

**Department of Health and Human Services  
Centers for Disease Control and Prevention  
Agency for Toxic Substances and Disease Registry**

**ATSDR's Annual Amyotrophic  
Lateral Sclerosis (ALS) Surveillance Meeting**



**July 30-31, 2013  
Summary Report**

**This document has not been revised or edited to conform to agency standards. The findings and conclusions in this report are those of the meeting presenters and attendees and do not necessarily represent the views of the Agency for Toxic Substances and Disease Registry.**

## Executive Summary

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Much remains unknown about what causes ALS. The National ALS Registry was established in 2010 to describe the incidence and prevalence of ALS, describe the demographics of ALS patients, and examine the risk factors for the disease.

This report provides information presented at the 2013 Annual ALS Surveillance Meeting. Each year the Agency for Toxic Substances and Disease Registry (ATSDR) holds this meeting to update stakeholders on the progress of the National ALS Registry and to discuss strategies to further enhance the Registry.

### Overview of the National ALS Registry

The ALS Registry Act, enacted as Public Law 110-373 in October 2008, directs CDC/ATSDR to establish and maintain the National ALS Registry. It is the only Congressionally mandated population-based registry for the U.S. ATSDR described the methodology used by the Registry. The Registry combines ALS data from existing national databases (i.e., Medicare, Medicaid, VA Health Administration, and the VA Benefits Administration) with information directly entered into a secure web portal by persons with ALS. In addition to registering, ALS patients are also asked to take brief online risk factor surveys. These surveys will help to answer questions about the potential risk factors for ALS.

An important aspect of the meeting is the discussion following each presentation. This discussion generates recommendations concerning Registry issues and suggestions for enhancing the Registry. ATSDR provided an overview of recommendations from the 2012 meeting and described the actions that have been taken regarding these recommendations.

ATSDR is also implementing several initiatives to strengthen the Registry including:

- the Research Notification System,
- the development of new risk factor surveys to be added to the Registry,
- the Biorepository Pilot Study,
- the State and Metropolitan-Based Surveillance Project, and
- new ATSDR supported ALS research funding opportunities.

### Redesigned National ALS Registry Website Demonstration

An ATSDR consultant demonstrated how the Registry website was redesigned in 2013. Many of the changes resulted from suggestions offered during the 2012 annual meeting. The site has been reorganized for clearer and more direct access to the main topic areas. It has been streamlined to make it more useful and easier to navigate. Changes to specific web pages and the addition of new pages were also presented.

### National Quantitative Data Findings

ATSDR described the data in the national databases used to populate the Registry. The criteria used in the algorithm developed to identify patients with ALS from the national databases were also explained. The algorithm was developed and tested for sensitivity and specificity through pilot projects conducted in Minnesota, Georgia, South Carolina, and an HMO consortium. The sensitivity was determined to be 0.87 and specificity was 0.85. Using this algorithm, a total of

36,610 cases of ALS were identified in the national databases for the period 2001–2009. These data were also presented by year, age, race, sex and geographic distribution.

#### [Research Notification Mechanism and Research Committee Update](#)

ATSDR described the Research Notification Mechanism and the development of the research committee. This is a system that connects ALS researchers directly with persons with ALS who are registered in the National ALS Registry and have indicated an interest in taking part in studies. ATSDR had received three applications. Applications were received from Harvard University, the Medical University of South Carolina, and jointly from the University of Miami and Massachusetts General Hospital.

#### [National ALS Biorepository Pilot Study](#)

An ATSDR consultant explained what a biorepository is, how they are being used in ALS research, and listed the existing ALS biorepositories. The goal of the National ALS Biorepository Pilot Study is to pilot methods for collecting and banking biological specimens from participants in the National ALS Registry. Information from this pilot study will be used to assess the potential for developing a comprehensive, national research resource associated with the National ALS Registry. The process for obtaining input into the draft ALS biorepository pilot study protocol was described.

Recruitment for the pilot study began in April 2013. To be eligible for the study, participants must be enrolled in the National ALS Registry. The specimens being collected include blood, urine, nail clippings, and hair clippings. Post-mortem collection is also being done. The status of specimen collection was described as of July, 2013 for the in-home study component and the post-mortem study component.

#### [NIH-ATSDR ALS Risk Factor Research Update](#)

Three research projects were presented. Each of these studies proposes to assess genetic and/or environmental risk factors of ALS. These projects were funded by ATSDR through a unique partnership with the National Institutes of Health (NIH). The projects include:

- *The Role of High Density Lipoprotein Particles in ALS,*
- *Environmental Risk Factors for ALS in a Representative Sample of the US Population,*  
and
- *Large Genome-wide Association Study in ALS using the NeuroX Genotyping Platform.*

#### [Registry Promotion and Outreach](#)

ATSDR's marketing and promotion strategy for the National ALS Registry involves working with partners throughout the country. Activities include generating awareness of the Registry; encouraging persons with ALS (PALS) to self-register; and engaging persons and organizations that interact with PALS in order to reach the largest number of potential registry participants. The metrics associated with visits to the Registry and new projects and features were also described. Although the Registry continues to be promoted through traditional printed materials and the print media, this effort has been expanded significantly to include social media messaging and online ads.

ATSDR cannot release the data in the Registry until it has been shown to be representative of the ALS population in the US. However, in an effort to assist in promotion and outreach for the Registry, ATSDR is providing qualitative data. Comparison of these data identify states that are lagging below the national participation rate in registering persons with ALS. This information is being shared with its partners at the ALS Association (ALSA) and the Muscular Dystrophy Association (MDA) to assist them in targeting their outreach activities.

ALSA has entered into a contractual agreement with ATSDR to help market the Registry. ALSA described the work they are doing. This work includes conducting a listening tour of all their chapters, through which ALSA learned about rewarding activities, needs, and challenges. Based on this information, ALSA described the development of a comprehensive toolkit. This toolkit has been distributed to its chapters and affiliated clinics and centers across the country. ALSA also described how they are engaging in outreach to health professionals, researchers, veterans, elected state officials, and the general public. Another innovative tactic is ALSA's strategy of reaching out to inform the public about the Registry through Minor League Baseball.

The Muscular Dystrophy Association (MDA) described the many areas in which their organization is providing essential ALS services such as: MDA clinics and MDA/ALS centers, legislation and health policy, equipment, education, outreach, support to patients and family members, and publications. Also described was the tremendous research commitment MDA has dedicated to ALS and MDA's many efforts in information dissemination about the Registry.

#### Metropolitan Area-Based ALS Surveillance

The objective of the metropolitan area-based ALS surveillance is to use the data to evaluate the completeness of ATSDR's National ALS Registry. To try and assure complete ascertainment of persons with ALS, the project had to identify and ask every neurologist who had diagnosed or provided care to an ALS patient in the specified metropolitan area from January 1, 2009 to December 31, 2011 to report cases. Eight metropolitan areas participated: Atlanta, Baltimore, Chicago, Detroit, Las Vegas, Los Angeles, Philadelphia, and San Francisco. The methods were described for identifying and recruitment of providers, case ascertainment, quality assurance, and for selection of reported cases for case verification. Results were described for the number of cases reported, age, race, ethnicity, sex, metropolitan area and by practice type. The limitations and recommendations for use of this type of active surveillance for ALS were also described.

#### American Academy of Neurology (AAN) Registry Task Force – ALS Performance Measures

An update was presented on the AAN Registry Task Force's development of ALS performance measures. The goal is to approach this from an outcome oriented perspective. The reasons were described for developing the quality outcome measures. The subcommittee members involved in developing quality measures were listed, as well as, the other organizations, ALS centers, and other groups. The process for developing measures and the attributes of a good quality measure were described. The format for measures was also described and the time required for developing a measure was broken down into the estimated time for each phase of development. The AAN ALS Performance Measurement Set was presented and examples of measures were reviewed. This effort is particularly relevant to the Registry because it underscores the importance of the information being gathered by the Registry, such as defining the number of persons with ALS and determining how many people are being treated and where. These data

will be absolutely crucial to determine the number of people who may be impacted by any quality outcome measure in development.

### [Les Turner ALS Foundation](#)

The Les Turner ALS Foundation described how the Chicago-based foundation was formed in 1977. An idea based on used books sales spawned the creation of the Mammoth Music Mart in 1978. This event continued for 25 years, providing funding to the foundation. Also described was how the foundation has grown over the years. Funds are being used to support ALS research at Northwestern University; the Les Turner/Lois Insolita ALS Center at Northwestern, and a wide variety of patient and family support programs. Ideas were discussed about how the Les Turner Foundation can help promote the National ALS Registry.

### [PALS Perspective on the Registry](#)

There were three PALS at the meeting. Each of the PALS shared his perspective on how he is dealing with the disease. They talked about what they have lost and what they have gained, about what is important in their life, and what is not so important. They shared their thoughts on the value of the Registry. They pointed out where the Registry needs to work harder. They recognized the challenges, and they offered their suggestions on how to make it better. And they thanked everyone attending for their hard work on the front lines and behind the scenes.

### [Mobile Service Locator Apps](#)

ATSDR's Geospatial Research, Analysis, and Service Program (GRASP), described the ALS Service Locator web application. This application was incorporated into the Registry web site in 2011. This mapping component uses geospatial analysis to locate the five nearest ALS clinics, ALSA chapters, and MDA offices based on the zip code entered by the user. An iPad app has also been developed and was released in September 2012. Also under development is an Android application.

### [OMB Continuation Package](#)

An ATSDR consultant explained that the Office of Management and Budget (OMB) is responsible for among other things ensuring that the policies of the Paperwork Reduction Act (PRA) are complied with by federal agencies such as ATSDR. The primary reason for the PRA is to ensure that when citizens are requested by government to do activities, that the completion of these activities should have the smallest burden possible. OMB approval of the Registry must be requested every three years. The current OMB approval is due to expire July 31, 2013. The ATSDR consultant described what is involved in the lengthy application process. Also described were some of the changes that will apply for this renewal and their impact. The timeline for the renewal process, which began in September 2012, was presented. The original approval of the application included terms of clearance, which would not allow the dissemination of results until it was clear to OMB that the results were representative of the U.S. ALS population. It is anticipated that there will be terms of clearance included with the renewal application which will allow for dissemination of the results with a disclaimer describing the limitations of the results.

### [Next Steps](#)

This session was intended to generate open-ended discussion. ATSDR opened the discussion with several questions related primarily to next steps in terms of releasing the Registry

information. Considerable discussion centered on the data elements that should be disseminated, the usefulness of including an online query tool with de-identified aggregate data, and the formats to be used to disseminate data.

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## Acronyms Used in This Document

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Acronym	Expansion
AAN	American Academy of Neurology
AANEM	American Association of Neuromuscular and Electrodiagnostic Medicine
AAPM&R	American Gastroenterological Association, American Academy of Physical Medicine and Rehabilitation
ACCP	American College of Chest Physicians
ACS	American Cancer Society
AD	Alzheimer Disease
AHRQ	Agency for Healthcare Research and Quality
ALS	Amyotrophic Lateral Sclerosis
ALSA	Amyotrophic Lateral Sclerosis Association
ALSFRS	Amyotrophic Lateral Sclerosis Functional Rating Scale
AMA	American Medical Association
ANCDS	Academy of Neurologic Communication Disorders and Sciences
AOTA	American Occupational Therapy Association
APHA	American Public Health Association
APOE	Apolipoprotein E
ApoA-II	Apolipoprotein A II
ApoL1	Apolipoprotein L1
APTA	American Physical Therapy Association
AQA	Ambulatory Care Quality Alliance
ASHA	American Speech-Language Hearing Association
ATSDR	Agency for Toxic Substances and Disease Registry
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
CPS	Current Population Surveys
CPS-II	Cancer Prevention Study II, ACS
CSF	Cerebrospinal Fluid
dbGAP	Database of Genotypes and Phenotypes
DME	Durable Medical Equipment
DNA	Deoxyribonucleic Acid
DoD	Department of Defense
DRS	Dysphagia Research Society
DTHHS	Division of Toxicology and Human Health Sciences, ATSDR
ELISA	Enzyme-Linked Immuno-Sorbent Assay
FDA	Food and Drug Administration
FTD	Frontotemporal Dementia
FY	Fiscal Year
GRASP	Geospatial Research, Analysis, and Service Program
GWAS	Genome-Wide Association Study
HCSC	Health Care Services Coordinators
HDL	High-Density Lipoprotein
HHS	(United States Department of) Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
ICD	International Classification of Diseases
IRB	Institutional Review Board
LC-MS	Liquid Chromatography-Mass Spectrometry
MAP	Measure Applications Partnership
MDA	Muscular Dystrophy Association
miRNA	Micro Ribonucleic Acid
MLB	Major League Baseball



<b>Acronym</b>	<b>Expansion</b>
MND	Motor Neuron Disease
NCEH	National Center for Environmental Health
NCQA	National Committee For Quality Assurance
NDI	National Death Index
NEALS	Northeast Amyotrophic Lateral Sclerosis Consortium
NGC	National Guidelines Clearinghouse
NGS	Next Generation Sequence
NIA	National Institute on Aging (NIH)
NIEHS	National Institute of Environmental Health Sciences (NIH)
NIH	National Institutes of Health
NINDS	National Institute of Neurological Disorders and Stroke
NLMS	National Longitudinal Mortality Study
NQF	National Quality Forum
NQMC	National Quality Measures Clearinghouse
OMB	Office of Management and Budget
PALS	Persons with Amyotrophic Lateral Sclerosis
PCPI	Physician Consortium for Performance Improvement (AMA)
PD	Parkinson's Disease
PON	Paraoxonase Enzymes
PRA	Paperwork Reduction Act
PSA	Public Service Announcement
PSP	Progressive Supranuclear Palsy
RCT	Randomized Controlled Trials
SALS	Sporadic ALS
SALSA	Southeast ALS Alliance
SBA	Small Business Administration
SES	Socioeconomic
SNP	Single Nucleotide Polymorphism
SOD1	Superoxide Dismutase 1
SOP	Standard Operating Procedure
SQL	Structured Query Language
STEEP	Dimensions of quality: safety, timeliness, effectiveness, equity, efficiency, and patient-centeredness
TDP-43	Transactivation Response (TAR) DNA binding protein-43
3' UTR	3 Prime Untranslated Region
UK	United Kingdom
US	United States
VA	(United States Department of) Veterans Affairs
VBA	Veterans Benefits Administration
VHA	Veterans Health Administration
WALS	Western ALS Consortium
WFN-ALS	World Federation of Neurology Research Group on Motor Neuron Diseases

**Centers for Disease Control and Prevention (CDC)  
Agency for Toxic Substances and Disease Registry (ATSDR)  
ATSDR's Annual ALS Surveillance Meeting**

**Minutes of the Meeting  
July 30-31, 2013**

## **Theme / Purpose**

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**Theme:** Status and Next Steps for the National ALS Registry

**Purpose:** Update stakeholders on the progress of the National ALS Registry and discuss strategies to further enhance the Registry for all stakeholders.

## **Welcome / Introductions**

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**Robert Kingon, MPA, Facilitator  
Carter Consulting, Inc.**

Mr. Kingon welcomed everyone, indicating that he would serve as the meeting facilitator. He acknowledged that the annual Amyotrophic Lateral Sclerosis (ALS) meeting is always a good conference, with great people participating and adding much to this endeavor. He noted that he is a retired CDC staff member who has been engaged in this type of work for some time following his retirement. He emphasized that during the meeting, they would be discussing preliminary information that had not yet been shown to be representative of United States (US) ALS population at this time. Therefore, attendees were requested to defer further dissemination of this information until more reliable information becomes available. Mr. Kingon then reviewed the ground rules, housekeeping, the agenda, and meeting procedures and called for introductions. A roster of those in attendance is included at the end of this document.

## **Opening Remarks**

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**Vikas Kapil, DO, MPH  
Associate Director for Science/Chief Medical Officer  
National Center for Environmental Health/  
Agency for Toxic Substances and Disease Registry**

Dr. Kapil greeted everyone and said that it was a pleasure and an honor to see everyone. Several years ago when this work first began at ATSDR, he was occupying the position currently occupied by Dr. Horton as Branch Chief. Thus, he has a very personal and warm feeling about this work and said he was thrilled to see the amazing progress that has been made over the past few years. He expressed gratitude for everyone's attendance, and emphasized the importance of convening this type of meeting to assemble the leading experts on this condition to help shape ATSDR's registry work.

ALS is a devastating fatal disease that impacts not only persons with ALS, but is also a tremendous drain on the families, friends, and loved ones of persons living with ALS. No cause has been readily identified, and the ALS Registry is a groundbreaking effort that helps scientists as they work toward finding a cure and better understanding of the risk factors for ALS. The Registry is making real progress.

ATSDR is very pleased with the progress that has been made over the past several years since going live in October 2010. The web portal has collected demographic and risk factor data on thousands of persons with ALS from all 50 states, and more people enroll every day.

Thousands of persons with amyotrophic lateral sclerosis (PALS) have been detected in the large existing administrative datasets, such as those from the Centers for Medicare and Medicaid Services (CMS) and the Veterans Administration (VA), which ATSDR is using to populate the Registry. ATSDR hopes to make the first ALS Registry report available in early 2014. The National ALS Registry also has some very exciting new initiatives, which ATSDR hopes will greatly enhance its utility. Examples include the Biorepository Feasibility Study, an online mechanism that links PALS directly with researchers, and a number of state and metropolitan surveillance activities.

Another issue that a number of people have asked about, ATSDR has gone through some transitions. Dr. Chris Portier retired as the director, and the agency is currently engaged in a national search for his replacement. Dr. Kapil saw Dr. Portier recently, who is on his way to a residential retired life in Switzerland and will be getting married in a few months. Dr. Robin Ikeda is the Acting Director. Despite the reorganization, new leadership, and time of transition, Dr. Ikeda asked Dr. Kapil to convey to everyone the tremendous support that this work has at CDC and ATSDR. ATSDR and CDC are linked sister agencies. CDC's Director, Dr. Tom Frieden, is also well aware of this work and is also extremely supportive of it. ATSDR and CDC fully support the goals and efforts of the National ALS Registry.

Dr. Kapil welcomed everyone once again to Atlanta and thanked them for their time, extended his best wishes for a very productive meeting, and said he looked forward to seeing and speaking with everyone during the breaks.

### **Ed Murray, PhD**

#### **Acting Director, Division of Toxicology and Human Health Sciences Agency for Toxic Substances and Disease Registry**

Dr. Murray reminded everyone that 2012 marked his first time attending the annual ALS meeting, at which time he reported that he was the Acting Director of the Division of Toxicology and Human Health Sciences (DTHHS). He has remained in that position for a little over a year. He also said during the 2012 meeting that this would be a steep learning curve for him, and it remained fairly steep. However, he learned a tremendous amount about ALS over the past year and said he thought they were very fortunate to have Dr. Horton and his group put so much energy and effort into this program. While he said he did not want to steal Dr. Horton's thunder, they were just notified that the ALS Registry would be receiving the CDC Director's Innovation Award for 2013. That is quite an accomplishment, and he requested that attendees take the opportunity to congratulate the group for this award. Dr. Murray emphasized that the effectiveness and success of the National ALS Registry depended upon the input from each and every partner. ATSDR has internal and external partners to help the agency work on ALS. He extended his welcome to the meeting, and wished everyone success.

## Overview of the National ALS Registry

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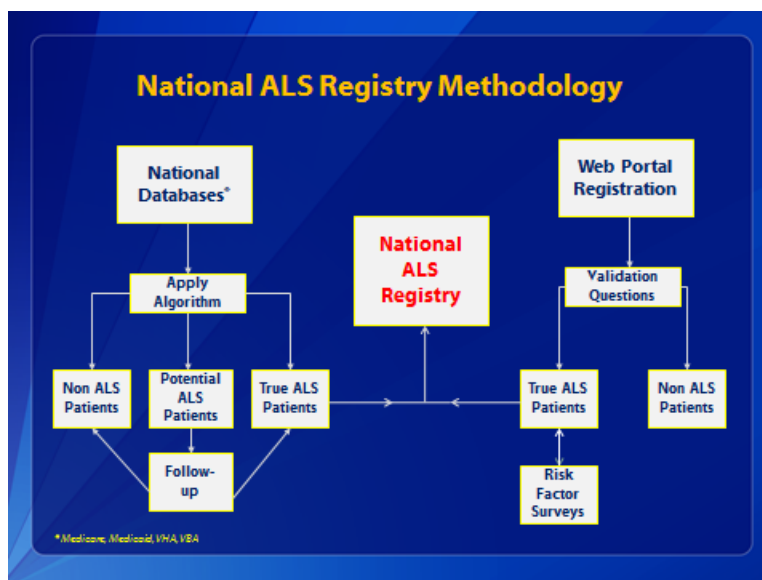
**D. Kevin Horton, DrPH, MSPH, CPH**  
**Chief, Environmental Health Surveillance Branch**  
**Division of Toxicology and Human Health Sciences**  
**Agency for Toxic Substances and Disease Registry**

Dr. Horton extended his welcome, and expressed his gratitude to everyone for taking time to attend. He stressed that ATSDR truly values everyone's input and cannot do this without its many supporters and their constituents, friends, partners, et cetera. This is not solely a CDC/ATSDR effort. This is largely a universal collaborative effort. Given that there were new participants in attendance, Dr. Horton began with a presentation of some background information to help familiarize everyone with the methodology of the Registry. He encouraged everyone to ask questions, challenge ATSDR, and offer feedback in order to help make the Registry better.

Regarding background, ATSDR is a small federal agency of the US Department of Health and Human Services (HHS). According to the last count, ATSDR employs approximately 200 individuals. While ATSDR is not a large organization, it is a sister agency of CDC. ATSDR is largely responsible for environmental health-related issues, especially those that affect people who are exposed to toxic substances. ATSDR also operates a number of registries, one of which is the National ALS Registry. ATSDR is co-located in Atlanta with CDC.

The ALS Registry Act was enacted as Public Law 110-373 in October 2008. To a large degree, this act was passed because of many of the people in the room. The act directs CDC/ATSDR to establish and maintain the National ALS Registry, which is the only Congressionally mandated population-based registry for the US. There have been other population-based registries for ALS in the US, but these have been more limited in scope. An example is the VA ALS Registry, which has done very good work. The National ALS Registry is truly a national registry in scope. As specified by the act, the intent of the National ALS Registry is to describe the incidence and prevalence of ALS, describe the demographics of ALS patients, and examine the risk factors for the disease. Lou Gehrig was diagnosed over 70 years ago. While good progress has been made in learning about the disease, much remains unknown about a definitive cause of the disease. As part of the Registry, PALS are asked to complete modules in order to gain more insight into the potential risk factors for ALS. As noted earlier, the Registry was launched in October 2010.

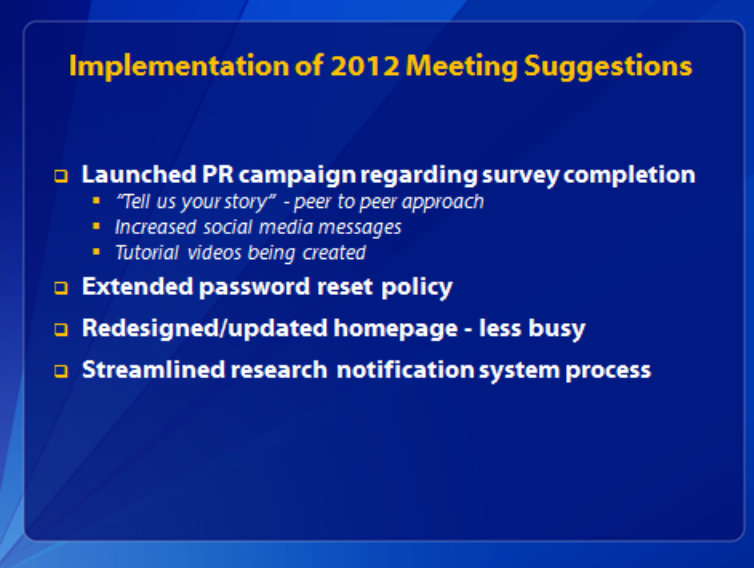
With regard to how the Registry functions, a two-pronged approach is utilized to ascertain ALS cases throughout the country. The first approach involves leveraging existing resources in the form of national databases to which ATSDR has access, including the following: Medicare, Medicaid, and a couple of datasets from the Veteran's Administration (VA). ATSDR created and vetted an algorithm from prior pilot efforts. One of the variables used in the algorithm is the International Classification of Diseases (ICD) code that is specific for ALS. That is a good indication that a person has ALS; however, ICD codes cannot be relied upon alone because coding errors do occur. Also important is prescription drug use. Given that Rilutek® (riluzole) is the only drug currently on the market for ALS that is approved by the Food and Drug Administration (FDA) and is extremely expensive, use of this drug is a sign that someone has the disease. Also an important signal is the frequency with which someone visits a neurologist. Once the algorithm is applied to the databases and people are divided into categories, those who are considered to be true patients are automatically entered into the National ALS Registry.



Those who are classified as non-ALS patients are not included in the Registry. Potential patients are those for whom there is not enough information to make a determination. These patients are placed in holding while awaiting additional data to determine whether they are or are not cases. The good thing about the approach of using existing databases is that PALS do not have to do anything.

The second approach is that anyone with ALS can have direct input into the Registry through web portal registration at [www.cdc.gov/ALS](http://www.cdc.gov/ALS). A series of 5 to 6 validation questions are posed. Depending upon the way a person answers, he or she will be asked to become part of the Registry or will be classified as not being a case and will not be asked to become part of the Registry. Those who are true ALS patients under the web portal approach are asked to take the risk factor survey modules, which will help to answer questions about the potential risk factors for ALS. While CDC and ATSDR do not interact with patients on a daily basis, those on the front lines do. This is why it is critical for neurologists, ALS Association chapters, Muscular Dystrophy Association (MDA), and everyone to help spread the word about the Registry in terms of enrolling and taking the extra step to complete the risk factor modules. There are currently 7 risk factor modules, covering such things as Demographics, Military History, and Smoking and Drinking History. PALS are asked to take the first 6 modules 1 time each, and the Disease Progression Module 2 times per year. The Disease Progression Module will be increased to 3 times for the first year at 0, 3, and 6 months, and then every 6 months thereafter. ATSDR heard from neurologists and others that perhaps 2 times per year is not sufficient, given that ALS is a very progressive disease. Understanding how a person's disease progresses over time would offer very valuable information for the ALS community at large.

During each ALS meeting, writers are taking notes. The feedback derived from the meetings is collated by ATSDR, and the agency implements many of the ideas that are offered. In terms of implementation of 2012 meeting suggestions, one idea was to engage in a public relations (PR) campaign regarding survey completion. As mentioned earlier, many PALS enroll but do not necessarily complete the survey. While it is not clear whether lack of knowledge about the surveys is an issue, launching a PR campaign will help to emphasize that point to patients. The Amyotrophic Lateral Sclerosis Association (ALSA) has conducted some PR campaigns, and

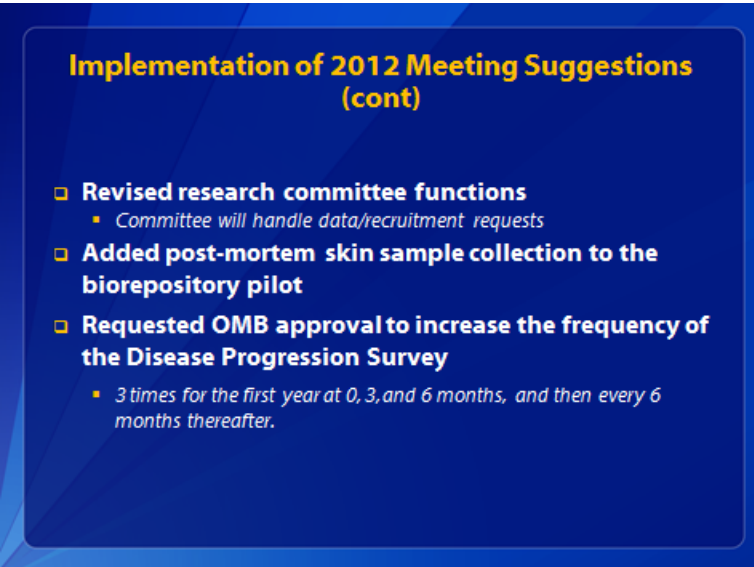


**Implementation of 2012 Meeting Suggestions**

- ❑ **Launched PR campaign regarding survey completion**
  - *"Tell us your story" - peer to peer approach*
  - *Increased social media messages*
  - *Tutorial videos being created*
- ❑ **Extended password reset policy**
- ❑ **Redesigned/updated homepage - less busy**
- ❑ **Streamlined research notification system process**

ATSDR is trying to conduct more as well. Another issue of concern raised is regarding the password reset policy. ATSDR heard from PALS that CDC IT policy requires PALS to reset their passwords every 60 days, and recognizes that this is an undue burden on patients. Even banks do not require passwords to be reset that frequently. ATSDR discussed this with the CDC IT personnel, and was able to convince them to extend the password policy to 180 days. The goal is to persuade them to extend it even further. Dr. Horton emphasized that this is not a Registry policy. It is a CDC data security policy.

In addition, ATSDR redesigned and updated the homepage. Some people thought that the previous version was very busy, so an effort was made to streamline it, make it more user-friendly, and bring it into a format that is more similar to the web pages on CDC's websites. The research notification system process has been streamlined. Now if researchers wish to use the Registry to recruit patients for their studies, the time it takes for ATSDR to supply that information to patients is shorter. The research committee functions were also revised. In the



**Implementation of 2012 Meeting Suggestions (cont)**

- ❑ **Revised research committee functions**
  - *Committee will handle data/recruitment requests*
- ❑ **Added post-mortem skin sample collection to the biorepository pilot**
- ❑ **Requested OMB approval to increase the frequency of the Disease Progression Survey**
  - *3 times for the first year at 0, 3, and 6 months, and then every 6 months thereafter.*

past, the thought was to have two different committees, one for data and one to handle recruitment requests. However, the decision was made to combine those functions under one committee. In terms of the biorepository, some of the researchers in 2012 mentioned that collecting post-mortem skin samples would be highly valuable. ATSDR was able to add post-mortem skin samples into the biorepository effort. In addition, Office of Management and Budget (OMB) approval was requested to increase the frequency of the Disease Progression Survey to 3 times for the first year at 0, 3, and 6 months and then every 6 months thereafter. This is important, given that the more data points that are known about a patient, the better the understanding of how the disease is affecting him or her.

Several initiatives are underway to help strengthen the Registry. It is not strictly a data collection effort, though that is a large component of the Registry. In terms of the research notification system, when the Registry came on line, a number of researchers approached ATSDR to express their interest in being able to use the Registry to recruit patients for clinical trials or other studies. ATSDR was able to modify the Registry such that researchers can now use it to recruit patients for their studies. The way this works is that when PALS enroll, they will be able to check a box to indicate that they want CDC/ATSDR to share their information with researchers. The good news is that a high percentage of PALS are signing up for this, and researchers are already using the Registry to recruit for various studies and clinical trials. This is a critical element of the system for linking PALS with researchers to learn more about the disease.


Additional risk factor surveys are also under development. It is known that the 7 risk factor modules that are currently available online are not enough. If it were up to ATSDR, there would be many more risk factor modules. However, OMB restricts the agency from overloading people with questions and questionnaires. For that reason, ATSDR has to be careful about the number of modules brought on line. New risk factor surveys in development include information on occupational and environmental exposures, injuries, clinical information and open-ended questions. The Open-Ended Question(s) module will offer an opportunity for PALS to articulate what they believe contributed to their particular case of ALS, or what their thoughts are in general about why people get ALS. This will be an open-field text box where people will be able to enter their data. ATSDR will review the comments and depending upon the feedback, it is possible that a module topic could be created based on the results. The surveys have been developed and tested by Stanford, and are currently being programmed into ATSDR's test portal by developers. The OMB renewal package, submitted this spring, for the Registry included the addition of these surveys. ATSDR anticipates OMB approval by July 31, 2013, with the surveys to come online later in 2013.

In terms of the proposed biorepository component, little is known about genetics in sporadic ALS. A feasibility study is being conducted for a biorepository to collect biological specimens



**Proposed Biorepository Component**

- ❑ Little is known about genetics in sporadic ALS
- ❑ Feasibility study being conducted for a biorepository to collect biological specimens (e.g., blood, tissue, hair, nails) from interested PALS who enroll in Registry
- ❑ Bioregistry would link risk factor surveys from Registry with specimens collected



(e.g., blood, tissue, hair, nails) from interested PALS who enroll in the National ALS Registry. The bioregistry would link risk factor surveys from the National ALS Registry with the specimens collected, which is anticipated to result in a very rich data source and to be extremely valuable to researchers. There are several existing ALS biorepositories that collect blood, hair, tissue, et cetera. However, they do not necessarily capture the extensive epidemiological data that ATSDR has (e.g., occupational history, residential history, et cetera).

The state and metro based surveillance component is intended to test the completeness of the National ALS Registry. Three state health departments and eight metro areas are now taking part and are engaged in an active data approach compared to the approach ATSDR is taking. Data collection focuses on cases from 2009 through 2011 and ATSDR hopes to publish this data in 2013 and 2014 to inform people about the findings.

New ALS research funding opportunities from ATSDR allow scientists to learn more about ALS risk factors and the disease burden upon PALS, family members, and caregivers. The results will help PALS and the scientific community better understand ALS, and will potentially help shape future risk factor modules for the Registry. ATSDR is in the process of accepting applications from scientists and researchers, and selecting those that are anticipated to enhance the Registry and advance knowledge about ALS. Depending upon the federal budget, and specifically the ALS budget, the hope is to make future funding available as well. The fiscal year 2013 funding announcement was posed by ATSDR/CDC on February 25, 2013 on [www.FedBizOpps.gov](http://www.FedBizOpps.gov), which is the mechanism by which the federal government advertises opportunities, and closed on March 25, 2013. Pre-solicitation proposal topics sought included the following:

- ❑ Epidemiological studies on potential ALS risk factors (e.g., cyanobacteria, environmental/occupational risks, statins)
- ❑ Epidemiological studies on the burden caused by ALS (e.g., costs of ALS, proximity of care, barriers for PALS in rural areas)

Chosen studies are to be awarded in mid-late summer, and future funding announcements may include different topics of interest to the National ALS Registry.



In closing, Dr. Horton emphasized that ATSDR cannot do this alone. Everyone must come to the table to pool resources to make this Registry the best it can be.

### **Discussion Points**

Mr. Harada suggested that a solution to the password issue may be to make it easier to reset passwords on the site by including a mechanism for password hints, secret questions, et cetera at the outset. The current requirement is to contact someone.

