

2016 Annual ALS Surveillance Meeting Executive Summary

Due to the limited information on the unknown cause(s) of Amyotrophic Lateral Sclerosis (ALS), 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 estimate the incidence and prevalence of ALS, describe the demographics of persons with ALS (PALS), and examine the risk factors for the disease. On August 5, 2016, the National ALS Registry published their second report on the prevalence of ALS in the United States in CDC's [Morbidity and Mortality Weekly Report \(MMWR\)](#).

ATSDR organizes the Annual ALS Surveillance Meeting to update stakeholders on the progress of the National ALS Registry, discuss the uses of Registry data, and to explore strategies to further enhance the Registry for all stakeholders. In late 2016, the Registry will launch the National ALS Biorepository with the primary goal of providing scientists access to the largest bank of bio samples in the US (e.g., blood, urine, tissue) for research.

Overview of the National ALS Registry – Dr. Kevin Horton

The US ALS Registry Act, passed in October 2008, directs CDC/ATSDR to establish and maintain a population-based ALS Registry for the U.S. Because ALS is a non-notifiable disease, the National ALS Registry developed a novel approach to identify and track ALS cases in the US. Data is derived from existing national databases (i.e., Medicare, Medicaid, Veterans Health Administration, and the Veterans Benefits Administration) in addition to information about PALS collected from the Registry's web portal. The National ALS Registry was launched by ATSDR in 2010.

The web-based portal allows PALS to enroll in the Registry and take brief risk factor surveys. The data from these surveys are being analyzed to better understand possible risk factors for ALS. Currently, ALS patients can complete any or all of 17 different risk factor surveys available on the Registry web site. With approximately 60,000 survey modules completed to date, these surveys may help to answer questions about the etiology and potential risk factors for ALS. Since 2010, the Registry has produced two annual reports, spanning three full calendar years (October 2010 – December 2013), as well as over 30 ALS publications. The prevalence and incidence rates within the United States were identified in previous ATSDR publications as 3.9 and 1.5 cases per 100,000 population, respectively. More detailed results from the Registry were also presented describing the demographic characteristics of the U.S. ALS population, as well as published data from select risk factor surveys that have already been analyzed. ATSDR continues to analyze the collected risk factor data.

ATSDR has also added multiple enhancements to the Registry, including:

- Implementing a Research Notification System to help researchers recruit PALS for clinical trials/studies,
- Funding for extramural research studies on etiology and risk factors,
- Launching the first National ALS Biorepository in late 2016, and
- Integrating a new online platform for researchers to request data and/or biospecimens.

These initiatives will help strengthen the work of the National ALS Registry by connecting PALS with research studies and clinical trials and by providing funding for studies which may help to determine risk factors for ALS. The National ALS Biorepository will be part of the National ALS Registry. Because it will include biosamples from persons enrolled in the Registry, these samples can be linked

with the data on risk factors collected by the Registry. Also, researchers can be granted access to data and specimens to help further ALS research.

ATSDR also works closely with its partners and collaborators, which provide invaluable insight into how the Registry can facilitate the efforts to defeat ALS. Being the first and only population-based ALS Registry in the U.S., the efforts being undertaken by ATSDR provide data on incidence, prevalence, demographics, and risk factors for ALS and is serving as a recruitment tool for research.

National ALS Registry 2012-2013 National Prevalence Estimates – Dr. Paul Mehta

The second report of the National ALS Registry identified 14,713 and 15,908 persons as definite ALS for the calendar years 2012 and 2013, respectively. The estimated ALS prevalence rate was 4.7 cases per 100,000 U.S. population for 2012 and 5.0 per 100,000 for 2013. Moreover, prevalence rates were observed to be higher in whites, males, and persons aged 60-69. The observed increase in prevalence rates was likely a result of improved data collection practices and public awareness.

