific outreach efforts in under-enrolled states would improve the

percentage of persons with ALS who enrolled in the Registry. The states participating in this project were Hawaii, Mississippi, New York, Utah, West Virginia, and Wyoming. The outreach efforts included the posting of targeted social media and graphics, outreach via partner-specific events, such as support groups and walks, and standardized phone calls by the local ALS chapter and clinic staff to persons with ALS served by their chapters/clinics. The results showed that all six states did have an increase in enrollment in 2018 as compared to the same time period in 2017. Regarding next steps, the Under-Enrolled States Outreach project was successful in bringing partners together to develop outreach methods that are now available to all states and in establishing methods to increase enrollment through outreach. The next steps in Phase II of the project are to focus on the higher populated and under-enrolled states of California, Florida, and Texas.

Recommendations from the 2018 Meeting

The purpose of the Registry's annual meeting is to update the ALS stakeholders on the progress of the Registry, to provide a forum to discuss challenges faced by the Registry, and to receive expert advice and discuss strategies to further enhance the Registry. In many ways, the annual meeting functions like an advisory committee to the Registry. The suggestions and recommendations that patients, caregivers, partners, and researchers provide are valuable and critical to the success of the Registry. There were 18 recommendations from 2018 that were presented in the following categories: Communications and Outreach, ALS Prevalence, Analysis and Existing Data, and Other. The activities that are being implemented to address each recommendation, the organization that is taking the lead on the recommendation, and the status of each recommendation were presented in several tables.

Communication & Outreach

ATSDR

This year, ATSDR created for the first time the National ALS Registry newsletter that features a patient spotlight and updates for partners and researchers. The goal of the newsletter is to increase awareness of the Registry and highlight the variety of resources and tools that are readily available on the ALS website. In addition to the newsletter, the redesign of the ALS website is another key marketing strategy ATSDR is focusing on in 2019. The new website will group subject matter topics by target audience so that users can navigate the new website efficiently. The Spanish website is also forthcoming.

Further communication outreach efforts from 2019 include:

- The first ever national training webinar for partners, with over 120 participants.
- Feature article on CDC's website for ALS Awareness Month.
- A "matte" article in community newspapers, which resulted in over 2500 placements.

Brunet Garcia

Since 2015, Brunet- Garcia has been working with the National ALS Registry to raise awareness of the Registry and also support partners, stakeholders and persons with ALS. Brunet- Garcia is supporting the Registry by creating new and innovative marketing materials such as graphics, posters, factsheets and more. In 2019, Brunet-Garcia created squeeze balls for patients and partners, appointment card reminders, and print materials to explain the importance of risk factor surveys and several posters in different content and design elements for partners.

Brunet-Garcia is continuing their work in the development of materials that explain the difference between the Registry and partner organizations.

ALS Association

The ALS Association is the only nationally affiliated not-for-profit health organization dedicated solely to ALS. The Association's nationwide network of 39 chapters provides comprehensive patient services and support to the ALS community. The ALS Association plays a vital role in promoting the work of the Registry through their chapters. For example, in 2019 the ALS Association conducted a series of focus groups of clinical staff in chapters to work cohesively on promoting the Registry. The focus groups also provided feedback and challenges about print materials and registration. Furthermore, the ALS Association requested help and support to their clinic staff and caregivers in understanding the process of practicing how to register online.

Overall, the ALS Association and their clinics promote the work of the Registry by holding ALS walks and engaging with persons with ALS about the importance of not only the Registry but also the Biorepository and have also collected specimens. The ALS Association continues to use their social media platform as a way to promote the Registry.

Muscular Dystrophy Association

The Muscular Dystrophy Association (MDA) is an umbrella organization that covers 43 neuromuscular diseases (NMDs), one of which is ALS. They offer a number of support services to the community, in addition to the research that they fund. MDA works as a partner with ATSDR to promote the Registry and in 2019 MDA has increased its social media promotion of the Registry considerably. In addition, MDA create regular online postings on their national site, including postings during ALS Awareness Month in May and the more traditional print media, such as MDA's Quest Magazine to reach a different target audience.

Furthermore, MDA has recently started a new effort to ensure that all of its staff are officially and adequately trained on the National ALS Registry. The new MDA Engage program is a community gathering event they recently hosted in Boston that focused on ALS and served as a great opportunity to share information about the Registry to the 80 patients and family members that attended.