Dr. Horton agreed that this was a good suggestion and a reasonable request.

Mr. Harada said he recognized the OMB's reasoning behind the restrictions, but he wondered about the rationale for some of the restrictions. If the neurology community thinks it is better to have more data points entered by patients, it was not clear why that would be restricted.

Dr. Horton agreed, and emphasized that they would ask 1000 survey questions if they could however, this would be an undue burden on PALS. The primary purpose of the OMB is to ensure that there is not an undue burden resulting from the number of questions members of the public are being asked. They also want to know whether another federal agency asked similar questions in order to ensure that efforts are not being duplicated.

Dr. Kaye added that during the second day of the meeting, she planned to explain the process and rationale in detail. This requirement falls under the Paperwork Reduction Act (PRA). Mr. Harada indicated that about 14 to 15 months before this meeting, he and many other PALS were involved in the creation of videos for the Registry for people in the ALS community to encourage them to register. However, these are still not posted. This is also a point of frustration for people.

Dr. Horton replied that anything ATSDR wishes to post on its website or distribute to the public has to go through the clearance process. These videos were somewhat different because this is not something that ATSDR typically does, so it has taken a while to get them through the clearance process. At this point, the videos were going through Institutional Review Board

(IRB) review. He agreed that the peer-to-peer approach is much stronger than a bureaucrat telling a person with ALS that it is good to register. Once approved, those videos will be housed on ALSA's website.

Mr. Harada inquired as to whether notification had been sent out to enrollees regarding the ability to participate in research.

Dr. Kaye replied that when this option was first added, an email was distributed once or twice. It is possible that people could have missed it.

Dr. Horton added that this is an effort on which they could potentially work with ALSA, MDA, and perhaps the Les Turner Foundation to tweet or re-tweet information about the opportunity to take part in these studies. He agreed that reinforcement and saturation are important so that people hear the message repeatedly. The same is true with regard to the risk factor modules.

Dr. Kasarskis congratulated Dr. Horton on how beautifully the National ALS Registry had come online, and what a wonderful spokesperson he is for it. It is very difficult to diagnose neuromuscular cases, and there is always an effort to screen out ALS mimics when evaluating patients. He pointed out that it would be of interest to know exactly who the people are who are sorted into the category of non-ALS via the algorithm, and what they eventually turn out to be. He recalled that it was previously stated that determining the outcome for these individuals would require a modification of the IRB, which would likely take another 12 months. However, this may be of interest. For example, there could be a pool of veterans who are seeking compensation under an ALS guise.

Dr. Kaye replied that most of the people in the non-ALS category never had an ALS code in their records. They are all "MND Other" or "Unclassified." They have not seen a neurologist. They are not on Rilutek®. They are perhaps not even coded correctly.

Dr. Kasarskis suggested that during the 2014 annual meeting, it would be interesting to see a report on that so that everyone can get a sense of who those individuals are.

Dr. Kaye responded that they could add this to the list for the next meeting.

Ms. Sanchez added that one difficulty in assessing those individuals is that Medicare and Medicaid have changed the rules regarding acquiring data from them. Once ATSDR identifies those who are determined to be ALS and possible ALS cases, they submit that to Medicare for further information so that ATSDR can match everything. Unfortunately, ATSDR can no longer obtain personal identifiers for people who are deemed to be non-ALS cases. It is still possible to determine what is included in the category.

Mr. Handsfield reminded everyone that in the past he spoke about projects to acquire more direct access to data from CMS. He did not know the full details given that he fully retired in December 2012, but he has been receiving occasional updates. There was a major breakthrough in May 2013 such that CMS, among other things, recognized that other federal agencies do have rights to these data provided that they have a legitimate need for them. Further, they are easing the data use agreements so that instead of having to worry about disposal of data, they will rely on their own records notices. In the first trial, CDC will have 25 seats to directly access the Chronic Condition Warehouse, which is the research level data for Medicare and Medicaid. He suggested contacting Henry Rolka for further information.

Dr. Horton agreed that it would be interesting to understand what the non-ALS classifications are and thought this would be possible if what Mr. Handsfield reported comes to fruition.

Dr. Sorenson added that at the beginning, a number of pilot projects were conducted to verify the data in these databases. The most common case that came through that was not ALS was Parkinson's Disease. While he did not recall the exact ICD-9 codes, this is off by one number from the 335.20 code. These are almost certainly coding errors that occurred.

Dr. Brooks endorsed Dr. Kasarskis's recommendation, because in many diseases, when looking at the core syndrome, the surround is just as important. This is particularly true for the VA. They saw a lot of non-core ALS type conditions. Ultimately, the value of this from the algorithm might just be miscoding. It may be something more profound.

## Redesigned National ALS Registry Demonstration

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**Courtney Darby**  
**Business Analyst**  
**CACI (Formerly Emergent)**

Ms. Darby indicated that she supports the National ALS Registry by helping to document the changes and functionality required for using the web portal. Although it gives the appearance of being excessive, the 180 day password reset policy stands. This was a change from 60 to 180 days. As Dr. Horton noted, the password policy is based on CDC IT security. A number of leaps were made in terms of providing more information for PALS on the Registry site. This includes various parts of the Registry and why they are important by categorizing and compartmentalizing links. Each section was broken down and an effort was made to better educate users on registry surveys, research, reports, videos, webinars, et cetera. Utilization of social media and video technology is increasing awareness, and participation and inquiries have spiked. Inclusion of even more information regarding why the surveys are important is on-going. ALSA has added videos of PALS discussing the importance of the Registry and incorporated it in the tutorial video sent to clinics, ALSA chapters, and MDA offices. Creation of additional tutorial videos on taking surveys is in progress.

Ms. Darby then guided participants through a tour of the ALS website, beginning with a brief flashback of what the site looked like at the time of the 2012 annual ALS meeting and then showing a high-level overview of how it appears and functions currently. Many of the changes were discussed during the last meeting, and have since been achieved. The original website was said to be too busy. It provided much of what is needed, but it was not well-organized, and basically gave the appearance of being a web page of links without true direction and guidance. Thus, an effort was made to place the emphasis on a few key areas, including the following:

- ☐ JOIN THE REGISTRY
- ☐ TAKE AVAILABLE SURVEYS
- ☐ LEARN ABOUT ALS
- ☐ GIVE FEEDBACK & GET HELP

The site was also streamlined by better categorizing the links, which resulted in a cleaner look and feel that ultimately makes navigation easier. The streamlining efforts resulted in giving each of those links/general topic areas a home.



The JOIN THE REGISTRY and LOGIN buttons are now the focus throughout, but are even more prominent and visible on the ALS home page. The site includes the ability to sign up for a PALS Account or a Public Account. The Account Notification Screen appears for users to agree to terms of usage. More surveys have been added, and it is now possible for users to see the completion status of all surveys taken and to request the reset of surveys they have started. Future add-ons include additional details of why surveys are so important to take, and also additional tutorial videos on taking surveys.

Visitors to the ALS web site/portal can now see clearer topic areas and pages with the addition of clear and direct access to the following:

- ☐ Registry Resources
- ☐ Feedback and Help
- ☐ Abstracts, Publications, and Reports
- ☐ Multi-Media Tools
- ☐ Take Surveys

The ALS Resource page is designated for general information about ALS and the Registry, which includes the following:

- ☐ Factsheets
- ☐ Patient and Provider Guides
- ☐ Resource Links
- ☐ Testimonials
- ☐ A page for ordering registry materials

The page designated for ALS RESEARCH NOTIFICATION is where researchers can apply to have enrollees informed of their study and where PALS can sign up and hear back from researchers directly.

The ALS Biorepository page is an important page designated for voluntary biorepository sample collection. This is essential for researchers and scientists to gather real data that help further

support scientific and medical progress. The alerts on the site are intended to spotlight events and programs like the ALS Biorepository Pilot Study.

The State-Metro ALS Surveillance Project page highlights participating states and metropolitan areas. Obsolete data was removed from this page, including the following:

- ☐ About DHS
- ☐ Retrieve State Information (Web Map)
- ☐ Retrieve State Information (Intranet)
- ☐ Update Web Map Data

Updates were added throughout the site, including the following:

- ☐ Access Registry Resources
- ☐ ALS Clinical Research Notification (PALS)
- ☐ Survey 7
- ☐ About ATSDR

It is also now easier to locate assistance by way of the Feedback and Help page. The areas for Publications and Conferences have also been broken out, making it much easier to access the following:

- ☐ Reports
- ☐ Papers
- ☐ Abstract presentations
- ☐ Non-scientific articles and announcements
- ☐ Conferences and events with ATSDR participation

Educational courses are also available and accessible on the Publications and Conferences page, along with contact information. The Multimedia Tools page includes videos, webinars, podcasts, e-cards, et cetera.

### **Discussion Points**

Dr. Kasarskis thought he remembered that in the past it was indicated that someone could not just set up a test account, and he wondered whether that capability was now possible. The layout of the new web page is still fairly dense with detailed navigation. While everyone in the room was likely to be very computer-savvy, not all patients are. He thought if personnel at his center were to encourage patients and help them by demonstrating how to use the system, they would have to have a test account. This would be beneficial in that it would increase the number of resource people available.

Dr. Horton responded that the functionality of the Registry, the enrollment process, and completion of the surveys did not change. The only changes were to the web page itself in terms of removing a lot of text, adding more boxes, et cetera. The enrollment process remains the same.

Dr. Kaye added that work is being done with the Health Education Group to create some videos regarding how to take the surveys and the different ways that questions can be answered (e.g., check boxes, drop downs). These should be finished in the next couple of months. The issue with test accounts is that they have the potential to create a nightmare for Ms. Sanchez and

herself as they try to analyze the data, given that they find obviously bogus accounts that people have made. There are approximately 200 accounts that are known to be bogus just by looking at them. It creates a lot of work to clean out the fake accounts.

Ms. Darby noted that they are technically not allowed to delete any records,

Dr. Kasarskis noted that with the VA electronic medical record, setting up and devolving a new template would involve the creation of a bogus patient like ZZ Duck. With two Zs, everyone knows it is a test account. A practice account like this would be helpful for learning how to navigate the Registry and enter data in order to help patients. Another example is that Turbo Tax<sup>®</sup> has instructions embedded in each section that offers guidance in bits and pieces for that one section.

Ms. Sanchez said that it is easy to determine that some accounts are fake, but she has found other accounts that required further assessment to determine whether they are fake or tests as well. While she understands that people want to practice in the system, there are no set criteria to create test accounts because they do not want people to do this within the actual National ALS Registry. People can still enter anything they want. Most of the time, she and Dr. Kaye can figure out fake accounts, but if someone does not include obviously fake data, it can be very difficult to determine. The 200 fake accounts they have found thus far were fairly obvious, but this raised concerns that there may be many fake accounts that are not as easy to figure out. Webinars are being completed that actually go through and show exactly how to complete the surveys and so forth. While it is not interactive, it does show step-by-step the different types of questions that are included, how to answer the questions, the different types of drop down and selection boxes, et cetera. Once the webinars are created, she thought they could at least look into the idea of something like the Turbo Tax<sup>®</sup> model. However, she was not clear how well that would work with the OMB and IRB processes.

Dr. Horton added that ATSDR is asking ALSA chapters and MDA offices to potentially help patients enroll. Even physicians and neurologists who have time can help patients enter data, which is a good way to learn the system as well.

Dr. Brooks inquired as to how many downloads of web buttons have occurred from the National ALS Registry.

Dr. Horton responded that Jay Dempsey would be covering this information during his presentation. They are also tracking the number of doctors who take continuing education modules. ATSDR is very interested in these and other metrics.

Mr. Wildman indicated that they have encouraged ALSA chapters to help patients enroll. While there was some confusion at the beginning, once a staffer goes through the modules, they can figure it out and it enhances their ability to help others. Although there is a learning curve, increasingly more chapters are engaged in actively helping patients.

Dr. Abrams inquired as to how much time is estimated to take a first-time patient to enroll in the Registry.

Dr. Horton responded that from start to finish (e.g., enrollment, completing the validation questions, going through the modules) would take approximately one hour. However, it is known that it is challenging for a late-stage patient to go through the risk factor modules. However, it is not necessary to complete all of the modules at once.



Mr. Harada agreed with Dr. Kasarskis that having test accounts should keep the program from having to identify bogus accounts. He noted that when he goes to Emory every week to have blood tests, there is a computer check-in process and that 5 minutes before he checks in himself and 5 minutes afterward, he is helping the people in line complete simple drop boxes. Therefore, he could understand how there could be some points of confusion. He asked whether the webinar would be available live or could be continuously viewed.

Ms. Sanchez replied that the webinar would be available for anyone to view at all times on the website. The decision has not been made about exactly where the webinar will be placed, but the best placement would likely be close to registry enrollment and where people are taking the surveys. Currently, there is a general instructions page that is linked in the surveys. It may be a good idea to have the webinar linked somewhere close to that as well.

Mr. Gibson said on average, it takes about an hour to actually complete registration and the surveys. This varies depending upon someone's familiarity with computers, as well as the number of "yes" responses that lead to more questions. ALSA recommends that people complete the first part and then go back to complete additional surveys, such that it is an exercise rather than a chore.

Mr. Handsfield asked whether there was any understanding of the percentage of PALS who have ready access to an online computer. Certainly, libraries are available. However, this raises an issue of accessibility. As mentioned earlier, ALS is a very expensive disease and many PALS are using Medicaid. Someone on Medicaid may not have the resources to get to a computer easily. He thought a number of questions need to be addressed as to how people interact with this system.

Mr. Gibson responded that this depends upon the geographic location. One of the startling things that ALSA found was that because there are a number of people with ALS who have access and are frequently online, that number is very small. While they do not yet have statistics, the chapters are now beginning to gain those as they go out with tablets to "hotspots." They were shocked living in a fairly large city with the lack that still exists in areas that would be thought not to have issues.

Dr. Horton noted that ATSDR has also worked with ALSA to provide tablet PCs to all of its chapters so that essentially, they are taking the Registry out to the people, especially those folks who do not have a computer, do not have internet access, or are not familiar with computers. ATSDR is likely going to do the same thing with MDA through all of its nation-wide offices as well. Any mechanism for getting people in front of a computer, whether it is giving them a tablet, or making arrangements so that people can call ATSDR's System Administrator, who can walk them through how to enroll and complete surveys if they are sitting at a computer, may be considered. People can also call an ALSA chapter to have someone help walk them through the system. This is not necessarily "one-size-fits all." A multi-lateral approach must be taken to get people in front of a computer so that they can enter their data.

## National Quantitative Data Findings

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### National Databases Analysis 2001-2009

**Marchelle Sanchez, MS**  
**Health Scientist**  
**Environmental Health Surveillance Branch**  
**Division of Toxicology and Human Health Sciences**  
**Agency for Toxic Substances and Disease Registry**

Ms. Sanchez reminded everyone that during the previous meeting, the 2001 through 2005 data were shown. During this session, she presented an update on the 2001 through 2009 data. The database sources include Medicare (2001–2009), Medicaid (2001–2007), Veterans Health Administration (VHA) (2001–2009), and Veterans Benefits Administration (VBA) (2001-2005). Medicare data includes inpatient and outpatient records for individuals receiving this benefit, and Part D benefits from 2006 through 2009. Medicare is a US government-provided insurance program for people age 65 or older, some disabled people under age 65, and people of all ages with end-stage renal disease. Individuals approved for Social Security Administration Disability Insurance Benefit or Supplemental Security Income because of ALS can begin receiving Medicare without a 24-month waiting period. Medicaid data includes inpatient, outpatient, and pharmacy records for individuals receiving this benefit. Medicaid is the US health program for individuals and families with low incomes and resources. It is an entitlement program jointly funded by the states and the federal government and managed by the states. VHA data includes inpatient, outpatient, and pharmacy records for veterans receiving health care benefits. Approximately 20% of veterans qualify for this benefit. VBA data includes records for veterans receiving pensions or compensation for service-related disabilities. ALS is considered service-related if it was diagnosed within 1 year of separation from active duty. While the VBA data have been acquired through 2010, the second set of data received has been very difficult to manage and clean-up, which is why it was not included in the 2006-2009 analysis. These are preliminary data only; therefore, data from VBA after 2005 and Medicaid data after 2007 were not included in the data charts presented during this session.

Ms. Sanchez explained the algorithm that was developed for identifying *ALS*, *Undetermined*, and *Non-ALS* patients, which are defined as follows [ \*In same source; \*\*Rilutek is the only prescription medication specifically used to treat ALS]:

#### ALS

- ☐ ALS ICD-9 in 1 or more years\*\* and death certificate or Rilutek®
- ☐ ALS ICD-9 in 2 or more years and neurologist visit\*\*
- ☐ Age ≤ 65, ALS in Medicare and neurologist visit
- ☐ ALS in one or more years and neurologist visit\*\* with ALS in another source
- ☐ ALS in 3 or more sources
- ☐ ALS in one year and ≥ 5 neurologist visits\*\*

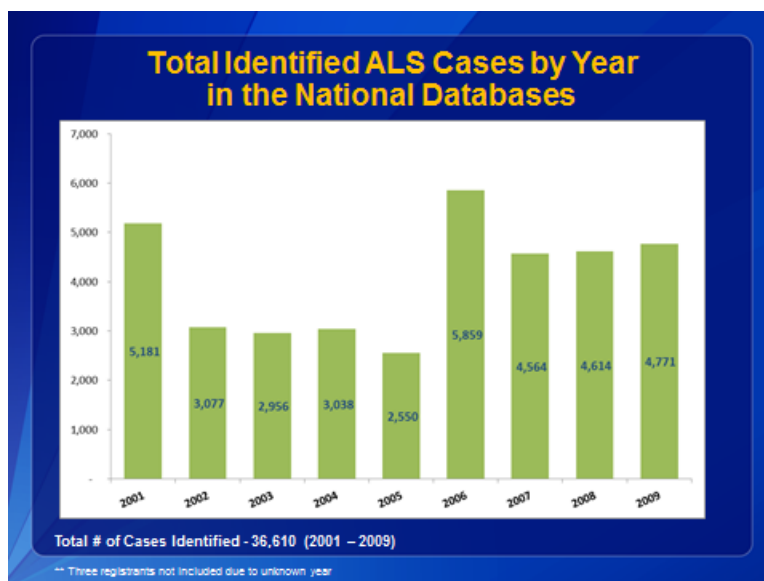
### Possible ALS

- ☐ MND in 1 year and ALS in 1 or more years after MND\*\*
- ☐ ALS in 2 years and no neurologist visit\*\*
- ☐ RX for Rilutek® only

### Not ALS

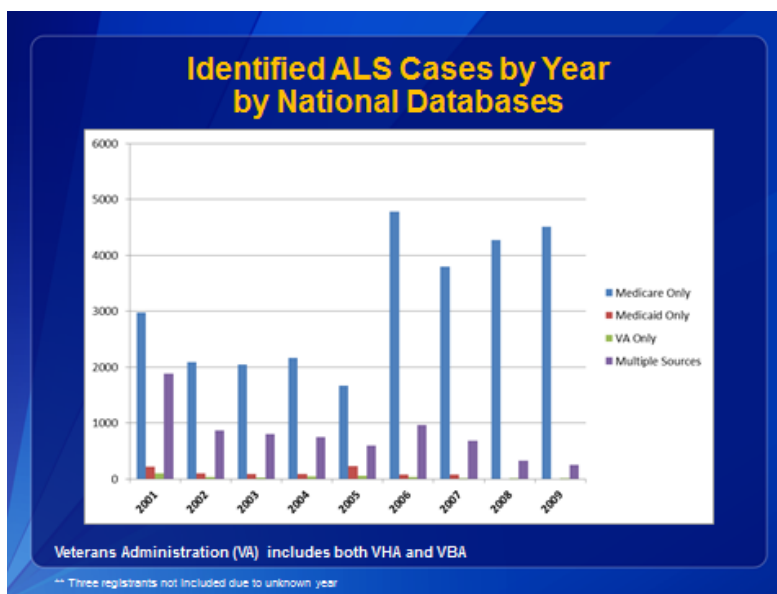
- ☐ No ALS visit and no prescription for Rilutek®
- ☐ ALS in 1 year and no neurologist visit\*\*
- ☐ Age < 18 years
- ☐ No ALS in any source
- ☐ Only "Other MND" codes listed
- ☐ Death certificate only

This algorithm was developed during the pilot projects conducted in Minnesota, Georgia, South Carolina, and an HMO consortium from 2006 through 2009. There were 4754 charts reviewed, with approximately 1800 confirmed ALS cases. Sensitivity was 0.87 and specificity was 0.85. Based on some of the new efforts, especially thinking about Part D of Medicare, there is discussion about possibly adding some criteria or assessing additional information from Part D to the algorithm to increase the detection of ALS cases. Ms. Sanchez invited any suggestions regarding what ATSDR could possibly do. Because of Medicare having Part D, ATSDR does not receive HMO information from Medicare. Therefore, if a Medicare patient is actually receiving an HMO benefit, ATSDR does not have their information. However, they could be receiving a Part D prescription, and ATSDR does have that information. This leaves the group of people who are "floating" from whom information may be captured in the "Definite" category, given that ATSDR does not have any further medical records for them.



In terms of the total identified ALS cases by year in the national databases from 2001 through 2009, 2001, and 2006 had spikes in the number of individuals identified. It cannot be said that these are incident cases, because they show up in Medicaid/Medicare. They may have already been diagnosed with ALS prior to showing up in these databases, so this is not based on date of diagnosis. In 2001, over 5000 cases were identified. The reason that year was somewhat

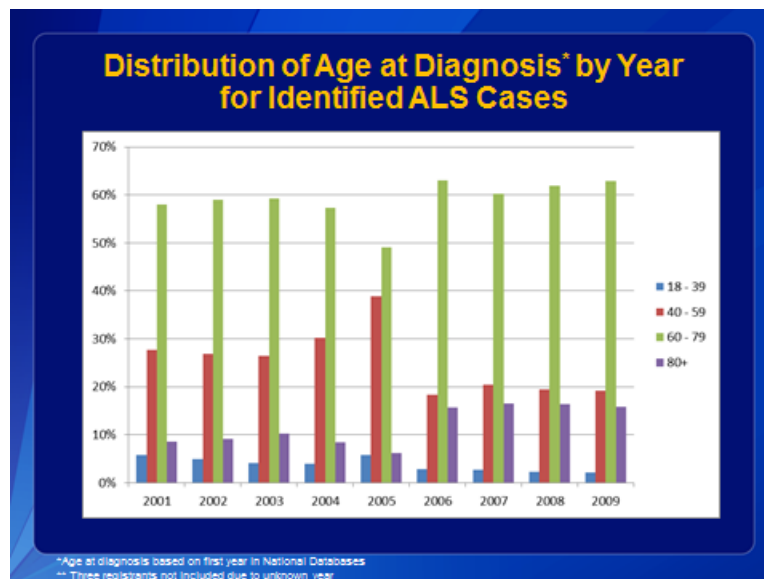
higher is because some prevalent cases were being identified from previous years. From 2002 through 2005, a lot fewer cases were identified than in 2006 through 2009. The larger number of individuals identified from 2006 through 2009 may be due in large part to two separate issues, the first being the change in rules for Medicare eligibility starting in 2003 removing the mandatory waiting period to receive Medicare benefits. The change took place in 2003; however, the changes took time before patients were able to benefit from the new rules. It would take approximately 3 years before changes would be noticed in Medicare enrollment, which is what ATSDR's data are showing. Part D prescription data became available starting in 2006, and therefore added an additional source of data to boost numbers based on the current algorithm (e.g., prescription for Rilutek®). Rilutek® is already part of the algorithm and would be expected to result in increased identification. The spike in 2006 may be due to additional prevalent cases being identified with the new rules in place and Part D added to the data available to ATSDR. A slight decrease in 2005 and a larger increase in 2006 are being further analyzed. Given that these are preliminary data, there may be changes after further analysis. However, the trend of increased ALS cases after 2006 is not expected to change.



The total number of identified ALS cases by year by national databases from 2001 through 2009 was 36,610. Medicare had the largest enrollment for ALS cases due to the population in Medicare being older (e.g., largely 65 plus). Medicaid had a low number of cases identified, which is due mostly to the fact that Medicaid services those with low/no income and largely serves children and young families. ALS is a disease that affects people usually between 55 to 75 years of age, so a low number of cases identified in the Medicaid data is to be expected. VA includes health and benefits, only available to Veterans. It is more likely for individuals to be identified in multiple databases, if not found in Medicare, although it is important to remember that VBA data after 2005 and Medicaid data after 2007 were not included in the preliminary data. Few cases after 2005 were identified in more than two sources, since VBA (part of VA) and Medicaid after 2007 were not included. The majority of cases identified in one source were from Medicare.

The age distribution for 60 through 79 year olds was consistent from 2001 through 2009. This category was also the largest for age distribution, which is consistent with the literature and age

at which most patients are diagnosed with ALS. Different reasons may account for unknown age at diagnosis, such as prescription data in Medicare and ALS visit in VBA data, since VBA



may not always include the date of birth in the file. The age distribution for 40 through 59 year olds was lower after 2006, and higher for the 80+ age group. ATSDR is further assessing the reasons for differences in the age distribution for 40 through 59 year olds and 80+ year olds. Race distribution was consistent between all years, with White being the largest category.

**Identified ALS Cases for Race by Year**

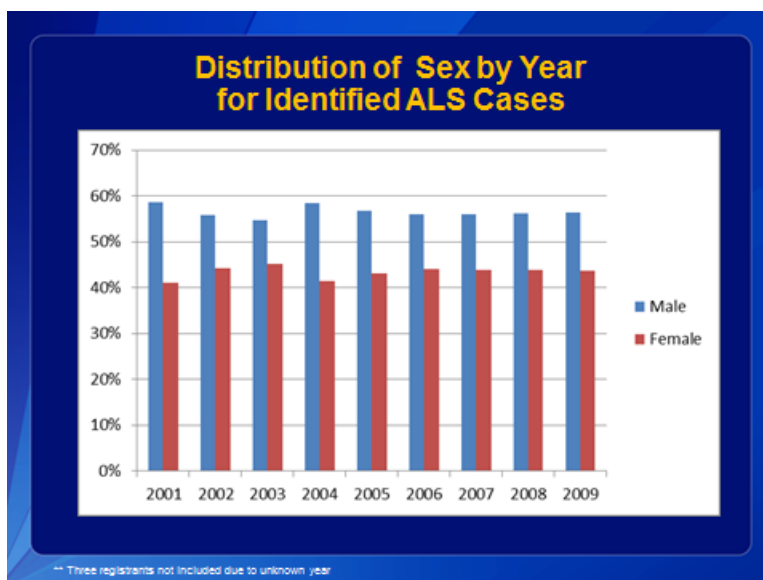
	2001		2002		2003		2004		2005	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
White	4,492	87%	2,868	87%	2,585	87%	2,647	87%	2,085	82%
Black	389	8%	247	8%	207	7%	194	6%	225	9%
Other	238	5%	136	4%	132	4%	166	5%	171	7%
Unknown	82	1%	28	1%	32	1%	31	1%	69	3%
Total	5,181		3,277		2,956		3,038		2,550	

	2006		2007		2008		2009		Total**	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
White	5,175	88%	3,938	88%	4,024	87%	4,203	88%	31,815	87%
Black	371	6%	352	8%	305	7%	305	6%	2,595	7%
Other	275	5%	248	5%	265	6%	230	5%	1,881	5%
Unknown	38	1%	26	1%	20	0%	33	1%	339	1%
Total	5,859		4,564		4,614		4,771		36,610	

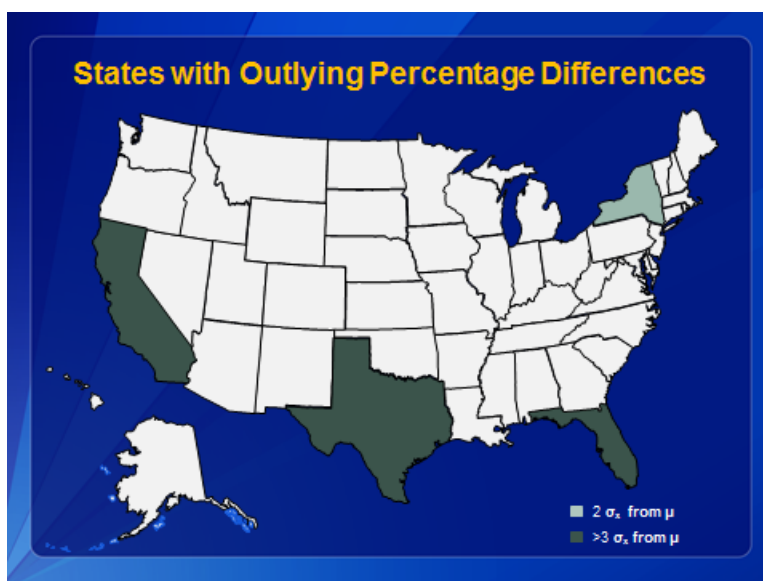
\*\*\* Three registrants not included due to unknown year

National databases have very inconsistent data on race, so only 4 categories are possible with the information, and race may not be included in some of the records or databases, or could just be wrong due to data entry or medical staff/billing professionals not having correct information. Sex distribution was consistent from 2001 through 2009, with a sex ratio for national databases of approximately 1.31. New studies show that the sex ratio has been on the decline, and is



currently about 1.3. Comparisons of the geographic distribution between the US population, based on 2010 Census data, and the national databases showed that the population percentage differences fit very closely to a normal distribution. This suggests that the national databases are doing very well at identifying ALS cases throughout the US.

In terms of states identified as outliers in the distribution curve, New York was 2 standard deviations below the mean. The national databases captured a larger percentage (7.13%) than the US population (6.28%). Florida was more than 3 standard deviations below the mean, with the national databases capturing a larger percentage (8.36%) than the US population (6.09%).



California and Texas were more than 3 standard deviations above the mean, with the national databases capturing a smaller percentage (California 8.09%, Texas 6.45%) than the US population (California 3.98%, Texas 8.14%). All outlying states have large populations, which could account for the differences. California has HMOs that are the main insurance providers for many Californians. The national databases do not have access to HMO insurance data, so

this could account for the large variation. Part D in Medicare may help identify some of those with Medicare HMOs in California, but prescription data alone is not currently a criterion for allowing cases in the national databases to become a “true” ALS case.

In summary, trends from 2001 through 2009 show an increase in identified cases after 2006. This is likely due to the new Medicare rules and availability of Part D prescription data beginning in 2006. Age at diagnosis showed consistent distribution for those 60 through 79 years of age across years. Further analysis is being done to assess trends for age groups 40 through 59 and 80+. There was consistent racial distribution across all years. The male to female ratio in the national databases was consistent at 1.31, with current studies showing a male to female ratio of about 1.3. Little difference was observed in geographic distribution between the national databases and the US population. States that were outliers in percentage differences included states with large populations. California has HMOs that provide a high percentage of insurance, Part D for Medicare HMOs could be beneficial, and prescription data alone will not move a case to “Definite ALS.”

### **Discussion Points**

Mr. Tessaro noted that like so many people with ALS, he was misdiagnosed by an orthopedic professional as having spinal stenosis. He is amazed at how many stories there are like that, and his sense is that orthopedic professionals are not clued into the high incidence of misdiagnosis. In terms of identifying cases, he wondered what type of outreach there has been or is anticipated to the orthopedic community in order to have them be much more cautious before they conduct a \$100,000 surgery. There are so many incentives not to do this surgery when it's wrong.

Dr. Kaye responded that the algorithm has no outreach to physicians at all. It is based only on what they include in their billing records. ATSDR looked at only records with an ALS code in them. In the pilot project, approximately 4500 medical records were reviewed that were matched to the administrative records, which is how the algorithm was built. Neurologists reviewed the medical records, so that they could determine true ALS cases based on a full medical record. That information was used to determine which of the elements in a billing record were best. However, ATSDR does not talk to any of the doctors about these records.

Mr. Tessaro said he realized it would not fit into the algorithm, clarifying that his question was larger because there seems to be a potent pool of information from orthopedists looking at this disease and thinking that it is pressure/spinal related. The last thing an orthopedic practitioner thinks is that it is not an orthopedic problem.

Mr. Gibson thought it was a great suggestion to reach out to orthopedists and other doctors, as well as neurologists.

Ms. Sanchez indicated that when ATSDR received the records from Medicare and Medicaid, they asked for all records that included any kind of ALS code regardless of the type of doctor. The algorithm would not be able to address orthopedists not recognizing that this is not an orthopedic problem.

In terms of the identified ALS cases by year, Mr. Harada asked when the self-enrollment registry opened.



Ms. Sanchez replied that the data she was showing had nothing to do with the web portal, and was all from national databases. The goal is to be able to link 2011 data in the national databases with the web portal data (i.e. self-registration) by Spring 2014 to determine how much of an overlap there is and create the first National ALS Registry report. Unfortunately, the self-registration web portal was not begun until very late in 2010. Therefore, no comparisons can be made between the two at this point. As Dr. Horton mentioned earlier, the national registry is a two-pronged approach to use the national databases along with the web portal. Once the two can be combined together, it will be interesting to see what the coverage is and whether the web portal is identifying people who have not been captured in the national databases.

Mr. Handsfield requested clarity regarding whether the data for age distribution by year included the enrollment database.

Dr. Kaye responded that they do have administrative data, but they cannot use date of diagnosis because the visit during which an individual receives an ALS code in his or her record is not necessarily the date of diagnosis. Someone may have been diagnosed a year before that, but it may have taken that long to be qualified for Medicare or VA benefits.

Regarding the HMO, Dr. Kaye clarified that there is a database that shows who has chosen to be included in an HMO for their Medicare benefits. The issue is that ATSDR does not have individual encounter data for those people because the HMO is just paid a per capita fee for each individual. Nobody has any information about the diagnoses of that person, whether they have diabetes, high blood pressure, ALS, or anything else. The only item for which there would be an individual record would be prescription data.

Dr. Brooks inquired as to whether ATSDR was ready to report what proportion of the Part D patients since 2006 are on Rilutek<sup>®</sup> relative to the total cases being identified in that group.

Ms. Sanchez responded that this information will be part of the paper to be published, because that is important to know. However, she did not have this information at the time of this session.

Dr. Sorenson asked whether all of the cases were de-duplicated. Ms. Sanchez replied that every case included in the data presented had been de-duplicated. If someone initially showed up in 2005, they were kept in that year and would not be included as a new case in 2006 or 2007.

Dr. Weisskopf asked whether variation of age and sex distribution by state was taken into account.

