

**Centers for Disease Control and Prevention
Agency for Toxic Substances and Disease Registry**

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



**September 1, 2011
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.

**Centers for Disease Control and Prevention (CDC)
Agency for Toxic Substances and Disease Registry (ATSDR)**

**Annual ALS Surveillance Meeting
September 1, 2011**

Theme / Purpose

Theme: Enhancing the National ALS Registry for all end-users.

Purpose: Updating stakeholders on the progress of the National ALS Registry and discussing strategies to further enhance the Registry.

Welcome and Introductions

**Jim Sacco, Facilitator
Atlanta, Georgia**

Mr. Sacco called the meeting to order, welcoming everyone and thanking them for their time and participation. He reviewed housekeeping and logistics, and then requested that everyone introduce themselves and state their role in the ALS Registry. The participant list is located at the end of this document.

Opening Remarks

**Christopher J. Portier, PhD
Director, Agency for Toxic Substances and Disease Registry/
National Center for Environmental Health**

Dr. Portier extended his welcome and gratitude to those in attendance, offering special thanks to Rob Tison and Rick Dumas, persons with ALS (PALS). He acknowledged that it is sometimes forgotten that these types of activities are intended for public health and public good, especially for those who are directly affected by these types of diseases. It is known that ALS is a devastating disease not only for the people who have it, but also for their families, friends, colleagues, and loved ones.

ATSDR's ALS Registry has accomplished incredible successes in just under a year, and Dr. Portier expressed his extreme pride in what the team developed during this short timeframe. There have been registrations from all 50 states during that period, demonstrating that the ALS Registry is truly national in scope. While there is currently no known cause of ALS, everyone is hopeful that with this registry in place and the numerous related activities, this groundbreaking effort will permit better understanding of the disease that leads to effectively curing or preventing it.

In conclusion, Dr. Portier emphasized the exciting new initiatives that the participants would hear about throughout the day, and stressed the importance of a bioregistry for future research. He apologized for having to make an early departure to attend a number of meetings, explaining that ATSDR was in the process of reorganizing and restructuring.

G. David Williamson, PhD
Director, Division of Health Studies
Agency for Toxic Substances and Disease Registry

Dr. Williamson added his welcome and appreciation for those in attendance, indicating that the annual ALS meeting is one of the most rewarding days of his year. He reminded everyone that during the first meeting, he talked about making “baby steps” but that at some point, they would make a “giant step.” This year marks the year of the “giant step.” This ALS Registry has received significant positive publicity, thanks to all who have helped to make it a reality. Nevertheless, the registry effort has reached only the “tip of the iceberg,” and there is much more work to do. Having this registry in place represents an opportunity to characterize the disease, as well as the people who have the disease. This registry is anticipated to make a difference, and Dr. Williamson thought that in a couple of years, they would look back and say, “What another giant step we have taken.” ATSDR believes the ALS Registry will serve as a model for other diseases and exposure registries.

He thanked everyone for all of the collaborations and the leadership they have provided to the registry to make it a reality. ATSDR continues to work to improve its relationship with current collaborators, and seeks opportunities to collaborate with others who are not yet involved. He noted that ATSDR relies on those who are involved to identify additional potential partners who should be brought into the fold so that they can contribute to this massive and important effort. There has also been increased participation and interest within CDC, and Dr. Williamson thanked their CDC colleagues for their support.

Discussion Points

- On behalf of patients with ALS and the Amyotrophic Lateral Sclerosis Association (ALSA), Mr. Gibson thanked Dr. Williamson and his team for all of the help they have provided for the registry. ALSA has been involved from the outset, and has had the opportunity to observe the “baby steps” it took to reach the current status of the registry. He stressed that diligent work is being done to continue to help enhance the system and help deliver some of the clues.
- Mr. Dumas wondered whether they might have the approval of the government to make a video that could be distributed to neurologists and other doctors to show the value of registering patients in ATSDR’s ALS Registry. He thought a gentle message that demonstrated value would increase the number of registrants by 10-fold.
- Dr. Horton responded that while anyone could launch a registry or surveillance system, one of the greatest challenges is to keep the message building, keep it alive, and keep it fresh. ATSDR tries to do this on a daily basis, but this is not just an ATSDR mission. It is a collaborative effort that takes everyone in the room and their respective organizations to get the word out. ATSDR does have the capability to create a video. They have made a video that is currently posted on the ATSDR website, and they hope that others will post it on their sites as well. ATSDR is trying to determine how to link the video made by Mr. Dumas that is on YouTube to the ATSDR site. It is one thing to have a government bureaucrat asking

people to take part in the registry, but it really drives home the importance when PALS make videos on behalf of the registry. People are getting the message, because they are giving ATSDR constructive criticism and recommendations. ATSDR assesses both to determine whether they are reasonable and feasible, and then tries to move forward to address criticisms and recommendations.

Overview of the National ALS Registry

D. Kevin Horton, DrPH, MSPH
Chief, Surveillance and Registries Branch
Division of Health Studies
Agency for Toxic Substances and Disease Registry

With regard to how the ALS Registry project originated, Dr. Horton emphasized that ATSDR does not simply jump into a project. For any study or surveillance activity, the agency begins with a feasibility assessment or study to ensure that for whatever method will be used, the research is sound and scientific. The ALS Registry was no different. ATSDR conducted four pilot projects during 2006 through 2009 in Minnesota at the Mayo Clinic, in Georgia at Emory University, in South Carolina by the State of South Carolina, and in an HMO consortium. The purpose of the pilot projects was to determine the feasibility of populating a national ALS registry using data from existing national databases, including Medicare, Medicaid, Veterans Benefits Administration, and Veterans Health Administration. These databases represent approximately 90,000,000 Americans. ATSDR entered into agreements to receive data on an annual basis from these sources; however, this was not an easy undertaking. Just because ATSDR is part of the federal government does not mean that government agencies will readily share their datasets. While there were challenges, ultimately the agreements were solidified.

Using data from the pilot projects, an algorithm was developed to identify people with ALS, which was then applied to these large national databases. The algorithm consists of a combination of select criteria such as ICD-9 code 335.20 (for ALS), Rilutek® use, and frequency of patient visits to a neurologist. It is known that ICD-9 codes contain coding errors, so they could not rely on these alone. It is also known that there is a high probability that people who take Rilutek® and those who make frequent visits to a neurologist may have ALS. The algorithm classifies patients into the following three groups:

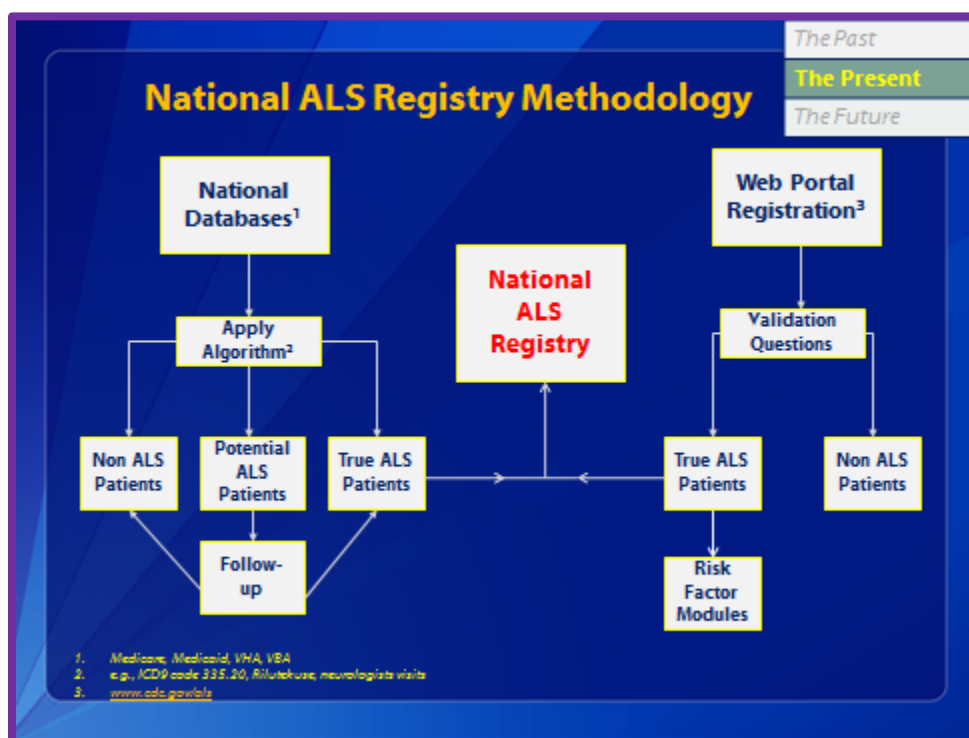
- ☐ True (it is clear from the algorithm that a person has ALS)
- ☐ Potential (there is insufficient evidence to place someone in a definitive or non-definitive category)
- ☐ Non-ALS (those that are clearly not ALS are not included in the registry)

Potential cases are not removed and are reevaluated when subsequent year's worth of data is received from Medicare, Medicaid, and the VA.