As the Registry continues to grow and mature, a third report is scheduled for release in 2017. This report will describe 2014 data, update ALS prevalence estimates for the U.S., and evaluate trends in ALS prevalence. Comparisons of Registry data with data collected in the State and Metro surveillance projects will help to determine the completeness of the Registry. Capture-Recapture statistical methodology will estimate the number of potentially missing ALS cases and will also be used to evaluate the completeness of the Registry. ATSDR anticipates releasing findings on Registry completeness in 2017.

Surveillance of ALS in Massachusetts – Alicia J. Fraser

In the 1990s and earlier, concerns had been raised regarding the number of hazardous waste sites in Southeastern Massachusetts, the suspected increase in ALS in this area, and the lack of ALS surveillance data. In 2003, Massachusetts General Laws were amended to establish the only statewide ALS registry in the U.S. During this same time period, Massachusetts received a research grant from ATSDR to develop methodologies for surveillance of ALS. As part of this effort, a surveillance study was conducted in Southeastern Massachusetts in an effort to determine the local prevalence of ALS and evaluate disease occurrence at sites located near hazardous waste. The prevalence that was found was 2.4 cases per 100,000, which is similar to what is reported elsewhere. However, from this effort MA developed more complete surveillance methodologies for their registry, which continue to be used today.

In 2004, ALS became a reportable disease in MA, and in 2008, the MA ALS Registry was implemented. The purpose of this Registry is to determine the prevalence and incidence of ALS throughout Massachusetts; investigate geographic patterns, as well as temporal trends; explore the impact of environmental factors on rates of disease; and develop and maintain a population-based database that can be accessible to researchers.

The findings of the MA ALS Registry were presented by source of reported cases, age of onset, and sex, for 2007 through 2011. ALS prevalence and incidence in Massachusetts was also described and compared with other registries and data in the literature.

The National ALS Biorepository Overview – Dr. Wendy E. Kaye

The National ALS Biorepository seeks to increase biological specimens available for ALS research by collecting specimens from a geographically representative sample of Registry participants. A 2013-2015 pilot study on the biorepository developed collection and storage methods for specimens collected from PALS in their homes and postmortem. In-home collection included blood, urine, hair, and nails. Postmortem collections included brain, spinal cord, cerebrospinal fluid, skin, bone, and muscle specimens. In-home specimens were collected from 330 PALS enrolled in the Registry, with representation from every state.

Data were presented describing the geographic distribution and demographics of the pilot study participants, as well as the specimen processing procedures. Recommendations were also presented regarding developing a National ALS Biorepository.

Recruitment of participants is essential to the functioning of the Biorepository. Measures have been taken to increase general recruitment for the Biorepository through integration with the Registry and improved contact with PALS. The Biorepository has also undertaken methods to improve specimen maintenance and collection, as well as assessing specimen demand and use to ensure efficient collection and distribution to researchers. Ultimately, through the integration of the Biorepository with the National ALS Registry, researchers can request samples and data from the Registry to be used for ALS research.

National ALS Registry Research Notification Mechanism Update – Dr. Paul Mehta

During enrollment in the National ALS Registry, PALS have the option to consent to be notified about opportunities to participate in external research studies and clinical trials. The Research Notification Mechanism connects researchers to PALS, facilitating their interactions, and advancing the process of recruitment. The process involves outside researchers submitting research proposals to ATSDR, with prior approval from their institution's Institutional Review Board (IRB), which are reviewed by ATSDR. If the research proposal is approved, eligible PALS are notified via email about the research project. Interested PALS can contact the researchers to be part of the research project. On average, over 95% of PALS who enroll in the web portal of the Registry elect to receive notifications. The Research Notification Mechanism has been extremely successful, with considerable increases in the number of notifications sent to PALS each year since its inception. Additionally, a large pharmaceutical company recently approached the Registry for assistance with clinical trial recruitment. This trial was a national effort with multiple clinics participating.