Ms. Sanchez indicated that while this calculation has not yet been done, it would be a very easy calculation to make. However, there did not appear to be a lot of variation.

Dr. Kaye added that there were more in the databases from Florida than would be expected, but this may be because they are older. There were fewer in California and Texas, which may be because their population distribution is younger.

In terms of the calculations for California, Dr. Nelson wondered whether the known Census populations for Kaiser in the state could be subtracted from the population count to get the percent difference or the difference corrected for that. A daily Census is available. Ms. Sanchez and Dr. Kaye agreed that this information would be helpful to know.

Regarding California, Mr. Handsfield suggested splitting the state between North and South. Doing so may show much higher numbers in the South than in the North, given that when people retire they move South.

Ms. Sanchez indicated that while ATSDR has some geographic distribution cities, with the information they have it may be somewhat difficult to do this, but it can be considered.

Dr. Bruijn wondered whether representation of various ethnic groups in those states could explain the difference.

Ms. Sanchez thought perhaps the Metro/State data could answer whether this has any effect on the outliers.

Dr. Kaye added that the Metro and State data suggest a lower rate of ALS among Hispanics. Whether that is a detection bias or something else is unclear, but it may have some impact.

Dr. Nelson pointed out that it would then be likely to have an impact on Florida as well. She also noted that in California it would seem very important to do something with the algorithm to capture the HMO population. In the Northern part of the state, Kaiser supplies care to about 25% of the population. That is a very large number, and it is a very large state with 36 million people. Also, it sounded like there were plans to leave the Rilutek<sup>®</sup> only patients in Part D in those states in the "Possible" category, but she suggested that consideration be given to combining that with death certificate data to move them into the "Definite" category.

Dr. Kaye clarified that Florida was higher than would be expected, while Texas and California were lower than would be expected. In terms of the Rilutek<sup>®</sup> only patients in Part D, all of the possibilities are being considered, in addition to the potential for conducting a small pilot study to determine what the results would be from moving them into the "Definite" category. The issue is that if they wait until there is a death certificate, they would not be counted at the preferable time. ATSDR would like to qualify and count them before reaching that point.

Ms. Sanchez added that they did not want to simply call them another "Possible" and do plan to assess this further.

Mr. Handsfield asked whether consideration had been given to recruiting the Kaiser Foundation to assist with this.

Dr. Kaye indicated that Kaiser was one of the pilots, and they cannot obtain identifiable data from them.

Dr. Horton indicated that Dr. Kaye and Ms. Sanchez are in the process of completing their analyses and writing these papers. The hope is to publish these data along with the Metro/State findings.

## Research Notification Mechanism and Research Committee Update

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**Vinicius C. Antao, MD, MSc, PhD**  
**Lead, Registries Team**  
**Environmental Health Surveillance Branch, DTHHS**  
**Agency for Toxic Substances and Disease Registry**

Dr. Antao presented a brief update on the Research Notification Mechanism and research committee. In addition to counting ALS patients and learning more about risk factors, one of the goals of the National ALS Registry is to provide a service to link patients and the research community. Through the Research Notification Mechanism, researchers are put directly in contact with persons with ALS enrolled in the National ALS Registry who are interested in taking part in new clinical trials and epidemiologic studies. As noted earlier, when patients register they can click a box to state that they wish to be notified about upcoming research opportunities. Researchers who wish to recruit patients for a clinical trial or project through ATSDR's mechanism submit a full study protocol, including recruiting materials, and proof of IRB approval to ATSDR. The package is then submitted to a committee that will judge the proposal. Once the request is approved, patients will receive recruiting materials in their email accounts and can directly contact researchers. ATSDR does not provide patient identities to the researchers. It is incumbent upon the patient to contact the researcher.

While this sounds like a simple mechanism, behind the scenes a lot of work is required. The first step was to develop a standard operating procedure (SOP) that had to be approved by all CDC clearances, and CDC IRB approval had to be obtained to move forward with the mechanism. A Research Committee also had to be assembled that is comprised of internal and external specialists in a variety of areas (e.g., neurology, epidemiology, bioethics, et cetera). A lot of work is also required to compile the data, because one of the features of this mechanism is that a researcher may select specific criteria (e.g., age range, time since diagnosis, sex, geographical information). Once specific criteria are selected, patients who agreed to participate are notified by email. Bulk emails are sent to the PALS who have agreed to receive them according to specific criteria that the researchers have selected.

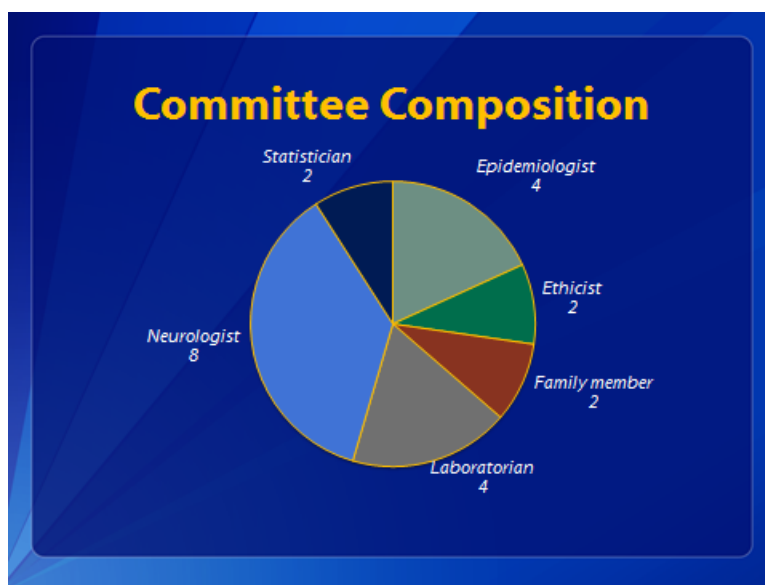
### Recent Applications

- University of Miami / Massachusetts General Hospital
- Harvard University
- Medical University of South Carolina



Recently, applications were received from Harvard University, the Medical University of South Carolina, and a joint application was received from the University of Miami and Massachusetts General Hospital. Dr. Antao emphasized that seeing the results of the work on this effort was one of his most gratifying experiences. When it was time to disseminate a notification, he went to a colleague's computer because it has all of the secure data. They began sending batches of emails, which took approximately 15 minutes. When he got back to his office, he had a voicemail from one of the researchers asking him whether he had begun sending notifications because the researcher was getting dozens of calls and emails. It was incredible that within 15 minutes, the patients were calling the researcher to participate in the study. He was truly amazed. Thus far, more than 5000 notifications have been sent to PALS. Some are duplicates, given that people may elect to participate in several studies. He encouraged all of the researchers to send a notification. This is a very simple process, and the approval process has been further streamlined. It is no longer necessary to wait for CDC's IRB to approve studies.

Expansion of the Research Committee was necessary to address access to biorepository specimens. The impression from the last annual ALS meeting was that the easiest way to handle this would be to expand the existing committee to include other specialties to deal with these requests. Now the committee will handle research notification, biorepository material release, and data release when it becomes available. The committee is



currently comprised of 2 statisticians, 8 neurologists, 4 epidemiologists, 2 ethicists, 2 family members, and 4 laboratorians. Given that members will serve on a rotational basis, there should not be a lot of burden on each member of the committee. At the outset, all members have to sign a non-disclosure agreement as required by CDC. When asked to review a proposal, reviewers will be asked to declare any conflicts of interest. The committee's recommendations are sent to ATSDR upon review by at least three researchers, and ATSDR will make the final approval decision.

Future tasks include development of standard operating procedures for data and material sharing, and development of procedures to review data usage and material requests.

## **Discussion Points**

Mr. Handsfield pointed out that this is related to the computer access issue, and expressed concern that all of this work is being done through computer access. In previous discussions, a number of PALS indicated that they do not have ready access to computers. This may add an undetected or undetectable confounder into the distribution of the answers. He wondered whether a mechanism was available or had been considered whereby someone who has placed their information in the Registry and indicated their interest in participating in research to designate an assistant or an assistance program (e.g., local ALSA or MDA office) to receive the message and contact them to indicate that a researcher is interested in using them in their research.

Dr. Antao responded that it would be up to the researcher to determine whether any bias is introduced in recruiting. This is an additional tool that they may use to recruit patients. Otherwise, they will have to rely on announcements in clinics, et cetera. He believes this mechanism is a plus in terms of recruitment. Regarding the patients who click the box and agree to receive notification will receive requests from the researchers. This is done as soon as approval is granted, and there is a very good turnaround on the part of the PALS in getting back to the researchers. He did not believe for this specific purpose additional assistance would be needed. Of course, ATSDR values ALSA, MDA, and the other advocacy groups.

Dr. Kaye added that in order to register, PALS have to provide an email address. From the experience with the biorepository in contacting people, it has been observed that some PALS are using an ALSA address. Thus, it appears that some chapters have created a way for PALS to use an email address there. That seems to be more on an individual basis than any kind of standardized forum.

Mr. Harada thought this was a wonderful tool, and that Dr. Antao's success story was great. While it may be cumbersome, he wondered whether there was a way to capture numbers or percentages in order to measure the success the tool is having.

Dr. Antao replied that they contact the researchers from time to time to obtain an estimate of the number of patients who have been recruited through the National ALS Registry mechanism. However, if they do not have that embedded in their questionnaire, which has probably already been approved, it is more difficult for the researcher to capture that information. Researchers have been asked to at least include an acknowledgement of this recruitment in published papers resulting from these studies.


Dr. Horton stressed that ATSDR is very excited about the new research mechanism. He requested that all of the support groups (e.g., ALSA, MDA, Les Turner) help to inform clinic directors and others in their organizations who conduct studies or clinical trials that this mechanism exists. This mechanism was built to help serve PALS and researchers, and was not necessarily the major focus of the Registry. The more this can be promoted, the better. He agreed that there must be a way to capture the metrics to determine who is taking part in these studies due to notification from the National ALS Registry, particularly given that this can help sell the story to Congress and decision-makers.

## National ALS Biorepository Pilot Study Update

**Wendy E. Kaye, PhD**  
**Senior Epidemiologist**  
**McKing Consulting Corporation**

Dr. Kaye explained that a biorepository is a collection of biological specimens (e.g., blood, urine, tissues) stored for future use by researchers. Biorepositories have been used in ALS research to identify genes associated with ALS (family studies), monitor response to treatment (clinical trials), and search for evidence of environmental causes (registries). ALS biorepositories could be used in the future to validate biomarkers (exposures, diagnosis), classify ALS subtypes (prognosis, treatment), and discover underlying pathobiology.

There are several existing biorepositories related to ALS, some of which are clinical and others of which are population-based. The following table outlines the existing biorepositories:

 <b>Biorepositories in ALS Research</b>			
Biorepository	Sponsor	Sample types	Number with ALS
<b>Clinical biorepositories</b>			
Northeast ALS Consortium (NEALS)	Consortium	serum, plasma, CSF, whole blood, extracted DNA, urine	5 clinical trials and 7 biomarker studies, each enrolling ~30-300 participants; ongoing open enrollment
NINDS Motor Neuron Disease Collection	National Institute for Neurologic Diseases and Stroke (NINDS, NIH)	DNA, cells	2021 persons
<b>Population-based biorepository</b>			
National Registry of Veterans with ALS	Veterans Administration (VA)	DNA (blood 85%, saliva 15%)	>1200 persons
<b>Brain banks</b>			
VA Biorepository (VAB) Brain Bank	Veterans Administration (VA)	brain tissue	not specified
MRC London Brain Bank for Neurodegenerative Diseases	Medical Research Council (MRC) London, UK	fixed and frozen human brain tissue and spinal cord; frozen CSF; extracted DNA/RNA	189 persons with motor neuron disease

The rationale for establishing a biorepository for the National ALS Registry is to correlate biomarkers with extensive epidemiologic data collected by the National ALS Registry; enroll a nationally representative, population-based sample of participants (not selected by geographic area, exposure, or clinical characteristics); and increase the number of biological specimens available for research on ALS.

The goal of the pilot study is to pilot methods for collecting and banking biological specimens from participants in the National ALS Registry in order to assess the potential for developing a comprehensive, national research resource associated with the National ALS Registry. The objectives of the pilot study are to maximize scientific potential, given the National ALS Registry parameters; maximize cost-efficiency; make recommendations for long-term sustainability; and recommend a process for providing access to researchers.

In March 2012, ATSDR convened a large meeting of experts in ALS, biorepositories, and biomarkers. A straw man protocol was discussed, and participants provided input into the draft ALS biorepository pilot study protocol regarding sample size and follow-up, specimens to be collected, and potential research uses. Some of the research considerations were for the biospecimens collected from participants to complement registry epidemiologic data; allow

comparisons with other studies; maximize scientific utility within National ALS Registry constraints; and be “future-proof” (e.g., amenable to emerging technologies and research priorities).

As part of the March 2012 meeting, lists of all specimen types suggested were posted in the room. Each attendee was given 3 or 4 tickets to use to place their votes on the specimens they thought were the most important. The following table illustrates the specimen collections considered and their potential for being useful in ALS:

Specimen consideration						
Characteristic	Blood	CSF	Urine	Saliva	Skin	Muscle
Proximity to CNS pathology	++	+++	+	+	+	+
Less molecular complexity	+	+	++	+++	++	++
Less invasive	++	+	+++	+++	+	+
Practicality of sampling	+++	++	+++	++	+	+
Ease of handling for storage	++	+	++	+	+	+
Resistance to exogenous drug contamination	+	+++	+	++	++	++
Candidate molecules to date	++	+++	+	+	+	+
Potential for DNA/RNA analysis	+++	+	+	++	+++	+++
+++ high; ++ moderate; + weak						

From: Otto et al, *Amyotrophic Lateral Sclerosis*. 2012 Jan;13(1):1-10.

This exercise resulted in the priorities being blood, urine, nail clippings, hair clippings, and saliva. Blood was the highest priority for specimen collection, and 5 tubes of blood will be collected in the order shown in the following table:

In-Home Collection					
Collection priority	Sample preservative	# tubes	ml / tube	Fractions	Potential analyses (examples)
<b>Blood</b>					
1	K <sub>2</sub> EDTA	1	10	White cells (buffy coat), red cells, plasma	DNA, proteins, red blood cell lipids
2	K <sub>2</sub> EDTA	1	6	Whole blood	Lead, other metals
3	Plain, (no anticoagulant)	1	10	Serum	Clinical biochemistries, metabolic products, other small molecules
4	PAXgene RNA	2	2.5	RNA-stabilized whole blood	Intracellular RNA
<b>Urine</b>		9	--	--	Electrolytes, environmental chemicals, metabolic products
<b>Nail clippings</b>		--	--	--	Metals
<b>Hair clippings</b>		--	--	--	Metals
<b>Saliva* (Oragene Collection Kit)</b>		2	--	--	DNA

For the second tube, everything has been certified metals free by the CDC laboratory for that collection. Saliva is at the very bottom, but if there is a problem with the blood draw (e.g., it fails or there are lab issues), patients will not be asked to do another draw. However, if they volunteer, another draw will be done. They will have the option of providing a saliva sample as a back-up so that there will be some deoxyribonucleic acid (DNA) on everyone. For all sample



collection, participants must be enrolled in the National ALS Registry. Post-mortem collection will also be done. Post-mortem participants must also be enrolled in the National ALS Registry. Eligibility is confirmed with the treating neurologist, and patients are followed prospectively. The specimens collected include brain, spinal cord; cerebrospinal fluid (CSF); muscle; bone; and hopefully skin will be added eventually. Brain collection is being done in collaboration with Boston University Brain Bank, which is doing all of the pathology and storage. Recruitment began in April 2013. The following collections had been made as of July 19, 2013 when Dr. Kaye had to have her slides cleared and into the system:

**In-Home Collection:**

- ☐ 53 specimens were processed
- ☐ 73 people were consented from 31 states
- ☐ 15 appointments were scheduled for a phlebotomist to collect blood

**Postmortem Collection:**

- ☐ 5 Health Insurance Portability and Accountability Act (HIPAA) releases were received
- ☐ Those 5 people were certified as eligible
- ☐ 2 of the 5 had been consented
- ☐ 3 consent appointments were scheduled (the Coordinator travels to people's homes to consent them in person and to obtain a signed authorization from their family)

The first person consented about a month ago passed away. ATSDR was notified at about 8:00 pm the evening before this meeting began, and by 6:30 am the collection was completed fairly smoothly for the first time. Everything was done within the timeframe promised to the family, and their family member was returned to the funeral home such that there was no interference with any funeral arrangements planned by the family.

Dr. Kaye decided that since a geographic distribution of the population is needed, she wanted a map with pins in it the old fashioned way so that she could walk by it every morning to see the status. Pins are inserted into the map when the bloods are processed and are back in ATSDR's lab, as shown in the following photograph of her map:



Dr. Kaye said she was proud to report that collections are not just from large cities. For example, blood samples have been collected from Wyoming; Hawaii; and North Dakota. As a pilot project, and in terms of feasibility, it is important to insure that recruitment is occurring throughout the US and in rural and metropolitan areas—not just from persons going to referral centers.

In terms of challenges, the response to recruitment emails has been slow. However, no other contact information is available in the National ALS Registry from which recruitment is being done. PALS receive an email from ATSDR regarding the project. McKing Consulting, who is in charge of the project, emails them again. However, there are issues with this approach because it is known that not all of these emails belong to the person being contacted. It is unknown whether everyone is receiving the message. In addition, not everyone is attached to his/her emails. For example, some people have indicated that they only check their email once per month. There is also a mechanism for people to volunteer and there was a burst of activity after ATSDR's colleagues at ALSA told people about the project. In terms of in-home collections, some potential participants do not want people coming to their houses. ATSDR is looking into making arrangements with a lab service where they could make appointments for people to go have their specimens collected there rather than in their home. There have been significant issues with finding reliable phlebotomists across the country who will make an appointment, show up when they say they will, and ship the samples back. In addition, there were issues during the high summer temperatures that required changes in packing and shipping procedures, which seems to have largely resolved the problem.

The biorepository has its own page on the ATSDR National ALS Registry website, which includes information about the project, the number of people to be recruited, the eligibility requirements, and a 1-800 number for people who are interested in volunteering. While it will not necessarily be possible to enroll all volunteers due to the requirement to try to make this geographically diverse and diverse in other aspects, at this point 75 people have been consented and 300 are needed. The ALS Biorepository contact information is as follows:

<http://www.cdc.gov/als/ALSBioRegistry.aspx>

or call 1-855-874-6912

### **Discussion Points**

In terms of the consenting model of going to everyone's house, Dr. Brady wondered if that would be the method going forward into a much larger project following the pilot study. Since the point of this pilot is to demonstrate feasibility going forward out of the pilot phase, it was not clear to him whether this method would make a large project infeasible. If the same method would be utilized going forward, he wondered if any thought had been given to developing a mail or telephone consenting model. A rate limiting step would be flying people everywhere. The VA has done this on the phone, with a 56% success rate for its brain bank. There is a relationship building process that takes a number of calls, but ultimately, people will volunteer.

Dr. Kaye replied that people are consented by telephone for the in-home component. Two Coordinators go through the consent forms with the person on the phone, and the participant signs the consent and mails it back. An appointment is then scheduled for the actual in-home visit. She agreed that consideration might need to be given to other models. For those who have done the postmortem donations, most of them have been their personal patients. There is something to be said for the personal touch, and being able to meet the family members to

make sure that everyone is agreeable with this. It is a big deal, and it is important to make sure everyone is comfortable. It is not clear whether that can be done over the phone.

Dr. Kowall added that the VA Biorepository does have a portfolio and does have contact with the family. Usually over a period of time, the families do get to know the staff and make the effort to identify themselves as a participant in brain donation. They are motivated, and a relationship is established for a period of time prior to death. It is important to have the right people with clinical maturity who are able to interact appropriately with the families, but the VA has shown that this can be done successfully long distance.

Dr. Pentz inquired as to how the VA's contacts are identified.

Dr. Brady responded that the initial recruitment was from the VA Registry. Subsequently, they began making contact through the local VA ALS clinic, they receive word-of-mouth referrals from other VAs, or people see the website and call. The process is similar to the ATSDR process.

Dr. Kaye added that 5 people had passed the eligibility screen, and 3 people have been through the eligibility screening, but she did not know whether they passed. Those 3 people were all volunteers. The process has gone more quickly with the people who volunteer, given that they did not call to volunteer until they talked with their families and decided that this was what they wanted to do. Their doctors are also quicker to call ATSDR.

Dr. Bowser inquired as to whether there were ways to cross-reference the other biorepositories for people who are interested in providing samples. For instance, he co-chairs the Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS) Biorepository that has 4000 subjects and over 20,000 samples. Patients are either donating through the NEALS Biorepository or contacting ATSDR about donating samples. There might be ways to cross-reference what they are collecting, which would enhance both registries.

Dr. Kaye responded that about 6 months ago, a meeting was convened to discuss how specimens would be released in the application process. One issue is that these data would be released de-identified, so there may be some significant IRB issues in trying to link these. ATSDR is aware that some people have provided specimens to more than one bank, and wants to ensure that if there are 300 ATSDR samples and 300 NEALS samples, they are really 600 different people versus there being 100 duplicates.

Dr. Boylan asked whether the patients from whom ATSDR is receiving postmortem tissue are the same as the patients providing blood samples. They have an ongoing relationship with most of the patients, though not all of them, from whom their center in Florida has received postmortem tissue. Some of them identify the center from the ALSA website where it is listed as a location that takes brain donations. Individuals who contact them unilaterally are generally highly motivated to participate in this, and contacts are typically via telephone and some by email.

Dr. Kaye indicated that while the recruitment processes are separate, many of the people who have been potentially recruited for the postmortem donation have also elected to only do the blood collection or to do both. This is somewhat complicated because of the fact that this project is being conducted as a contract, and there is a hard end date for when this project has to be completed. Recruitment of people for the postmortem collection has been tailored for those people who are more progressed in their disease, so that donation occurs within the timeframe. In an ongoing project, those criteria could be different.

Dr. Bowser noted that one potential way to address the de-identifying issues is that there is a universal de-identifying system. They are now involved in trying to use a universal de-identifier that follows the subjects forever via medical records. This would be a way to cross-reference and cross-fertilize.

Ms. Bledsoe asked whether consideration had been given to how some of the challenges with the in-home collections would be addressed, particularly in terms of the phlebotomists.

Dr. Kaye replied that the phlebotomists pose the greatest challenge. There are two complications, one of which is collection of specimens other than blood. Consideration will have to be given when discussing feasibility about whether continuing to include nails, hair, and urine is worth the effort. If just collecting blood, laboratory services could be used like Quest Diagnostics or LabCorp who are willing to engage in a national contract to draw and ship the tubes. The other complication is that the budget would have to be tripled. When ATSDR began to run into some issues, they tried to locate other companies that do this. Some of them want to charge upwards of \$700 per household visit.

Regarding some of the VA statistics mentioned by Dr. Brady, Dr. Tessaro pointed out that an earlier slide showed that the last VA data were from 2009, a year after ALS was accepted as a veteran disease. He wondered why they had not been able to capture 2010, 2011, and 2012 or at least 2010 and 2011 data. That seemed like a long time given this registry and an overly populated community.

Dr. Brady replied that he is not a member of the VHA patient data warehouse, so he could not respond to that question.

Dr. Kaye indicated that ATSDR has the health data through some point in 2011, but just did not present it this time. The VA is more responsive and can provide data in a much more timely fashion than CMS, given that the VA data are real-time.

## **NIH-ATSDR ALS Risk Factor Research Update**

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### **Introduction to NIH-Sponsored ALS Risk Factor Research**

**Amelie Gubitz, PhD**  
**Program Director, Neurodegeneration**  
**National Institute of Neurological Disorders and Stroke**  
**National Institutes of Health**

Dr. Gubitz indicated that the three research projects to be presented during this session were facilitated and funded through a very unique partnership between ATSDR and the National Institutes of Health (NIH). In Spring 2012, ATSDR expressed interest in supporting some investigator-initiated ALS risk factor research, but they had a limited amount of funds available. ATSDR approached NIH and asked whether such projects were available, and NIH carefully and diligently reviewed all pipeline applications. Selection was based on multiple criteria. Only projects that had gone through NIH peer review or internal review were considered. They all had received highly meritorious scores, but had not been awarded yet. From an administrative perspective, these projects were "shovel-ready." There was also a desire to focus on projects that lent themselves to a one-year period of support, which was the intent of ATSDR. The most important consideration was that all of the projects propose ALS risk factor research, one of the

important missions of the National ALS Registry. Also important was to support projects that were very different in nature and proposed to assess a variety of genetic and environmental risk factors of ALS. NIH was able to identify the following three peer-reviewed NIH projects that were very suitable for the research mission of the National ALS Registry:

- ❑ Role of High Density Lipoprotein Particles in ALS  
Teepu Siddique, MD, Northwestern University Feinberg School of Medicine
- ❑ Environmental Risk Factors for ALS in a Representative Sample of the US Population  
Marc Weisskopf, PhD, ScD, Harvard School of Public Health
- ❑ Large Genome-wide Association Study in ALS using the NeuroX Genotyping Platform  
Bryan Traynor, MD, Laboratory of Neurogenetics, National Institute on Aging

In June 2012, project overviews were presented during the Annual ALS Surveillance Meeting. In September 2012, one-year "Notice of Grant Awards" were released just prior to the end of the fiscal year. Updates were presented during this session on these three projects.

### **Role of High Density Lypoportein Particles in Amyotrophic Lateral Sclerosis**

**Teepu Siddique, MD**  
**Northwestern University**  
**Feinberg School of Medicine**

Dr. Siddique clarified that he could only relate to what is important in ALS from his point of view. In 1985, he suggested that genetic molecular techniques could be applied to ALS. This turned out to be a very fruitful direction of research that resulted in the first gene identification and the first animal model of any neurodegenerative disease. The second major paradigm shift occurred recently when the importance of the autophagy-lysosome degradation pathway of proteins in ALS pathology was discovered. Analysis of autopsy specimens has revealed pathologies or sub-pathologies of ALS and ALS/dementia that are positive for ubiquitin, p62, ubiquilin2 and transactivation response (TAR) DNA binding protein-43 (TDP-43), pointing towards impaired protein degradation as a bottleneck in the disease.

The third aspect of ALS that has been overlooked is the mechanism of disease in the superoxide dismutase (SOD1)-linked form of the disease, which is apparently different from other forms. This work began in 2006 with the discovery of an association with the paraoxonase enzymes (PON) region of chromosome 7 in sporadic ALS (SALS), in which specimens of patients were very clearly separated from familial disease and from dementing disorders. Because these enzymes detoxify certain pesticides and toxic agents, they became the first environmentally related genes that were linked to ALS. Further studies of the paraoxonase enzymes PON1 and PON3 in the plasma indicated that their levels were significantly elevated in SALS patients, although the activities were similar. PON1 and PON3 are found on high density lipoprotein (HDL) particles that contain multiple proteins with several functions including lipid and cholesterol transport and protecting lipoproteins from deleterious oxidation. Similar particles are also found in the cerebrospinal fluid (CSF). With research support provided by the ATSDR, Dr. Siddique's group has conducted work to further characterize HDL-particles in the plasma and CSF of SALS patients using cutting-edge high-throughput technologies that can quantify the levels of multiple proteins present in these particles. This approach allows for the first time to determine how HDL particle composition changes in a neurodegenerative disease, and if these changes are causally linked to the

disease process. Dr. Siddique's team is also determining whether the genes for the HDL-associated proteins contain variants that are associated with risk of SALS and whether these changes are related to alterations in HDL particle composition. Using advanced gene targeting techniques, he has created transgenic mouse models to study the effects of over-expressing HDL components. The results from this work have begun opening paths to therapies that seek to rescue potential dysfunctional HDL states found in ALS.

### **Environmental Risk Factors for ALS in a Representative Sample of the US Population**

**Marc Weisskopf, PhD, ScD**

**Associate Professor, Departments of Environmental Health and Epidemiology  
Harvard School of Public Health**

Dr. Weisskopf urged everyone to accept the results he was about to present as a preliminary snapshot, given that more work must be done. He reminded everyone that he and his team are taking advantage of a study known as the National Longitudinal Mortality Study (NLMS), which is based on Current Population Surveys (CPS) administered by the US Census Bureau and US Bureau of Labor Statistics. Each CPS is a national stratified cluster sample of US households, and is meant to be representative of the US civilian non-institutionalized population. This survey has a very high response rate of approximately 96%. Many of the labor statistics about the US economy come from this survey. Other investigators have linked the CPS with the National Death Index (NDI) in order to follow them for various causes of mortality. Dr. Weisskopf and colleagues are assessing how these factors relate to ALS as identified by the linkage with the NDI.

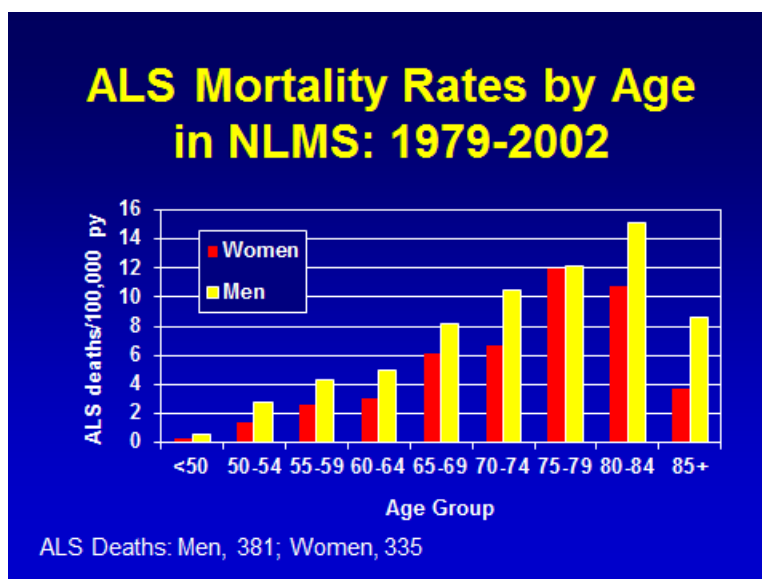
Age distribution by sex in the NLMS spans all age groups, though it is clearly weighted somewhat toward younger age groups, who have lower rates of ALS and will take longer to develop it. Approximately 2.4 million people are followed by NLMS. The age distribution by sex is illustrated in the following table:

<b>NLMS Age Distribution by Sex</b>		
	<b>Men (%)</b>	<b>Women (%)</b>
<b>&lt;15</b>	228,778 (20.2)	219,113 (17.9)
<b>15-24</b>	193,191 (17.1)	199,904 (16.3)
<b>25-34</b>	192,561 (17.0)	208,074 (17.0)
<b>35-44</b>	164,514 (14.5)	175,381 (14.3)
<b>45-54</b>	128,640 (11.4)	139,059 (11.3)
<b>55-64</b>	106,209 (9.4)	119,257 (9.7)
<b>65-74</b>	75,955 (6.7)	96,071 (7.8)
<b>75-84</b>	35,446 (3.1)	55,207 (4.5)
<b>85+</b>	7,062 (0.6)	14,311 (1.2)
<b>Total</b>	1,132,356	1,226,377

In terms of the study design, cases are identified from death certificates. There are pluses and minuses from that, but in the context of this study, that is essentially the only way to ascertain



cases. ALS deaths are identified by ICD-9 code 335.2 through 1998 or ICD-10 code G12.2 after 1998. Basically, a Cox proportional hazards model is used to follow people from the date they complete the CPS until they either die from other causes, die from ALS, or to the end of the follow-up period of 2002. The CPS began in 1973, was administered again in 1979, and subsequently has been administered yearly since then. The electronic version of the NDI began in 1979, so death follow-up is from 1979 forward. However, through linkage with the Social Security Administration (SSA), the investigators can identify who died prior to 1979. Thus, consideration can be given to the people who responded in 1973 and 1978, but their follow up begins in terms of this study in 1979. The death follow-up was completed through 2002 in January 2013. They have a lot of linkage through 2006, and hope to complete that in the near future. However, if the experience with 2002 is any indicator, it may take longer but would certainly add a lot of extra follow-up.



With regard to the ALS mortality rates from NMLS from 1979 through 2002, there were 381 deaths from ALS among men and 335 among women. The distribution of mortality rates per 100,000 person years is similar to what is observed in other places. This is mortality not incidence, so it is going to be delayed slightly. The highest mortality rates are observed in 75 to 79 or 80 to 84 age ranges, and deaths are slightly higher in men.

One of the primary risk factors of interest for this study was military service. This came out of prior work with the Gulf War stories and the earlier paper Dr. Weisskopf published from his study of the American Cancer Society (ACS) dataset that seemed to suggest that military experience was associated with ALS. In the NLMS, the questions were posed as follows:

- ☐ "Did (name/you) ever serve on active duty in the U. S. Armed Forces?"
- ☐ "When did (you/he/she) serve?"
  - ▶ WW2: 12/1941-12/1946
  - ▶ Korean war: 7/1950-1/1955
  - ▶ Vietnam war: 8/1964-4/1975
  - ▶ Other

Contrasting that with the study conducted by Dr. Weisskopf et al in the ACS Cancer Prevention Study II (CPS-II), the questions posed were as follows:

- ☐ "Were you in the U.S. Armed Services?"
- ☐ Based on reported years served:
  - ▶ WW2: 1942-1944
  - ▶ Korean war: 1950-1953
  - ▶ Vietnam war: 1965-1973

While the breakdown of years served vary slightly between the two studies, they are more or less in the same range. In addition, in CPS-II the questions were only asked of men. To orient this to what was found previously in the older report from 2005, overall about a 50% increase hazard ratio was found for service in the military for ALS. This seemed to be reasonably consistent across war periods or periods of service. There were 63 deaths in the non-military group who did not serve. The data were weighted heavily toward people who served in WW2, with 116 deaths from ALS. There were 36 deaths among those who served in Korea, 4 among those who served in Vietnam, and 36 among those who served during other periods. In the original report, this was interpreted as there not being a significant amount of variation in terms of when a person served. Importantly, there were extremely few cases among those who served in Vietnam, so the numbers are fairly unstable for that [Weisskopf et al., Neurology, 2005].

In terms of the distribution of the NLMS characteristics by military service, women were asked whether they served in the military. However, many fewer responded to that and many fewer were in the military. For the purposes of the current study, Dr. Weisskopf restricted the age range to people who were 25 years of age or older at the time they answered the CPS.

<b>Characteristics by Military Service</b>		
<b>NLMS, ages 25+</b>		
	<b>Non-Military</b>	<b>Military</b>
<b>Men</b>		
<b>N</b>	<b>434,837</b>	<b>268,904</b>
<b>White, non-Hisp (%)</b>	<b>85</b>	<b>73</b>
<b>Some college educ. (%)</b>	<b>41</b>	<b>41</b>
<b>Women</b>		
<b>N</b>	<b>387,552</b>	<b>5,081</b>
<b>White, non-Hisp (%)</b>	<b>73</b>	<b>78</b>
<b>Some college educ. (%)</b>	<b>42</b>	<b>62</b>

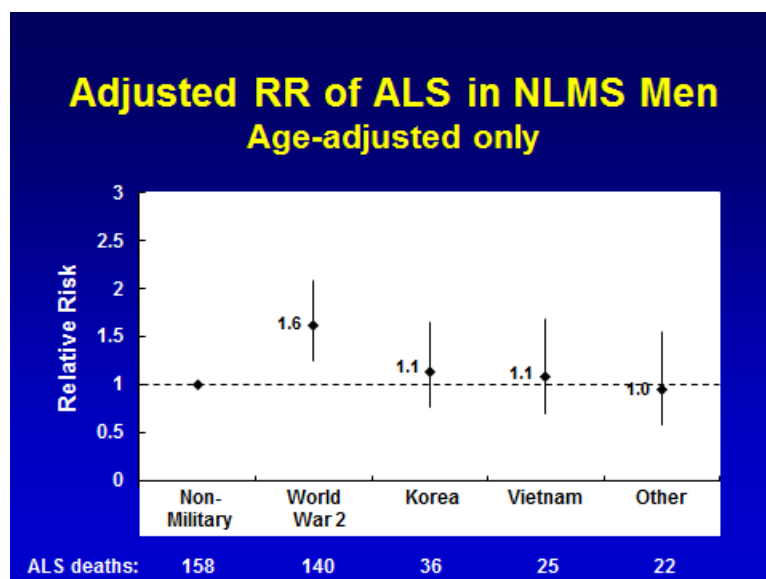
Approximately one-third of men served in the military. That is of note, because the ACS database had about the exact opposite at two-thirds. Of those who did not serve, 85% were white, non-Hispanic. Also striking is that the education level is virtually identical between those who served and who did not serve in the military. That was not the case in the ACS database. Those who served in the military in that database had a much higher education level than those



who were not in the military. The picture for women is slightly different in that many fewer women served in the military; they were predominantly white, non-Hispanic; and they generally had higher education levels than those who did not serve.

In terms of just the simple age-adjusted relative risk or hazard ratios these produce, a significant increase from having served in the military of about 30% is observed. When race and education are adjusted for, that decreases slightly and just loses significance at the 95% level of confidence. For women, the confidence intervals are much wider because there are smaller numbers. However, it appears similar if not slightly stronger, at least in the effect estimate. What is intriguing is the distribution among periods of service in NLMS, which is shown in the following table:

<b>NLMS Veteran Status</b>		
<b>Age 25+</b>		
	<b>Men</b>	<b>Women</b>
<b>Period of service</b>	<b>N (%)</b>	<b>N (%)</b>
<b>Vietnam</b>	78,448 (29.1)	1,097 (21.6)
<b>Korea</b>	44,547 (16.6)	406 (8.0)
<b>World War 2</b>	90,316 (33.6)	1,102 (10.8)
<b>World War 1</b>	2,534 (0.9)	14 (0.3)
<b>Other</b>	53,231 (19.8)	2,462 (48.5)



At this preliminary stage, the effects are being seen much more strongly related to WW2 service. ALS deaths are heavily weighted toward people who served in WW2 (n=140). The 36 deaths of those who served in Korea is the same number from the ACS CPS study. There were 25 deaths among those who served in Vietnam, and 22 who served during other time periods. The numbers remain similar when adjusted for age, race, and education. There still seems to be a signal at this stage targeted to WW2 veterans. With women, it remains difficult to tell because the numbers are so small, but something certainly seems to be observed among WW2 veterans for women as well.

One of the beauties of the NLMS is that there is a lot of socioeconomic data to potentially use as covariates. When this is taken advantage of and adjustment is made for a variety of items, it appears that this does not change the basic result just shown. Other items still need to be addressed. Unfortunately, smoking data are not available for everybody in the NLMS. Actually, because of the way the CPS is set up, it is trickier data to handle. An effort is still being made to ensure that all of the data possible are acquired and are accurately linked. Various other analyses need to be considered as well. The investigators may want to limit the analyses to the head of household who is actually reporting on himself or herself, or limit the ICD-9 as the majority of cases in the ACS database were identified by ICD-9. They want to test the proportional hazard assumption about equal follow up, and at this stage are focused on the distribution of service and education in the ACS database. Aside from just adjusting something, they are focusing on the idea that maybe what they have is some type of effect modification. The ACS database was essentially created by volunteers calling anyone they knew and signing them up, so it is in no way representative. If it actually wound up recruiting a particular type of person and particular type of veteran, it is possible that an effect is being observed that is restricted to that group in the ACS dataset. All sorts of other variables can be stratified upon to determine whether this pattern holds in those other strata.

Other factors to be explored include smoking and lead exposure. There was a preliminary suggestion of an increase in risk for ALS among smokers. The data are preliminary and more data are currently being sought. This question was not asked at the same time as all of the other CPS, so data linkage is more complicated and is ongoing. In terms of lead exposure from occupational work, the investigators first had to convert the job-exposure matrix based on 1980 Census codes to one based on 1990 codes. That is complete and lead issues are now being explored.

### **Discussion Points**

Dr. Brooks inquired as to whether any of the WW1 veterans were also WW2 veterans, and if there were any ALS cases in that subgroup.

Dr. Weisskopf replied that none were coded as WW1 veterans and no ALS cases showed up for that time period. That may be a very selected group because of the ages they would have had to be at the time they were recruited into this survey. Another vagary the investigators are currently ironing out is potential multiple service in two periods. However, they do not have the full details of this yet.

Dr. Kasarskis asked whether the investigators have data regarding duration of service. For example, his father was drafted into WW2 for the duration of the war, which was open-ended. However, some of the other conflicts were more time-delimited.

Dr. Weisskopf said that unfortunately they do not, which is a major limitation of the CPS-II data.

Dr. Sorenson asked what the overall mortality rate per 100,000 person years is for ALS. The ICD-9 code 335.2 is not actually the ALS code. It is 335.20, so depending upon how they obtained the data, they could be collecting a broader population than just ALS.

Dr. Weisskopf agreed that this was a very good point. While he could not remember precisely off the top of his head, he thought it was approximately 2 or somewhat under 2 per 100,000. He said he would check to determine whether they maintained the extra coding so it could be limited down further.

Dr. Kaye suggested assessing ICD-9 by itself. She recently read approximately 1000 to 1500 death certificates for the Metro project, and 15% of them in G12.2 were progressive supranuclear palsy (PSP). It was 15% regardless of the state.

Dr. Weisskopf responded that this is a major issue they want to address. Studies have been published on how the ALS death rate increases with ICD-10. Also, it is more likely that the WW2 veterans would have been captured under ICD-9. The ACS study also included a question that was not in the CPS that asked, "Do you have any other major illness?" In those data, anyone who said "yes" to anything was excluded. This question was not included in the CPS dataset, but they can lag the follow-up and only start 5 years after they answered the survey to avoid any prevalent cases of ALS who had it while they were answering the survey, and which might skew the results. Those are two very important issues, and Dr. Weisskopf believes that the ICD-9 question is going to be particularly important.

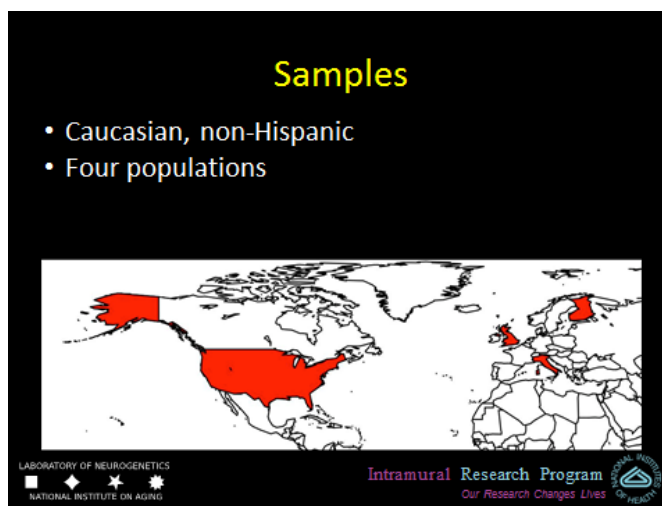
### **Large Genome-Wide Association Study of ALS**

**Bryn Traynor, MD, PhD**

**Investigator, Neuromuscular Diseases Research Unit**

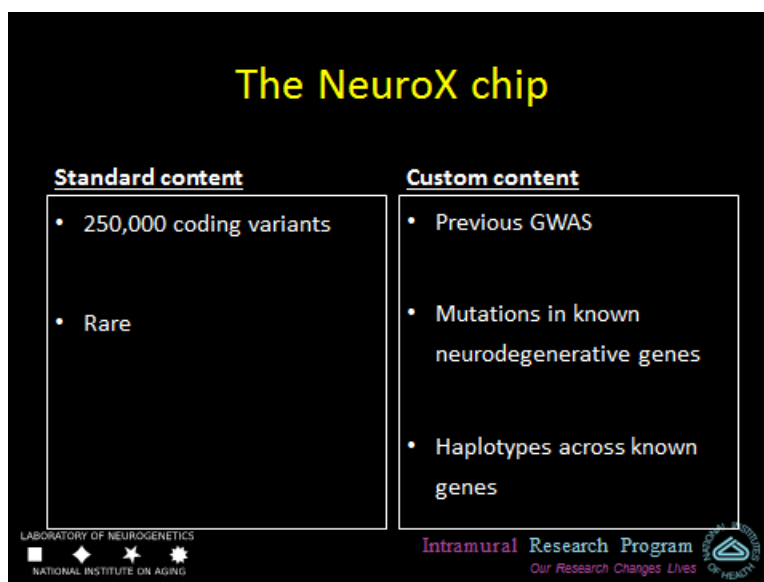
**National Institute on Aging (NIA), National Institutes of Health**

Dr. Traynor reminded everyone that the overall aim of this study was a large scale genome-wide association study (GWAS) of ALS that has the power to identify new genetic loci. Until recently, it really was not feasible for one group such as his to conduct such a large scale study because of the cost of the chips. However, the cost has decreased over time making studies such as this increasingly feasible.



The sample is comprised of non-Hispanic Caucasians taken from four different countries, including the US, the United Kingdom (UK), Finland, and Italy, with a little of Sardinia included for good measure as well. This illustrates that this is, in fact, a national and international collaborative effort. In fact, many of the people attending this meeting were very familiar with this project because they provided samples. In addition, many of the samples were obtained from the Coriell Biobank at the Coriell Institute for Medical Research. This demonstrates just how important these public biobanks are. They form the basis for many studies that come later, such as this genetic study.

The other aspect to consider about this study is the platform, or the chips used to assay the samples. In terms of background, in 2010, the National Institute of Neurological Disorders and Stroke (NINDS) organized a meeting in Washington, DC of various principal investigators from various laboratories around the world who were interested in different fields of neurology to design a chip that would work across all neurodegenerative diseases. Unfortunately, the funding was not available at that time to move forward with that chip design. Therefore, NIH took it upon themselves to design the chip and christened it "NeuroX" to reflect the neurological bent, aspect, and emphasis of this chip. As with everything else at the NIH, they try to make everything publically available as quickly as possible. Dr. Traynor said he was pleased to report that the NeuroX chip is publically available so that other researchers throughout the world can purchase it for their own use. There has been a tremendous amount of interest in the purchase of this chip, which he thought reflected the reasonable job they did on designing it.



The NeuroX chip has a standard content, which consists of the 250,000 coding variants across the genome. These are rare coding variants, so in contrast to previous GWASs where the focus was on variants that were common, these are specifically within the genes and they are specifically rare. The other aspect of the NeuroX chip that really makes it exciting is the custom content. Basically, there is the standard content for the exome chip and on top of that 30,000 SNPs can be selected. This is known as the custom content. NIH chose the previous chips for GWAS of ALS, Parkinson's disease, Alzheimer's disease, and all of the mutations of known neurodegenerative disease. In the case of ALS, for example, that would include all of the known mutations (e.g., SOD1, TDP-43, et cetera). Each of these genes is well-represented on this particular platform, so if there is an instance where ALS is actually due to a gene that is known as an Alzheimer's gene but also is involved in ALS, this particular chip will pick that up.

The first batch of chips was received in December 2010. Over 11,000 samples have been successfully genotyped to date, and the analyses of these data are ongoing. In fact, the laboratory as a whole has genotyped over 30,000 samples in a 6-month period. This shows how the advances in genomic technology are helping to accelerate the pace of genetic discovery. Those 30,000 samples help the lab to be more accurate and have better quality control in this particular platform for just the 11,000 ALS samples of cases and controls.

In terms of how this project fits in with the National ALS Registry and how it can be used to leverage the understanding of the disease, the NeuroX chip itself is going to be publicly available. Furthermore, all of the raw data from this project will be made publically available at the time of publication. The advantage of that is two-fold. First and foremost, researchers can access these data, download it, and incorporate it into their own work. Secondly, NIH will feed back to Coriell all of its knowledge about which samples carry which mutations. Researchers will then be able to contact Coriell to request specific samples. For example, an investigator could request samples that have only a TDP-43 mutation. If the National ALS Registry could be used to collect additional samples, this will be very important for the future because the power for these studies comes from the numbers.

### **Discussion Points**

Dr. Gubitza asked whether the data from this very large GWAS would go into the Database of Genotypes and Phenotypes (dbGAP). She routinely surveys access requests to the ALS datasets in this database, and has found that the ALS datasets are frequently being accessed for data mining by the broad research community.

Dr. Traynor replied that NIH really likes dbGAP, thinks it is well-run, and it is their preferred database. He agreed that the number of requests received by dbGAP is impressive.

## **Registry Promotion and Outreach**

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### **ATSDR and CommunicateHealth**

**Jay Dempsey**  
**Health Communication Specialist**  
**Office of Communication**  
**Agency for Toxic Substances and Disease Registry**

**Marchelle Sanchez, MS**  
**Health Scientist**  
**Environmental Health Surveillance Branch, DTHHS**  
**Agency for Toxic Substances and Disease Registry**

Mr. Dempsey indicated that he works directly with the National ALS Registry Team on some of the marketing and promotion of the Registry. There is a basic communication strategy in place, which is to work with partners throughout the country to generate awareness of the National ALS Registry; encourage PALS to self-register; and engage persons and organizations who influence people with ALS in order to reach the largest number of potential registry participants. The target audiences include the following:

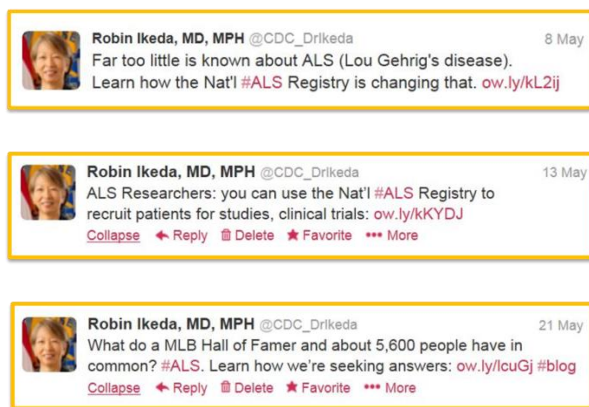
- ☐ PALS
- ☐ Family members

- ☐ Specialized health care providers (e.g., neurologists, physical therapists)
- ☐ ALS researchers who work with patients
- ☐ ALS support organizations or entities

There have been additions to the National ALS Registry website, which were demonstrated earlier in the day. In terms of some of the metrics associated with visits to the website since its launch in November 2010 through June 2013, there have been 93,946 views. There have been 51,139 views since last year, which is an increase of over 8000 views since the 2011/2012 period. This suggests that some of the marketing efforts are working. The website is updated constantly to be a more comprehensive source of information. Specific areas were expanded for different audiences, and new projects and features added. Some of the new features include the state and metropolitan area-based ALS surveillance projects, which are helping to evaluate the completeness of the National ALS Registry. Also new is the research notification system, which informs PALS about new research studies (e.g., clinical trials, epidemiological studies). In addition, the biorepository study was launched to evaluate the feasibility of collecting biospecimens (e.g., blood, saliva, and tissue) from individuals enrolled in the National ALS Registry.

An effort is also being made to connect PALS and their caregivers with as many ways as possible to connect to registry information. The ALS Service locator app was launched in September 2012 and has been downloaded 289 times since that time. This is a mobile app that is designed to be accessed from Apple's iOS platform, which means that it is accessible on an iPhone, iPad, and any of Apple's other devices. It can be downloaded from Apple's iTunes store. This app uses the GPS service of an i device to locate available ALS resources in a user's area. A version of the app for the Android platform is currently in development.

Social media continues to be utilized as a way to share information about the National ALS Registry. The following examples were used for NCEH/ATSDR's Acting Director, Dr. Robin Ikeda, Twitter profile:



ALS is now being tagged with a #, which permits anyone who wants to search for a particular topic on a social media platform, such as Twitter, to quickly see all of the messages being said about that particular topic. This has been a great benefit in the last couple of years in terms of being more "plugged in" to the conversation that is occurring about ALS on Twitter and being able to leverage CDC/ATSDR's message about the Registry into that conversation in a more opportune way. CDC/ATSDR's Twitter feed reaches over 170,000 people and Dr. Ikeda's feed has over 6500 followers. Unique opportunities are also taken to share information, such as the public service announcement (PSA) from Tommy Johns:



Another unique opportunity was a three-part series about ALS recently aired by CNN. There is a reporter on CNN named Suzanne Malveaux, whose mother lives with ALS, so she did a story about her mother and all of the struggles she has faced. In addition to the piece on her mother, Ms. Malveaux highlighted a couple of other stories of PALS. Knowing that she was reporting the story, Mr. Dempsey was able to get in touch with her to let her know about the Registry, and she told him that she would share some information about the Registry itself after the initial piece aired. Though he did not see the last component of the series, he thought that she did share information, given that there were a couple hundred calls on the information line asking about the Registry. Earlier in June the series aired on CNN's international channel. Thus, the story of ALS is getting some attention.

Ms. Sanchez reminded everyone that Patient Guides, Provider Guides, Fact Sheets, Quick Start Guides about how to quickly register in the National ALS Registry, Continuing Education Guides, and Doctor Office Posters have been developed for distribution in a variety of settings. She noted that samples of these materials were located on the display table in the back of the room. As of July 8, 2013, registry product distribution was as follows:

Product Type	ALSA	MDA	Clinics, Centers, Physicians, General Public	Total
Patient Guides	2425	475	1150	4050
Provider Guides	775	200	375	1350
Fact Sheets	1475	550	1200	3225
Quick Start Guides	1400	375	625	2400
Continuing Ed. Guides	350	150	225	725
Doctor Office Posters	625	175	500	1300
Total	7050	1925	4075	13050

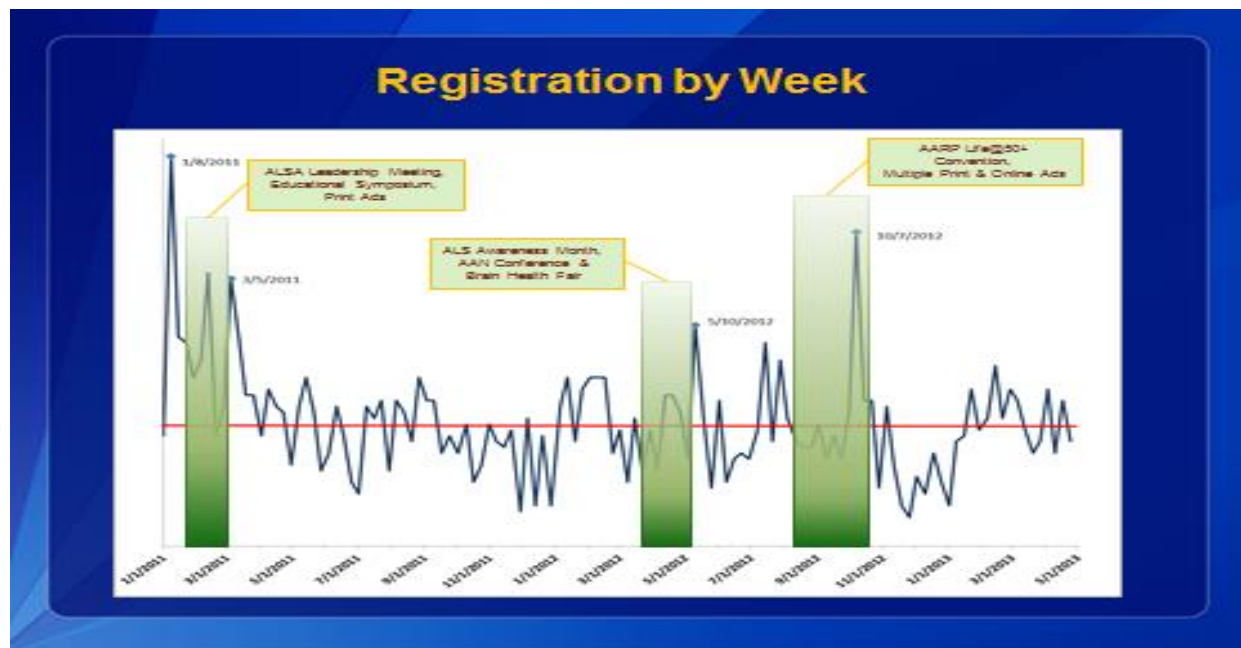
While many materials were disseminated early on when the Registry was first begun, unfortunately they have not had as many requests in the past year. These products are still available to anyone who is interested and interacts with ALS patients.

Other efforts to promote the Registry have been through print and online ads to targeted audiences, including veterans, patients, neurologists, and caregivers. Ad placement and audiences are reflected in the table on the following page:



Ad Placement	Audience	Dates	Type
Military Times	PALS	Aug - Nov, 2012	Print
American Veteran	PALS	Spring 2013	Print
AAN Patient	PALS	Sept - Dec, 2012	Online
Neurology Today	PALS	Sept - Dec, 2012	Online
Neurology Now	PALS	Sept - Dec, 2012	Online
AARP	PALS	Sept 2012 - Mar 2013	Online
Quest (MDA)	PALS	Oct 2012 - Sept 2013	Print
Neurology Now	PALS	Oct 2012 - Jan 2014	Print
AAN Professional	Neurologists	Sept - Dec, 2012	Online
Neurology	Neurologists	Sept - Dec, 2012	Online
Caregivers Magazine	Caregivers	Sept 2012 - Feb 2013	Print

The publications listed above reach thousands of subscribers each. For example, while exact circulation data are not available for all publications listed, it is known that *American Veteran* has a subscriber base of 250,000. For the AARP online banner ads, it is known that well over 1,000,000 “impressions” were delivered during the run from 9/12-3/13. However, only 1300 click-throughs to the ALS Registry page were recorded during this time. There does not seem to be a strong enough presence or helpfulness with the AARP online ad to continue doing that, unless a better way is found to get people to click through.



In terms of registration by week from January 2011 through the end of April 2013, Ms. Sanchez highlighted a couple of dates during which registration was higher. In January 2011, registration was still really new and there was still a lot of interest. In March 2011, there was somewhat of a spike prior to which there were three events, including the ALSA Leadership Meeting, the Georgia Educational Symposium, and the circulation of the print ads. There was a spike on May 10, 2012. May is ALS Awareness Month and there were also the American Academy of Neurology (AAN) Conference and the Brain Health Fair, which are believed to have contributed to this increase. There was also a nice increase in October 2012 subsequent to the AARP



Life@50+ Convention and the release of multiple print and online ads. This was also the second year anniversary of the Registry, which they wanted to further promote as well. Registration for the last week of May 2013 increased, which is thought to be related to ALS Advocacy Day in Washington, DC. A lot of the advocates returned to their chapters and promoted information regarding the Registry to their chapters and cities, which would have increased awareness of the National ALS Registry.

Registration also increased in mid-June 2013, which is thought to be the result of the arrival of the ALSA toolkits in clinics. In addition, the Major League Baseball (MLB) events were beginning, and ALSA is working with them to help promote the Registry. There was a significant increase in the first two weeks of July 2013, with the continuation of MLB events. In addition, ALSA was in Syracuse for the All Star Game and some Minor League Baseball games. As Mr. Dempsey noted, subsequent to the CNN series, the agency received a considerable number of telephone calls asking about the Registry. The majority of the calls were from patients who have already registered, but wanted to reset their password. She had not yet had a chance to review those data to determine whether there was a spike in registration, but there was a large volume of calls.

CommunicateHealth has also created web buttons for ATSDR with a focus on appealing to minorities, athletes, veterans, and rural populations. The buttons include images and language developed to reach the intended target audiences. Anyone is free to post these buttons on other websites that are trying to promote ALS awareness. Clicking on the buttons takes users directly back to the National ALS Registry. That also helps to generate a greater audience for the Registry. CommunicateHealth is also working on some videos and webinars. The video titled *Veterans: Fight Back Against ALS* will have interview footage from veterans who have joined the National ALS Registry. It will emphasize that veterans are twice as likely to be diagnosed with ALS as the general population. The video titled *Be Counted: Your Role in the Data Gathering Process* will provide overview of the data gathering process for the National ALS Registry in a creative and engaging way using animation and graphics. The webinars will focus on an overview of the National ALS Registry, the risk factor surveys, and the research notification tool.

The following is an example of an infographic tool that will answer frequently asked questions (FAQs) about the National ALS Registry's enrollment process, and can be used in the same way as the web buttons:



## The National ALS Registry: Get The Facts

The National Amyotrophic Lateral Sclerosis (ALS) Registry enables persons with ALS to fight back and help defeat ALS (Lou Gehrig's Disease). By signing up, being counted, and answering brief questions about your disease, you can help researchers find answers to critical questions.

**Learn more at [www.cdc.gov/als](http://www.cdc.gov/als) or (800) 232-4636**



### Who can sign-up?

Anyone with ALS

**No computer?** Don't worry! A family member, caregiver or friend with a computer can help you. You can also contact your local ALSA chapter or use the computer at your public library





### What do I need?

- A computer with an internet connection
- An email address

### What if I need help?

Caregivers and others can help you in person or even over the phone



### Will my information be private?

- YES! Only approved registry scientists can see it, NOT employers or insurers
- You CANNOT be looked up in the registry by name

### What kind of information is collected?

- Basic demographics (e.g., age, sex, height, weight)
- Military history
- Physical activity
- Family history





### Do I need to update my information?

YES! Every six months – you'll get an email reminder

## YOU JOINING



More information for research

↓

A better understanding of ALS

↓

The chance to help create a better future for persons with ALS

## Discussion Points

Mr. Harada inquired as to the length of the timeframe for the total figure of 13,050. Ms. Sanchez clarified that the figure was since 2010 when the Registry was first launched.

Dr. Boylan added that ALSA has printed and distributed some of these products itself, so the total is actually significantly larger.

Ms. Sanchez noted that one of the reasons for the decline in requests to the agency may be because ALSA is picking up production and distributing information for ATSDR.

Dr. Weisskopf wondered whether Kaiser has any type of publications for its members where ads could be placed. In addition, he wondered whether there was a way of knowing where people accessing the web portal were coming from.

Ms. Sanchez responded that they do not have the capability with the web portal to find out where someone comes from. Asking this question could raise major OMB issues. However, placing ads in publications through Kaiser and other HMOs has not yet been considered. Brainstorming continues in terms of where ads can be targeted, and that would probably be a very good area to consider next.

Mr. Tessaro pointed out that with the exception of *Military Times*, one could argue that the demographics of the readers of the publications in which ads have been placed represent an older demographic. In terms of social media, he wondered what attempt was being made to reach a younger demographic (e.g., family members, sons and daughters, nieces and nephews) of PALS who are really the ones with the energy and wherewithal to organize and get a family member registered. While he said he did not know whether there was a correlation, as someone who is in the philanthropy business for ALS, the way MDA raises money is not to target themselves. They raise funds targeting families, and there is a much different approach to helping families. PALS may be wrapped up in the psychology of ALS and not be thinking about the bigger picture; however, the family is always thinking about the bigger picture. MDA raises more money for ALS research than anyone else in the world. That is a good place to start, given that the population that supports that work is huge. There might be about 600 people at one of their Galas, 400 of whom are under 40. They are family members and are very active.

Ms. Sanchez indicated that *Neurology Today* is for anyone who has neurological issues and is geared more toward family members. Ads were placed in *Caregivers Magazine*, but that has more of a focus on people in the medical field who are delivering care. This can be taken into consideration. They are looking for ways to reach out to patients and family members, and know that they are not reaching everyone they would like to. They have explored WebMD®, but there are some issues with that. She welcomed any additional suggestions about where family members are getting information. They do communicate with MDA and ALSA to acquire more information. One of the reasons they contracted CommunicateHealth was to help determine the areas the agency is missing.

Dr. Horton added that advertising is just one way in which they are trying to reach people. He reiterated that this is truly a collaboration. ATSDR largely relies on ALSA chapters, MDA offices, neurologists, and others to spread the word about the Registry. The neurologists are the first line of treatment, and there is nothing more powerful than a neurologist who has just diagnosed someone to inform them about the National ALS Registry. While a small percentage

of the budget is being used for advertising, word-of-mouth will likely result in “more bang for the buck.”

Dr. Abrams suggested having some spokespeople for the National ALS Registry to Tweet, blog, and put information on Facebook to get the relatives of patients to get involved and understand the importance of the Registry. Some suggestions include former New Orleans Saints player Steve Gleason and MDA's National ALS Ambassador Nancy O'Dell.

Ms. Sanchez indicated that they are working very closely with CDC's Office of Communication, and Mr. Dempsey is working with the communications contractor. They do want to reach out to these people and others for assistance in promoting the Registry and its importance.

Mr. Harada suggested that additional information be offered about the significant restrictions placed on the agency in terms of advertising and what can and cannot be said about the Registry based on OMB, IRB, et cetera. He emphasized that about 15 PALS made YouTube videos in May 2012 at the DC conference, which were still not approved to publish.

Ms. Sanchez emphasized that they are restricted in what messages they can communicate; however, they can still get the word out and let people know.

Dr. Brooks inquired as to whether ATSDR was keeping track of the downloads of the web buttons.

Mr. Dempsey responded that they have some metrics on the original web button that had the familiar image of Lou Gehrig. Approximately 200 people have visited the site to acquire that button. What he did not have was the exact number of how many people have actually posted the button on their page. That has proven somewhat more difficult to track efficiently. They can count individual page views as well.

Dr. Brooks indicated that when they developed the Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS) app, they did demographics and found almost half and half Android. He wondered whether ATSDR planned to produce an Android app.

Dr. Horton responded that they are currently working on an Android app.

Ms. Sanchez pointed out that the web buttons and infographics shown are in the process of being finalized and have not gone live at this point. It will be nice to see whether these new products generate more web traffic.

## **Agency for Toxic Substances and Disease Registry**

**Tom Hicks**

**Public Health Advisor**

**Carter Consulting, Inc.**

Mr. Hicks noted that he had been working with the National ALS Registry Team since the Registry was launched in 2010. During this session, he reported on how ATSDR is using the qualitative enrollment data to inform outreach by sharing this information with its partners at ALSA and MDA to assist them in targeting their outreach activities for increasing registry participation. Since the Registry was launched in 2010, PALS have registered from every state and the District of Columbia. However, ATSDR cannot release the data in the Registry until it has been shown to be representative of the ALS population in the US. However, ATSDR can provide qualitative data with which comparisons can be made.

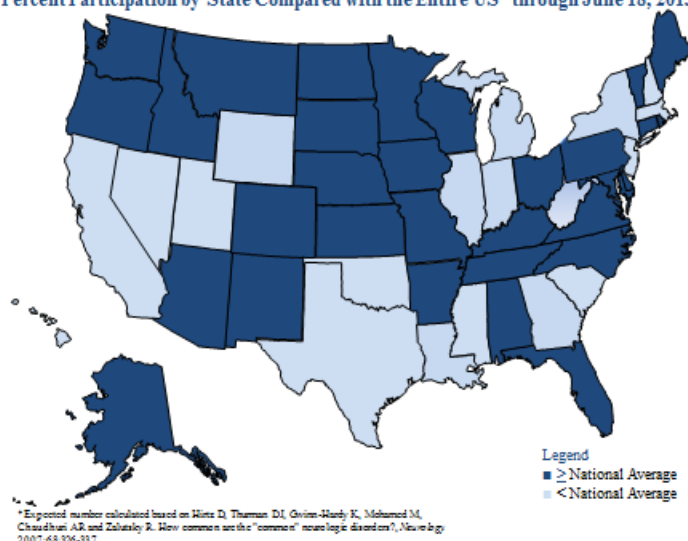
Each month, ATSDR determines the cumulative number of PALS registered. The data are assessed from the date the Registry was launched on October 19, 2010 through the 18<sup>th</sup> of the current month. The number of persons who have registered is determined for the US as a whole and for each state. This number is compared to the expected number of ALS cases [Expected number calculated based on Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR and Zalutsky R. How common are the "common" neurologic disorders? *Neurology* 2007;68:326-337].

Using the prevalence and incidence estimates in the paper by Hirtz, ATSDR calculated one year of prevalence for 2011 plus one and a half years of incidence, representing 2012 and one half of 2013. This expected number of ALS cases is incremented every 6 months in January and July to add in the newly diagnosed cases of ALS. This determines the overall number of expected ALS cases for the US. This same method is used to calculate for each state. From there, the percent participation is determined for the US and each state by dividing the number of PALS who are currently in the Registry for the US and each state by the expected number of ALS cases. This results in the identification of states that are above and below the percent participation for the US. As of June 18, it was determined that the following 19 states and the District of Columbia were below the national percent participation average. The 19 states include the following:

California	New Hampshire
Georgia	New Jersey
Hawaii	New York
Illinois	Oklahoma
Indiana	South Carolina
Louisiana	Texas
Massachusetts	Utah
Michigan	West Virginia
Mississippi	Wyoming
Nevada	

The following map depicts the percent participation by state compared with the entire US through June 18, 2013:

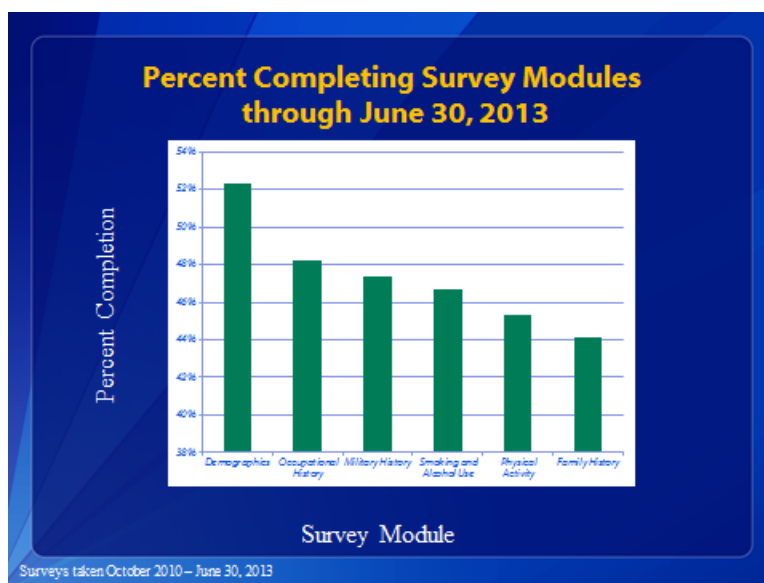
Percent Participation by State Compared with the Entire US\* through June 18, 2013



The states shaded in dark blue are those that are equal to or above the national average, while those shaded in light blue are the 19 states and the District of Columbia, which are below the national average and are considered to be lagging in participation.

ATSDR also assess those states for which no PALS have registered for the last two months. As of June 18, 2013, the District of Columbia, New Hampshire, West Virginia, and Wyoming had no new PALS registering for the last two months.

Each month, this information is sent to the national offices of the ALSA and MDA. ALSA and MDA use this information to help target their outreach efforts through their local chapters and offices to increase participation in the Registry.



Mr. Hicks also shared the most current information available regarding the percent of PALS who are completing the risk factor surveys. Through June 30, 2013, for the 6 risk factor surveys the percent completion ranged from approximately 44% for the Family History Survey up to about

52% for the Demographic Survey. This qualitative information can also be used to help target outreach efforts to increase completion of the survey modules.

In conclusion, it is important to acknowledge that there are limitations in using qualitative data. For example, these data only represent qualitative enrollment data relative to the US national average participation. It does not differentiate between states that are near the US average from those that are lagging far behind. However, ATSDR does believe that the qualitative data are helpful in targeting outreach efforts.

### Discussion Points

Dr. Brady asked whether consideration had been given to what avenues might be taken to increase the completion rates across the board, including the self-administered ALSFRS.

Mr. Hicks replied that consideration has been given to this issue. The use of social media has been increased, and other efforts are being made.

Dr. Horton reiterated that this also pertained to everyone helping spread the word about the Registry. Anytime ATSDR has an opportunity to attend conferences, such as ALSA's May Advocacy Day, they do. It is one thing to enroll, but people must take the survey modules as well. It is unclear whether people do not understand that there are survey modules, which ATSDR is assessing. He emphasized that "it takes a village."

Mr. Wildman indicated that a major part of ALSA's messaging to its chapters is to make sure that people not only enroll, but also take the surveys. ALSA will continue this messaging. He noted that the surveys completed the most are the first ones.

Dr. Horton responded that it was not clear whether the decline in taking the surveys was due to survey fatigue or other issues. However, it is important to note that people do not have to take all of the surveys at one time. If people are fatigued, they are encouraged to return later to complete more surveys.

Dr. Kasarskis recalled from earlier meetings that ALS is a reportable illness in Massachusetts, so he wondered why that state was lagging. An initial pilot study was conducted in South Carolina with highly integrated datasets, so it was not clear why that state seemed to be lagging.

Dr. Horton responded that Massachusetts does have a state registry, and ATSDR has spoken to them a number of times. ATSDR would like to cross-reference its data with Massachusetts data at some point. These are two separate registries.

Ms. Charleston, the ALS Registry Coordinator for Massachusetts, indicated that in speaking with some neurologists, they believe that people who are registered in Massachusetts think that they are also registered in the National ALS Registry. They are trying to get the word out that the Massachusetts Registry and the National ALS Registry are different, and encouraging patients to voluntarily register in the National ALS Registry.

Dr. Kaye responded that the South Carolina pilot study was conducted using databases just as the algorithm is done for the national dataset, so it is just that they are not registering. The people in South Carolina would not know that they were part of the other study anyway. In terms of the surveys, as part of ATSDR's package to OMB, they were asked similar questions.

As it turns out, the people who have registered fall nicely into two categories: takers and non-takers. Of those people who completed at least one survey, 87% completed 5 or more. The rest of them did nothing. She does not believe that it is survey fatigue. Instead, there are people who are interested in providing this additional information and those who are not. The demographics of the takers and non-takers do not really differ. Some people who have not taken the surveys may simply not know that they are available, but part of it is their personal preference.

Dr. Antao added that in the beginning, the old website may have been one of the problems. When a person registered, they would go back to the home page and would have to voluntarily search and go to another page to take the surveys. In the streamlined website, after registration is complete, enrollees are taken straight to the surveys page. A spike was observed in the number of surveys taken after the website was redesigned. ATSDR is trying to do as much as possible to direct people to the survey, which is the most important part of this registry in his opinion.

Dr. Brady quipped that he thought now that they had new buttons without New York Yankees on them, the Massachusetts enrollment would go sky high.

Mr. Harada asked whether any type of messages are sent to people after a certain period of time to remind them that they have uncompleted surveys. He also wondered whether any questions are asked in the surveys about who made the diagnosis and who gave a second opinion. This would help identify trends and help to inform where to concentrate. For example, there is probably a trend of neurological practices in a state. While there are two main diagnosing clinics in Georgia, but it seems to him that they need to get to some of the practices. There has to be a trend in terms of who is making the diagnoses, because not everyone is diagnosed with ALS.

Dr. Kaye replied that based on the state-based surveillance projects, only 50% of cases are diagnosed in a referral center. For the metro surveillance project, 90% are diagnosed in a referral center. There seems to be a bias that people who do not live in a large metropolitan area are more likely not to see a referral center ever.

Mr. Harada said that reinforced even more the importance of determining who the initial diagnosing physician was.

Dr. Kaye stressed that many of these people never saw a specialist ever. They only saw a general neurologist. In terms of follow-up on pending surveys, emails are sent out once or twice to remind people that they have open surveys. From a human subject's perspective, this is a voluntary process. Therefore, ATSDR can remind people but cannot nag them so there is a fine line.

Dr. Kowall suggested that it might be beneficial to distribute a general email to everyone to inform them that the website has been redesigned and it is now easier to complete the surveys.



**Amyotrophic Lateral Sclerosis Association**

**Steve Gibson**  
**Chief Public Policy Officer**  
**Amyotrophic Lateral Sclerosis Association**

**Patrick Wildman**  
**Director, Public Policy**  
**Amyotrophic Lateral Sclerosis Association**

Mr. Gibson noted that this is ALSA's second year of marketing the Registry. They knew that the first year would be comprised of trying to understand and develop some strategies. They primarily focused on that because they wanted to engage in a thorough listening tour with all of the chapters, which included many patients, doctors, and researchers. They found out about a lot of important and rewarding activities, and learned that probably one of the best mechanisms for enrolling additional patients is through patients. That is why they developed a video with patients sharing what is important and why it is important. They also learned what should go into a toolkit for ALSA chapters. As they begin to develop the strategy, three obstacles arose that were unanticipated. In DC, they have a different name for the acronym "IRB" where many of their great ideas become held up. Not to criticize the process, but when ALSA first began this endeavor, they felt the frustration that many of the participants in the room were feeling. Hopefully, that will change, but it is important to understand why information may not yet be widely available. It is not for lack of good ideas, but is instead that the IRB process can be daunting, as with the videos Mr. Harada was part of that were filmed over a year ago in May.

In addition, ALSA learned there is a major education gap, or perhaps differences of opinion about what the Registry really means. When ALSA developed some suggested bill language for Senator Reid and Congressman Engel to introduce, they really took the best of all registries and worked with ALSA's Chief Scientist, Dr. Bruijn, to determine what was really needed. They did not want a spreadsheet with a list of names. Instead, they wanted a powerful research engine. As they continue to work on this endeavor, there are still some knowledge gaps between people. Sometimes, people do not understand why a list of names cannot just be pulled and that this really is an important research project.

Also not anticipated were the challenges of trying to reach people who are not connected to the internet, or did not have a mechanism to enroll. While ALSA knew there would be some sort of divide and works closely with its chapters and centers to provide tablets and hotspots, they did not realize how wide the gap would be. Even people with some access may not have extensive skills in terms of navigating the internet, and may not be accepting of completing online information. It can take significant convincing to get some people to complete personal and private information online.

ASLA developed a toolkit and has been reaching out through all of its chapters and mechanisms to disseminate information, including "how to's." In terms of direct marketing, they focused on the states that were under-enrolled when ALSA first began this project, as well as the states that have low enrollment. Through the listening tour, they determined some of the key audiences who are important to address. They learned that many children of people with ALS are the ones who actually enroll their parents. They are more tech savvy, they are more familiar with tablets, and it is a lot easier to get them to help their parents answer these questions. They are also engaging in outreach to health professionals, researchers, veterans, elected state officials, and the general public. For those involved in this crusade for some time,

it is easy to forget that this is a rare disease and many people are not familiar with it. He invited further ideas and requested information about possible key contacts in any of the states with low registration levels.

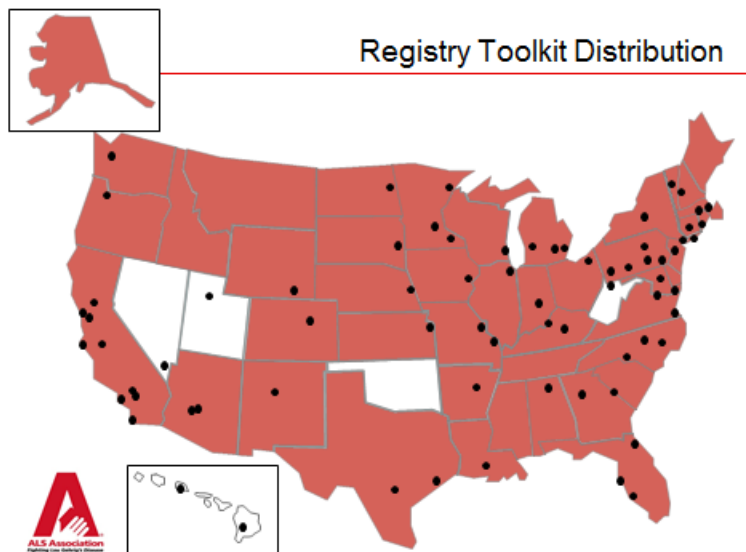
Mr. Wildman shared information about the toolkit developed for ALSA's chapters. It is pretty comprehensive, and they shared some information about it during last year's Annual ALS Meeting before it was cleared by IRB. It includes a comprehensive notebook that offers background information about the Registry, and informs chapter staff and volunteers about how they can promote the Registry and how they can assist in enrollment. In addition to being very detailed, it is very turnkey and makes it much easier for staff and volunteers to get the word out. Checklists of activities are included, as are lists of places they can go to spread the word about the Registry and enroll PALS. It also includes a lot of giveaways (e.g., brochures, stress balls, buttons, stickers, et cetera). They really try to spread the word at large events, including walks. The toolkit has been a very successful and beneficial resource.

#### National ALS Registry Toolkit



7

Once the toolkit was produced, ALSA reached out to its chapters to see how many they needed. The numbers depended upon how many care services staff they had who were going out into the field. Every chapter received at least two toolkits, and most received about five. The toolkits were also provided to all of ALSA's affiliated clinics and centers so that they could disseminate these materials in the clinics, and they also reached out to other organizations and partners. Mr. Wildman shared a map showing where the toolkits have been disseminated, indicating that they have clearly been able to blanket the country with these materials. There are a couple of gaps, most notably Oklahoma.



In May, they did identify people who agreed to help ALSA get the word out in that state. They are trying to ensure that their chapters and other partners are getting these materials so that they can get them into the field and into the hands of patients and families.

Mr. Gibson reminded everyone that one of ALSA's tactics is reaching out to people through baseball, primarily because most people associate Lou Gehrig with baseball, and also because ALSA has established relationships with baseball that puts them in front of the general public. ALSA began the campaign with Minor League Baseball, which contrary to what some people in big cities may think, last year 41 million people attended Minor League Baseball games. This has been a very effective way to get the word out, because with Minor League Baseball, ALSA can really plan their program. Before they went to the teams, ALSA got involved with the management of Minor League Baseball (e.g., Advertising Managers, Promotion Managers, et cetera) and helping them to understand the importance of this campaign. It helped that ALSA is one of the official charity partners of Minor League Baseball, but when they shared information about the project, they were really empowered because they know ALS is a horrific disease they want to help cure, and because they had no idea of the connection between ALS and the military. Almost every team in the country, minor or major, has some sort of dedication that honors our veterans. They automatically agreed to include this in one of their military nights, and it really helped ALSA to "get it's foot in the door."



ALSA has held events with over 30 teams this year, many of which were in states that are under-enrolled. For the teams that do sign up, these are treated as campaign events, and most chapters attach something about how to sign up for the Registry. Many of the teams that were signed up during the winter meetings actually went to the ALSA chapters before the chapters went to them, which is very encouraging. ALSA worked with the teams to help plan their events, such as having a patient throw out the first pitch. On game day, the Tommy John PSA about the Registry is played before the game, during the game, and through some of their spots. ALSA is also allowed to have a table where they can pass out camouflaged balls or information to enroll. In most places, ALSA is provided with a room where people can enroll in the Registry. If patients are not there, the game day announcers are provided with a script to go through what the Registry is, how important it is, and what it actually means. The awareness that has been generated through these events is tremendous. Further information about these events can be found at: <http://www.alsa.org/als-care/veterans/strike-out-als/strike-out.html>.

Mr. Wildman indicated that ALSA is also traveling to various target states that are lagging in enrollment to hold Registry events. Some of the events in which ALSA participates include the AAN's annual meeting, the International BIO Conference, AARP's conference, and the American Public Health Association (APHA) Conference. ALSA often plans a Patient Symposium and works with a local chapter to educate patients about the Registry, answer questions, and give them opportunities to enroll. ALSA representatives take tablets to the conference so that people can actually enroll during the symposium.

ALSA is also engaged in a lot of online outreach. During last year's ALS meeting, they shared a draft of ALSA's website changes. Unfortunately, that is still going through IRB. However, it does have easy-to-find information about the Registry. An important point to make is that it targets different constituencies—not just patients. That addresses the point made earlier about family members. One section is devoted to family members and caregivers that encourages them to speak with their loved ones about the National ALS Registry. They are making many efforts to reach PALS through various mechanisms. The website will also be more interactive, including the videos that were created with PALS. People will be able to film their own videos and upload them themselves. Again, peer-to-peer communication is the most powerful form of communication in terms of getting the message about the Registry and its importance across.

ALSA plans to engage in some online advertising as well, which will be highly targeted. This is also going through the IRB clearance process. In addition to Facebook, Google, and WebMD®, a variety of other mechanisms are being considered. ALSA is working with ATSDR and CommunicateHealth to make sure that efforts are congruous and are not being duplicated. ALSA is also placing some print ads. There are 15-, 30-, and 60-second versions of the Tommy John PSA and it is available in a variety of formats. Mr. Wildman played a version of the video.

Mr. Gibson stressed that he could not emphasize enough the issue of confusion about patients enrolling in the national versus local registries. The confusion may actually lie in the fact that patients are enrolling in so many programs, registries, et cetera. When patients receive a diagnosis, they may enroll in a clinic, a chapter, for Medicare, the VA, et cetera. This highlights the importance of a variety of outreach methods and tools.

### **Discussion Points**

Ms. Bledsoe expressed an interest in hearing about what might be done to address some of the IRB issues.

Mr. Wildman replied that some of it has to do with the materials developed initially in terms of messaging. After completing the first year of the contract and having materials returned to them redlined, they have a better sense of what can be said that will not violate the IRB restrictions. Other exterior factors have come into play, particularly with the package that is going through the IRB process currently that have to do with the OMB renewal. When ALSA submits an IRB package for clearance, they try to make sure they are ready to submit another one as soon as that one is cleared.

Dr. Horton added that the National ALS Registry Team is very small and is pulled in many directions. Recently, they had to focus on renewing their OMB package so everything else was set aside, including IRB. IRB approval is tricky for ATSDR as well. It is not necessarily an easy process. The CDC IRB process in general has improved, but they are constantly bombarded with other non-ALS submissions and the National ALS Registry Team has to get in line behind the next group. He agreed with Mr. Wildman that understanding what language is suitable is beneficial. For example, the CDC IRB does not like the word "cure." They cannot say that the Registry is going to cure this disease or even lead to a cure. ALSA has gained a good appreciation for the way the federal government operates. Everything is a process, and they have to do the best they can.

Ms. Bledsoe indicated that there are many issues related to biobanking, and they are trying to address them in a number of ways in terms of educating the IRBs on the importance of this work, and letting them hear from the patients themselves for whom this is so important.

Mr. Gibson pointed out that this needs further exploration because everybody has their own rules, and for a very good reason. They have observed this with the FDA setting protocol, but then becoming more aware of a horrific disease like ALS and realizing that people only have a short lifetime, and are then willing to make changes. ALSA had a series of meetings that followed their hearing last year that have all been very positive in terms of developing guidelines for speedier drug trials, et cetera. Perhaps there is an opportunity to do the same thing about this disease, because this is a different disease than most others that people deal with.

Dr. Kasarskis agreed with ALSA's strategy for outreach, and acknowledged that there is clearly not any one mechanism that is going to work. In terms of putting a lot of energy into targeting

physicians, following their clinics they have a group meeting. During one of their group meetings someone asked about the Registry and whether he had told the patient about it, and he thought, "Damn. No I didn't." It is understandable. Obviously, he is involved in the National ALS Registry because he is interested in this, but the clinics are incredibly intense and in a single clinic visit a patient may have so many needs that research does not take precedent over mobility, drooling, going to the bathroom, et cetera. Certainly, materials should be provided to clinics and physicians. However, he advocated against putting too much emphasis on that because the people who see these patients get so wrapped up with other issues, in addition to the department chair and institution wanting to see productivity bar graphs. He remembered a presentation on burnout and stress from doing the clinics, but it is not doing the clinics, it is lack of time and the number of bosses who are each looking over clinicians' shoulders to see how productive they are and how much money they are generating. That is where the stress arises. A balanced approach is critical.

Mr. Gibson responded that they have heard these comments from others, and are using the awareness approach. Perhaps the care service person who works in the clinic can take some responsibility for enrolling patients. ALSA just wants to ensure that clinicians are aware of the Registry.

Dr. Abrams asked whether other organizations like hers are bound by IRBs if they want to promote the Registry and engaged.

Dr. Horton responded that they are not. ATSDR has a contract with ALSA, making ALSA their agent. Thus, ALSA is bound by the CDC's IRB. Assuming that a partnership is formed with MDA, they will also have to follow IRB protocol. However, organizations with no allegiance or obligation to CDC can say what they wish.

Mr. Kingon inquired as to whether this is tied to the contract. Mr. Horton replied that it is.

Mr. Wildman pointed out that while the national association has a contract with CDC and is bound by IRB requirements, the chapters are not and are free to say whatever they wish.

### **Muscular Dystrophy Association**

**Jane Larkindale**  
**Vice President, Research**  
**Muscular Dystrophy Association**

Dr. Larkindale noted that while Annie Kennedy has been involved with this program for a long time, MDA had another event underway during this meeting that precluded her from attending, but she sent her apologies.

Given the conversation that just transpired regarding IRB, she clarified that at this time MDA does not have a contract with CDC. Therefore, she emphasized that the information she would present focused on efforts in which MDA has engaged because they believe them to be very important. As they move forward, they hope for a more formal agreement and hopefully will be able to do a lot more than possible thus far.

In terms of background, MDA is a national organization. Unlike ALSA, MDA is not chaptered. That means that if they are required to adhere to IRB rules, all of MDA will be covered by IRB rules. The advantage of that is that anything they decide to do on a national level will be

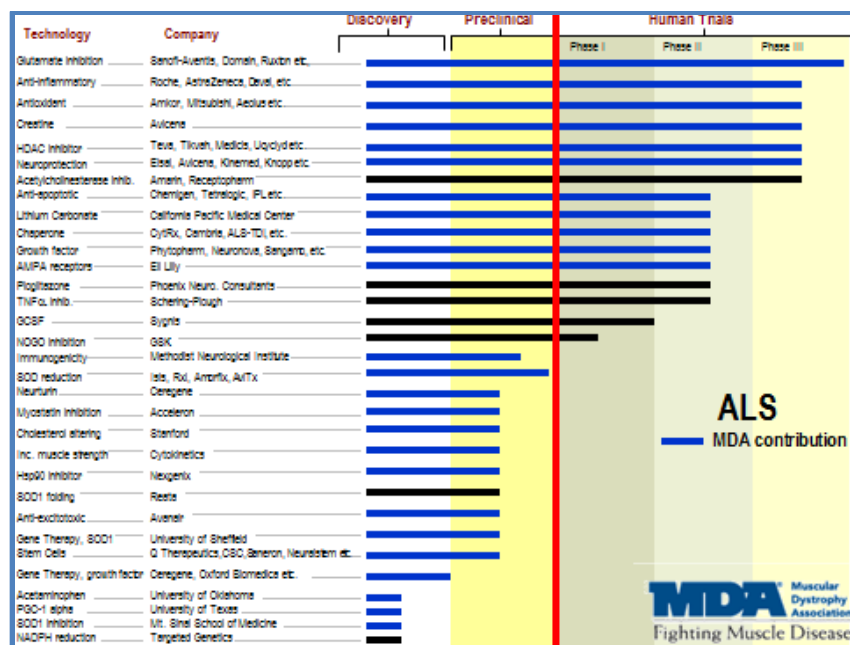
covered across the country. MDA has offices in every state across the US; 200 clinics nationwide, 42 of which are specifically designated as ALS Centers; and 5 of the ALS Centers are networked to ALS Clinical Research Centers.

MDA covers a lot of essential services, including MDA clinics and MDA/ALS centers; legislation and health policy; durable medical equipment (DME) repair and modification; support groups and educational seminars; home visits; outreach and emotional support; equipment loan program; influenza vaccination; websites resources; MyMuscleTeam; and publications. MDA currently has 42 MDA/ALS Centers, as well as an additional 50 MDA Adult Clinics. Those on the average have about 12% ALS patients. MDA support 140 different support groups that include PALS, though not all of those are specific to ALS, but many of them are. In an average year, MDA sponsors about 100 seminars serving the ALS-inclusive community. While many are ALS-specific, some are more general in nature and include topics of importance and interest to a wider NMD community.



In addition to working with patients, patient communities, and clinicians, MDA also has a tremendous research commitment and is very proud of its research program. Since MDA's inception, \$290 million has been dedicated to ALS research and services; \$25 million is dedicated to ALS research currently, representing 71 grants; and \$30 million has been dedicated to MDA's partnership with ALSTDI, which represents funding through both MDA AQ and ALSTDI. The majority of the 71 grants are for basic research. The following graphic reflects the pipeline for everything that is in development for ALS:





In addition to supporting research, MDA also works hard to try to assemble people to discuss this issue. Last year, they started a new symposium series comprised of small, focused symposia. Each year the aim is to have one neuron symposium, one muscle symposium, and one translational symposium. These are comprised of small focus groups dealing with specific issues. If there is a specific issue that needs to be addressed pertaining to the National ALS Registry, one of these symposia could be utilized.

Probably more importantly, MDA started a National Annual Conference Series several years ago. These alternate between scientific and clinical meetings. The scientific meetings are aimed at researchers and industry, and usually have about 500 participants. This year it was so popular, registration had to be closed. The clinical conferences are aimed at physicians and allied health professionals. Again, this is a great audience for getting the word out, because it is not just clinicians.

In terms of how MDA has been promoting the National ALS Registry, the Registry has placed ads in *QUEST*, MDA's news magazine. Until recently, MDA also had a paper magazine titled *ALSN*, which was a specific ALS news magazine. These have now been combined, and MDA has only one print magazine. *ALSN* still exists online. The Registry has been advertised in both of those. Those magazines are read as much by caregivers and families as they are by patients themselves. The print circulation is about 130,000 people. Full-page National ALS Registry ads have run from November 2010 through the present. Other publications include *MyoBlast* and *Clinic Connect*, which go to the clinical community and are online newsletters. MDA also talks on Facebook, YouTube, Twitter, et cetera. MDA's media people try to send out multiple tweets per day, and the Registry is certainly mentioned many times.

With regard to deliberate information dissemination efforts about the National ALS Registry, MDA has reached out to the members of the MDA PALS/CALS community through MDA publications; MDA websites button/links; exhibit space at MDA-sponsored meetings (including national conferences); information at seminars, support groups, local events; new patient



registration packets and MDA clinics; and information from MDA HCSCs and MDA Clinic Teams. MDA has reached out to MDA staff nationwide through staff trainings; monthly DDHCS calls and ATSDR update distribution; supplying field office distribution from the national office and online replenishment for seminars, support groups, local events, new person registration packets, and MDA Clinics; and inclusion of updates and reminders in MDA's internal staff publications and Intranet site. MDA has reached out to MDA-supported researchers through publication articles; advocacy alerts; and exhibit space at MDA-sponsored meetings, including national conferences. MDA has reached out to MDA-supported clinicians with materials distributed from the MDA field offices to the MDA clinics; presence of MDA HCSC at MDA Clinics; publication articles; advocacy alerts; and exhibit space at MDA-sponsored meetings, including national conferences. MDA has reached out to MDA community supporters (e.g., volunteers, donors, sponsors, Congressional champions, et cetera) with advocacy alerts (The MDA Voice, Take 5, et cetera), MDA publications; and National ALS Registry materials and displays at MDA events, seminars, clinics, symposia, support groups, et cetera.

### **Discussion Points**

Dr. Horton thanked MDA for everything they have done, pointing out that their tweet and Facebook post volume has been fantastic.

## **End of the Day Questions Section**

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**Robert Kingon, MPA, Facilitator**  
**Carter Consulting, Inc.**

During this session, Mr. Kingon called for any additional comments, questions, and / or suggestions.

### **Discussion Points**

Based upon a quick scan, Dr. Brooks noted that less than a handful of the MDA ALS clinics or ALSA clinics have the National ALS Registry on their websites. However, he could not make any correlation between the presence of that and enrollment in the states. Both clinics in Georgia have it on their websites, but Georgia has low enrollment. In North and South Carolina, one out of five clinics has National ALS Registry on their websites. While he did not know what the issue was, he would imagine that one effort would be to figure out how to get more buttons on more clinic websites.

Recalling the discussion earlier in the day regarding male to female ratios in terms of prevalence, Mr. Kingon wondered whether those ratios hold with regard to registrations and takers and non-takers of the risk factor survey modules.

Dr. Horton replied that they have not assessed this in detail, but preliminary information suggests a very high Caucasian population, with a male to female ratio of about what would be expected. Many of the demographics on the web portal side appear to resemble the administrative data side.

Dr. Antao added that takers are slightly younger than non-takers. That is the only difference in terms of their demographics.

Dr. Bowser wondered whether the decline in completion of the risk factor surveys had any relationship to people who were enrolling via tablets from home visits and then subsequently not having access to that tablet again, or not receiving further home visits from people with tablets that would enable them to take those modules later. If this is an issue and they could identify the individuals who enrolled once by tablet, perhaps they could do a quick mailing of subsequent modules.

Dr. Horton responded that while this could be a factor, he did not know the answer and was not sure whether they would ever be able to acquire this level of detail.

Mr. Gibson pointed out that this depends upon where the person enrolled. If it was during a walk or other type of event, the person would have had time to complete only a small amount. For the most part, ALSA has observed that the care service professionals go out to do this and actually go through the entire process at that time. PALS also make frequent visits on clinic days, so that offers another opportunity. However, he agreed that they should keep statistics on this.

If computers are an issue, Dr. Brady wondered whether a paper-based version could be created that could be scannable, like a Teleforms scannable form that would go into the same database as the web portal. While he understood that there would be Paperwork Reduction Act and other issues, a response is a response regardless of whether someone was clicking on a computer mouse or filling out a piece of paper.

Dr. Horton replied that they have been hesitant to put this in a paper format that could be mailed or distributed at walks, primarily because they do not want to bias the data. For example, if a person who has never been in the military sees a military module, they may decide to skip over it because they think it does not apply to them. While logistically they could hire someone to enter the data, that is not really the issue.

Ms. Sanchez added that one of the issues involved with administering paper surveys is that these surveys were designed based on previously designed surveys from Stanford, and adapted to be self-administered for web use. In addition, they are designed to have skip patterns so that if a person answers one question, something else might be grayed out because they do not need to answer it. Normally during these types of surveys, a surveyor would be giving these questions to a participant, so they would know if a person said "no" to a question and that they should skip something. However, a person taking a survey with no assistance may not realize they should skip certain questions depending on how they responded to others, which has the potential to cause a lot of issues with the data.

Regarding survey completion rates, Mr. Wildman noted that one of the items in the new patient packet is the Registry. ALSA instructs its chapters to follow up to ensure that people complete all of the surveys, and to continue to follow up until all of the surveys are completed. Clearly, much more work needs to be done in this area. Setting up a system to track patients would be beneficial, but this raises IRB issues. Nevertheless, ALSA is very conscious of the need to increase the completion rate and is trying to think of creative ways to address this issue.

Dr. Horton said that while he understood what Dr. Kasarskis was saying about having limited time with the patient and not wanting to overload them, he wondered whether he provides his patients with a packet of information that includes a checklist of things they should do. If so, that may be a good place to insert the Registry literature so they could read it at their own leisure. Some physicians are doing this.

Mr. Harada requested clarification about the number of modules, whether the percentages they were shown earlier were based on that number of modules, and if a second set of modules had been added at the 12-month mark.

Dr. Horton clarified that there are currently 7 modules, and that the percentages shown earlier included 6 modules. The 7<sup>th</sup> was not included because it is the one that is taken multiple times. The second set of modules has not been brought on line yet, but that series of new modules is anticipated to begin appearing on line before the end of the year.

Mr. Harada asked whether the issue had been either that when people signed up, they do not complete the modules at that time or people just did not sign up.

Dr. Bowser responded that people can go back later to complete modules. They could start with one or two, and then return later to respond to the rest.

Dr. Abrams inquired as to how ATSDR accounts for those who have died during the process.

Dr. Horton responded that they run the data through the National Death Index annually to determine who is deceased.

Mr. Wildman pointed out that there is a tremendous opportunity for ALSA, MDA, ATSDR, and others when the new survey modules come on line to remind people that if they have not completed the existing modules, they should do that as well.

Dr. Horton indicated that for the Quality of Life Survey, an automatically generated email is sent to enrollees at their 6-month anniversary to remind them that it is time to take the survey again. They are trying to make it as user-friendly as possible, and do not necessarily expect a patient to check with the Registry every day. They are busy living their lives and taking care of themselves, so they are trying to do anything they can like the automatically generated email to prompt PALS to take a survey.

Dr. Boylan asked what approximate proportion of patients has completed the Quality of Life Survey even once.

Dr. Kaye replied that this is somewhat complicated due to trying to figure out who has taken it once and who has taken it more than once, but it is approximately 50% plus or minus.

Mr. Wise wondered whether there were any restrictions to locking people into the website once they sign up to let them know that it could take up to an hour to complete every module, instead of allowing them to complete one or two and come back at another time.

Ms. Darby responded that based on information from ATSDR's developer, if someone was dropped from the site, it would save his/her data.

Dr. Kaye added that forcing people to stay on until the modules are completed would be against IRB rules. This is a voluntary activity, so they cannot force people to answer the modules.

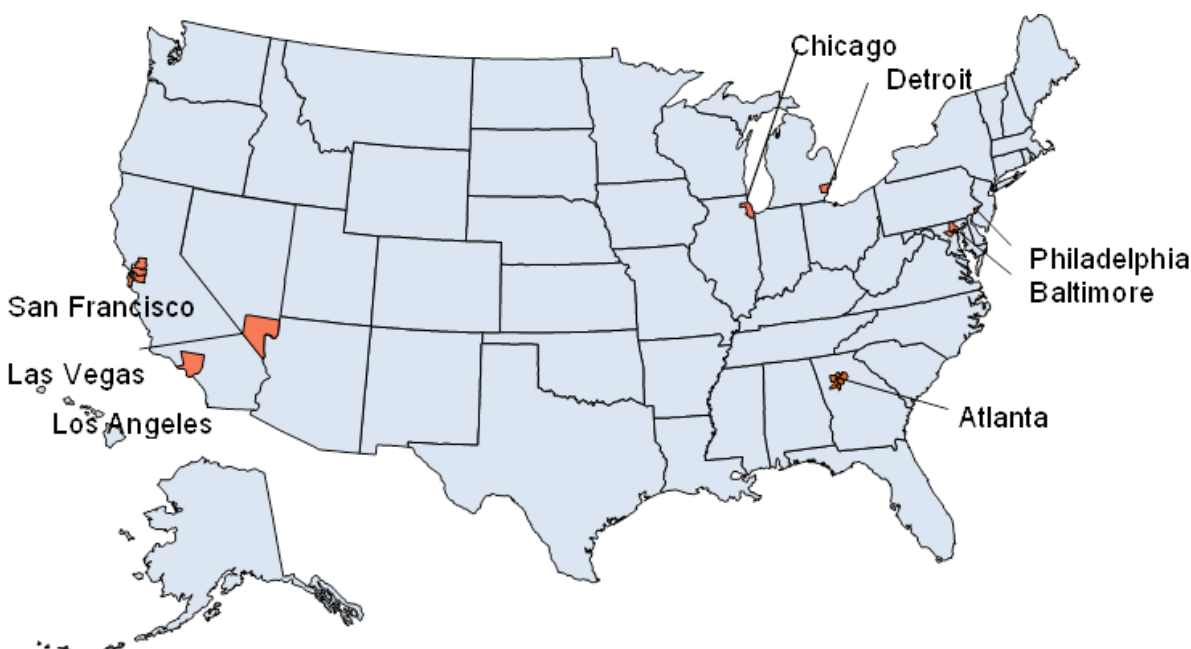
## Metropolitan Area-Based ALS Surveillance Update

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**Laurie Wagner, MPH**  
**Research Associate**  
**McKing Consulting Corporation**

Ms. Wagner noted that she and Dr. Kaye collaborated to develop this presentation. The metropolitan area-based ALS surveillance project was funded by ATSDR. In order for the metropolitan areas to participate, they had to have a minimum of 1.5 million population. The metropolitan areas in Florida, New Jersey, and Texas were excluded because that information was captured in the state-based ALS surveillance project. Areas were selected to over-represent minority populations. McKing Consulting approached state and local health departments about participating. Ultimately, 8 metropolitan areas were recruited. Participating metropolitan areas include: Atlanta (5 Counties), Baltimore (City + Baltimore and Howard County), Chicago (Cook and DuPage Counties), Detroit (1 county), Las Vegas (1 county), Los Angeles (1 county), Philadelphia (1 county), and San Francisco (5 counties).

### Participating Metropolitan Areas



The objectives of the metropolitan area-based ALS surveillance are to identify and ask every neurologist who had diagnosed or provided care to an ALS patient in the specified metropolitan area from January 1, 2009 to December 31, 2011 to report cases; and use the data to evaluate the completeness of ATSDR's National ALS Registry.

In terms of methods, in each metropolitan area providers were identified who see ALS patients. A comprehensive and current list of practicing neurologists was created to contact identified ALS specialists. Sub-specialties unlikely to see ALS patients (e.g., pediatric neurologists) were removed. Providers were contacted via a combination of mailings, phone calls, faxes, and

office visits. For recruitment, there was a slight variation for each area. However, the typical protocol was to phone providers using the list that was developed, mail/fax packets to providers, make several follow-up phone calls, and conduct office visits. Recruitment efforts were ceased once case reports were received, it was determined that a provider had no eligible cases to report, or providers refused. Outreach included attendance at local neurological society meetings, the AAN Annual Meeting, the NEALS Annual Meeting, and the International Symposium on ALS/MND Annual Meeting. Outreach also included meeting with ALS specialists at ALS referral centers in most of the metropolitan areas, and coordination with local ALSA chapters and national ALSA.

For case ascertainment, case reports were collected from the specialists who diagnosed or cared for ALS patients from January 1, 2009 through December 31, 2011. In some cases, additional information was provided such as ICD-9 Codes (335.20, 335.21, 335.22, 335.23, 335.24) and eligible zip code lists. Specialists completed case reporting forms and submitted them to the surveillance project that included identification, demographic, and diagnosis information. Ms. Wagner showed an image of the case reporting form, noting that it did not take very long to complete once patients were identified. The more time-consuming effort involved identifying patients.

For quality assurance, case verification forms were also supplied to the reporting neurologists. Completed forms were returned for 10% to 20% of the reported cases. ATSDR's consulting neurologist, Dr. Sorenson, subsequently reviewed the verification forms. The forms included signs and symptoms and a copy of the most recent EMG report, if available. For case reporting completeness, death data ICD-10 (G12.2) were assessed to identify potential cases that were not reported, and identification of a neurologist to report the case if possible. This was a lengthy process. For all areas, except California, the reports were received by McKing Consulting and Ms. Wagner and Dr. Kaye did most of the matching. California did its own matching and requested their own data. After the death data were requested, an attempt was made to identify the reporting neurologist. Sometimes that began with a general physician and required backtracking to determine the neurologists and ask them to report the cases.

In terms of the methods used for selection of reported cases for verification, there was systematic selection of cases. Requests were made based on the number of ALS patients seen by the practice. If a practice saw 1 to 4 cases, they were asked to complete case verifications for all of their patients. Twenty percent of cases were selected for verification from practices seeing 5 to 20 cases, and for those seeing 21 to 50 cases 10% of cases were selected for verification. Dr. Kaye conducted systematic selection and then the practices were notified to complete case verification forms. In some cases, the surveillance specialists would know whether a patient was very young, had a very long illness, or was noted as unclassifiable by the reporting physician. Some of these were over-selected, but not all were selected based on these criteria. Ms. Wagner shared a copy of the ALS Medical Records Verification Form, which included more symptoms and background of the disease itself versus the demographics included in the other form.

With regard to some of the results of the case ascertainment for the metropolitan areas, 2636 neurologists were contacted. Of those, only 275 actually stated that they diagnose or treat ALS patients, 320 said that they did not diagnose during the specified timeframe but that they would, and 2017 indicated that they do not diagnose or treat ALS patients. This was similar to what was found with the states. The majority of neurologists in the areas did not diagnose or treat ALS patients. In terms of the practice size of each participating neurologist by each metropolitan area, the majority belonged to small (49%) followed by super-sized practices

(34%), and the remainder were medium (10%) and large (6%). In terms of the reported cases by reporting practice size by metropolitan area, the majority of practices that reported were super-sized. This differed from the states because about half of the practices were super-sized and the rest were other-sized. For the metropolitan areas, the majority of cases were from super-sized practices or the large referral centers. It is important to note that none of the results include Las Vegas, given that it was difficult to get started there, it took a long time to complete, and was just closed out the week before the ALS meeting. The types of providers reporting cases by metropolitan area included ALS specialists (38%), general neurologists (59%), family/internal medicine/general practice (2%).

In terms of the results of case reporting, 2302 cases were expected, and 2473 cases were reported. Once data were de-duplicated and/or mistakes removed, there were 2189 unique cases which resulted in a period prevalence of 7.58 per 100,000 population. As a reminder, this still does not include Las Vegas and the numbers may change slightly in the final report once Las Vegas data have been added.

Regarding the age distribution of reported cases compared with Census data for all ALS cases reported in this project, the age distribution for the metropolitan areas is a lot younger, and as would be expected for those with ALS, the age of reported cases was somewhat older. With respect to the racial distribution of reported cases compared with Census data for the metropolitan areas, the majority are White and there is fairly good representation of other races. While there were not quite as many minority cases reported as would be expected based on the Census data, the project did have a significant number of ALS cases reported among Black, Asian, and Other racial groups. The ethnicity distribution of reported cases compared with Census data is similar however; there were many reported cases with unknown ethnicity. If the unknowns were determined to be Hispanic, then the ethnicity distribution of the ALS cases would be very close to that of the Census for the metropolitan areas. Sex distribution was very similar for reported cases compared with Census data. The project's data show a 1:3 ratio of males to females as seen in the Registry and the newer literature.

## EI Escorial Rating of Reported Cases by Metro Area

EI Escorial Criterion	Atlanta		Baltimore		Chicago		Detroit	
	#	%	#	%	#	%	#	%
Definite	164	58.4	105	78.4	118	27.4	56	38.9
Probable	49	16.0	15	11.2	126	29.2	48	33.3
Probable Lab Supported	20	7.1	2	1.5	68	15.8	21	14.6
Possible	45	16.0	10	7.5	61	14.2	17	11.8
Not Classifiable	7	2.5	2	1.5	58	13.4	2	1.4
Total	281		134		431		144	

With regard to the El Escorial Criteria rating of the reported cases received by each metropolitan area, most cases fell within the Definite (46%) and Probable (23%) categories. In terms of the El Escorial rating by practice type, groupings were made by referral centers and compared to other practice types. If practices were referred to as referral centers by ALSA or MDA, those referral centers were used. There was little difference between the results of the referral centers versus other types of practices for these classifications.

## **El Escorial Rating of Reported Cases by Metro Area (continued)**

El Escorial Criterion	Los Angeles		Philadelphia		San Francisco		Total	
	#	%	#	%	#	%	#	%
Definite	211	38.7	65	57.0	305	56.5	1024	46.8
Probable	165	30.3	27	23.7	75	13.9	501	22.9
Probable Lab Supported	50	9.2	6	5.3	43	8.0	210	9.6
Possible	71	13.0	16	14.0	110	20.4	330	15.1
Not Classifiable	48	8.8	0	0.0	7	1.3	124	5.7
Total	545		114		540		2189	

Regarding time from onset of symptoms to diagnosis of reported cases by each metropolitan area, several categories were established, including: < 6 months, 6-8 months, 9-11 months, 12-14 months, 15-17 months, ≥ 18 months, and Unknown. Most cases fell into the ≥ 18 months category (31%). They are prevalent cases, so they may have been diagnosed a while ago and that would be why they were classified there. Several fell into the < 6 months category (17%). The dementia status of reported cases by practice type (referral centers versus others) was very similar for a total of 5% with dementia and 87% without. This may be somewhat lower than expected, but 8% were of unknown status. Familial ALS status of reported cases by practice type was identified more by referral centers than by other practice types.

Turning to the results of case verification, these were the reports that were completed for 10% to 20% of all of the reported cases that were sent to Dr. Sorenson to review. He came up with his own determination. A total of 328 cases were requested from the metropolitan areas, and 309 were received from the reporting physicians. This was much higher than in the states. Part of that may be that much was learned from the processes utilized in the states. It takes a lot of follow-up, phone calls, and tracking to get the completed forms back. This was implemented from the first day of the metropolitan area surveillance project. In terms of the age, race, ethnicity, and sex distributions of the requested case verifications compared with those received and all ALS cases for the project, the results were very similar. This merely verifies that there was good representation of all ALS cases reported.



The assignment of EI Escorial criteria on case reports compared with the EI Escorial criteria assigned by the consulting neurologist were very similar. The only difference was that the case reporting form included a “Not Classifiable” category. When the consulting Neurologist, Dr. Sorenson conducted his verification, he did not use the “Not Classifiable” category, however he determined some cases to be “Not ALS”. The EI Escorial criteria assigned by Dr. Sorenson for each metropolitan area included a total of 248 Definite, Probable, and Probable Lab Supported; 57 Possible; and 4 Not ALS. The following table illustrates the concordance of the cases reported versus Dr. Sorenson’s EI Escorial determination, with the squares highlighted in turquoise being the ones that matched exactly:

## Case Report vs. Consulting Neurologist EI Escorial Determination

		Consulting Neurologist's Determination				
		1 (Definite)	2 (Probable)	3 (Probable Lab Supported)	4 (Possible)	5 (Not ALS)
Reporting Providers' Classification	1 (Definite)	111	23	-	12	2
	2 (Probable)	36	11	4	6	-
	3 (Probable Lab Supported)	17	5	3	4	-
	4 (Possible)	13	5	-	27	2
	9 (Not Classifiable)	6	10	4	8	-

Dr. Sorenson’s determination of the 28 non-classifiable cases included 6 Definite, 10 Probable, 4 Probable Lab-Supported, 8 Possible, and 0 Not ALS.

Regarding the results of the death data used for quality assessment, 1256 death certificates were received for the project. Of these, 685 matched the case reporting database, and 414 potential new cases were identified. The difference between those remaining after the match and those requested was about 160. These 160 turned out not to be ALS and were removed. The metropolitan areas were able to follow up and identify 84 of the 414 and get case reports submitted to the project, leaving 330 potential cases unreported. It remains unclear whether these are definitely ALS, but they were not eliminated because of other reasons. It is possible that some cases may have fallen outside the timeframe of the study that were not ascertained.

In summary of the general findings, most neurologists (>75%) in the metropolitan areas do not diagnose or care for persons with ALS. That applies to states as well. Most cases were reported by ALS referral centers. The number of de-duplicated case reports was close to the expected number. Age and sex distributions of reported cases were similar to those reported in the literature. The percentage of cases with familial ALS and dementia was lower than expected. Less than 2% of verified cases were determined to be “Not ALS.” There was no significant difference in the percentage of “Not ALS” determinations between referral centers

and other neurologists. Approximately 72% of “Non Classifiable” cases reported were determined to be ALS by Dr. Sorenson.

In terms of limitations, active surveillance is extremely time-consuming. It is very rewarding, but is a slow process. The reliance on neurology office staff to determine if the practice cared for ALS patients is difficult. Physicians are not responsive to requests. Most VA medical centers could not participate because of decisions by their individual privacy officers. Death certificate data are very difficult to obtain and to use. Hospital discharge data are not available for most areas. No hospital discharge data were received for the metropolitan areas at all, although the data were requested for each study area.

With respect to recommendations, this type of surveillance is good for evaluation but not for ongoing surveillance. Retrospective case reporting works best, but there were still problems because doctors forgot about older cases, did not have access to old records, and had retired and/or passed away. Case verification is an important process. Case verification should continue to be distributed between referral and non-referral centers.

### **Discussion Points**

Dr. Horton said he thought what Ms. Wagner, Dr. Kaye, and their group had shown was that this methodology for tracking cases is very laborious, very expensive, and not all neurologists want to participate. Although ATSDR had not seen the official findings from McKing Consulting at this point, in his mind, this supported the national approach.

Regarding time from onset of symptoms to diagnosis, Dr. Kasarskis noted that roughly a third of the cases were classified in the  $\geq 18$  months category. This seemed to be somewhat in contrast to what is observed in most places. Typically, the time from the onset of new progressive weakness to a confirmatory secondary opinion is in the 12-month range. The  $\geq 18$  months struck him as being very long, and he requested further information about the definition.

Dr. Kaye responded that there are two issues. The first issue is that about a third are prevalent cases who were diagnosed before 2009, but were still being seen by a doctor in 2009. There is probably some bias for people forgetting some of those, so a survivor issue is probably occurring in that particular group. In addition, the dates were taken out of medical records. If there was a duplicate case with several records, the date of symptom onset and date of diagnosis in each record did not even show the same year sometimes. Thus, the accuracy of the dates is questionable.

Ms. Wagner added that they found with duplicate cases, many times the diagnosis came at the time they saw a particular physician rather than being based on the other physician.

Regarding that the FTD was lower than anticipated, Dr. Bruijn imagined that in this type of collection and with the different cognitive tests and level of expertise in this, that was probably what accounted for this.

Dr. Kaye said she did not think so, because they were just comparing referral and non-referral centers. It is still only 5% even from a referral center, which one would think would do more.

Dr. Brooks emphasized that they found more deaths in the ALS death certificates than through case ascertainment. The learning point for him was that ALS needs to be a reportable disease.

That should be one of the policy recommendations that should come out of this study, particularly if they were going to move forward with the National ALS Registry.

Dr. Kasarskis thought the one variable they did not hear about was how many people may have moved into one of these metropolitan areas from outside, and may have been diagnosed elsewhere.

Dr. Traynor said he thought that the idea behind reportable diseases was for something that might have a societal impact in terms of communicability, such as infectious diseases and certain types of cancers. As much as he would love for ALS to be reportable, it was not clear to him whether it fell within that rubric.

Dr. Horton responded that most reportable diseases are infectious. It is also important to note that it is largely up to the discretion of the states to decide what diseases they want to be reportable. CDC publishes a recommended list, but the state legislators have to declare a disease reportable.

Dr. Brooks thought they should not be limited by what they were looking back at. As Thomas Jefferson said, "I am the most powerful citizen of the United States right now," and Dr. Brooks wanted to go on record to say that any environmentally caused condition should be a reportable disease.

Dr. Horton agreed that this would certainly make their job much easier. However, in the absence of reportable disease status, the national approach appears to be the best methodology. He reiterated that taking a state and metropolitan approach is very time-consuming and expensive.

Dr. Traynor said he was not totally sold on the idea of making ALS a reportable condition, given that there might be a backlash from various groups. However, if that was the way the group wanted to proceed, he understood.

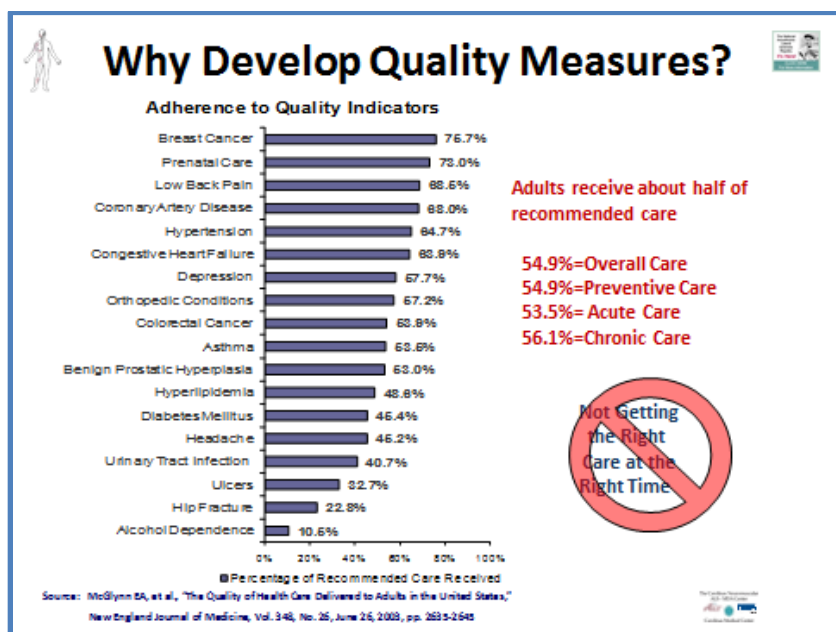
Dr. Kasarskis pointed out that cancers would fall analogously like ALS. Dr. Kaye indicated that all cancers are reportable, except basal cell skin cancers. Cancer is different because when the decision was made to have cancer registries, CDC was allocating funds for them. States had to agree to make cancer a legally reportable disease in order to obtain funding, which is how the cancer registries in the US were ramped up in such a short period of time. There were only 3 registries before 1982, and by 1990 there were 45 to 50.

Dr. Horton added that 1 in 3 people will be diagnosed with cancer, so it is more prevalent in terms of disease. He was sure that had something to do with cancer being a reportable disease. He also indicated that Dr. Kaye and her group would be developing manuscripts that are anticipated to be submitted in fall 2013. Many of the state- or metro-specific journal articles will have incidence and prevalence rates where possible. Thus, this will be a good source of data for anyone who is interested in how common ALS is and the disease characteristics.

## AAN Registry Task Force: ALS Performance Measures

**Benjamin Brooks, MD**  
**Carolinas Neuromuscular/ALS-MDA Center**  
**Carolinas Medical Center**

Dr. Brooks presented an update on the AAN Registry Task Force's development of ALS performance measures. He explained that the reasons for developing ALS performance measures are to determine how many ALS cases there are in order to help treat them, and to provide evidence that something has to be done. The goal is to address this from the point of view of outcomes. Using any metric, US health care is not the best in the world. The US ranks very high using metrics about specialized "rescue" care, and ranks in the middle using metrics about general care. By all metrics, US health care is far the most expensive. Another reason to develop quality measures is to assess adherence to quality indicators. The following graphic shows adherence across a number of disease:



Overall, adults receive about half of the recommended care in the US. Therefore, even if people with ALS are being counted and treated, it is important to ensure that they are receiving appropriate care. The act of measurement usually has improved quality of care (e.g., the Hawthorne Effect). Use of measures has become accepted by payers and large health care systems with respect to making sure that care is being provided, but there are hundreds of quality measures across many conditions. It is easy to develop measures for some conditions, but neurological conditions are particularly difficult. The consequence of not developing measures is that the condition will be ignored by health care providers, insurance, et cetera. Into the breach, the AAN and other organizations think that this should be done disease by disease.

Regarding the use of guidelines versus measures, there is a lot of work to convert guidelines to measures. For example, if a patient is admitted with an ischemic stroke, then aspirin should be given within 48 hours. What if the patient is on another antithrombotic? What if the patient is

allergic? All of these details must be considered as well. In terms of the professional organizations involved in developing guidelines, AAN has been very involved. Other professional organizations include the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM), the American College of Chest Physicians (ACCP), the American Gastroenterological Association, and the American Academy of Physical Medicine and Rehabilitation (AAPM&R). All of these organizations have journals and websites to disseminate guidelines. AAN has a long history of implementing "Quality Improvement in Neurology: Implementation of Clinical Practice Guidelines Phase I: Quality Measures Development." The subcommittee members involved in developing quality measures are listed as follows:

<b>AAN QMR Subcommittee Members</b>	
Christopher Bever, Jr., MD, MBA, FAAN (Chair)	
Richard M. Dubinsky, MD, MPH, FAAN (Vice-Chair)	
John R. Absher, MD, FAAN	
Eric Cheng, MD, MS	
Charles C. Flippen, MD	
Daniel B. Hier, MD, MBA	
Donald J. Iverson, MD	
Rita Richardson, MD	
David Z. Wang, DO	
<b>AAN Staff</b>	
Sarah T. Tonn, MPH, Associate Director, Clinical Quality and Performance Evaluation	
Rebecca Swain-Eng, MS, Manager, Performance and Implementation	
Gina Gjorvad, Project Manager, Performance Measurement	

Others have helped, including the following:

#### Professional Organizations

- ☐ American Occupational Therapy Association (AOTA)
- ☐ American Physical Therapy Association (ATPA)
- ☐ American Speech-Language Hearing Association (ASHA)
- ☐ Dysphagia Research Society (DRS)
- ☐ Academy of Neurologic Communication Disorders and Sciences (ANCDS)
- ☐ National Quality Forum (NQF)
- ☐ Physician Consortium for Performance Improvement (PCPI) American Medical Association
- ☐ National Committee For Quality Assurance (NCQA)

#### Quality Organizations

- ☐ Agency for Healthcare Research and Quality (AHRQ)
- ☐ Ambulatory Care Quality Alliance (AQA)
- ☐ National Quality Measures Clearinghouse (NQMC)
- ☐ National Guidelines Clearinghouse (NGC)

#### ALS Centers

- ☐ The Forbes Norris MDA/ALS Research & Treatment Center at California Pacific Medical Center
- ☐ The Carolinas Neuromuscular/ALS – MDA Center at Carolinas Healthcare System
- ☐ The Eleanor and Lou Gehrig MDA/ALS Center at Columbia University Medical Center

- ☐ University of Kentucky ALS Association Certified Center
- ☐ University of Texas Health Science Center-San Antonio MDA/ALS Center
- ☐ The Les Turner/Lois Insolia ALS Center–Northwestern University

### ALS Research Groups

- ☐ Amyotrophic Lateral Sclerosis Research Group
- ☐ NorthEast ALS (NEALS) Consortium
- ☐ World Federation of Neurology Research Group on Motor Neuron Diseases (WFN-ALS)
- ☐ Robert Packard Center for ALS Research at Johns Hopkins
- ☐ Western ALS (WALS) Consortium
- ☐ SouthEast ALS Alliance (SALSA)

### Patient Organizations

- ☐ Muscular Dystrophy Association–ALS Division
- ☐ ALS Association
- ☐ Les Turner ALS Foundation

A number of ALS measurement sets have been developed and have either been published, are in press, or are still being developed, including the following:

- ☐ Parkinson's disease (published in *Neurology*<sup>®</sup>)  
[www.aan.com/globals/axon/assets/8002.pdf](http://www.aan.com/globals/axon/assets/8002.pdf)
- ☐ Epilepsy (published in *Neurology*<sup>®</sup>)  
[www.aan.com/globals/axon/assets/8092.pdf](http://www.aan.com/globals/axon/assets/8092.pdf)
- ☐ Stroke and Stroke Rehabilitation  
[www.aan.com/uploadedFiles/3Practice\\_Management/2Quality\\_Improvement/1Quality\\_Measures/1All\\_Measures/2012%20Stroke%20and%20Stroke%20Rehab%20Measurements.pdf](http://www.aan.com/uploadedFiles/3Practice_Management/2Quality_Improvement/1Quality_Measures/1All_Measures/2012%20Stroke%20and%20Stroke%20Rehab%20Measurements.pdf)
- ☐ Dementia  
[www.ama-assn.org/ama1/pub/upload/mm/pcpi/dementia-measures-specifications.pdf](http://www.ama-assn.org/ama1/pub/upload/mm/pcpi/dementia-measures-specifications.pdf)
- ☐ Distal symmetrical polyneuropathy (in press)  
Confidential copy can be emailed
- ☐ Amyotrophic Lateral Sclerosis (in press)  
Confidential copy can be emailed
- ☐ Muscular Dystrophies (in development)

The process for development in measures includes consideration of six dimensions of quality, including safety, timeliness, effectiveness, equity, efficiency, and patient-centeredness (STEEP). Performance measures can be process, outcome, structural, composite, and/or surrogate. Most current performance measures are process. A performance measure includes a numerator statement that indicates what the clinician needs to do to successfully complete the measure (e.g., document in the medical record that they discussed falls with the patient). It also includes a denominator statement that indicates the eligible patient population, diagnosis,

timeframe for measurement (e.g., yearly, every visit, other time period), and age and gender limitations. Exceptions for a measure include medical reasons (e.g., medication contraindication), patient reasons (e.g., patient refusal), or system reasons (e.g., no insurance). Documentation links exclusion to the measured process, CPT II codes can be developed for each measure, and ultimately eSpecifications and eMeasures will be developed.

The key to a good measure is for it to be evidence-based, linked to outcome, actionable by physician, feasible to collect and it should fill a gap and have well-defined specifications. Evidence links care to better outcomes. Ideally, the evidence should be randomized controlled trials (RCT)-based; however, the reality is that RCTs are typically performed when needed for FDA approval. Care about history-taking, examination, and counseling or education are not RCT-based. They are usually observationally-based on single case studies. There must be a balance between greater efficacy versus greater eligibility. An RCT may not be conducted on a homogenous population, such as the patients they see. In terms of gap in care, widespread variations of care means that gaps in care may not be consistent. Gaps in care may have temporal trends. The cystic fibrosis model has assessed that specifically, and there have been recent publications by the MDA with respect to how the cystic fibrosis model might be very good moving forward in terms of bringing everyone in line with the same rule. Examples of no gap in care include neuroimaging for patients with acute stroke, and beta-blockers for persons with myocardial infarction.

The format of a quality measure is that it should be evidence-based; follow guidelines implemented in practice; and be actionable, feasible, and based on a gap in care. Data sources include administrative claims data (CPT II codes combined with ICD9 and CPT I code), clinical lab data, registry data (groups of measures), and electronic health record data (eSpecifications (human readable) and eMeasures (computer readable in XML)). Selection of the medical evidence can be made from: 1) the Medical Librarian (Literature search: Embase, Cochrane, National Guideline Clearing House ( [www.guidelines.gov](http://www.guidelines.gov) ), PubMed, others; 2) PCPI Evidence-based Checklist (Individual Guideline Review and Approval using PCPI checklist); and 3) Desirable Attributes of Measures. There must be more focus on outcomes (not just process, though process is still the most common type of measure); safety (even though evidence may not be as strong); overuse (choosing wisely), not just underuse; and care coordination, which may either prevent adverse outcomes or reduce utilization. The following example represents a good format for a quality measure:

Best examples: IF-THEN or ALL-SHOULD

"If a PD patient is having persistent medication-induced hallucinations or delirium not improved by PD medication adjustments, then a trial of quetiapine or clozapine should be used"

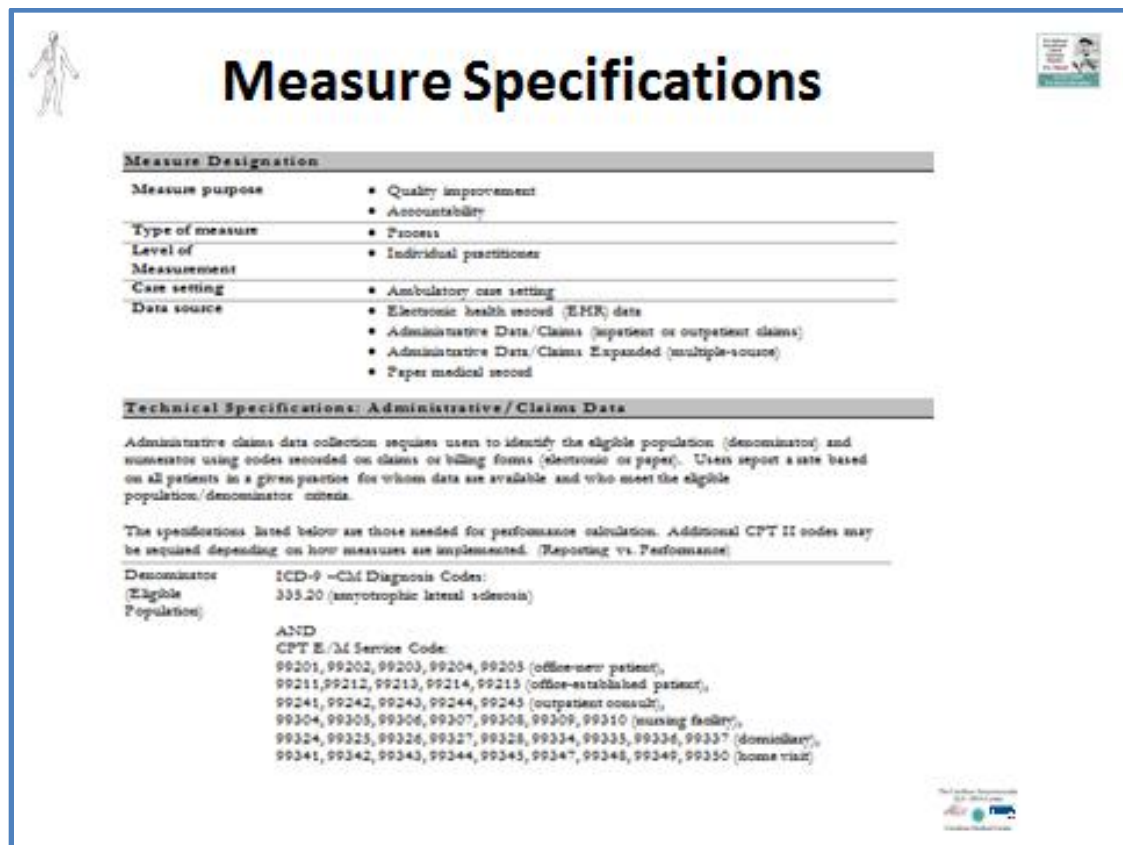
"All patients with PD should be asked at least annually about the occurrence of falls"

A quality measure should be expressed as a ratio with a denominator (eligible persons), and a numerator (persons who received care), and then exclusion must be accounted for (medical, patient, system). The development process for a measure is 6-12 months total, with a planning phase (2-4 months), in-person meeting with people involved, measure refinement (1-3 months), public comment period (30 days), revisions in response to public comments (1-2 months), approvals (1-2 months), and a beta testing process (6-9 months total).

The working group composition for ALS was led by Dr. Brooks and Dr. Robert Miller, and a large number of people were involved from a variety of areas, including medical societies; physician and provider associations/organizations; employer and health plans; society staff,



methodologist, AMA/PCPI staff; and patient advocacy/society groups. Preliminary work included measurement development and identification of working group members. The following is an example of a measure designation:



**Measure Specifications**

**Measure Designation**

Measure purpose	<ul style="list-style-type: none"> <li>Quality improvement</li> <li>Accountability</li> </ul>
Type of measure	Process
Level of Measurement	Individual practitioners
Case setting	Ambulatory case setting
Data source	<ul style="list-style-type: none"> <li>Electronic health record (EMR) data</li> <li>Administrative Data/Claims (inpatient or outpatient claims)</li> <li>Administrative Data/Claims Expanded (multiple-source)</li> <li>Paper medical record</li> </ul>

**Technical Specifications: Administrative/Claims Data**

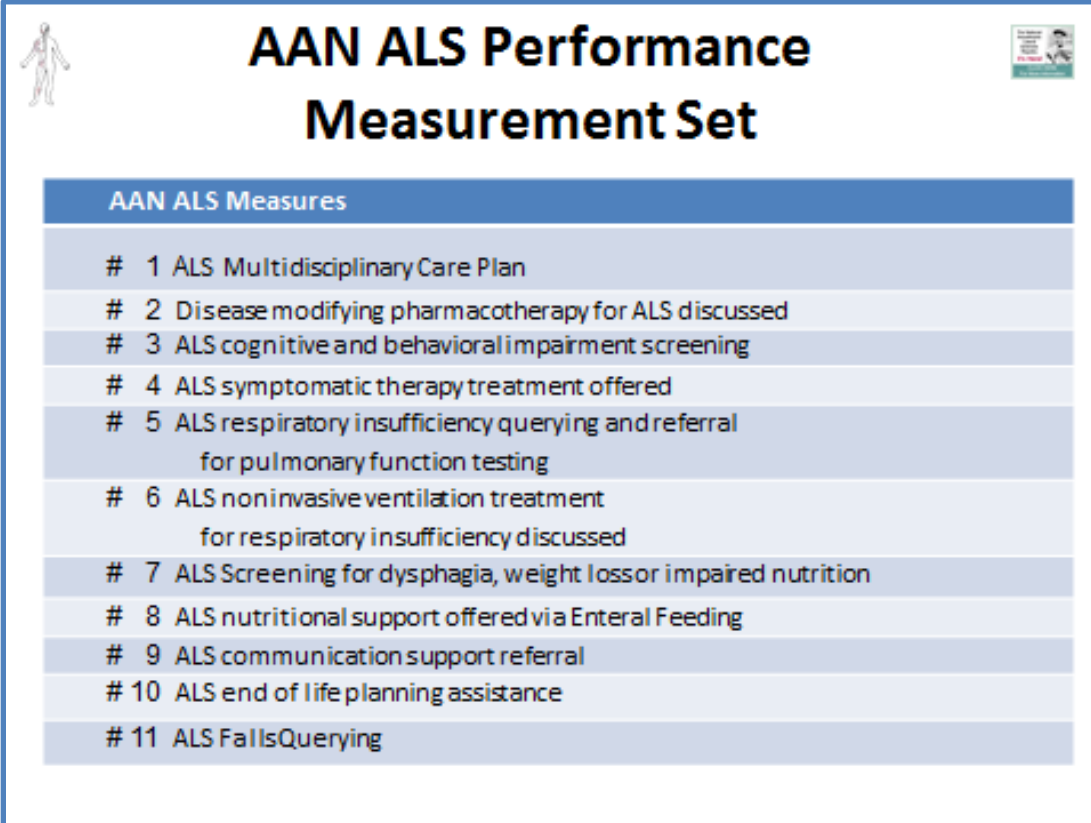
Administrative claims data collection requires users to identify the eligible population (denominator) and numerator using codes recorded on claims or billing forms (electronic or paper). Users report a rate based on all patients in a given practice for whom data are available and who meet the eligible population/denominator criteria.