ALS is not a disease that requires mandatory reporting, but ATSDR believes that the ALS Registry Act is the next best thing because it set in motion ATSDR's opportunity to move forward to create and maintain an ALS registry. The ALS Registry Act was enacted as Public Law 110-373 in October 2008. It directs ATSDR to establish and maintain the only national population-based ALS Registry in the United States (US). The purpose of the registry is to

describe the incidence and prevalence of ALS, describe the demographics of PALS, and examine potential risk factors for the disease. Current information regarding prevalence and incidence is based on small studies that are extrapolated to the US. The beauty of the ALS Registry is once it includes a complete years' worth of data and subsequent data, it will provide insight about the true burden of ALS in the US. In Dr. Horton's opinion, one of the most important pieces of the registry is the ability to assess the potential risk factors for ALS. There are numerous theories pertaining to what causes ALS. ATSDR is moving forward to collect information about a person's disease through risk factor surveys. The surveys ask questions about military service, occupation, demographics, family history of ALS, et cetera that may shed light on potential causes. ATSDR is very pleased with responses from PALS. A significant amount of risk factor data has been collected, which is largely due to groups such as ALSA, the Muscular Dystrophy Association, the scientists in the room, and patients telling people how critical this registry is.

The ALS Registry methodology is depicted in the following graphic:



The registry takes a two-pronged approach, the first of which is the algorithm. Because not everyone will appear in the large national databases, it was important to have another mechanism to identify cases. To that end, a National ALS Registry web portal was created. Patients can enroll directly through the web portal by answering a series of previously validated/vetted questions, which helps ATSDR ensure that no one is “falling through the cracks.” A very important component of the web portal is that once a patient enrolls, he or she can take the brief risk factor surveys on-line. As with the algorithm approach, patients enrolling are categorized into True and Non-ALS cases. True patients are included in the registry and can go on to respond to the risk factor modules. These data can be obtained and analyzed quickly, and can

then be compared against the national database. Merging of the national data with the web portal data is the method by which ATSDR will arrive at the first complete dataset.

New registry initiatives include state/metro-based ALS surveillance projects; a feasibility study of a national ALS Bioregistry from enrolled PALS (e.g., collecting blood, tissue, CSF); ALS Registry clinical trials notification mechanism; and new ALS risk factor surveys. ATSDR is especially excited about linking patients directly with researchers, particularly given that it can be difficult for researchers to recruit people into clinical trials.

Discussion Points

- Dr. Gubitza wondered whether there is a mechanism in the registry for patients to provide longitudinal data about their disease progression.
- Dr. Horton replied that there is a “Quality of Life” module that tracks a person’s disease over time. Patients are asked to take this module twice a year, while they are asked to take all other surveys one time. Once they take the “Quality of Life” module, it is grayed out. After 6 months, PALS receive emails indicating that it is time to take their quality of life module, and the link to the module is reactivated. PALS have been taking the survey at their 6 month anniversaries. Some PALS have mentioned that they are not receiving these emails, so ATSDR is working on this issue. It would be very helpful for everyone to help the agency remind people that this module is available and that ATSDR would like them to take it twice a year.
- Mr. Tison inquired as to when estimates for prevalence and incidence from the registry might be expected, and whether there is a method to determine percent of PALS registering at the web portal.
- Dr. Kaye responded that they will be able to do this, but it will be a little bit longer before this is possible because they have to merge what is in the portal with national data to have a full year of information. They will also be able to determine what percentage of PALS register. People will be linked so that they are included only once.
- Dr. Horton acknowledged that this is not a quick process and that people with ALS do not have a lot of time and want to know what the numbers are. While ATSDR wants to let people know what the numbers are, it is an ATSDR policy and a public health surveillance policy that data have to be complete before they are released. ATSDR wants to be able to give a complete, population-based picture of the true incidence and prevalence of this disease. They hear the concerns loud and clear about how long the process is taking. It is not that it is taking ATSDR a long time—this is a classic public health approach. For example, when cancer registries first began, it was two to three years before the first dataset was published. It is important to ensure that the data are correct and complete.
- Mr. Tison requested a forecast date for incidence and prevalence estimates.
- Dr. Horton replied that the answer is not easy. The web portal went live in October 2010. Usually, surveillance systems or registries operate on a calendar year. ATSDR is taking the same approach, so when they release the first year’s worth of data; they want it to be for a full calendar year. However, they have to at least get through the end of 2011 to have a

complete year of data from the portal. The complication is that some of these administrative databases have a lag of a year or more. It will probably be around the first quarter of 2013 before ATSDR will be able to release any numbers.

- Dr. Kaye added that the VA is not an issue. Given that the VA uses electronic medical records (EMRs), ATSDR receives data from them largely in real time. The problem is with Medicare where a large number of cases are coming from, and for which there is approximately a 2-year lag. They have a new contractor, so that lag time is getting much shorter. She agreed that it would probably be around 2013. There is a rating system for state cancer registries. States receive the highest rating if they can publish their data within 18 months of the close of year. That would mean that data for the 2011 calendar year would be available in the summer of 2013. ATSDR is aiming for something in that timeframe, and quicker if possible because they are aiming for the best.
- In terms of merging the portal and database information to create a new database, Dr. Brooks wondered what the half-life of that new database would be and how the views of the registry would be updated.
- Dr. Horton replied that once the first years' worth of data is released and they get into a routine, theoretically they will be able to release data on a schedule similar to that of the cancer registry. That is, an annual update is anticipated. In terms of making the data public, ATSDR anticipates letting scientists have use of these data; however, ATSDR has made it clear from the outset that the agency takes privacy and confidentiality to the extreme, so these will be de-identified data.
- Dr. Bowser asked how they would ensure that a patient is not enrolled twice. For example, a patient may have moved from the VA in Boston to Wisconsin and self-registered.
- Dr. Horton responded that personal identifiers (e.g., social security numbers) are being utilized for the administration databases. For the web portal, those registering are asked for the last 5 digits of their social security numbers. ATSDR will be able to merge on that to ensure that a person is not counted twice. Regardless of whether someone thinks they are in one of the large national databases, everyone is being encouraged to enroll in the web portal, primarily because ATSDR would like for them to complete the surveys.
- Mr. Gibson pointed out that while prevalence and incidence are important components of the registry, it was also emphasized from the outset that it is important to allow researchers to have access to information collected. He wondered when it would be possible for researchers to see what has been collected in terms of the entire registry rates collected this far, including the pilot projects and the biorepository.
- Dr. Horton responded that at this point, the bioregistry is a pilot. They have to make sure that it does what they think it will do. Data are not being collected for the bioregistry for ATSDR. There are others who are experts at analyzing blood and tissue, so ATSDR wants to make sure that biological samples are allocated to those who want to analyze them. There will be a process to ensure those making requests are who they say they are. The data are being collected so that the scientific community at large can use them. Data are being rolled out in phases, so data from ATSDR's dataset will be published before anything will be released from the bioregistry.

- Mr. Gibson asked whether the response rate was known for those who are due to complete the 6-month disease progression module who actually fill it out.
- Dr. Horton responded that this number changes daily. A spike was observed in the number of people taking the ALSFRS (ALS Functional Rating) "Quality of Life" survey. When assessing the response numbers over all 7 surveys, this one is at the bottom.
- Mr. Sacco pointed out that it is a really important goal for advocacy organizations that collaborate with the CDC to support such efforts. If he receives an email from an organization he belongs to versus CDC, he is more likely to respond to that. He asked whether any thought had been given to enhancing response to the email ticklers.
- Mr. Dumas added that periodically receiving email updates (perhaps every 6 weeks or quarterly) to offer any news would be beneficial. For example, information could be reported about the number of people registering. The more the registry is in the front of everyone's minds, the more likely the information is to receive exposure in the press and the more likely people are to participate.
- Dr. Horton asked whether Mr. Dumas received an email prompting him to take his follow-up "Quality of Life" survey.
- Mr. Dumas said he received an email indicating that his password had expired. He did receive assistance from some of the people in the room and was able to get back on-line, so he completed his follow-up survey about 9 months after he originally registered.
- Dr. Brooks asked whether password expiration was being used as a way to capture/recapture to figure out whether people are still alive. This seems to be creating more havoc for patients than it helps the registry. He wondered whether there was a way to assess the password expiration practice and what they were achieving from it.
- Dr. Horton responded that to determine whether a person is still alive in the database, on an annual basis the data are applied to the National Death Index (NDI) database. And they will be able to tell us, yes this person is alive, no this person is not alive. Password expiration has to do with CDC IT security. It is not up to ATSDR. CDC takes confidentiality very seriously, so part of CDC's IT protocol is that a person entering data on-line must update their password every 60 days. They realize that this is an undue burden for persons with ALS, and are working with the CDC IT group to try to extend this beyond 60 days. In all honestly, the hassle of having to change passwords every 60 days probably keeps a lot of people away from the registry.
- Mr. Tison reported that while he was not notified in 6 months, he completed the survey anyway.
- Dr. Horton acknowledged that if people are automatically notified that a survey is waiting for them, it is likely to drive the response rate up.
- Mr. Johnson emphasized that his group is closely monitoring the email notification situation on a daily basis, and is working diligently to address this issue.

- Mr. Sacco recapped that it sounded like one outcome of this meeting would be for everyone to think collectively about suggestions to enhance access to the 6-month update survey, within the constraints of the federal bureaucracy.

Updated Web Portal Demonstration

Greco Johnson
Business Analyst
Emergint

Mr. Johnson reported that the registry was updated on August 28, 2011. At that time, five new components were added to the registry, one of which was the National ALS Registry Alert. This alert will be utilized to notify patients of situations when the registry may be down to undergo maintenance, when new services are available, et cetera. Another new component added was the "Clinical Research" webpage: <https://wwwn.cdc.gov/ALS/ALSClinicalResearch.aspx>. This page provides brief information about ATSDR efforts to work with clinical researchers, clinicians, and patients to link them together with respect to clinical research projects. This section includes brief information about ATSDR's efforts to create this clinical research mechanism, the Congressional mandate, and an explanation of the Institutional Review Board (IRB).

There is now a "State-Metro ALS Surveillance" section: <https://wwwn.cdc.gov/ALS/ALSStateMetro.aspx>. This section provides information about existing state and metro surveillance projects funded by ATSDR. States currently taking part include Florida, New Jersey, and Texas and cities include Atlanta, Detroit, and Philadelphia. Links are provided to participating states' sites, and information is included about future analyses. Also created was an "ALS Bioregistry" section: <https://wwwn.cdc.gov/ALS/ALSBioRegistry.aspx>. This section explains ATSDR's intent with this registry, and includes links to more detailed information about the process to develop the bioregistry.

What used to be the "ALS Clinic Locator" was updated and is now the "ALS Service Locator." This was enhanced to find not only the five closest clinics, but also the five closest ALSA chapters and MDA offices in one's area. Mr. Johnson shared a sample map. The "Publications and Reports" page was updated, and a "Featured Items" section was added. The "Featured Items" section collects information regarding how visitors heard about the National ALS Registry (e.g., Family Members/Friends, Advocacy/Support Group, Doctor/Physician, News/Media, Twitter/Facebook, ATSDR Website, Internet Search, Other).

The "Registry Resources" section includes a number of resources that can be used by PALS and researchers, including the National ALS Registry Video, the National ALS Registry Podcast, an ATSDR ALS Webinar, About ATSDR Video, the ICYOU healthcare video website: National ALS Registry Video, Send a Registry e-Card, and Add the Registry Button to Your Website. The "Frequently Asked Questions" section is probably one of the most important sections in the site. It includes responses to questions about ALS, the ALS Registry, and the website. The summary report from last year's annual surveillance meeting, *Morbidity and Mortality Weekly Report (MMWR)* articles, and notifications can also be found on the website. A link is also included to the system administrator, which allows PALS, researchers, and others to ask questions about the website or about the registry. These questions go directly to the Registry Support Team. Mr. Johnson then demonstrated the registration process.

Discussion Points

- Dr. Horton indicated that many people who have visited the site are reporting that they heard about it through ALSA. He thanked ALSA for their support, and pointed out that this helps ATSDR assess how funds and / or other resources should be utilized to reach out to other groups or organizations to help get the word out. He also emphasized that when a person enrolls, their data are not stored in this system. The data in the system are swept away at midnight every night to a computer that is not linked to an on-line computer. ATSDR wants to emphasize to patients and everyone that this is a very secure system. CDC's IT group has assessed the system to ensure that it cannot be hacked and that the data cannot be compromised.
- Dr. Brooks asked what the process is for submitting corrections about clinic information in terms of whether the information should be sent directly to ATSDR, or if it has to be submitted directly to the group from which the data originated (e.g., ALSA or MDA).
- Mr. Johnson replied that questions/comments submitted through the contact system and administration page go directly to the Registry Support Team. The mapping system in the website is updated based on feedback.
- Dr. Horton added that they received the lists of clinics from MDA and ALSA. ATSDR has debated about whether to include private practicing physicians in freestanding offices; however, because these are subject to change frequently, they decided to include only ALSA and MDA clinics at this time.
- Dr. Brooks indicated that he sends updates frequently to MDA and ALSA. He wondered what ATSDR's process is for going back to them for their most recent updates.
- Mr. Sacco suggested having a system in place for ATSDR to receive updates from ALSA and MDA to determine whether enhancements are correct.
- Mr. Johnson indicated that they could do this.
- Mr. Tison noted that the map did not show clinics in Charlotte, North Carolina or Winston Salem, North Carolina. Perhaps this is showing chapter addresses, not clinics. Regarding clinical trials notification, he wondered whether time since disease onset would be considered. If not, this may be a very frustrating feature for PALS, of which a high percentage may be excluded from those trials about which they are informed.
- Dr. Kaye replied that there would be a presentation in the afternoon on this topic and requested that Mr. Tison hold this question until that time.
- Dr. Kasarskis indicated that he typed in their zip code and the zip code for Boston (40503) and the map does not come up. He wondered whether the "Clinic Locator" that was up was live or was just a demo PowerPoint.
- Dr. Kaye responded that Dr. Kasarskis could be having a browser issue.
- Dr. Kasarskis indicated that he has Safari on an iPad.

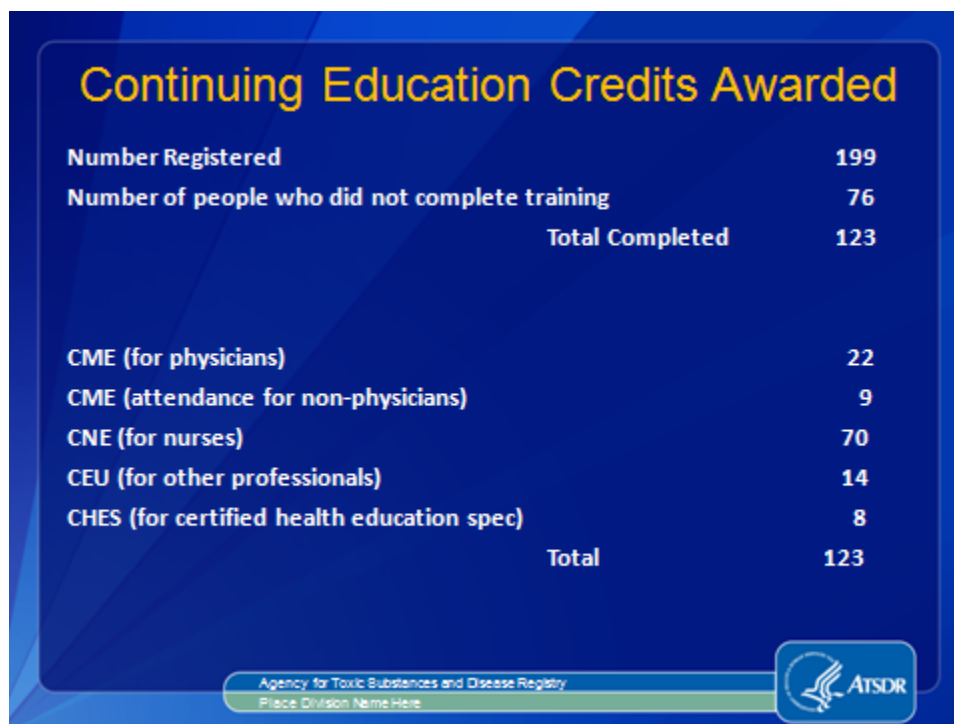
- Mr. Johnson explained that because Apple and Adobe are not compatible and this is a flash application there are problems when using Apple products. It is explained in “Frequently Asked Questions” that this application is best used with Internet Explorer 8 or higher.
- Dr. Kasarskis emphasized that this is a major defect, given that a patient is going to become frustrated with this issue.
- Dr. Horton responded that for a standard desktop, the application should work fine. It is the tablets on which the application does not work. ATSDR recognizes that many PALS use tablets. While there is not a quick fix, addressing the issue of compatibility with iPads and Androids is on ATSDR’s “To Do” list.
- Mr. Johnson added that the team has made a point to take this issue to the IT department leadership at CDC. There is an approval process to make any changes, so they must follow that process.
- Dr. Kasarskis asked whether there is a demonstration of a patient account that everyone can access that goes through the process of how to register and how to access modules that might help clinicians guide their patients.
- Mr. Johnson replied that during the next quarter, the intent is to have a tutorial built on the website that takes a PAL step-by-step through the registration process. There has also been discussion about the creation of a demonstration tool. They would like to receive input from PALS about what would be the most beneficial. The decision was made to develop the tutorial video first and then possibly to create demonstration software that could be distributed on CDs to show persons wishing to register what to expect without actually putting them in the registry.
- Dr. Horton added that for now, there is a single PDF “How To” file currently available that walks people through the steps.

CME Training Module Update

Brian Tencza, MEd, Team Lead, Educational Services
Kim Jenkins, Health Education Specialist
Division of Toxicology and Environmental Medicine
Agency for Toxic Substances and Disease Registry

Mr. Tencza and Ms. Jenkins presented an update on the educational ALS module, which is an interactive module for health professionals. Mr. Tencza explained that this module offers a clinical overview of ALS and addresses current clinical practice recommendations for diagnosis, treatment, and management of patients with ALS, including communication strategies. The module also covers information on the importance of standard diagnostic coding procedures for diagnosis of ALS patients in clinical practice, as well as information on the new National ALS Registry and the importance of ALS patient self-enrollment in the registry. Product materials development included a combination of audience input, educational expertise, and content

expertise. The methods used included Instructional Design, Formative and Post Education Evaluation, Structured Writing, and Risk Communication (e.g., Message Mapping). Ms. Jenkins reported that they receive evaluation data from CDC's Office of Continuing Education on a quarterly basis. Of the 199 registrants, 76 did not complete the training and 123 completed the course. Of those completing the course, 22 were physicians, 9 non-physicians, 70 were nurses, 14 were other professionals, and 8 were certified health education specialists.



Occupational categories for all 199 registrants included Academic/ Educational (12), Healthcare (112), Military (2), Non-Profit Organizations (13), Other (18), Other Government Agencies (12), Private Industry (2), Public Health Agencies (26), and Unknown (2).

CDC is approved as an Authorized Provider by the International Association for Continuing Education and Training (IACET), and is accredited by all national accrediting bodies to provide continuing education credits. CDC / ATSDR offer free continuing education credits, which is a major strength since most of the time people have to pay for courses to obtain continuing education credits.

Over 21,000 people accessed the tool kit on the website inside the module. Of note is that as a federal agency, CDC websites are not permitted to have cookies. The top 7 pages in the website are shown in the following table:

Page	Hits
ALS Definition	1126
Communicating with the Patient	1150
Clinical Assessment	832
Welcome Page	683
Treatment and Management	586

ALS Risk Factors	510
Overview of Module	494

Those who completed the course were required to take a post-test to receive their continuing education credits. There were 26 evaluation questions. To give everyone a general overview, Ms. Jenkins reviewed the results from 10 of the 26 questions. In addition to the post-test questions, the learners were required to complete the 26 evaluation questions in order to receive their CEs. The evaluation questions pertained to the following topics, with the combined percentage of those agreeing and strongly agreeing shown in parentheses:

- ☐ Content and learning materials addressed need or gap in knowledge (95%)
- ☐ Module is written at appropriate difficulty level (98%)
- ☐ Length and pace are appropriate (98%)
- ☐ Content demonstrated expertise in subject matter (97%)
- ☐ Online learning was a good medium for content (95%)
- ☐ Instructional strategies helped learn content (89%)
- ☐ Training effectively met educational needs (94%)
- ☐ Can apply knowledge gained from training (95%)
- ☐ Content relevant to learning objectives (99%)
- ☐ Availability of CEs influenced decision to participate in training (91%)

The post-test questions are as follows:

- 1) Which of the following statements regarding Amyotrophic Lateral Sclerosis (ALS) is INCORRECT?
- 2) Which of the following cases is consistent with a diagnosis of ALS?
- 3) Which of the following statements regarding ALS is INCORRECT?
- 4) Recommended strategies to communicate effectively with ALS patients include all of the following EXCEPT
- 5) All of the following are principles and practices of managing patients with ALS as described in the 2009 American Academy of Neurology systematic review of management strategies EXCEPT
- 6) Treatment modalities for patients with ALS may include which of the following?
- 7) All of the following are true regarding the epidemiology of ALS EXCEPT
- 8) ALS risk factors suggested in the scientific literature may include all of the following EXCEPT
- 9) Which of the following statements regarding the etiologic or pathologic mechanism of ALS is/are TRUE?
- 10) Which of the following statements regarding different classification of ALS is FALSE?

- 11) Treatment and management strategies for patients with ALS include all of the following EXCEPT
- 12) All of the following are true regarding the purpose of the National ALS Registry EXCEPT
- 13) The benefits of the National ALS Registry include all of the following EXCEPT
- 14) All of the following are true regarding the importance of the development and implementation of standard diagnostic coding procedures for ALS patient medical records EXCEPT
- 15) Which of the following may mimic ALS and should be considered in the differential diagnosis?
- 16) All of the following are consistent with clinical manifestations of ALS EXCEPT
- 17) Diagnostic testing to rule out conditions that may mimic ALS may include all of the following EXCEPT
- 18) All of the following diagnostic test results are consistent with ALS EXCEPT
- 19) The following statements are true regarding the methodology involved in collecting and synthesizing data for inclusion in the National ALS Registry EXCEPT
- 20) Which of the following statements are true regarding the importance of encouraging patient self-enrollment in the National ALS Registry?

Participants have to score 80% or above on the post-test in order to receive continuing education credits, but those not scoring in this percentile are permitted to retake the post-test. The questions are not simple, because it is important to make sure that people understand the content.

The team has some innovative ideas such as creating games and scenarios, but they must ensure that materials, graphics, functions, et cetera are 508 compliant so that they are accessible to all people.

Mr. Tencza indicated that with all of their products, they conduct follow-up surveys with users at 6 and 12 months to determine whether they are applying what they learned, although there are some constraints with regard to confidentiality. They also conduct a limited item analysis to determine whether any questions need to be revised or removed. For example, if everyone is missing a particular question, perhaps the content was not covered sufficiently in the module. Some of the comments from learners have included the following:

- ☐ Many say "Excellent" or "Good"
- ☐ Learned a lot
- ☐ Helpful
- ☐ Refreshed knowledge of clinical assessment
- ☐ Easy to understand and apply
- ☐ Keep up good work
- ☐ Some issues with the CE process

The only aspect people were really critical about was the difficulty encountered when they attempted to obtain their CE post-test information on the CDC CE website. However the Division of Toxicology and Environmental Medicine does not have control over the CE process, since this is handled by another area in CDC. Mr. Tencza and the rest of the team conducted a formative evaluation with 9 physicians who were all very positive about the module. In his experience with physicians, Mr. Tencza has found that they like to be in control of the pace rather than having it dictated to them. For physicians, being able to work at their own pace was a positive aspect of the module.

In terms of next steps, the team will continue to monitor learners' input and make adjustments as needed. Development of a new module for ALS patients that walks them through the registration process is in progress, with the on-line module to be formatively tested in October 2011. The product can be found at the following sites:

ALS module website:

<http://www.atsdr.cdc.gov/emes/ALS/>

Educational resources:

<http://www.atsdr.cdc.gov/emes/index.html>

Discussion Points

- Dr. Horton indicated that this is not only for those who work with ALS patients regularly, but also is intended to help those who perhaps do not know a lot about ALS to learn more, and to receive continuing education credits. ATSDR is trying to think of all aspects of who interacts on a regular basis with ALS patients (e.g., physicians, advocacy groups, et cetera). He asked whether the response rate was higher than normal.
- Mr. Tencza replied that the response is higher than for the average product they develop.
- Dr. Brooks thought the products were great and that this was great for allied health care providers as part of a disease-specific certification program. However, he did not feel that 20,000 hits was a lot. His hospital department receives this number of hits in a month. He wondered what the goals were in terms of deploying this module, and whether they felt they had achieved their goals.
- Mr. Tencza replied that as an instructional designer, his goal is for people to be satisfied with the training. In terms of getting the product out, they need to assess the marketing. Getting the word out and getting people to use products is challenging with all of their products.
- Dr. Horton said the most challenging thing about the registry is to keep it moving, keep it fresh, and keep people coming in. They use the typical channels such as Twitter, Facebook, working through advocacy groups, et cetera. Additional marketing ideas are welcomed.
- Mr. Sacco noted that even most healthcare providers who are interested in public health do not think to go to ATSDR first.

- Dr. Sorenson reported that CME is undergoing a significant amount of change, with major flux right now about how CME will be done. One of the latest additions is the requirement to include self-assessment modules. This is already included in the ALS CME training module. He wondered whether the certificates being issued include self-assessment credits and where they are in terms of the new CME requirements.
- Mr. Tencza responded that he needed to find out more about the requirements, but that he knew they went above and beyond the CME requirements in terms of the assessment. They administer post-tests. The old version of CME did not require post-tests. They basically required an assessment determined through Yes/No questions such as: Do you feel you mastered this content? Having to show mastery of the content makes the CMEs more valuable.
- Dr. Sorenson felt that they were meeting the requirements with the self-assessment. He encouraged them to double-check their alignment with the CME changes, given that self-assessment credits will become increasingly more important components of CME in the next year.
- Mr. Gibson wondered whether having dedicated computers in clinics was a possibility for the future so that perhaps social workers could help patients register. Clinics are busy and when a person with ALS first goes into a clinic site, the registry is not their first priority.

State / Metro-Based ALS Surveillance

Wendy E. Kaye, PhD
Senior Epidemiologist
McKing Consulting Corporation

Dr. Kaye reported on the state- and metro-based surveillance project. ATSDR executed two contracts to conduct state and metro surveillance. Currently, the participants in the project include Atlanta, Chicago, Detroit, Florida, New Jersey, Philadelphia, and Texas. They hope to add two additional sites in California. The purpose of this project is to help ATSDR assess the completeness of the National ALS Registry. McKing Consulting Corporation is actively receiving case reporting from physicians, while the national registry is receiving self-reporting and administrative data. As mentioned earlier, these two approaches will ultimately be compared to determine how well the national registry is doing.

Participating State and Metropolitan Areas



State / metro surveillance is an incredibly time-consuming process, which is why it is being done only in selected areas. First they had to identify all of the neurologists, which seems like it would be a simple process. Some states have licensing boards and / or neurological societies that have lists of neurologists, while others do not. To identify neurologists who diagnose or provide care for ALS patients, lists of neurologists were obtained from outside vendors, state licensing boards, and others. Neurologists not expected to treat or diagnose ALS patients in the target area were removed from the list. Neurologists were contacted to determine if they

Contacts with Neurologists through July 31, 2011

	Florida	New Jersey	Texas	Phila- delphia	Detroit	Atlanta
Total	778	396 242*	834	144	335	225
Diagnoses and/or treats ALS patients	358	182 49	269	26	39	58
Does not diagnose and/or treat ALS patients	420	213 182	513	116	49	134
Unknown	0	1 11	52	2	247	33

* Neurologists in Philadelphia, Delaware, and New York who treat New Jersey residents

diagnosed or treated ALS patients. Every neurologist who diagnosed or treated a patient diagnosed with ALS from January 1, 2009 through December 31, 2011 was asked to report cases. The table on the previous page illustrates the magnitude of this undertaking.

A brief abstraction form including demographics, date of diagnosis and El Escorial Criteria is completed on each ALS patient. The abstraction form has only 15 items. Given that sometimes neurologists do not agree on the diagnosis of ALS, a more detailed Medical Records Verification form will be completed on up to 20% of the cases and submitted with an EMG, if available, to the consulting neurologist for verification of diagnosis. These forms will be submitted to the consulting neurologist, Dr. Sorenson, who will assess them further so that the investigators can determine whether there are any reporting issues in certain areas. Annually, death and hospital discharge data will be evaluated to identify possible cases of ALS not reported to the surveillance project. When physicians can be identified, they will be contacted to examine reasons for not reporting. The following is an actual form:

Date Completed ____/____/____		Form Approved OMB No. 0923-0043 Exp. Date 04/30/2014	
Name of person completing the form _____			
Job Title _____			
Name of Practice _____			
Phone number (____) ____-____			

<p align="center">ALS Case Reporting Form</p> <p><small>This form should only be completed for individuals meeting the El Escorial Criteria for diagnosing ALS including definite, probable, and possible ALS. The diagnosis of ALS requires the presence of each of the following:</small></p> <ol style="list-style-type: none"> 1. Lower Motor Neuron signs (by clinical, electrophysiological, or neuropathological examination) in 1 or more of 4 regions (bulbar, cervical, thoracic, and lumbosacral). Signs of lower motor neuron degeneration include: slowed movements, increased muscle tone or spasticity, spastic gait, muscle atrophy and fasciculations. 2. Upper Motor Neuron signs (by clinical examination) in 1 or more of the 4 regions. Signs of upper motor neuron degeneration include: slowed movements, increased muscle tone or spasticity, spastic gait. 3. Progression of signs within a region or to other regions. <p>Definite ALS = Upper Motor Neuron + Lower Motor Neuron signs in 3 regions</p> <p>Probable ALS = Upper Motor Neuron + Lower Motor Neuron signs in 2 regions with Upper Motor Neuron signs rostral to Lower Motor Neuron signs</p> <p>Probable ALS, lab supported = Upper Motor Neuron + Lower Motor Neuron signs in 1 region with evidence by EMG of lower motor neuron involvement in another region.</p> <p>Possible ALS = Upper Motor Neuron + Lower Motor Neuron signs in 1 region or Upper Motor Neuron signs in 2 or 3 regions, such as monosymptomatic ALS, progressive bulbar palsy, and primary lateral sclerosis.</p>		<ol style="list-style-type: none"> 6. Race (as reported by subject – check all that apply): <input type="checkbox"/> Asian <input type="checkbox"/> Black/African American <input type="checkbox"/> White <input type="checkbox"/> Unknown <input type="checkbox"/> Other: _____ 7. Ethnicity: <input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Non Hispanic or Latino <input type="checkbox"/> Unknown 8. Country of Birth: _____ 	
<p>Demographic Information</p> <ol style="list-style-type: none"> 1. Subject Name: Last Name _____ First Name _____ Middle Name or Initial _____ Suffix _____ 2. Address: Number _____ Street _____ City _____ State _____ Zip Code _____ 3. Social Security Number (last 5 digits only) ____-____-____ 4. Date of Birth: ____/____/____ (mm/dd/yyyy) 5. Sex: <input type="checkbox"/> Male <input type="checkbox"/> Female 		<p>Diagnosis Information</p> <ol style="list-style-type: none"> 9. El Escorial Criteria as determined by an ALS specialist (check one) <input type="checkbox"/> Definite <input type="checkbox"/> Probable <input type="checkbox"/> Probable (lab supported) <input type="checkbox"/> Possible <input type="checkbox"/> Not Classifiable 10. Date of Diagnosis ____/____/____ (mm/yyyy) 11. Date of Onset of Symptoms ____/____/____ (mm/yyyy) 12. Provider Making the Report <input type="checkbox"/> Neurologist (ALS specialist) <input type="checkbox"/> Neurologist (other) <input type="checkbox"/> Physiatrist <input type="checkbox"/> Family/Internal Medicine/General Practice 13. Does the patient have dementia diagnosed by a neurologist? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know 14. Does the patient have an immediate family member (parent, sibling, child) who has/had ALS? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know 15. Payer Type (check all that apply) <input type="checkbox"/> Medicare <input type="checkbox"/> self-pay <input type="checkbox"/> Medicaid <input type="checkbox"/> Veterans Administration <input type="checkbox"/> HMO <input type="checkbox"/> Other <input type="checkbox"/> Private Insurance 	

Public reporting burden of this collection of information is estimated to average 5 minutes including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed and completing and reviewing the data collection of information. An agency may not conduct or sponsor and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC/ATSDR Information Collection Review Office, 1600 Clifton Road NE, MS D-74, Atlanta, GA 30333; ATTN: PRA (0923-0043).

There have been some unique challenges. Texas is a vast geographic area with medically underserved areas. The geographic proximity to large medical referral centers outside of the state is problematic in New Jersey, which is close to Philadelphia and New York City. Florida has large transient populations.

With respect to conclusions about providers, state differences in access to specialized medical services complicate getting an accurate count of neurologists who diagnose and/or treat ALS patients. Approximately 55% of neurologists do not treat or diagnose ALS patients. In each state or region, there are a handful of major ALS treatment centers seeing 50 or more patients.

In these three states, it is estimated that more than 50% of the expected cases are seen in major treatment centers. Although, major treatment centers treat and diagnose a significant number of ALS patients, to account for all ALS patients in a geographic area, all neurologists must be contacted to ensure complete and unbiased ascertainment.

Cases reported through July 31, 2011 in the three states that have begun collecting data are reflected in the following table:

State	Cases Reported	Practices Reporting
Florida	186	9
New Jersey	95	7
Texas	275	15
Total Reported	556	31
Expected Number	4219*	
*Based on 2010 Census data;		

The total number of cases reported for Florida, New Jersey, and Texas had increased to a total of almost 900 as of August 31, 2011. On August 31, 2011 Dr. Kaye picked up the data from one ALS referral center in Atlanta. Reporting is working, but it is slow and the investigators have had to do some of the abstracting themselves.

Conclusions about case reporting are that most neurologists are supportive of the project. Smaller practices may need more direct assistance abstracting records. Referral centers and some universities have required local IRB approval, which has added some time to the project. Reimbursement for case reporting has been helpful for recruiting physicians, especially those with large practices.

Discussion Points

- Dr. Horton emphasized that this illustrates the two approaches being taken with this registry. It is going to be very interesting for ATSDR to receive the results from McKing Consulting Corporation that show how many cases they are discovering in these state and metro areas as compared with what is in the National Registry. If McKing Consulting Corporation is finding more cases than the registry has, ATSDR will have to tighten up the registry approach to ensure that they are finding all of the cases.
- Dr. Kaye indicated that the state data will be provided to ATSDR in the Summer of 2012, and the metro data will be provided in 2013.
- Responding to a question regarding how much is paid for each case, Dr. Kaye indicated that the compensation is \$100 dollars per case.

- Mr. Tison inquired as to what incidence rate was being used for the expected number of cases per 100,000 population.
- Dr. Kaye replied that they are using the National Institutes of Health (NIH) paper that was published a couple of years ago that states an incidence of 2 per 100,000 and a prevalence of 4 per 100,000, and they used the 2010 Census data. It is recognized that one of the reasons for the registry is to better understand incidence and prevalence; however, this offers at least a baseline estimate to help the participating states and metro areas measure their progress.
- Mr. Tison thought some of the original pilot programs were particularly interesting, especially the South Carolina project with thorough case ascertainment. He wondered when they may expect a published peer-reviewed journal article from South Carolina. He thought it would be very informative for incidence and point prevalence, and may offer the ALS community some hint of the outcomes they will not see for another year or more from the ALS Registry.
- Dr. Kaye replied that two papers had been through clearance and were accepted for publication, the first of which was published in the journal *Muscle & Nerve*. The second article is anticipated to be published in 2011 based on what Dr. Kaye has heard from South Carolina.
- Dr. Horton added that if possible, they plan to put the findings from the registry under the publications link on the website. The goal is to have a repository of various papers that will be useful to PALS and the scientific community. He noted that Dr. Sorenson has a paper from Minnesota that will soon be published. Dr. Sorenson reported he was awaiting clearance from CDC.
- Dr. Knorr inquired as to whether the McKing Consulting Corporation data that would be submitted to ATSDR would show individual level data, and whether they would be comparing the names and not just the Social Security Numbers (SSNs).
- Dr. Kaye responded that the names and the last 5 digits of the SSN would be compared. The names that are in the state and metro areas that are not in the National ALS Registry will not be added. This is for comparison purposes only and describes the differences in demographics between the two populations. Under their agreements with the states for the release of the identifiers, these individuals cannot be added into the national system.
- Ms. Bledsoe asked why some referral centers, IRBs, and universities have required local IRB approval and whether the activity is being perceived as research instead of public health reporting.
- Dr. Kaye replied that CDC determined this project to be research because two different surveillance methods are being compared. The state health departments in New Jersey and Florida determined the project to be surveillance versus human subjects research. Atlanta, Detroit, Philadelphia, and Texas determined the project to be research. Two states are releasing the data under a Health Insurance Portability and Accountability Act (HIPAA) permitted release. Under the IRB there is a "Waiver of HIPAA Authorization" and a "Waiver of Consent." All of this took a year to straighten out.

- Regarding the pilot project, Mr. Gibson noted that South Carolina was one of the few states that had a collection of data unlike any other states. He wondered whether that was still the case.
- Dr. Kaye responded that South Carolina has between 20 and 30 different databases (e.g., Medicare, Medicaid, medical, hospital discharge, emergency department, law enforcement, et cetera) that they can tap into for any one project. For each project, they determine which databases would be the most useful and then they have to obtain permission to use those data for a particular project. This is the only state that currently has this capability, although other states are interested in creating similar systems and have been referred to South Carolina to learn more.

National Qualitative Data Findings

Wendy E. Kaye, PhD
Senior Epidemiologist
McKing Consulting Corporation

Dr. Kaye noted that the PowerPoint she was using for this presentation was not included in the handouts due to the constraint that they are not permitted to release the data until they know they are complete. ATSDR has been informed that only qualitative information may be reported. Dr. Kaye shared two maps that showed the percentage of cases they believe they have captured in each state, compared with the NIH incidence and prevalence data being utilized. 2000 Census data were used because 2010 was not available. For every state in the country, they have designated a percent rural population and a percent urban population. Nearly every city has been designated as either urban or rural. The investigators went through six months' worth of data from the registrants and assigned them urban or rural status based on the city of their address. They then assessed the percent who had registered urban or rural compared with what the Census data showed.

California has one of the lower percentages, but that state has a huge number of people. Alabama has a really large differential between the percent of people registering from rural areas compared with rural populations in Alabama. However, that state has the highest percentage of people registering in relation to the number of people with ALS believed to be residing in the State of Alabama. This raises a question regarding whether perhaps a different strategy should be used to encourage registry participation in Alabama than in other states. The same is true in Maine, which has very high representation in terms of overall registration. However, Maine has a very large differential in rural populations registering.

In terms of the percentage completing survey modules, nearly 46% have completed the Demographic module. The Family History and Physical Activity modules have the lowest completion percentages. These are the two most difficult modules to navigate because the Physical Activity module asks about physical activities in different periods in one's life, while the Family History module asks about parents, siblings, and children. Those with large families will have to take longer to complete this module. The percentage completing the Quality of Life and Disease Progression module is rising, although they have not yet been able to assess the

percentage of first-time versus second-time completions for this module. This information will be available in 2012. Though still not the percentages she would like to see, Dr. Kaye said she would argue that for voluntary surveys, the participation rate is really quite high.

Discussion Points

- Dr. Nelson noted that some death certificate data have suggested that there is a Southeast to Northwest gradient of frequency of mortality rates. She wondered what the investigators thought about that and whether they felt they could trust the mortality data. She emphasized that it was not a criticism, but based on the map it made her wonder whether the rates are just higher in the North.
- Dr. Kaye responded that she could answer this better once they have a year of registry data. As noted, they are currently following the NIH paper that states an incidence of 2 per 100,000 and a prevalence of 4 per 100,000 without trying to adjust it for that suggested gradient.
- Dr. Horton added that hopefully all of the data they are collecting can be used to validate or compare with other studies. For example, it appears that people who serve in the military are twice as likely to develop ALS. Once ATSDR has complete data from the military module, they will be able to conduct their own analyses. The usefulness of this registry will be better realized once they begin analyzing the data.
- Dr. Kasarskis noted that Kentucky has the same urban versus rural split as Alabama. This did not surprise him, and he indicated that they had a few off line conversations about this because this may reflect the accessibility of Internet use and how savvy people are at using mechanisms that may be taken for granted.
- Dr. Kaye replied that they also assessed poverty and education levels, neither of which seemed to explain the urban / rural difference. However, access could be an issue.
- Since the national registry will not be backfilled with the state data, Dr. Brooks wondered if there were any plans to assess whether deployment of the state-based registry has any positive or negative Hawthorne effects on national registry registration. He was concerned that at the street level, physicians may be telling people they do not have to worry about being registered. Because they are receiving \$100 per case to enter the patient at the street level, there could be a negative effect and this should be assessed.
- Dr. Kaye responded that if there is an effect, it will have a negative effect on the study because the purpose is to determine whether the current strategies (e.g., self-registration and the administrative data) miss people. The states are not actively telling people about the national registry except to say that they are engaging in this effort to help support evaluation of the national registry. In terms of physicians telling people not to register, the investigators are being very clear that the data physicians provide will not be added to the national registry. However, she agreed that whether there is an effect should be assessed. She had visited one clinic at the time of this meeting. Even though they are not a major participant, they were actively telling people about the registry. That has not changed because of their participation in this project.

- Regarding the high response rates in the Northwest, Dr. Sorenson indicated that there are very high reporting rates in Minnesota, Iowa, North Dakota, and South Dakota. The primary reason for that is because the ALSA chapter in Minneapolis covers those areas. If they covered all of Wisconsin, it would be blue as well. Minnesota is virtually identical to the numbers quoted in the NIH publication, with an incidence of 1.7 per 100,000 and a prevalence of 4 per 100,000. These numbers are very similar to what would be expected. In terms of the ALS database of people who registered with ALSA chapters, there is virtually a 100% capture rate of ALS cases in all four of those areas as a result of partnering with ALSA. ALSA chapters are highly promoting the registry, and there is an exceptional participation rate because of that. This highlights the importance of partnering with ALSA and the MDA.
- Mr. Tison requested a copy of the first map to share on ALS forums in order to use peer pressure for enrollment. He also wondered whether there was a method in place to overlay incidence and prevalence data with Census population data by zip code to automatically look for clusters at some point when those numbers are reliable.
- Dr. Kaye replied that they would have to get clearance to release the maps, but if they can, they will be happy to make those available. When the registry was launched, there was a "Terms of Clearance" statement from the Office of Management and Budget (OMB). OMB has the power to shut them down without much notice, so the investigators are trying to be very cautious about their actions. She did not include the maps in the handouts for that reason. Nevertheless, she agreed that peer pressure could be highly beneficial. Regarding overlay of incidence and prevalence data with Census population data by zip code, ATSDR is in the process of developing an analysis plan for how to use the data. While this was not on the list, it could be added to the list to consider.
- Dr. Horton added that on a monthly basis, Dr. Kaye and others provide this information to the ALSA national chapter and the MDA national office. They inform clinical directors about how their state is performing based on ATSDR data.
- Mr. Gibson cautioned that if information is posted on some boards, all they will be doing is answering questions on those boards. This information should be shared more widely.
- Dr. Knorr said they have heard people question whether they need to register in the national registry, so they have a mailing going out through the ALS chapter to make it clear to people that they are encouraged to register in the national registry in addition to the Massachusetts registry.
- Dr. Kaye indicated that the FAQ link on the website includes a question about why it is important to register with the MDA or ALSA as well as the national registry. Perhaps this needs to be given more prominence so that word gets out.
- Dr. Horton expressed appreciation for making the distinction.
- Dr. Knorr suggested adding, "There are no other national registries" to the FAQs.
- Dr. Gubitza noted that the state registries may not be as comprehensive as the National ALS Registry, so an important part of the message is to emphasize that ATSDR is accruing more

data, additional data, or different data in the national registry and that is why patients should enroll.

- Mr. Wildman emphasized the importance of disseminating the information ATSDR shares with them. ALSA has been working with members of Congress and others to try to convince OMB to permit ATSDR to share more information. It is extremely important for people with ALS to receive feedback and to know that their data is making a difference and that they are being counted.
- Dr. Horton stressed that ATSDR would love to share the data they now have, at least to let people know they are making progress. However, they must adhere to the OMB "Terms of Clearance" with regard to what information is released. They do not want to jeopardize the entire project. ALSA and other groups have approached OMB, but it is unclear whether this will have an impact.

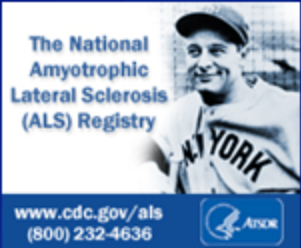
Registry Marketing Update

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

Mr. Dempsey reported on National ALS Registry marketing efforts over the last year. The strategy was to work with as many partners as possible to generate awareness of the registry and encourage persons with ALS to self-register, and to engage persons and organizations who influence people with ALS in order to reach the largest number of potential registry participants. To achieve that goal, a number of audiences were identified, including PALS, family members, specialized health care providers (e.g., neurologists, physical therapists), ALS researchers who work with patients, and ALS support organizations or entities.

As discussed earlier, some major updates have been made to the ALS web portal. Mr. Dempsey highlighted one of the great, user-friendly tools now available on the page—the web button. The web button allows bloggers or other websites to place this image on their respective pages. Visitors to those sites can click on the button to go directly to the ALS

ALS Registry Web Button:



- **Updated Web site**
 - More comprehensive source of information
 - Specific areas for different audiences
 - user-friendly tools (Web button)
- **Being used on a number of different websites (e.g., ALSA chapters, NEALS, MDA, PALS websites)**
- **Podcast also linked from page**

Registry web portal, or call the 800 number provided for more information. E-cards are also available to send. To send an e-card, a short web form can be completed and the e-card can be sent to anyone who might be interested in the ALS registry. The first thing they open is the image of Lou Gehrig that says “Strike out ALS” and then a short animated feature imbedded within the web page opens to the message inside. Then the user can click back to the website and go from there.

Particularly exciting for Mr. Dempsey is that some of the efforts over the past year are related to social media, which he has been working on the most. He emphasized that social media is not the “be all, end all” of marketing. It is not the magic tool that solves all marketing issues. However, it is a great tool for reaching people through a brand new channel. What is exciting about social media is the interactive nature of this mechanism. While a website is a great tool, it is a one-way dispensing of information. With channels like Facebook and Twitter, people are able to see a message and interact with others about that message. CDC’s Facebook currently reaches 151,000 people, which is a significant audience, and this number grows every week. In February or March of 2011, that number was 90,000. The Facebook page is set up to display information from CDC and ATSDR. There are about three posts per month across CDC’s various social media channels, including Facebook and Twitter, which highlight specific information to ALS audiences. For example, the following post in May 2011 highlighted ALS Awareness Month:



CDC
May is ALS Awareness Month.

Currently, there is no accurate picture of who has ALS. ATSDR wants to change that. The National ALS Registry gathers information to help scientists learn more about ALS, also known as Amyotrophic Lateral Sclerosis or Lou Gehrig's disease. The more people living with ALS participate in this registry, the more accurate registry information will be.

ALS-Lou Gehrig's Disease – Learn More
www.cdc.gov

Far too little is known about ALS (Lou Gehrig's disease). Learn more about how the National ALS Registry is changing that.

May 11 at 3:15pm · Share

63 people like this.

Lorie Ann Walley You have that Right! So do I, want to change that!
May 11 at 3:18pm

Sherry Anderson SOMBODY I KNEW BREIFLY DIED FROM ALS.
May 11 at 3:18pm

Lorie Ann Walley My brother passed away in my arms 02/05/2010 from this monster! I was his main caregiver! :(
May 11 at 3:20pm

Janette Cochran Sohm My Uncle Bob died from ALS in Jan 1990.
May 11 at 3:31pm

Mandy Ladd-Lueshen My husband has been living with ALS since his 30th birthday...
May 11 at 3:33pm

Susie Deeds Knowledge "IS" Growth...Education "IS" The Key...!~
May 11 at 3:37pm

Tammy Jo McNulty What happened to Kelly's comment?
May 11 at 4:05pm

Tammy Jo McNulty Those with ALS and Alzheimer's test positive for Lyme. Check it out...
May 11 at 4:06pm · 8 people

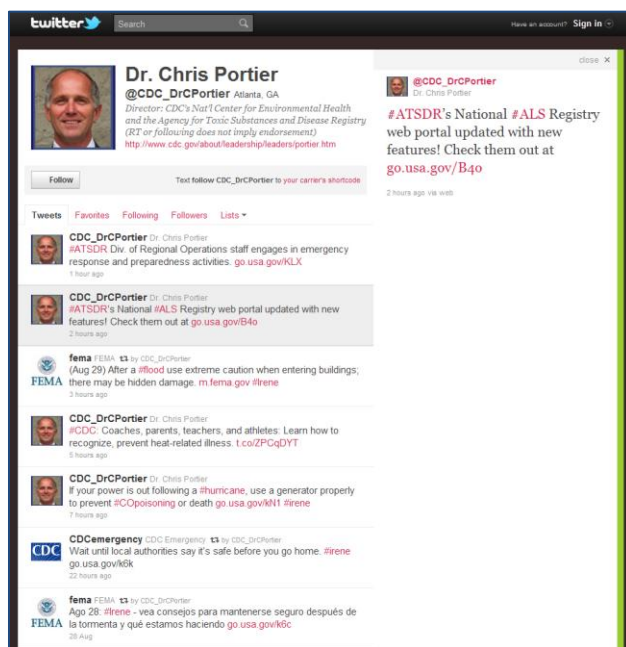
Denise Longman Dr Martz was very ill with ALS then he got treated and got completely better with Antibiotics for the Lyme borreliosis which was actually causing the ALS. Bacteria are being found to cause so many chronic diseases...we need a complete overview of all the neuro diseases like ALS, MS, CFS/ME, Parkinson's, Fibromyalgia - even Schizophrenia - all could be caused by infection.
May 11 at 4:51pm · 9 people

Susan Brinchman May is also ElectroSensitivity Awareness Month and Multiple Chemical Sensitivity Month, just so the CDC doesn't forget.
May 11 at 6:43pm · 3 people

There is a short paragraph from CDC about ALS and the ALS Registry, and there is a link to the ALS website. This post got 63 “likes.” Many comments were received from people sharing how ALS has touched their lives. For example, several people said they know someone living with ALS. This post highlights the interactive nature of the Facebook page. So far this year, there have been 3 ALS-related posts on this Facebook page. That has generated 127,000 plus impressions since the February 2011 post. An impression means people actually saw it in their Facebook newsfeed. The post generated just over 200 visits to the ALS page. While 200 plus is not a substantial number, it is still 200 plus people who might have learned more about ALS, who might have registered, or who might have convinced a family member living with ALS to register.

ATSDR has also been leveraging CDC Twitter channels in the past year. CDC has a main Twitter page to share general health information, as well as information about programs on which CDC and ATSDR are working on. A few posts have been made on Twitter related to ALS in the past year. CDC's Twitter feed reaches over 42,000 people. Dr. Portier, ATSDR's Director, has been very active on Twitter since June 2011. He reaches 1300 followers, and

those numbers are growing as well. Since February 2011, Twitter has been able to track 187 visits to the ALS webpage, and that information has been re-tweeted 85 times. The following is an example of a tweet that Dr. Portier posted earlier in the week:



An ALS page has also been set up on Flickr, which is an online photo sharing tool designed by Yahoo that basically allows people to post photo albums to a web page where users can comment or share the pictures on their own website. The Flickr album has received over 1,300 visits. ATSDR has been trying to capture the ALS team while they are interacting with various ALS communities, presenting during conferences, et cetera. There are also some great photos of members of the ALS team sharing exhibits, such as this one:



ATSDR is certainly not ignoring traditional media. Some future plans are to continue engagement via the traditional media in 2012. An article has recently been submitted to AARP, which ATSDR hopes will be published in the October 2011 issue. Mr. Dempsey is still awaiting confirmation about that, but he pitched a really great story to them and ATSDR believes this would be a great way to get the message to the audience who reads AARP. The agency also

knows that building relationships with bloggers is going to be an important way to disseminate information. People are sharing increasingly more information through blogs and their own personal websites. Thus, ATSDR is trying to develop working relationships with bloggers and people who host websites who can share information on ATSDR's behalf. The agency is also working on potential partnerships with major league sports franchises. There is obviously a connection to Lou Gehrig and the Yankees. ATSDR would love to partner with a major league sports franchise to engage in some awareness building, which would be a tremendous opportunity. They hope to pursue this effort in the coming year.

Discussion Points

- Dr. Brady asked whether people are self-disclosing personal health information as a function of coming onto ATSDR's Facebook page, and he wondered whether CDC's IRB or others had raised any concerns about that.
- Mr. Dempsey replied that he had not observed that anyone had personally disclosed on any of ATSDR's social media channels.
- Dr. Horton added that ATSDR cannot control what people say. Obviously, CDC/ATSDR can remove any inflammatory remarks. He also did not recall anyone ever directly disclosing. If someone does disclose he did not know whether they would actually do anything about it, but he agreed that it was an interesting question.
- Dr. Kaye agreed that this is a major issue. The Food and Drug Administration (FDA) has been developing guidance related to social media and clinical trials for quite some time, but this has not yet been published. Everybody is "flying blind" and doing the best they can. If someone discloses public health information about an adverse event on Facebook rather than contacting the investigator, consideration would have to be given to what responsibilities a site has to submit that information to the correct place. Clearly, there are many potential issues related to using Facebook for very specified research activities.
- As a member of an IRB, Dr. Brooks pointed out that if a patient discloses, that is their responsibility, not ATSDR's.
- Mr. Tison wondered whether there is a possibility of having a specific Facebook page for the registry. He is overwhelmed with information and does not care much about all CDC information. He is extremely interested in newsfeeds related to the registry specifically, and would enthusiastically support a specific registry Facebook page.
- Mr. Dempsey replied that he and Dr. Horton have discussed this previously. Their initial thoughts were that CDC's Facebook page has such a large following, it made the most sense at the time to leverage that following rather than to try to build a following "from scratch," which takes considerable time and manpower. It is worth pursuing again if the interest is significant enough to sustain a Facebook page or Twitter feed that can constantly push out enough information to keep it relevant for ATSDR's users.
- Dr. Sorenson asked where the registry website comes up on the list when a search is done for ALS or Lou Gehrig's disease.

- Mr. Dempsey replied that it should be the first page; if not the first “hit” that is seen on Google. They just conducted an audit of all of the information shared on ATSDR websites. The ALS registry page now ranks #1 in terms of user-friendliness and usability. Google search rankings were also incorporated into that score.
- Mr. Gibson pointed out that Facebook is very challenging. Because there are so many postings to follow on the CDC page, it may be advantageous for ATSDR to have its own page. He asked whether ATSDR had taken the opportunity to reach out to any military publications, groups, et cetera. Whether it is on Capitol Hill or in the general public, unless a connection is made to a disease, it will be just one more acronym. Many people support veterans, so connecting the disease to the military could be advantageous. It is amazing how many veterans’ groups and active military personnel do not know the connection.
- Though not specific to ALS, Dr. Horton indicated that ATSDR is working on the Camp Lejeune contaminated water investigation. For this project, ATSDR is reaching out to military non-governmental organizations (NGOs) to spread the word about this investigation. They are making in-roads with this approach and could explore using the same channel for ALS.
- Mr. Dumas reported that he is active and has well over 100 friends on Facebook who have a connection to ALS. Oftentimes it will be a parent, a friend, et cetera. The benefits are that it is a fabulous way to gain exposure for fundraising. During the previous weekend, there was a sky dive in Northwest Georgia. While he was not sure of the total number of participants, there were constant messages through Facebook. There is a newsletter publication out of Marietta, Georgia that reaches 401,000 veterans every month. He offered to connect ATSDR with the editor so that they could perhaps develop a focused statement to disseminate via this publication. It is known that those who have served in the military have a higher percentage of onset than the general population. He is not really concerned about anyone on Facebook knowing that he has ALS; however, he does not really talk about his symptoms. