

2017 Annual ALS Surveillance Meeting Executive Summary

Amyotrophic Lateral Sclerosis (ALS) continues to be a mysterious fatal disease with no known cause(s) for approximately 90-95 percent of those diagnosed with the disease. It is for this reason that the Agency for Toxic Substances and Disease Registry (ATSDR) established the National ALS Registry in 2010. The primary purpose of the ALS Registry is to describe the incidence and prevalence of ALS, to describe the demographics of ALS patients, and to examine the risk factors for the disease. In 2016, the ALS Registry published the second report on the prevalence of ALS in the United States in CDC's *Morbidity and Mortality Weekly Report (MMWR)*.

Each year the ATSDR organizes the Annual ALS Surveillance Meeting to update stakeholders on the progress of the National ALS Registry, The National Biorepository, the Registry data and its implications, and to discuss strategies to further enhance the Registry for all of the stakeholders. In January 2017, the National ALS Biorepository was initiated with the primary goal of assembling the largest bank of ALS blood and tissue samples in the US and making them available for research.

Opening Remarks

Dr. Patrick Breyse, Director, National Center for Environmental Health and the Agency for Toxic Substances and Disease Registry, provided the opening remarks for the 2017 meeting. Dr. Breyse acknowledged the huge resource this meeting represents by bringing together clinicians, researchers, persons with ALS and other ALS advocates to help move the science forward. He briefly mentioned the President's budget, which reduces NCEH funding by approximately \$25 million over recent funding, including elimination of the National ALS Registry funding. However, he underscored the importance of this important work and therefore hoped that the funding would be restored. Dr. Breyse also pointed out the progress that has been made by the Registry since it was launched in 2010.

Overview of the National ALS Registry

The background and methodology of the National ALS Registry was described beginning with the enactment of the US ALS Registry Act, passed in October 2008. This act directs CDC/ATSDR to establish and maintain the National ALS Registry. Because ALS is a rare and non-notifiable disease there was not a reliable method for determining the number of cases of ALS in the US, who has the disease, or other factors about ALS. The Registry was launched in October 2010 to describe the incidence and prevalence of ALS, to describe the demographics of ALS patients, and to examine the risk factors for the disease.

The methodology for identifying ALS cases was described, which uses data from national administrative databases (i.e., Medicare, Medicaid, and the Veterans Administration) in addition to the information entered into the online Registry web portal by persons living with ALS. In addition to enrolling, persons with ALS can also answer questions regarding their disease and complete any or all of 17 risk factor surveys on the Registry web site. These surveys will help to answer questions about the potential risk factors for ALS.

But the Registry is doing much more than just counting cases. Some of the initiatives that are now ongoing as part of the Registry include:

- Funding to support ALS research
- Launching the National ALS Biorepository in January 2017
- Maintaining the Research Notification System to connect persons with ALS to clinical trials and epidemiological studies

- Implementing the use of a Global Unique Identifier (GUID) to link data across studies and trials
- PALS have participated in
- Launching a researcher data/biospecimens platform for requesting data and biospecimens for use by researchers
- Publishing journal articles including ATSDR-funded research & research that used the Registry to recruit participants
- Partnering with organizations including; the ALS Association, Muscular Dystrophy Association, Les Turner ALS Foundation, and Brunet-Garcia Advertising

Discussion about Research and Registry Activities

A high-level overview about research and Registry activities was presented, which included the next MMWR report to be released from the Registry, risk factor surveys, funded research, the Research Notification System, and manuscripts currently in development. The third *National ALS Prevalence Report* will cover the calendar year 2014. Hospice data will be included in the report for the first time, which may increase the case ascertainment counts. As of August 1, 2017, nearly 70,000 risk factor survey modules had been completed by persons living with ALS. Requests have been received from researchers for the risk factor survey data, which is now being released. These data are being made available for research with certain restrictions. ATSDR is also funding extramural research to learn more about ALS etiology and risk factors. To date, 12 research studies have been funded, with one additional study to be funded within the next few weeks. The Registry is also assisting ALS patients in locating research studies and clinical trials and determining if they meet the eligibility criteria for participation. The Research Notification System is designed to help researchers recruit for their studies and clinical trials. When a person enrolls in the Registry, he/she may choose to receive notifications about clinical trials and studies that they are eligible for. Over 100,000 emails have been sent to Registry participants thus far. A listing was also presented of 10 manuscripts that are currently under development or have been submitted to journals.

Update on the National ALS Biorepository

A brief history and update on the National ALS Biorepository was described. A pilot project ran for about four years from 2012 until 2015. The pilot study enrolled 330 Registry participants to provide biological specimens including blood, urine, hair, and nails. An additional 30 Registry participants were enrolled to donate tissues postmortem. At the end of the pilot study, a number of recommendations were made including the continuation of collecting most of the specimens collected during the pilot study. Based on these recommendations, the National ALS Biorepository was launched in January 2017. The process for enrolling in the Biorepository was described for new and previously enrolled Registry participants. From January – July 15, 2017, the Biorepository has collected 133 in-home blood and urine specimens, 30 saliva specimens, and 1 postmortem tissue donation. The process for researchers to request samples from the Biorepository was also described.

Registry Communication and Outreach

ATSDR

ATSDR provided an overview of the communication and outreach efforts being used to increase awareness of the National ALS Registry and to encourage persons with ALS to participate in the Registry. ATSDR recognized the outstanding work being done by its partners to raise awareness. But more attention needs to be focused on understanding who the target audience is and what messages should be used. To that end, ATSDR has used many different routes this year to reach the audience. A few of these include; the creation of a new video, new digital media, and a website makeover, currently in progress. In addition to its existing partners, ATSDR is also exploring new partners who may be able

to provide insights to where patients and clinicians are and can help bring everyone to the table to work together.

The ALS Association

The ALS Association described the many facets of the organization that are working for people with ALS through their public policy, research, and care efforts. Between 150-180 research studies are funded each year by the Association. They are also working through the 39 chapters and over 130 clinical partners to provide outreach to support the Registry. The Association's newly created National ALS Registry Taskforce has been instrumental in revitalizing the Registry section of their website by helping to identify the need to relocate it to a much more prominent location on the Association's website. This move has significantly improved its visibility, resulting in 250,000 views per month. The use of social media to further awareness of the Registry has also been increased significantly in 2017. Also described are new and innovating strategies, some in place and others planned, to increase enrollment in the Registry such as assisting under-performing chapters to develop strategic plans and holding Best Practices meetings at upcoming ALS Association conferences.

Muscular Dystrophy Association

Kristin Stephenson, Vice President of The Muscular Dystrophy Association, explained that MDA is committed to saving and improving the lives of individuals living with neuromuscular disease. She stressed the importance of the organizations and individual stakeholders working together because each has a role to play to ensure that the Registry is successful. MDA sees its role as not only promoting the Registry, but also telling people why the Registry is important and why it is important to be part of it. She described the different disorders served by MDA, their funding commitment for ALS research and support services, and provision of care through its 150+ ALS Care Centers. MDA also advocates for public policies that impact therapy development, and provides ALS support groups and medical equipment to ALS patients.

MDA's many different channels, which are used to promote, advocate for, and to talk about the Registry to its stakeholders were also described. Some of the communication channels include social media and the more traditional print media, such as MDA's *Quest Magazine*, which can reach persons who may not be connected to the internet. Their outreach efforts employed over the last year were also presented, as well as, areas that MDA is exploring to make the messaging more impactful as it moves forward.

Les Turner ALS Foundation

The Les Turner ALS Foundation has been serving persons living with ALS and their families in the Chicago area since 1977, making it one of the oldest independent ALS groups in the world. The Foundation's mission is to: advance scientific research into the causes, treatments, and prevention of ALS; provide people living with ALS, their families, and caregivers exceptional clinical care and support services; and to increase awareness and education of ALS. The distribution of their funding was described in the areas of research, patient care, and patient and family programs.

The Les Turner ALS Foundation uses a personalized approach to promoting the National ALS Registry, which is very consistent with the way that it approaches other ALS efforts. This approach is evident in their promotion and outreach efforts to patients and family members through clinic and home visits, support groups, annual patient education meetings, and outreach to medical professionals. Other uses of the media, educational efforts, and events, such as the ALS Walk for Life are also used to promote the Registry. The National ALS Registry Direct Enrollment Program is another very personalized effort provided by the Foundation whereby a Registry Associate works with persons with ALS in their homes

to assist them with enrolling. The Les Turner Foundation also presented some of the feedback they have received directly from patients, both positive and negative about the Registry. The feedback they have received on the Biorepository has been particularly good.

Brunet-Garcia

Brunet-Garcia has been working with the National ALS Registry since 2015 to help raise awareness of the Registry, which will lead to increased enrollment and completion of the risk factor surveys. To this end, Brunet-Garcia is continuing to work to develop and implement a strategic communications plan. One of the many underlying critical elements of the plan is to recognize the importance of helping people understand the benefits and value of the Registry. Brunet-Garcia explained the methodology and importance of ensuring that what they are doing is relevant and effectively communicates to persons living with ALS, their family, researchers, clinicians, and other audiences. Some of the highlights of their work include the following accomplishments:

- Created social media that is relevant to the caregivers as well as persons living with ALS
- Created a motion graphic video and infographics which build upon “ALS Research Counts on You”
- Worked with the Registry team to create an engaging website landing page
- Collaborated with Registry partners on a variety of articles

In all of Brunet-Garcia's accomplishments is a consistency of creating materials which communicate a very concise and clear message to a variety of audiences.

Under-Enrolled States Outreach Project

This project was initiated based on recommendations from the 2016 Annual Meeting. The previously conducted Georgia Pilot Project was reviewed in terms of its purpose, methods, results, and implementation. An update was provided on the pilot project and the strategies to increase Registry enrollment in the seven states through partner collaboration with the ALS Association, MDA, and the Les Turner ALS Foundation were presented.

The objectives of the Under-Enrolled States Outreach Project are to provide data which may be used to target outreach activities to increase Registry enrollment in specific areas of states that are enrolling persons with ALS at a lower rate than the average rate for the US. The data are now available for distribution to the ALS Association, MDA, and the Les Turner ALS Foundation. The next steps are to develop plans, to focus outreach efforts on under-enrolled counties within the seven states for a six month period, and to evaluate the impact on enrollment for these states.

Open Panel Discussion

An open panel discussion session was held to focus on answering the questions of:

- What works and does not work when it comes to enrolling patients?
- How can Registry awareness be better raised among minority groups, persons living with ALS, and rural providers?

The presenters for this session responded to the questions from the meeting participants and the participants offered their insights into approaches that are working or appear to have promise. There was a healthy discussion of the barriers to enrolling, such as cultural issues where some races may find it difficult to enroll and provide their data to the federal government, and barriers where populations do not have internet access and populations who are living in rural areas. There was agreement on the need for simple metrics. The discussion also included concerns such as the lack of access to enrollment data that informs the local chapters and clinics of which specific cities or counties are under-enrolled. Another area is the need to enhance education about the Registry for neurologists and their

staff. There was also discussion regarding when would be the best time to discuss the Registry with newly diagnosed patients.

End of the Day Questions

During this session, the floor was opened for meeting attendees to ask questions or make comments regarding any ALS issues or concerns.

Update from Pharma

Mitsubishi Tanabe Pharma America

Dr. Jean Hubble, Vice President, Medical Affairs, reported on the background and studies related to RADICAVA™. Dr. Hubble's presentation is not available for dissemination because it contains unpublished data.

Cytokinetics, Inc.

Dr. Sarah Kulke, Senior Medical Director, presented on two investigational products currently under development for ALS at Cytokinetics, Inc, Tirasemtiv and CK-107. Neither of these compounds are approved for the US at this time. Tirasemtiv is in a Phase 3 clinical trial. The findings of the Phase 1 trial were that muscle function could be improved with this compound. The Phase 2 clinical trial was also described. There were some findings that were encouraging, but there were also some tolerability issues with Tirasemtiv. The findings of these trials encouraged the investigators to move forward to the Phase 3 trial. Cytokinetics, Inc. recruited for the Phase 3 study through the National ALS Registry's Research Notification System. The results of the Phase 3 trial are anticipated to be presented at the ALS-NMD meeting this year.

Cytokinetics, Inc. also recently began the Phase 2 treatment study, Functional Outcomes in a Randomized Trial of Investigational Treatment with CK-2127107 to Understand Decline in Endpoints – in ALS (FORTITUDE-ALS). CK-107 is known to have the same mechanism of action as Tirasemtiv, but it is known not to cross the blood-brain barrier (BBB). The theory is that would lead to less of the tolerability or side-effect issues.

National ALS Registry Data Update

Outside researchers may now request data for use in their research studies from the National ALS Registry. The data that is available has been collected through five of the Registry's 17 risk-factor modules including: demographics, occupational history, military history, smoking/drinking history, physical activity, and family history of neurological diseases. The application process that researchers are required to follow in order to request the data was described. Once the application is approved, ATSDR provides the researcher with a unique de-identified dataset, as well as a matching data dictionary.

Open Panel Discussion: Persons Living with ALS Perspective on the Registry

Ms. Janine Cory, Acting Director of Communication, pointed out that this session would serve as a very helpful reminder for everyone that each point of data on a slide represents a patient, and that it is important not to lose perspective about why this Registry exists and what is important. With that in mind, this panel was comprised of persons living with ALS and their families who shared their perceptions of the National ALS Registry.

ATSDR Funded Studies

Research is a critical component in learning more about the etiology of ALS and its risk factors. 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. The following ATSDR-funded studies were presented by their principle investigators during the 2017 Annual ALS Surveillance Meeting and further information can be found on the National ALS Registry website.

[Environmental Risk Factors and Gene-Environment Interactions in ALS Risk and Progression](#)

[A Prospective Comprehensive Epidemiologic Study in a Large Cohort in the National ALS Registry: Identifying ALS Risk Factors](#)

[A Population-Based Ohio ALS Repository and a Case-Control Study of ALS Risk Factors](#)

[Identification and Validation of ALS Environmental Risk Factors](#)

[ALS Risk in Latin Americans: A Population-Based Case Control Comparative Study with Three European Population-Based Cohorts](#)

[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](#)

Next Steps: Recommendations and Strategies for Strengthening the Registry

In this session there were six panelists, consisting of a representative for: the National ALS Biorepository, the ALS Registry, persons living with ALS, researchers, the pharmaceutical industry, and ALS advocacy organizations. Each panelist shared their observations about how the Registry could be used to advance research and the future directions he/she would like to see.

In addition, this session attempted to review all of the suggestions and recommendations which had been offered from the attendees throughout the meeting, to determine if any had been missed, to add any additional recommendations, and to prioritize them.

This session was also opened for meeting participants to ask questions and to provide expert advice and guidance to Registry staff pertaining to challenges encountered by the Registry, strategies, and recommendations to maintain and further enhance the Registry.

Closing Remarks

Dr. Paul Mehta thanked the participants for their attendance and closed the meeting.