The specifications listed below are those needed for performance calculation. Additional CPT II codes may be required depending on how measures are implemented. (Reporting vs. Performance)

Denominator (Eligible Population)	<p>ICD-9 -CM Diagnosis Codes:</p> <p>335.20 (amyotrophic lateral sclerosis)</p> <p>AND</p> <p>CPT E/M Service Code:</p> <p>99201, 99202, 99203, 99204, 99205 (office-new patient),</p> <p>99211, 99212, 99213, 99214, 99215 (office-established patient),</p> <p>99241, 99242, 99243, 99244, 99245 (outpatient consult),</p> <p>99304, 99305, 99306, 99307, 99308, 99309, 99310 (nursing facility),</p> <p>99324, 99325, 99326, 99327, 99328, 99334, 99335, 99336, 99337 (homebased),</p> <p>99341, 99342, 99343, 99344, 99345, 99347, 99348, 99349, 99350 (home visit)</p>
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Topic nomination was defined by gaps and variations in care, reference list guidelines, recommendation list for topic, guideline review checklists, work plan, and other documents. A public comment period and review of the specifications have been completed. The measures were revised and have been approved by the AAN and PCPI, but at another level, none of the process measures were approved pending the beta testing that has to be ongoing. The development of these measures is being limited by Medicare, because they want more outcomes-based measures. Maintenance of certification, health plans, and research also come into play.

The AAN ALS Performance Measurement Set is shown in the following table:

The graphic is a rectangular box with a blue border. In the top left corner is a small icon of a human figure. In the top right corner is a small logo for the American Association of Neurological Surgeons (AAN). The title "AAN ALS Performance Measurement Set" is centered at the top in a large, bold, black font. Below the title is a table with a blue header row and 11 data rows. The header row is labeled "AAN ALS Measures". The data rows list 11 measures, each preceded by a hash symbol and a number.

AAN ALS Measures
# 1 ALS Multidisciplinary Care Plan
# 2 Disease modifying pharmacotherapy for ALS discussed
# 3 ALS cognitive and behavioral impairment screening
# 4 ALS symptomatic therapy treatment offered
# 5 ALS respiratory insufficiency querying and referral for pulmonary function testing
# 6 ALS noninvasive ventilation treatment for respiratory insufficiency discussed
# 7 ALS Screening for dysphagia, weight loss or impaired nutrition
# 8 ALS nutritional support offered via Enteral Feeding
# 9 ALS communication support referral
# 10 ALS end of life planning assistance
# 11 ALS Falls Querying

Dr. Brooks reviewed the ALS Multidisciplinary Care Plan measure in more detail, pointing out that the difficulty is the group of people who do not go to ALS centers and those who do and how to define that measure and that concept. He also showed an example of the measurement component (numerator, denominator, exceptions); supporting guidelines and other references for the guideline; the relationship of the measure to the desired outcome (the importance of the measure); opportunities for improvement; a figure illustrating national quality strategy aims and priorities, and a figure illustrating Measure Applications Partnership's (MAP) family of measures populating a core measure set and program measure sets. All 11 ALS measures were submitted to MAP, only 2 of which were approved, and 9 were not approved pending beta testing.

TABLE A2. MAP INPUT ON PQRS MEASURES UNDER CONSIDERATION (continued)

Measure # and NQF Status	Measure Title	Federal Program Alignment	MAP Conclusion and Rationale	Additional Findings
M2806 Not Endorsed	ALS Cognitive Impairment and Behavioral Impairment Screening	MUC: PQRS FIN:	Do not support	Public comment from AAN does not support MAP's conclusion.
M2807 Not Endorsed	ALS Communication Support Referral	MUC: PQRS FIN:	Do not support: Measure does not adequately address any current needs of the program	Measures assessing referrals are not considered to drive improvement; measures should assess if proper care was received. Public comment from AAN does not support MAP's conclusion.
M2809 Not Endorsed	ALS Multidisciplinary Care Plan Developed or Updated	MUC: PQRS FIN:	Support Direction: Not ready for implementation, should be submitted for and receive NQF endorsement	Public comment from AAN does not support MAP's conclusion.
M2862 Not Endorsed	Disease Modifying Pharmacotherapy for ALS Discussed	MUC: PQRS FIN:	Do not support	

Measure Applications Partnership MAP Pre-Rulemaking Report 2013  
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TABLE A2. MAP INPUT ON PQRS MEASURES UNDER CONSIDERATION (continued)

Measure # and NQF Status	Measure Title	Federal Program Alignment	MAP Conclusion and Rationale	Additional Findings
M2810 Not Endorsed	ALS Noninvasive Ventilation Treatment for Respiratory Insufficiency Discussed	MUC: PQRS FIN:	Do not support	Public comment from AAN does not support MAP's conclusion.
M2811 Not Endorsed	ALS Nutritional Support Offered	MUC: PQRS FIN:	Do not support	Public comment from AAN does not support MAP's conclusion.
M2812 Not Endorsed	ALS Respiratory Insufficiency Querying and Referral for Pulmonary Function Testing	MUC: PQRS FIN:	Do not support	Public comment from AAN does not support MAP's conclusion.
M2813 Not Endorsed	ALS Screening for Dysphagia, Weight Loss or Impaired Nutrition	MUC: PQRS FIN:	Do not support:	Public comment from AAN does not support MAP's conclusion.
M2814 Not Endorsed	ALS Symptomatic Therapy Treatment Offered	MUC: PQRS FIN:	Do not support	Public comment from AAN does not support MAP's conclusion.

Measure Applications Partnership MAP Pre-Rulemaking Report 2013  
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In order for this to have any impact on the treatment of patients with ALS, it is important to define the number of patients who have this condition, how many people are being treated, and to what degree they are meeting the criteria for being treated.

### **Discussion Points**

Dr. Horton inquired as to if and how the Registry could contribute to this effort.

Dr. Brooks replied that he thought a proper definition of all of the patients with ALS in the country is very important. The metropolitan data are important in terms of the number of people who may or may not be going to centers, as well as the number of people who die who may never have been treated by a doctor or ALS center. It will be absolutely crucial to determine the number of people who may be impacted by any quality outcome measure in development.

Mr. Harada asked what would constitute “good” in Dr. Brooks’ mind, and once the metrics are captured, what he thought a proposed corrective action plan would be to correct gaps.

Dr. Brooks replied that this is a problem across many diseases. The cystic fibrosis model, which has been endorsed by the MDA, is a model of trying to ensure that everyone achieves the same level of performance. They have done this at the Carolinas Neuromuscular ALS/MDA Center by developing a very intense internal audit called “Disease-Specific Certification,” which they have been working through the Joint Commission. Based on the guidelines, the first 4 metrics were identified that they wanted to meet and then they tried to meet them. He stressed that it is hard to meet them, and that the difficulty is in the details. It is the same model as flying an airplane. Several items have to be checked off before taking off, and if everything is not in place, there is no take-off. For the care of an individual patient, certain information should be known about that patient. For instance, they have gone through the first cycle of “Disease-Specific Certification” and are the first to be endorsed in the country and the world in that respect for ALS. However, the next step is much harder in trying to define whether they can really achieve meaningful outcomes for people. For example, they have been considering the deployment of non-invasive ventilation, and have implemented a pneumococcal immunization program to prevent pneumonia to treat an outcome from ALS that has been observed.

## **Les Turner ALS Foundation**

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**Wendy Abrams**  
**Executive Director**  
**Les Turner ALS Foundation**

Dr. Abrams shared that it was an unusual beginning that brought her to the Les Turner ALS Foundation as its Executive Director 35 years ago. She met Les Turner in 1977, after he was diagnosed with ALS. She used to play tennis with his brother-in-law. As she sat in that first meeting when they were asking for volunteers, her hand went up and she asked, “Who was Lou Gehrig, and what was his disease?” She has since learned about both Lou Gehrig and Les Turner very well. Les was only 36 when he was diagnosed and died two years later at age 38, leaving a wife and three young sons. Les Turner, a Chicago area businessman, husband, and father, was diagnosed with ALS in 1976. Frustrated by the lack of information and research on ALS at the time, he and his family and friends started the foundation in 1977, just a year before his death. Before he died, he had an idea based on used book sales. He was sitting in his wheelchair and his wife was throwing out some old records. This spawned the idea that

resulted in the beginning of the Mammoth Music Mart in 1978. They contacted Dick Clark of American Bandstand who thought it was a wonderful idea, endorses the foundation, and became its National Honorary Chairman. Mammoth Music Mart was an 11-day sale of donated music items, including old 78 rpm records and 45s, sheet music, musical instruments, 8-tracks, cassettes, and eventually CDs. This began with a tent the size of a couple of football fields in a very prominent shopping center in the Chicago area, and began collecting music from the public. That single event provided the funds needed to create the first ALS Research Laboratory at Northwestern in 1979. The event continued for 25 years, closing in 2002 due to the changing music formats. However, Dick Clark continued as the National Chairperson for all 25 years and remained a staunch friend and supporter until his death. Unfortunately, while this was Les's idea, he did not live to see the first Mammoth Music Mart.

Today, the foundation's ALS research is conducted in two laboratories at Northwestern, one headed by Dr. Teepu Siddique since 1991 and the other headed by Dr. P. Hande Ozdinler since 2008. They have each made enormous contributions to the field. After Les Turner died, the founders did not know other ALS patients, but quickly patients and families were calling the foundation because of the awareness brought about by the Music Mart. In 1986, the Les Turner/Lois Insolia ALS Center at Northwestern was formed. It was the beginning of a multidisciplinary center. At that time, the center had one physician scientist, one doctor, and one nurse. Today, the center has 5 neurologists; a pulmonologist; 3 nurses; speech, OT, nutritionist, and genetic counselors; and other allied health professionals and vendors who offer diagnosis, second opinions, and management of the disease and options for best quality of life.

Les Turner ALS Foundation patient and family support programs are free and are available to ALS patients and their caregivers who reside in the foundation's service area, which includes Chicago and its collar counties, as well as portions of Indiana. The Home and Community Services Team is comprised of 5 patient advocates, 3 nurses, and 2 social workers. The role of this team is to:

- ☐ Enhance the continuity of care between center visits
- ☐ Provide ongoing disease education and address specific concerns
- ☐ Provide practical information on quality of life and daily living
- ☐ Provide home environment safety assessment, adaptations, and equipment
- ☐ Facilitate communication between patient, family members, and the healthcare team
- ☐ Share information regarding disability, Medicare, Medicaid, private insurance, and other financial options
- ☐ Guide access to care through state programs and caregiver services, and explore additional means to maximize assistance
- ☐ Assist with advance directives, including living wills, medical powers of attorney, and other end of life issues
- ☐ Provide social service support and intervention to improve communication and assist in conflict resolution
- ☐ Consult with home health agencies and hospices to coordinate care
- ☐ Conduct in-service education for home health agencies, hospices, case management groups, assisted living facilities, nursing homes, a patient's employer, and other community organizations
- ☐ Provide bereavement Support

Additional program services include the following:

- ☐ Telephone, e-mail, and referral support
- ☐ Support group meetings for patients, families and caregivers
- ☐ Durable medical equipment loan banks
- ☐ Communication equipment
- ☐ Ralph Russo Patient and Family Services Grant Program
- ☐ Dan Nelson ALS Respite Grant Program
- ☐ Stuart Rosen ALS Transportation Program
- ☐ Educational materials and programs

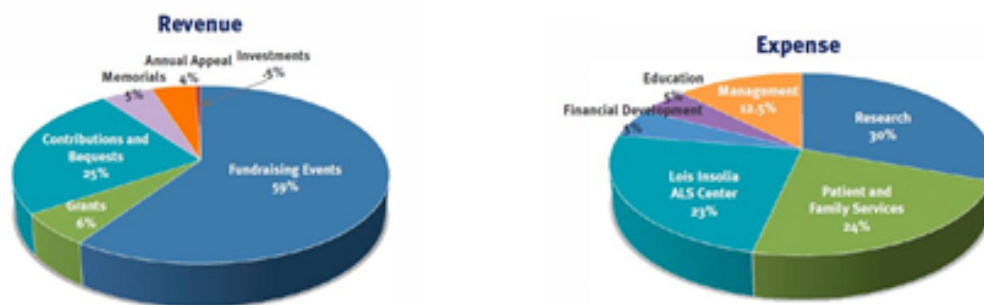
Fundraising events include the following:

- ☐ ALS Walk4Life
  - ▶ Arts4ALS
- ☐ Run4ALS
  - ▶ Strike Out ALS 5k
  - ▶ Iron Horse 5k
  - ▶ Chicago Marathon
  - ▶ Shamrock Shuffle
- ☐ "Hope Through Caring Award Dinner"
- ☐ ALS Awareness Month Tag Days
- ☐ Third Party Events:
  - ▶ Gary Griffith Golf Outing
  - ▶ Holla for ALS Casino Night
  - ▶ And many more...
- ☐ Partnership with:
  - ▶ The Chicago Bandits, Women's Professional Fast Pitch Softball
  - ▶ The Schaumburg Boomers, Men's Minor League Baseball

Over 59% of the foundation's income comes from special events fundraising, so they are very active and visible in the area. The ALS Walk4Life is the foundation's signature event. Now entering its 12<sup>th</sup> year, it has raised over \$7 million. Last year, there were 6000 walkers and their families at Soldier Field, which is where the event will be on September 22, 2013. The Run4ALS program is gaining ground, with several 5Ks, marathons, and half-marathons being held this year. Next year, there are plans to expand into other endurance sports. The foundation also has a flourishing Young Professionals Group, which offers great energy and hope for the future. They also have three local celebrities as spokespersons: Keith Van Horne of the 1985 Super Bowl Bears; Jonathan Eig, author of "Luckiest Man: The Life and Death of Lou Gehrig;" and Lin Brehmer, local on-air personality from the most popular station, WXRT.

The Les Turner ALS Foundation has a Board of Directors of 23 and an office staff of 10. They are continually striving to improve fundraising to grow the programs that have been created in

## Les Turner ALS Foundation 2012 Year-In-Review



Eighty-three cents of each dollar spent goes directly to our research and our patient services programs



the Chicago area. In 2012, 83 cents of each dollar spent went directly to the foundation's research and patient services programs. Each year this changes, but lately increased funding has been allocated to patient care and support. This depends on financing from the year before. The foundation is very conservative, and does not give away any funds unless they have raised them. Their budget for next year will be based on 2013 income and the needs of the research facilities. The foundation serves approximately 90% of the Chicago area ALS population, serving over 600 patients annually. The foundation is also a founding member of the International Alliance of ALS/MND Associations and the host of the ALS Nursing and Allied Health Professional Symposium, which will be held in Chicago November 7-10, 2013.

## PALS' Perspective on the Registry

**Ed Tessaro**  
**Retired/Philanthropy**  
**MDA for ALS/St. Jude's Hospital/CF**  
**Alpharetta, Georgia**

Hello again. I'm Ed Tessaro. I am at 5 years for symptoms and 4 years ago diagnosed. I want to begin by acknowledging Steve and ALSA for having the gumption to get this started many years ago for the national registry. I know that is hard to do. I did not realize that it was the only one authorized by Congress, so I am feeling pretty good that I'm in this privileged class. The bio of an ALS patient takes a lot of forms. I guess I want to begin by telling you that sympathy is



nothing we deal in, and I'll speak for Ted and Joe a little bit. We're all about the future. I've really lived two lives, the one that ended 4 years ago when I was diagnosed and I realized the consequences, and the one that began that very next day. I'll tell you sitting here that the one that began the next day is better. I'm sure that the doctors in the room will recognize that when you take away one capability, or you lose the ability to do something, you appreciate more what you have, you develop more of what you have, and you end up putting more into what you can do as opposed to worrying or fretting about what you've lost. So, I sit in front of you as a very optimistic guy and someone who has found a sense of purpose in assisting you all in this very difficult task. I do it every day. I sit on a cystic fibrosis board. There are also 30,000 patients with cystic fibrosis. It's an odd connection to the number of people diagnosed with ALS. I find the same thing in that community, and I am here to tell you that it's a good life when you can join in this kind of a purpose.

Talk about having good fortune, I should say that Ted and I are involved in the first stem cell transplant clinical trial in the nation right here at Emory. There are 15 of us originally who have a million and a half stem cells in our spines. So, all of that work is in some way the result of the work you all have done as well. What the 10-year ALS clinic at Emory has been able to accomplish is what I think you're accomplishing all over the country. I'm very impressed. I also have a philosophical point to make. That is, the example is federalism in our own politics. It's a wonderful thing when there's a great system of checks and balances among people and bodies of government. That's why we're the envy of the world politically. But, it sometimes works to our detriment in science as it does in politics, because everybody has an agenda and everybody has common interests, and goals, and objectives. Sometimes, we don't share what we need to share. That's a little bit of self-interest, but it is also the nature of what we do. We take great pride in it, we want to own it, and there is a pride of authorship. So, this national registry that is what we're here for is such a great idea because it cuts through all of that and allows the science to be advanced, not just by one ALS clinic, or 55 across the country, or 72 across the country for MDA, but all over the world. It enables us to go further and not have this long, painstaking process to get from A to B. That's a good thing, and I hope we can do more of it.

The point I made yesterday about social media—I believe what Kevin said about self-reporting is the answer to this. There is a lot of process to try to get information, and there is a lot of pushback to giving it appears. What I think we can do is go to those families—I will repeat what I said yesterday. I saw Dr. Ikeda on Twitter with a hashtag, but how many followers does she have? Steve Gleason has 37,000 followers on his Twitter account. Ted and I both know Steve, and that's the way to communicate. We have a social media explosion in this country, and it can go to the kids, and nieces, and nephews of PALS. My kids are in their 30s and they are hugely active on this now. That's the community that might get the family to pull in and register—not just us old guys or young guys in Joe's case. I would invite us to not run an ad in *Rolling Stones*, but to get into 2013 the way that people 30, 40, and 50 are communicating. That's the way we can get a registry started. I know that's not part of the process that we're talking about today, but I think that's going to be the solution. I think that's the only way we self-report. I just ask you to continue to be fierce advocates. I'm so impressed with everything you've done, and I have met some great people today. Don't feel bad about us, because we're doing fine even if we're physically much impaired. What you're doing makes me feel better. I won't speak for 30,000 people, but if they could all feel here, I think they would feel better than maybe they did two days ago. Thank you for what you are doing. Myself, my family, and a lot of people really appreciate it.

**Joe Wise, Veteran  
Rineyville, Kentucky**

I concur with Ed that this second life is certainly more fulfilling and rewarding knowing that you're possibly involved in helping someone else down the road. I was diagnosed in 2007, and am what is known as a creeper. I don't know if that is a technical term that we can use in the Registry data, but it may be something to look at. I am probably not a good candidate for a research trial, but somebody might want to have my brain and spinal cord to study. Primarily my role in Kentucky now is to advocate in Washington, DC. I go every year, and have been going for the last 4 years. It is really encouraging to see all of the "movers and shakers" behind the Registry really advocating on behalf of it, and trying to raise money to support it. What is encouraging about this meeting is that it gives us new ammunition, because we see the same folks—the same Congressman and maybe the same staffers every year, and we are basically asking for the same things every year. But now it will be encouraging to have the data and other information. Certainly, this is more good information to give the Congressmen because they are always wanting more "bang for the buck" and say "I gave you this much money, or helped you get it. What am I getting from it?" All of this is certainly very encouraging to me.

As far as going forward, I do not really have anything prophetic or new to add to the Registry. Most of the business and other issues have been covered. I am a simple guy. I am not a medical guy, or a stat guy, or even a political guy. I'm just a veteran who was stricken in his 40s with this disease, so I look at things in simple terms. I don't understand the IRB and some of the drawbacks. It seems like they hinder good efforts. Why does someone have to check a box to be included in research? Why does Massachusetts have their own registry when they could report directly to this one? I'm sure there are a million reasons why, but that is the way I look at things—simply. I don't know if you have utilized the Paralyzed Veterans Association or the VA, but those are really good organizations that could possibly help with getting the word out about the Registry. I would certainly pursue all military options. "Military" is a very big buzzword around the country, with a lot of support, so I would definitely look into every option possible to try to help them do the work for you.

I don't pretend to understand everything that was discussed here in the last couple of days. A lot of it was very far over my head, but what I do understand is that the Registry is probably the single most important thing that PALS can do to help themselves. The way we can get that across is through the peer videos. I think that plea and push from PALS would certainly be helpful. As far as under-enrolling states, I know if you want to capture the attention of the people of Kentucky, you really have to go to the organizations or communities where Kentucky is really good, and that is basketball, bourbon, and horse racing. It's not baseball. Probably not everyone in Kentucky knows how to operate a computer. In some areas, we even have to pump in sunshine. But, they all know how to work a television set, so the more things that can go out across TV would be a way to reach folks. In some of the under-enrollment areas, maybe you could go to the industry in that particular state to try to pursue that avenue. Unfortunately, this is my personal opinion, but I think until we have a national spokesperson who really is an "A Lister" or Hollywood-type sports figure, someone in those arenas who can really get on board to push the Registry, it's going to be a difficult challenge to get the kind of notoriety that it needs. Like I say, that's just my personal opinion. Hopefully, no one comes down with ALS, but I really feel like that is what it needs. Even if you're not a baseball guy, maybe you've heard of Lou Gehrig. But, some of the other Hollywood celebrities who have been doing PSAs just don't have the clout that they used to. Thank you very much for inviting us. I really have enjoyed it.

**Ted Harada**  
**Board Member, Georgia Chapter ALS Association**  
**Atlanta, Georgia**

I apologize in advance if my thoughts are a little random. Bob asked me to speak this morning, and I'm never at a loss for words as you've seen, but I did try to jot down some thoughts. First and most importantly, I would be remiss if I didn't thank everyone in this room for your hard work, what you do behind scenes, or as doctors and nurses and researchers on the front lines. Ed and I were talking yesterday at lunch, and I said this before over a year ago in another forum, no one wants to be on the receiving end of an ALS diagnosis, but I would not necessarily want to be in the person's shoes who every week is putting themselves on the opposite end—giving that diagnosis to patients every week of their lives. They get in the medical business or become a doctor to help people, and then sit by helplessly. What you guys do is tremendous. A phrase I like to use is that what you do puts the humanity into a very inhumane disease. From a patient perspective that is very much appreciated, and we recognize your end and your difficulties as well.

I do consider myself somewhat of an ambassador for the ALS community. As Ed said, I'm in a trial and this has given me an opportunity to get in contact with thousands of ALS patients. I get plenty of feedback and plenty of questions. I am going to give some of my thoughts. First, I think this is great and I understand it, which gives me an advantage. I've been to so many meetings, so I get it. But, I don't think most of the community does and I think the fact that they don't is risking the Registry becoming irrelevant—not to the researchers in this room but to the patients in the community themselves. I don't think they see what's in it for them. It has been open since 2010, and there is really nothing yet to report. Statistically that's just the way it works. You have to collect it. That's not me saying you guys have done anything wrong. I think we need to manage expectations, so we may need to have a timeline on the Registry that tells people that the Registry was approved in 2008, in 2010 it went live, our expectation is that by 2013 we will have a paper out about the metro surveillance, in 2014 we expect to be able to deliver X. We have to start managing the expectations. That may be out there, but if it is, it is not known very well. Perception versus reality. The more that is communicated, the better the community will receive it.

What I hear a lot of times is that patients feel that there is not a lot of transparency based on the fact that they are going to DC to raise money, or lobby for money year after year. They want to feel included in what is going on in terms of how that money is being spent and what the result and return on investment is for that money. The more information you can give them, or when at least to expect that information, the better. As I said yesterday with that research information, if we can start saying, "Hey, we communicate with 500 PALS about these trials," again, it's a result. You're showing progress. You're showing what the Registry is being utilized for. People can understand that, and it gives them something to hang on to and helps them to realize the benefit. The other thing is what the Registry can and cannot do. I don't think everyone understands the nature of the Registry. I don't think most people understand the limitations of the Registry—limitations placed on it by an IRB. There are a lot of savvy patients, but there are also a lot of patients who do not have an interest in learning everything about what an IRB is or how the OMB impacts it. I think some high-level fact sheets and education would definitely help.

There is some concern about duplications. I read that a lot from people, especially when you're talking about the bioregistry. I don't know if that is legitimate or not. I can see the concerns. I have a doctor next to me who runs a brain repository. I promised myself to Emory. The

question raised to be asked is, "Are we doing just one more repository, and is there lack of sharing, or if we pooled the money, would we get better "bang for our buck?" I don't know the answers to these questions, and they may not be the right questions. But, there is a perception issue about whether it is a smart decision and if so, why. Again, if we could just get that information out there. I think the more you talk to the community, the better. I never read an exit interview or survey that said, "My boss talks to me too much." Everyone I read said, "There was no communication," or "I had no idea what was going on in the company," or whatever the case may be. I think this is a similar scenario.

We talked a little bit about internet limitations. Maybe it is a little tough to understand, but there is always the monetary factor, the rural factor, the age factor who maybe have not embraced technology. Is there a possibility to set up as a secondary option when getting information from the clinics for them to call in to complete the survey. I heard one of the ladies say that doing a paper version would be difficult, and I heard her say that a lot of times it's phone-in surveys because the operator can skip 3 if 2 was answered "no." Certainly, that would be a little more expensive I imagine, but don't make it the first choice. You could even do it by appointment if you had to. They could call in to make an appointment when they have someone available, or whatever the case may be. Find a mutual time for them to do the survey over the phone. That could eliminate some of the internet issues we discussed.

Following up from last year, I wasn't here last year, but one of the big questions I received from patients was, "What were the actions taken from last year's meeting? Was it productive?" I'm sure many of you knew a great man, Rob Tison, who was here and put a lot of work into trying to give feedback. Just a really good person, and a very smart person. One of the questions I received was, "What was done with that?" How were the questions that were raised last year resolved? I'm sure they all were resolved. I'm sure action was taken, but if not everyone realizes it, it doesn't do any good. I always go back to when I was Managing Director at FedEx for 15 years. I got an employee survey one time that said, "Our frontline employees didn't receive their 3-day training," so I told the managers to put a sign in the training room that said, "This is your 3-day training." For the next survey, the answer to "Did you receive your 3-day training" was "Yes, I did receive my 3-day training." This was not because we did anything different. It was just because we put a sign in there telling them what it was. My point being is that if they don't know what is happening or what was done, they may not even realize what great things you have done with the feedback.

I wanted to hit on something Ed said earlier about social media. I even said to Ed yesterday, "You know, I don't think social media is a problem. I think we're doing a good job with it." Then I did some homework last night and looked on social media to find information about the Registry. I didn't find a lot. When I went to the Registry page itself, there are Facebook and Twitter buttons on the bottom that keep tallies of how many people recommended it via Facebook. When you hit the Facebook button, it lets you recommend that site. After I recommended it, I was the 29<sup>th</sup> person to recommend the ATSDR specific registry page. After I tweeted it, I was the 21<sup>st</sup> person to tweet that page. There have been more than 21 tweets about it, but not specifically from that link. Then I went to Twitter and did #als to look for anything about the Registry. Most of what I found, unfortunately, was people asking questions about the Registry (What has been done? Is there any new information?). I looked for things about signing up. I think I found one Tweet from Dr. Ikeda that was shown yesterday that just said, "Hey, there's been updated information on the Registry." I didn't really find too many relevant things in the last couple or three months that were pushed out by CDC or anyone else for that matter. I think what we saw yesterday about one of the stats was, "Well, we see it in May." It's not surprising because in May we go to Washington, DC and Dr. Wharton comes and

talks to us about the Registry and importance, so there is probably a big social media push then, and maybe in July after the All Star game advertising and whatnot. But unlike cancer where everyone knows someone who is impacted, if you are not impacted by ALS all of the time, you're not going to remember. You are not going to remember 6 months or a year from now when your friend got diagnosed with ALS, "Oh, I saw something about a year ago about a registry." If you're not constantly pushing it out, then it's not going to be in the front of people's minds. There almost needs to be a regular schedule that gets pushed out via social media to keep it relevant. I think we all have a role in that. Obviously, I shamed myself and said, "Well, I'm not doing a good job of pushing it out. I'm an advocate. I'm on the Board of Directors for the Georgia ALS Association. Georgia is lagging. Why am I not Tweeting this regularly?"

You know, we all play a role. I just want to reiterate that this is not criticism. This is about opportunities for improvement. It's feedback from the community. Again, I cannot say enough about how much I appreciate all of the hard work you do in front of and behind the scenes. So, thank you from the bottom of my heart.

## Mobile Service Locator Apps

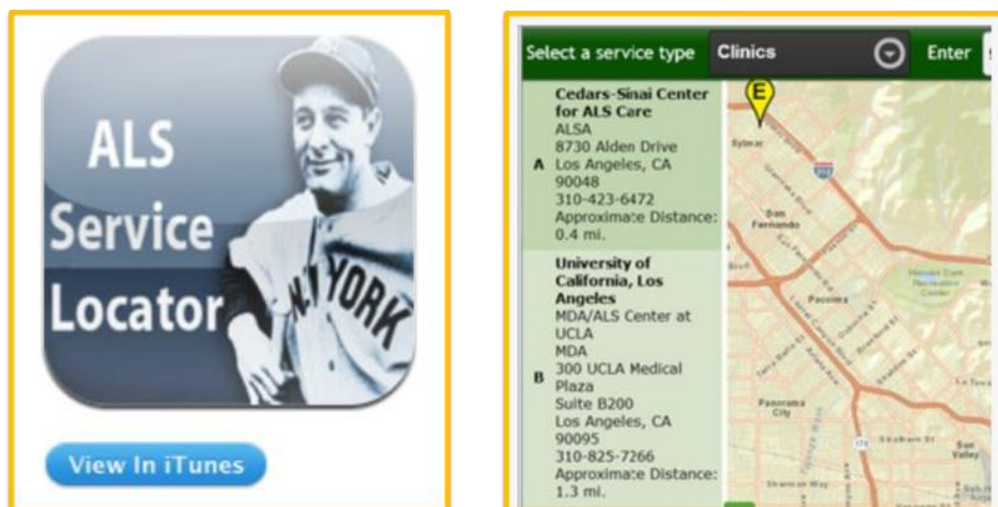
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**Lance Broeker, Technical Lead  
Geospatial Research, Analysis, and Service Program  
Division of Toxicology and Human Health Sciences  
Agency for Toxic Substances and Disease Registry**

Mr. Broeker indicated that he was filling in for his colleague, Andrew Dent, who was originally scheduled to present but could not attend and sent his apologies. He also clarified that this presentation was not his original presentation, but was something that a colleague of his did in November 2012. Though it was somewhat technical in nature, he made a few modifications in the last few hours to change the scope somewhat and make it less technical. He apologized in advance if it was too technical.

In terms of background, the Geospatial Research, Analysis, and Service Program (GRASP) is within NCEH/ATSDR in the same division with Dr. Horton and his team. GRASP is a multidisciplinary team comprised of about 30 team members, which is involved with geospatial sciences. Their domain lies with anything that deals with mapping and geospatial sciences, spatial analysis, demographic analysis, application development, and geospatial sciences in general.

A couple of years ago, the ALS Team approached GRASP because they were interesting in developing an ALS Service Locator web application. Because there was a mapping component and geospatial analysis, that fit precisely in GRASP's domain. In 2011, GRASP released the ALS service web application. This is a fairly simplistic application, which allows someone to enter a zip code to locate the 5 closest ALSA chapters or MDA offices to that zip code. Technically, this is accomplished using a single structured query language (SQL) server 2008 database that understands geospatial types, can calculate line of distance, et cetera. This is available directly off of the landing page at CDC, and is shown in the following illustrations:



There are some disadvantages to a web application of this nature. For example, flash cannot support it on iOS devices, such as iPad or iPhone. iOS devices are very popular, especially among people who may have some dexterity issues because they are typically much easier to navigate. Flash is a separate install typically, so in order to add it to a Windows device, it will have to have the flash install to support it. Flash often consumes browser and system resources and may compromise the overall performance. For this application, this is not so much of a problem, but it can be a pain to get this application and identify the 5 closest facilities. As a result, the ALS Team approached the GRASP Team again. Although iOS applications have been in use for a while; the government culture has been somewhat slow to adopt the technology. There was a lot of interest, but the government is an environment where people need to be educated about the technology, there are also security concerns, et cetera. It was not so much of a technical issue as it was an administrative issue in terms of obtaining the proper authorization to push these types of applications out.

Even though the government was a little “late to the game,” ALS approached GRASP to see if they could build a Native iOS application, which would be available directly in the iTunes store that could be downloaded and installed directly, and would permit the use of the features available in the iPad to navigate a map and use various other features. GRASP developed the iPad application, which was released in September 2012. Since then, there were 312 downloads as of July 1, 2013. Mr. Broeker apologized for not having more statistics on that, but from his recollection, the stats are interesting because they have some geographic information about where this application has been downloaded. It has actually been downloaded worldwide by people in Europe, Asia, et cetera. These ALS facilities are domestic, so it is unclear why it is being downloaded internationally. The ALS Service Locator iPad application is more or less the same concept as the web application, but has a slightly different interface. There are some pull-down menus to filter based on clinics, ALSA chapters, or MDA offices. It is important to note that this is available for iPad only at this time, not iPhone.

In terms of the technical architecture of these applications, the first application was a Flex web-based application. The second one was an iPad Native app. The applications are more or less the same, and they do the exact same types of things. What was interesting to GRASP and somewhat unknown at the time, was that they were actually able to utilize the same source code for both of these applications. Even though they are completely different operating systems and completely different environments, the development environment was Flash

Builder, which allows the compilation of a Flash application, Native iOS, and Android applications and supports the Blackberry platform. When data are updated, both applications are updated simultaneously.

In terms of next steps, the GRASP team is currently working with CDC's informatics laboratory to develop and test a Native Android application. Given that this effort is in its infancy, Mr. Broeker was unable to predict a timeframe for availability of this app. He noted that during his brief attendance during the meeting, he heard a gentleman from Kentucky saying that in his area, people may not be connected. The iPad is not the cheapest device on the market, so this type of application may not be available to people with limited financial resources or limited computer access. The cost of an Android tablet is typically in the \$200 to \$400 range versus the starting price of an iPad at \$400 to \$500, depending upon the features selected.

### **Discussion Points**

Dr. Horton noted that ALSA and MDA compiled the lists of clinics and offices for ATSDR, ATSDR merged the lists and submitted the merged list to the GRASP team, and the GRASP team created the app. He emphasized that ATSDR needs ALSA and MDA to keep the lists current as new ones come on line, and that ATSDR will approach them periodically to acquire updated lists. The ALSA and MDA sites have lists of their facilities, but this merges the two together and offers the "best of both worlds."

Mr. Gibson added that the hope was that no matter where a patient is diagnosed, they can find services in their area.

Dr. Antao inquired as to whether they could make this application available for the iPhone as well.

Mr. Broeker indicated that they are technically capable of doing this. It is more or less a form factor issue depending upon what they want to do with the mapping. The current iPad application could be reconfigured for the iPhone. The major issue would be the form factor. For example, the iPad does not have the same number of pixels as the iPad. One of the most interesting things about developing this type of application is that the issue does not lie in the time investment in the app development so much as it does in the design, look, feel, and overall flow. These aspects are quite challenging and time-consuming.

In terms of the question about why the app has been downloaded overseas, Dr. Brooks indicated that the British and the Dutch want to see how this works and add other capabilities such as emergency departments. Having done this with the ALSFRS, Android is going to be using the code system, so it should be easier and the charge should not be as much for the Android. He said he believes the iPhone really needs to be pushed forward, because the demographics are roughly half and half, with the Android beginning to overtake the number of people who have other capabilities.

Dr. Horton invited feedback, during or after this meeting, about whether there are other applications that PALS think would be helpful in terms of how they might relate to the Registry.



## OMB Continuation Package Status

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**Wendy E. Kaye, PhD**  
**Senior Epidemiologist**  
**McKing Consulting Corporation**

Dr. Kaye reminded everyone that OMB approval for the National ALS Registry must be renewed every three years, and was due to expire at midnight July 31, 2013.

In terms of background, since the mid-20<sup>th</sup> Century, there has been a growing recognition that the federal government can be a burden to individuals. Primarily this is related to the Census and the Small Business Administration (SBA). This mostly pertained to activities citizens were asked to complete for which there was a penalty for non-compliance. Given that there is a penalty to citizens for non-compliance, the notion was that the government should make completion as least burdensome as possible. A series of laws were passed known as the Paperwork Reduction Act. Dr. Kaye has completed about 15 packages, which are always very large and require a lot of paperwork, so it is not a reduction of paperwork for them.

OMB enforces the Paperwork Reduction Act. They conduct a scientific review, cost-benefit analysis, and policy implications review. They have the authority to review decisions that the agency has made about PRA determinations, because sometimes they will decide that something does not need to be submitted to OMB. In the case of the biorepository, ATSDR was awarded a clinical exemption, so they did not have to obtain OMB approval. There are very specific categories, but OMB has the right to review those and disagree.

There is a lengthy application process that includes a requirement to estimate the burden to participants and include information about what will be collected, statistical analyses, and all of the materials participants would be asked to complete. Previously, they were able to provide a Word document of the surveys to be administered; however, the rules have changed and now the screenshots have to be provided. For the surveys already posted on this web portal, it is not a problem to capture screenshots for submission. However, screenshots now have to be provided for surveys that have not yet been developed and approved. This added an extra complication, because mock-ups of the screenshots had to be created without the actual coding behind the application to make them work.

OMB approval is for a maximum of three years. Sometimes less than three years are approved if a project can be completed in less time. Renewal must be sought every three years, and there is no difference between the initial application and the renewal application as far as paperwork is concerned. Renewal also requires an update on the project's progress, an indication of any changes that are desired and what they are, and current burden estimates based on reality. The first time an estimate was made about the anticipated burden, how many people would take a survey, and how long it would take. The second time the information was based on what actually occurred.

As noted, the OMB approval for the National ALS Registry was due to expire at midnight. However, the renewal process was begun in September 2012. There were two public comment periods, one 60 days and one 30 days. Those are to give the public an opportunity to comment and know what is occurring (e.g., transparency in government). The 60-day public comment period began on February 7, 2013 when it was announced in the *Federal Register* and closed on April 12, 2013. The 30-day public comment period began May 8, 2013 and ended on June

6, 2013. The full application cannot be submitted to OMB until the 60-day public comment period has closed and revisions have been made based on public comment. While Dr. Kaye could have submitted this on April 15, 2013, there was a lag because at that point they had some data they thought would be helpful and wanted to be able to include that in the application. That turned out to be a wise decision.

While she hoped to be able to announce the approval of the package during this meeting, unfortunately she had not heard anything officially. The comments they have received from OMB have been good, and they have been able to respond to OMB's questions within a day or two. OMB had everything at this point, had made counters, and the counters were accepted by ATSDR. The original approval included terms of clearance, which would not allow the dissemination of results until it was clear to OMB that the results were representative. There will likely be terms of clearance again, although they are likely to differ. One of the terms will be somewhat of a disclaimer on the limitations of the representativeness, and the terms will probably state that as long as the disclaimer is included, ATSDR will be allowed to publish the results.

### **Discussion Points**

Dr. Brooks asked whether there would be ramifications if the package was not approved by midnight, and whether the Registry would have to close.

Dr. Kaye responded that the law reads that if no word is received from OMB and they do not disapprove, the package is approved. However, CDC has never pressed that option because if they did that, every package they submit may be disapproved if the deadline arrived and OMB was not ready to make a decision. OMB is friendlier than it used to be, and there are a few lapses. Therefore, even if they are not ready to grant final approval, they can offer an extension. A lapse is not anticipated.

Mr. Harada inquired as to whether they were asking for approval to publish the results, or just to keep going.

Dr. Kaye responded that the purpose of the new application is to add the risk factor surveys (n~10), to continue to use the risk factor surveys that are already available on the web portal, and to disseminate the data that have been collected. This was a major package. She thanked everyone for their cards and letters, because ATSDR was able to utilize this to support the package requests.

Assuming that OMB approval is received, Mr. Tessaro requested an educated guess about what the lag time would be for dissemination of the information.

Dr. Kaye replied that OMB will likely want a disclaimer included. The current issue for ATSDR is the need to combine the existing data and the portal data, and the slight lag in receiving the data from CMS. They are still waiting for the 2011 Medicare data, and it will have to be processed (e.g., cross-linked with the Registry data, de-duplicated, etcetera). Assuming that approval was imminent, the report would probably be completed by early Spring 2014.

Dr. Horton emphasized that a lot of PALS want to know how many people are self-enrolling. He asked whether she had a sense of whether ATSDR would be able to share general numbers. Heretofore, they have not even been able to articulate how many people have self-enrolled.

Dr. Kaye responded that they probably would be able to share that type of information. The main issue for OMB, which differed from any other conversation she has had with them ever, was a concern that ATSDR's data would show fewer cases than expected, would be misinterpreted, and would result in less support for ALS. OMB does not want to do anything that would be detrimental, which is positive.

As the data were presented, Dr. Brooks pointed out that under-counting would be a possibility.

Dr. Kaye responded that OMB typically is not concerned with under-counting. They are more concerned with over-counting.

In having submitted 15 different packages, Mr. Kingon inquired as to how many different OMB desk officers she has dealt with. He noted that one of his last positions at CDC was in the Office of Program Planning and Evaluation, and anytime there was a change in desk officers, one of his jobs was to bring them to CDC to educate them about the agency. Some of them had a public health background, but many did not. A lot depends upon the desk officer and their perspective.

Dr. Kaye responded that she had dealt with about 5 officers, and noted that ATSDR uses the same desk officer as the Environmental Protection Agency (EPA) rather than CDC's desk officer. That also results in education issues sometimes, given that it is still public health.

Dr. Horton emphasized that it was not that ATSDR did not want to share the information that had already been captured. They simply cannot release that information, but hopefully they would hear some good news soon. Any time they attend a public meeting or conference, the first question asked is, "How many people have enrolled?" It is awkward not to be able to let people know.

Mr. Tessaro asked for clarification about who was meant by "they" in terms of the Spring of 2014 publication.

Dr. Kaye clarified that ATSDR Registry staff will perform the analysis, write the report, and disseminate it.

## **Next Steps and Strategies for Enhancing the National ALS Registry for All End-Users: Open Discussion**

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**Robert Kingon, MPA, Facilitator**  
**Carter Consulting, Inc.**

Mr. Kingon indicated that this session is intended to generate open-ended discussion, and that Dr. Antao has prepared some questions related primarily to next steps in terms of releasing the information and in what formats. The questions are as follows:

- ☐ What data elements do you think are vital to disseminate?
- ☐ Would having an online query tool with de-identified aggregate data be useful for the community?
- ☐ What formats should be used to disseminate data?

## **Discussion Points**

Dr. Kasarskis thought of the first question as two-pronged in terms of what would be scientifically interesting and what would have public relations value for sustainability of the Registry. Perhaps the patients for ALS would be the spokespersons for the latter in terms of what the patient public would like to see in terms of the dissemination efforts.

Mr. Harada responded that some raw numbers would be beneficial in terms of how many people have enrolled. He thought the supposition at the outset was 3 per 100,000.

Dr. Kaye clarified that the supposition was 4 per 100,000 prevalence and 2 per 100,000 new cases each year.

Mr. Harada said he thought patients would be interested in some of the scientifically relevant information as well, because it impacts their lives. One question he receives a lot from the community via social media is, "How does enrollment compare to what has been found through medical, VA, and death certificate data?" It would also be beneficial to indicate whether any risk factors have been identified.

Dr. Brooks said he would recommend consideration of the online query tool with de-identified aggregate data. That has been very successful for breast cancer in Finland.

Dr. Antao noted that Dr. Kaye told him that would be a difficult sell for OMB.

Dr. Kaye added that one of the issues for OMB is that the portal data is obviously a subset of everyone, because not everyone registers and not everybody completes surveys. That geography is different from the cases. Having answered the cluster calls for cancer for 10 years, she understood the issue that they did not want people to draw a line based on what may not be very good information. Comparing the people who have registered to those found in the databases, the geographic distribution is very similar. Comparing people who complete surveys versus those who do not, there is no difference in individual states. ATSDR does not have permission from CMS or the VA to distribute their data.

Dr. Antao noted that perhaps they could share distribution by gender, age groups, et cetera and not geography.

Dr. Brooks recommended beating the competition within CDC. They should assess what was presented for deaths through 2009 to come up with something that supports it or is different. That is a major hurdle for ATSDR.

Dr. Gubitz requested clarification about the format in which data would be released, in terms of whether there would be something placed on the website that the patient community could read (e.g., a status report of registry), or if the release would be through peer-reviewed more research style papers. She also inquired as to when the datasets would become fully available to the research community, epidemiologists, and others for high level data mining.

Dr. Antao responded that they hope to disseminate all of those items. The plan is to develop reports, publications, and make data available for researchers that would go through the research committee.

Dr. Horton pointed out that the federal government in general, at least at ATSDR/CDC, is trying to move away from large reports. No one wants to read a 50- or 100-page report. The

approach has been to publish in peer-reviewed journals. Given that ATSDR has a lot of data, especially in terms of risk factor data, he envisioned that much of those data would be submitted for publication in peer-reviewed journals. It is possible that a basic report could be developed with numbers of cases, incidence, prevalence, et cetera. Or perhaps they could create a fact sheet that is easily digestible. He invited suggestions during or after this meeting.

Dr. Bruijn noted that one confusing issue is that it is unclear what the current predicted prevalence and incidence numbers really mean. Even on their own websites, they do not have figures that gel with NINDS entirely. All of that is complicated even for a scientific researcher, so for the lay community it is quite difficult. She thought as a community it was important to understand what the numbers really mean.

Dr. Bruijn pointed out that one thing they must remember is that it is unlikely a particular risk factor will be highly apparent from the Registry. The Registry will offer some interesting clues, which researchers and scientists will have to further explore and validate. While everyone has an expectation that the answer will be clear and solid from the registry, she believes it is a stepping stone to a lot more investigation. She thought they should be very clear about communicating this message.

Dr. Horton indicated that as soon as ATSDR releases the first set of findings, they envision making the de-identified datasets available to researchers who request them. This likely will be done through the committee mechanism. Consideration is being given to whether a de-identified dataset should be placed on the website for people to download, or if they should go through the committee.

Dr. Boylan suggested considering taking the approach that is sometimes seen in peer-reviewed papers now. For example, if a paper reports granular data on a patient set, it is considered supplemental data that becomes available and is posted with the electronic version of the manuscript so that people can download it for hypothesis testing. He suggested trying to democratize this to make it easy for investigators to access the data, especially if it has already been peer-reviewed.

Dr. Bowser pointed out that various levels of and venues for dissemination must be considered. When mention was made earlier of a publication, it was unclear to him where that would be disseminated. If a report is just on the website, perhaps only the same tech savvy people who might have registered and completed surveys will see it versus those who do not have access. Given the initial intent of the Registry, the first top level approach might be a shout out to say "Look, in the last X years we have registered X number of people in every state. We accomplished what we planned. We were successful. Thanks to everyone who participated across all of the states." That could be followed by dissemination of a multitude of different types and levels of reports at different time intervals, which would allow people to digest the highest level of information first. Subsequent reports could share incidence and prevalence ratios that were observed from the data across all of the states. That could be followed by reports that dig deeper into the metro reports. This would guide readers through the process. A multitude of people are going to look at the data, some who are more savvy and some who are less. If heavy detailed reports are quickly disseminated, most people will be lost.

Dr. Kasarskis stressed that what Drs. Bruijn and Bowser said was crucial. He could see the danger in releasing the report as being perceived as, "We have arrived on the mountain top, and now this is a done deal." Rather than a finished product, this is a milestone. The first 10,000 people could be labeled as ALS Registry Pioneers. Any reports that are distributed

should be used to generate enthusiasm for patients around the country to work with the Registry to make it grow. Information should be released about plans for the future (e.g., work being done to refine questions, biorepository work) to educate the public in general about how all of this fits into a puzzle. There is a danger in fizzling interest when the report is just a step along the way versus a definitive answer. It is a matter of educating the public about how all of this fits into getting answers to why ALS occurs. That is really crucial to build enthusiasm for the Registry among the public.

Dr. Berry pointed out that it was also important to recognize that as researchers look at these data, what they will need in order to perform further analyses are very good descriptions of the methods. Publishing a methods paper about how the Registry was developed, how the data were collected, and guiding researchers to where there are and are not data to support the analyses they may want to perform will be very important. It is difficult to get methods papers published sometimes, so perhaps that could be matched with the top line results to develop one manuscript that informs the scientific and patient communities.

Dr. Sorenson did not think for this project getting a methods paper published would be a problem.

Dr. Kowall pointed out that when ATSDR is finally allowed to release some specific data, that would be a major opportunity to leverage further enrollment. There should be a lot of strategic thinking about what could be said in press releases, various media, national television, et cetera that will likely be seen by people who otherwise might not be aware of the Registry. Consideration should also be given to alternate methods to enroll via telephone or paper. ATSDR must capitalize on what will be a fleeting opportunity.

Dr. Horton indicated that when CDC/ATSDR is working on site-specific or disease-specific findings, they develop a communications plan. If it includes other stakeholders, such as with EPA, shared talking points are developed so that everyone is in harmony. He anticipated a similar effort when the Registry data are released. Undoubtedly, everyone associated with ALS will start receiving phone calls (e.g., ATSDR, ALSA, MDA, Les Turner) and they should all be harmonious in their communications plans.

Mr. Harada said he thought that what patients really wanted was knowledge for ammunition, meaning that many patients do not believe that this is as rare a disease as currently described, and that it does not receive the funding or attention that it deserves. He agreed with the comments about managing expectations and enthusiasm levels, but emphasized the importance of remembering that the reality of this disease is that the public is constantly changing and evolving.

Dr. Traynor agreed with Mr. Harada in that he thought they needed to start moving away from the idea of calling ALS a rare disease, especially in the context of two pieces of information. First, lifetime risk of ALS is about 1 in 450 to 1 in 500. That is a significant number, especially when compared with other neurodegenerative diseases. Second, all of the estimates for incidence of ALS are based on a diagnosis of ALS. They do not include the other end of the clinical spectrum, namely frontotemporal dementia (FTD). If ALS and FTD are considered to be one disease, incidence increases appreciably. The most common neurodegenerative disease is probably Alzheimer disease (AD), the second is Parkinson's disease (PD), the third is FTD, and the fourth is ALS. Combining FTD and ALS suggests how common this might be.

Dr. Kasarskis suggested it may be helpful to the public for ATSDR to articulate some clear goals or milestones for the 5- to 10-year period. This would help people to understand that this is an organic, living, expanding effort rather than something static. Every stock coming also publishes "Forward Thinking Statements" and labels them that way. Given all of the exigencies of OMB, it would be beneficial to state some realistic milestones. This is an educational piece for the public. ATSDR could discuss the hurdles, which is important because patients may not have any insight into OMB and IRB issues. To some degree, ATSDR needs to communicate the fruits of all of the lobbying efforts and the labor of the patients, patient services organizations, and others. The statements would also be communicated to funding agencies, Senators, et cetera.

Mr. Gibson agreed that this is important, but cautioned ATSDR. Once data can be released, he suggested that it would be as important to go back to show what they have learned in infographics and high level discussion. Some people are focused on prevalence or how many people have this disease. That is important, but is not the sole focus and is one reason this registry is not an MS/ALS registry. The MS folks really wanted the numbers and already had a powerful research engine. They did not need this to be what they already had. He thought it was important to share lessons learned along the way, because there will be a lot of important findings that if not shared, people will say, "You have this database. It's worth how much?"

Mr. Wildman underscored the importance of communicating that this is definitely an ongoing project. He remembered when the portal went live in 2010 and the comments they received about the surveys not asking the questions that PALS wanted to answer. ATSDR responded to this and is adding new surveys, including the open ended survey where people can enter what they think contributed to their ALS. Some of the new surveys were developed based on feedback from people with ALS. It is important to communicate that, and that they are part of this process.

Dr. Brady suggested that it would be important to highlight that ATSDR has also released a broad agency announcement. Many people are waiting to hear about studies that may be funded going forward that are tied into the Registry. When the data are released, they should also highlight all of the research that has been funded that is or is going to make use of the Registry. It is important to show that the Registry is being tapped into and enhanced with specific research projects. ATSDR has to show that it is giving back.

Dr. Boylan pointed out that highlighting and discussing to the extent possible the additional studies being facilitated through the notification process is also an important way to make people aware of other registry efforts and show broadened impact beyond just the initial registry effort.

Dr. Horton indicated that consideration was being given to adding a page on the website that lists all of the studies ATSDR is supporting, as well as the research being conducted by investigators who are recruiting through the Registry. There is a lot of value in sharing that information with the public and Congress.

Dr. Nelson pointed out that people will also be interested in geographic distribution, and inquired as to the lowest level of geographic resolution at which ATSDR planned to present the data (e.g., prevalence or incidence variation by state or region of the country).



Dr. Kaye responded that initially, the data would be reported at the US level. If she understood her conversations with OMB correctly, reporting prevalence and incidence variations by state or region would require subsequent permission for the portal and national dataset data.

Dr. Horton added that while ATSDR has had internal discussions about the importance of reporting at least down to the state level, they will have to assess OMB's latest terms of clearance.

Dr. Brady stressed that ATSDR had a room full of people who would gladly come to their support if they found they were struggling.

Dr. Brooks pointed out that CDC has already reported state level data on deaths.

Dr. Kaye said she had a conversation with the people doing the death data for ALS, and they were having problems with the death certificates, so she thought they were pooling it. The issue is that for the Registry, ATSDR is combining data that are not traditionally used (e.g., billing data) and self-reports that have not been verified. There are some concerns that there may be geographic variations in who receives Medicaid services, for example, which would have absolutely nothing to do with the disease itself but may have to do with the ability to complete all of the paperwork to obtain benefits. OMB wants to make sure that ATSDR shows that they do not believe issues such as this are occurring before they start disseminating data. If ATSDR can show that those are not confounders, then OMB will permit the state level data.

Mr. Wildman mentioned that one purpose of the state and metro projects was to verify the completeness of the national registry and determine whether there were gaps.

Dr. Kaye added that the state and metro projects might be able to address the issue regarding whether large groups of people are being missed when combined with the information supplied by the doctors who are not being captured in either self-reports or the national dataset. OMB approved that data collection as well, so combining all of those things together will hopefully make a convincing argument.

Dr. Weisskopf indicated that he also does some work in autism, and pointed out that CDC routinely publishes the changing rate in autism. There are plenty of questions over whether that is real. He wondered why ALS was different.

Dr. Kaye responded that they do not have OMB clearance for that activity, and probably did not have to get it because of the way they are collecting the data. If they did not have to acquire OMB clearance, then OMB cannot tell them they cannot report that. ATSDR was issued a clinical exemption for the biorepository because the only data being collected from individuals has to do with lab processing (e.g., time the specimen was drawn, whether hair is permed or colored, et cetera) to interpret the lab results. Because they received a clinical exemption, they did not have to submit a package to OMB or receive any terms of clearance, and can release any data they think is appropriate.

Dr. Abrams asked whether the assumption should be made that the information that is released about the Registry may or may not affect funding through NIH or the Department of Defense (DoD). Constituents frequently ask what they can talk to their legislators about. If constituents are being asked to support the Registry, they will ask how that will affect funding down the line for other efforts.

Mr. Gibson thought this was a great point, and pertained to what was said earlier about communications plans. It is important to be very thorough about what the data mean and do not mean. He could already envision some disagreements about the numbers. One ALS organization now says 40,000 people have ALS, but has no background about that number. Their thinking is because people are living longer on ventilators, but that may or may not be true. This disease is so horrific; many people have been left to develop their own theories. Therefore, it is critical to be careful with how information is communicated.

Dr. Bruijn thought that communication could also be focused in the opposite direction to make a very positive statement about how the Registry has demonstrated the need for more funding from different areas, and for even engaging the National Institute of Environmental Health Sciences (NIEHS) again where there are opportunities to conduct studies.

Mr. Gibson stressed that this is why we need to focus on the research and not simply the numbers. As they say on Capitol Hill, "Tell your own story." If ALS numbers are compared to Alzheimer's or Parkinson's, they are very small. However, discussing what it is like to live with ALS levels the playing field in terms of garnering more resources.

Mr. Tessaro disagreed. He said he thought a lot of different groups could do whatever they wanted to with the data, because everyone has a hundred different reasons for the data. While he could not answer for the one person in Nevada who is a donor and feels like he is out of the loop, to try to do an inside, top level control of the data might satisfy a couple of desires, but will miss the large community. He was much more interested as a PALS to have and then parse it whichever way he wanted. He would hate to have someone limit or be overly cautious about what he could see in order to answer a small problem.

Mr. Gibson clarified that he did not say to limit the data. He was not saying not to share, but was rather saying to be very explicit about what is being shared and what it means to provide the necessary narrative around the data release.

Ms. Charleston asked whether CDC could partner with more state departments of public health in order to acquire more information at the state level.

Dr. Kaye replied that unless ATSDR decides to conduct a new project, the state and metro projects have concluded.

Ms. Charleston inquired as to whether this could be considered in the future to expand the Registry or work on getting more data.

Dr. Kaye responded that unless the state public health departments were willing to share identifiable data, it was unclear how this would help the Registry. ATSDR is not allowed to add any new registrants identified in the state or metro projects, because the purpose is for comparison only.

With respect to moving forward, Dr. Brooks noted that one issue is getting information into the Registry. They heard about the iPad app for finding clinics, but more apps and different media are needed to get the data into the Registry. He liked Dr. Kasarskis's idea of a 5-year plan. They should be looking forward to be responsive to the different types of media, how to get younger people involved, et cetera. He thought the WWII observation made by Dr. Weisskopf needed to be resolved. The VA has defined that there was a Gulf War I hit, but there may or may not have been a Korean War hit, and that has to be resolved. He asked to what degree the

ATSDR registry is working with the Millennium Project, which is the military aspect of all of this, particularly since ALSA is pushing the military connection.

Dr. Horton said that he could not speak to the Millennium Project. The military module drills down by branch of service and wartime theatre deployments, so they will likely be able to capture Vietnam versus other deployments.

## Closing Remarks

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**D. Kevin Horton, DrPH, MSPH**  
**Chief, Environmental Health Surveillance Branch**  
**Division of Toxicology and Human Health Sciences**  
**Agency for Toxic Substances and Disease Registry**

Dr. Horton thanked everyone for attending, and expressed ATSDR's gratitude for them taking the time out of their busy schedules. He emphasized that their feedback is vital in terms of making the Registry better. While it was always good to hear feedback in person, he reminded everyone that there is a feedback link on the web site that anyone can use to send the Registry Team an email. The Registry Team reads every comment and, where feasible, implements reasonable recommendations that can help the Registry. He also welcomed those who were new to the group, such as Wendy Abrams from the Les Turner ALS Foundation. This is a very important organization, especially in Chicago, so ATSDR looks forward to working with her and her group moving forward. He thanked the existing partners such as MDA and ALSA, emphasizing that their assistance is critical in helping to move the Registry forward. Dr. Horton thanked Dr. Brooks for discussing the AAN initiative. Obviously, ATSDR is willing to help with that effort in any way they can. He also expressed gratitude to the PALS who attended, and acknowledged the challenges they may have faced in doing so. He thanked them and their caregivers who escorted them to the meeting for their time and effort, and called for a round of applause for all of them.

Dr. Horton expressed his hope that everyone could understand some of the challenges that the Registry Team faces as a program and as a registry. It is easy for people on the outside to jump to conclusions and say that ATSDR is not moving quickly enough. In reality, it is the opposite. They are moving as quickly as they can, but there are many limitations and hurdles (e.g., IRB, OMB, et cetera). They want the data out the door as quickly as anyone, including the patients. That being said, he thought they were getting close to turning a corner. Many participants have been attending these meetings for years, and perhaps in the beginning it was difficult to see the "light at the end of the tunnel." However, hopefully after some of the presentations during this meeting they could see that they were getting close to the "finish line" but there remained a number of activities that ATSDR must complete before they can cross the "finish line." He expressed his hope that by this time next year, the data will have been released and there can be discussions about where to go from there.

In terms of the findings, based on the presentation from Ms. Sanchez, the national administrative data approach is working to capture thousands upon thousands of cases. This is good news for the Registry. Hopefully, when that is coupled with the web portal data, ATSDR will be able to complete its first dataset. Being able to share the data is obviously one of the goals of the Registry. Whenever analysis is completed of a specific component of the Registry, the plan is to disseminate it as soon as possible. People are very eager for the data, especially PALS, and ATSDR is eager to publish the data. He thought by the end of the year some of the

state and methods papers would be published. He reminded everyone that while ATSDR is asking a lot of questions through the survey modules, there are many other questions that are not being asked through this mechanism. For that reason, they want researchers to use the Registry as a recruitment tool to answer whatever questions PALS have. This tool was developed to help PALS and researchers connect. He expressed his hope that researchers would take an active part in the process by developing hypotheses and using the Registry as a recruiting tool.

ATSDR is very excited about the biorepository pilot study. Some people think they are just counting cases. While they are doing this, they are also engaged in a lot of other efforts they believe will enhance the Registry. He emphasized that the purpose of the biorepository pilot study is to determine whether it will be feasible to take this to scale. ATSDR does not want to use taxpayer money to duplicate what someone else has done. However, if they can show that there is a need for a full-blown biorepository that will help fill gaps, obviously consideration needs to be given to moving forward with that. Dr. Kaye's group has been investigating what other biorepositories exist and what they capture. Perhaps there is not a need for ATSDR to have a biorepository, but they do not know this yet. Nevertheless, it is still exciting to see that PALS around the country, with the help of ALSA and MDA, are taking this seriously and are donating blood, tissue, and hair. They have also had their first brain donation. That is incredible and speaks volumes to how dedicated the PALS are in this effort. ATSDR is also supporting other valuable studies, and it is important to highlight that work as well.

Promotion of the Registry is critical. ATSDR was not so naive to believe that all they had to do was build it and people would come. They know that people are diagnosed with ALS every day, and they really need to get in front of them. The help from organizations is greatly appreciated, and the peer-to-peer approach is fantastic. As soon as the peer videos emerge from IRB, they will be uploaded. There must continue to be a collaborative effort to sell the Registry every day, and make people aware of how critical this initiative is. ATSDR hopes to bring the results of the state and metro surveillance project online in the fall. That will be a good starting point, because once papers start being published, ATSDR will be at the point of releasing the first report. It is also important to seize upon new and emerging technology to sell the Registry, whether it is through a new app or giving MDA and ALSA tablets so they can take the Registry to the people. MDA and ALSA have also done a good job of re-tweeting ATSDR's tweets and having their own tweets about the Registry. As mentioned, everyone must be harmonious and strategic about how the data are released and in what format. Over the next 6 months or so, ATSDR will reach out to everyone for more feedback and for assistance in developing talking points for everyone's use. When the data are released, it is very likely that everyone will begin receiving calls, so it is important to prepare for that.

With no further business posed or questions and comments raised, Dr. Horton wished everyone safe travels and officially adjourned the 2013 Annual ALS Surveillance Meeting.

## Participant Roster

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**Wendy Abrams**

Executive Director  
Les Turner ALS Foundation  
Skokie, IL 60077

**Vinicius Antao, MD, MSc, PhD**

Registries Team Lead  
Surveillance and Registries Branch  
Division of Health Studies  
Agency for Toxic Substances & Disease  
Registry  
Atlanta, GA 30341-3717

**James Berry, MD, MPH**

Neurology  
Massachusetts General Hospital, East  
Charlestown, MA 02129

**Marianna J. Bledsoe, M.A.**

Independent Research Professional/Consultant  
Silver Spring, MD 20904

**Robert Bowser, PhD**

Chair and Professor of Neurology  
Barrow Neurological Institute  
Phoenix, Arizona 85013

**Kevin Boylan, MD**

Director, ALS Center  
Department of Neurology  
Mayo Clinic  
Jacksonville, FL 32224

**Christopher "Kit" Brady, PhD**

Director, Scientific Operations  
VA Biorepository (151C)  
VA Boston Healthcare System  
U.S. Veterans Administration  
Boston, MA 02130

**Benjamin Rix Brooks, MD**

Director  
Carolinas Neuromuscular/ALS-MDA Center  
Department of Neurology  
Carolinas Medical Center  
University of North Carolina School of Medicine  
Charlotte, NC 20807-1885

**Lucie Bruijn, PhD, MBA**

Chief Scientist  
The Amyotrophic Lateral Sclerosis Association  
Washington DC 20005

**Alicia Charleston, MPH**

Massachusetts ALS Registry Coordinator  
Massachusetts Department of Public Health  
(MDPH)  
Boston, MA 02108

**Jay Dempsey, MED**

Health Communications Specialist  
National Center for Environmental Health/  
Agency for Toxic Substances & Disease  
Registry  
Atlanta, GA 30341-3717

**Steve Gibson**

Chief Public Policy Officer  
The Amyotrophic Lateral Sclerosis Association  
Washington, DC 20005

**Amelie K. Gubitz, PhD**

Program Director, Neurodegeneration  
National Institute of Neurological Disorders  
and Stroke  
National Institutes of Health  
Bethesda, MD 20892

**James Handsfield, MPH**

Retired/Statistician/Consultant  
Centers for Disease Control and Prevention  
Office of Surveillance, Epidemiology and  
Laboratory Science  
Public Health Surveillance and Informatics  
Program Office  
Atlanta, GA 30333

**Ted Harada**

Board Member/Georgia Chapter ALS  
Association  
Atlanta, GA 30329

**Thomas Hicks**

Public Health Advisor  
Carter Consulting, Inc  
National ALS Registry Program  
Agency for Toxic Substances & Disease Registry  
Atlanta, GA 30341-3717

**D. Kevin Horton, DrPH, MSPH**

Chief  
Surveillance and Registries Branch  
Division of Health Studies  
Agency for Toxic Substances & Disease  
Registry  
Atlanta, GA 30341-3717

**Val Kapil, MD**

Acting Deputy Director, Chief Medical Officer  
CDC/NCEH/ATSDR  
Atlanta, GA 30341

**Edward J. Kasarskis, MD, PhD**

Professor, Neurology  
University of Kentucky and VA Medical Centers  
Kentucky Clinic  
Lexington, KY 40536-0284

**Wendy E. Kaye, PhD**

Senior Epidemiologist  
McKing Consulting Corporation  
National ALS Registry Program  
Agency for Toxic Substances & Disease  
Registry  
Atlanta, GA 30341-3717

**Robert Kingon, MPA**

Facilitator  
Carter Consulting, Inc.  
Rapid City, MI 49676

**Neil Kowall, MD**

Chief of Neurology and Professor of Neurology  
VA Boston Healthcare System and Boston  
University  
Boston, MA 02130

**Jane Larkindale, DPhil**

Muscular Dystrophy Association (MDA)  
Tucson, Arizona 85718

**Carolyn Minnerly**

Director of Outreach Services  
Muscular Dystrophy Association (MDA)  
Tucson, Arizona 85718

**Oleg I. Muravov, MD, PhD**

Medical Epidemiologist  
National ALS Registry Program  
Agency for Toxic Substances & Disease  
Registry  
Atlanta, GA 30341-3717

**Ed Murray, PhD**

Acting Director, Division of Toxicology and  
Human Health Sciences  
Agency for Toxic Substances and Disease  
Registry  
Atlanta, GA 30333

**Lorene M. Nelson, PhD**

Associate Professor, Division of Epidemiology  
Department of Health Research & Policy  
Stanford University School of Medicine  
Stanford, CA 94305-5405

**Rebecca D. Pentz, PhD**

Professor of Research Ethics  
Emory School of Medicine  
Atlanta, GA 30322

**Meraida Polak, BSN, RN**

Director of Clinical Research  
Emory ALS Center  
Atlanta, GA 30322

**Marchelle Sanchez, MS**

Health Scientist  
Agency for Toxic Substances and Disease  
Registry  
Division of Toxicology and Human Health  
Sciences  
Environmental Health Surveillance Branch  
Atlanta, GA 30341

**Judith "Judy" Smith**

Public Health Analyst  
National ALS Registry Program  
Agency for Toxic Substances & Disease  
Registry  
Atlanta, GA 30341-3717

**Eric Sorenson, MD**

Mayo Clinic  
Rochester, MN 55905

**Shari Steinberg**

Epidemiologist  
Centers for Disease Control  
Atlanta, GA 30333

**Edward Tessaro**

Retired/Philanthropy  
MDA for ALS/St. Jude's Hospital/CF  
Alpharetta, GA 30005

**David J. Thurman, MD, MPH**

Medical Epidemiologist  
Neurology/Epidemiology  
National Center for Chronic Disease Prevention  
and Health Promotion  
Centers for Disease Control and Prevention  
Atlanta, GA 30341

**Bryan Traynor, MD**

Investigator  
National Institute on Aging  
Bethesda, MD 20892

**Laurie Wagner, MPH**

ALS Surveillance Specialist  
McKing Consulting Corporation  
Atlanta, GA 30341

**Marlena Wald, MPH**

Consultant, CACI-Emergent  
NCEH-ATSDR  
Atlanta, GA 30341

**Marc Weisskopf, PhD, ScD**

Associate Professor  
Harvard School of Public Health  
Dept. of Environmental Health, EOME  
Boston, MA 02215

**Patrick "Pat" Wildman**

Director, Public Policy and Communications  
The Amyotrophic Lateral Sclerosis Association  
Washington, DC 20005

**Joe Wise**

Rineyville, KY 40162