Les Turner ALS Foundation

Founded in 1977, the Les Turner ALS Foundation is one of the oldest ALS groups in the world aiming to serve persons living with ALS and their families in the Chicago area. They provide wide-ranging ALS care through patient service programs including local support groups, community educational programs and in-home consulting. In addition, the Les Turner ALS Foundation has a National ALS Registry Associate and their main objective is to meet with patients in clinics and at the comfort of their homes to provide information about the importance of the Registry and help persons living with ALS successfully enroll in the Registry. They estimate that about 85% of the individuals they serve are currently enrolled in the Registry.

In 2018, the Les Turner ALS Foundation has promoted the National ALS Registry through monthly features on their website, marketing the Registry from their social media channels, print newsletters, annual education meetings for medical professionals and more. They also promote the Registry in 5 support groups in the Chicagoland area.

Update from Pharma

Biogen

Dr. Cho, associate Medical Director presented on several Biogen clinical trials, including the EMPOWER Phase III study with dexpramipexole, which did not demonstrate any difference in efficacy with placebo. Although the Phase III study failed to demonstrate the prespecified efficacy, the study provided an opportunity to examine the rich datasets generated from the study with over 800 patients to reshape the approach. Key findings from this assessment suggested the need to evaluate genetically validated targets in defined patient populations, pursue the most appropriate modality for each target, implement biomarkers of target engagement and disease activity in early-stage studies, and employ sensitive clinical endpoints.

Biogen is also focusing on applying what has been learned from genetic targets, such as SOD1 and C9orf72, to target sporadic ALS.

Dr. Cho presented on a number of other studies that are in Phase I and Phase III development, including Toferson, an antisense oligonucleotide (ASO) targeting SOD1 mRNA. The hypothesis is that if the SOD1 protein levels are reduced, this may slow disease progression. The first report of tofersen in participants with SOD1-ALS supports its continued development. A Phase III study with tofersen has been initiated called VALOR, which is currently enrolling patients with SOD1 mutations who demonstrated weakness attributable to ALS. The treatment duration for VALOR will be 6 months.

Other studies were described which focus on sporadic ALS and the assessment of a potential complementary therapy for muscle strengthening.

Persons Living with ALS Perspective

An open panel including three persons with ALS provided their journey living with ALS and perspective of the Registry. Each participant expressed their appreciation for the Registry and for the meeting. Participants also provided helpful insights on ways to better promote the Registry and Biorepository.

ATSDR-Funded Research Update

ATSDR provides funding to support ALS research studies to help the ALS community learn more about the disease and to also help prioritize new risk factor modules for the Registry. Principle investigators presented updates of the following ATSDR-funded studies:

- Environmental Risk Factors for ALS: Critical Time Periods and Genetic Interactions
- Identification and Characterization of Potential Environmental Risk Factors for ALS Using the ALS Registry Cases and a Control Population
- Novel Extracellular Vesicle and Molecular Biomarkers of Environmental Exposure and Disease Progression in ALS
- Metabolomic Signatures Linking ALS to Persistent Organic Pollutant Exposures
- A Population-Based Ohio ALS Repository and a Case-Control Study of ALS Risk Factors
- Case-Control Studies Nested in National ALS Registry to Evaluate Environmental Risks
- Antecedent Medical Conditions and Medications: Associations with the Risk and Prognosis of ALS
- Identification and Validation of ALS Environmental Risk Factors

National ALS Registry Action Items for 2019/20:

We recognize that the success of the Registry depends on the collaboration of all the stakeholders. During the coming year we will continue to work collaboratively with the partner organizations and other stakeholders to implement the following new recommendations:

- Create new materials about how to sign up for the Biorepository.
- Create new materials explaining the importance of risk factor surveys and their completion.
- Explore universal branding for ALS.
- Identify new and better ways to engage minority populations to join the Registry.
- Provide increased guidance to neurologists on the most effective way to engage PALS about the Registry.
- Provide registration information to PALS at multiple time points.
- Have someone designated or information about the Registry available at the doctor's office.
- Randomly order surveys for each participant to help increase completion rates.
- Place information about the Registry on the same side of the appointment card as the appointment information.
- Have a checklist or card for Registry participants to note user ID and password.
- Have a Registry practice site/test account for partners and clinic staff. Alternatively, have a webinar that steps partners/clinic staff through registration and a sample of surveys.
- Have a central location for information on all ALS Biorepositories.