In 2015, ATSDR began distributing brochures describing the notification system to neurologists, clinics, and ALS organizations to inform PALS about this benefit of the Registry. The National ALS Biorepository is scheduled to launch a similar system in fall 2016. This additional system will allow researchers to request samples for research. In addition, the Registry has received numerous requests from researchers for access to the Registry data. The Registry seeks to have a mechanism for researchers to request data in 2016-2017.

[Clinical Trial Notification using the National ALS Registry – Dr. Sarah F. Kulke](#)

This presentation was done by Dr. Sarah F. Kulke of Cytokinetics. Cytokinetics used a tool to recruit Registry-enrolled PALS for a large Phase III study, known as VITALITY-ALS, which stands for Ventilatory Investigation of Tirasemtiv and Assessment of Longitudinal Indices after Treatment for a Year in ALS. Tirasemtiv is a drug intervention. The study is across many countries with 80 treatment centers. There were several hurdles to clear regarding clearances for emails to send out, but all was ultimately resolved. The National ALS Registry Notification Mechanism is an excellent means of alerting patients in the United States with ALS about clinical trials. The Registry staff was very responsive and understanding of the challenges faced by their partners in industry. We highly recommend using the Registry for anyone in the process of recruiting for a clinical trial in ALS.

[ATSDR Preliminary Analyses Related to ALS Mortality & Disease Progression – Ted Larson](#)

Mr. Ted Larson discussed three preliminary analyses being conducted by ATSDR related to ALS mortality and disease progression. The first analysis was the calculation of ALS mortality rates, excluding deaths from other motor neuron diseases. The second analysis is fitting a survival model using data from active participants in the ALS Registry. The third analysis is fitting a multistate model for disease progression in ALS registrants. These analyses are underway at ATSDR using both national and Registry data. An estimation of national ALS mortality rates, with the exclusion of other motor neuron diseases, is important to provide more precise rate estimates. We believe that the National ALS Registry is a rich database that, using survival and multistate modeling, will begin to shed light on questions related to patient mortality and disease progression.

[Registry Promotion and Outreach: Carter Consulting, Inc. - Tom Hicks](#)

This presentation described the marketing and promotion of the Registry. ATSDR's strategies for marketing the Registry uses both digital media and traditional media, such as pamphlets, fact sheets, posters, and exhibits presented at ALS conferences. Examples of the digital media being used include: online newsletter articles, digital ads posted in partner organization publications, CDC feature articles, social media and other graphics.

The Registry works closely with large organizations who interact directly with PALS, such as the ALS Association, the Muscular Dystrophy Association, and the Les Turner ALS Foundation in order to reach the largest number of potential Registry participants. Recommendations from the previous year's annual meeting were discussed. Some of the recommendations include: to clarify and manage the expectations of what the Registry will do, to develop articles for partner newsletters to highlight the enhancements of the Registry, and to improve branding of the Registry. All of these recommendations have been implemented or are in the process of being implemented.

[Registry Promotion and Outreach: Brunet-Garcia/Global Prairie – Anna Jaffee, Kaylie Wallace, and Erin Bunyard](#)

Brunet-Garcia Advertising has been contracted to increase awareness and engagement with the National ALS Registry through developing a communication outreach plan. Their communication objectives are

to raise awareness of the Registry among PALS and their families and caregivers; to target, inform, and educate PALS of the latest happenings and updates from the National ALS Registry; and to increase self-registered PALS in the Registry and encourage the completion of risk factor surveys. A tagline was created – “ALS Research Counts on You”.

A digital media campaign was developed and is being managed by Global Prairie to increase awareness of the Registry and to support its objectives.

[Registry Promotion and Outreach: The Les Turner ALS Foundation – Andrea Pauls Backman and Judy Richman](#)

The Les Turner ALS Foundation (LTALSF) was founded in 1977, when the family and friends of Les Turner, an ALS patient, aimed to provide resources for ALS research and share the findings of this research. With the first ALS Research Laboratory opened in 1977, the foundation currently has three dedicated ALS research laboratories. In addition to the laboratories, Les Turner supports other patient service programs such as in-home consulting, support groups, and community educational programs to over 90% of the ALS population in the Chicago region. LTALSF described how, in addition to being a champion of community outreach, their 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. Directly funded programs at LTALSF get \$.88 of every dollar received in program funding. Les Turner promotes the National ALS Registry through a dedicated Registry page on their website, monthly features on the foundation homepage, social media announcements, and inclusion of links in e-newsletters.

[Registry Promotion and Outreach: Muscular Dystrophy Association \(MDA\) – Kristin Stephenson](#)

The mission at MDA is to fight to free individuals — and the families who love them — from the harmful effects of muscle-debilitating diseases so they can live longer and grow stronger. MDA does that through supporting ALS families, being committed to ALS Research, and promoting the National ALS Registry. This is being done at MDA's National Care Center Network, MDA's National Clinical Conferences, as well as, through regional and local promotion opportunities, and other education and outreach opportunities.

[Registry Promotion and Outreach: Amyotrophic Lateral Sclerosis Association \(ALSA\) – Patrick Wildman](#)

The ALS Association (ALSA) strives to keep their Chapters in the know about the Registry through monthly newsletters and other communication efforts. The Chapters are encouraged to maintain and expand their patient outreach as well. There are ALSA Certified Centers and Affiliated Centers throughout the country. Outreach and education continue through conferences and meetings, Advocacy Days, Registry Events and Symposiums, and training. ALSA has also partnered with Minor League Baseball to raise awareness of the Registry through many promotional events and trade shows.

Registry Promotion and Outreach: McKing Consulting Corporation - Promotion of The National ALS Registry to Non-referral Centers – Heather Jordon

The focus of this presentation was to provide information and data on a pilot project to conduct educational and promotional outreach activities at non-referral center neurology practices in the U.S. The project informed neurologists and the staff about the Registry and encouraged neurologists to inform their patients about the Registry, thereby increasing the self-enrollment information and data in the Registry. The results of the project to-date were presented. The project plans to evaluate the effectiveness of the educational and promotional outreach activities by reviewing enrollment rates before and after the project period.

End of the Day Questions

During this session, the floor was open for meeting attendees 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.

DAY TWO

Capture-Recapture Statistical Analysis - Dr. Lorene Nelson

Dr. Nelson reviewed the estimated prevalence of ALS in the U.S. for 2010 - 2011 as reported in the July 25, 2014 CDC Morbidity and Mortality Weekly Report (MMWR) and updated in the 2016 MMWR Surveillance Report. An assessment was performed to determine the relative contributions of case-finding methods for identifying ALS case totals to determine the best case-finding methods. The application of capture-recapture methods was used to estimate the undercount of ALS cases for the 2010 - 2011 report. Medicare and web portal were determined to be the most important case-finding methods (together they identify 94% of all cases). This information will be used to identify potential gaps in the Registry and develop strategies to identify missing cases.

ATSDR Funded Research Update

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 2016 ATSDR-funded studies are listed below and were presented by their principle investigators. More detailed information about these and previous studies can be found on the National ALS Registry website at www.cdc.gov/als.

- Ecological Study to Evaluate Spatial Relationships between ALS and Potential Environmental Risk Factors
Walter Bradley, MD, DM, FRCP
University of Miami

- A Prospective Comprehensive Epidemiologic Study in a Large Cohort in the National ALS Registry: Identifying ALS Risk Factors
Hiroshi Mitsumoto, MD, DSc
Columbia University Medical Center
- Identification and Validation of ALS Environmental Risk Factors
Stephen Goutman, MD
University of Michigan Health System

PALS Perspective on the Registry

There were four PALS in attendance at the meeting. All of the PALS provided their perspective on the ALS Registry, offering their positive feedback, as well as constructive criticism on ways to improve the Registry. PALS participation throughout the meeting provided vital input into how to best use the Registry for all stakeholders. Their involvement in the meeting discussions also provided a unique perspective for researchers and neurologists.

End of the Day Open Discussion

During this session, the floor was open for meeting attendees 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.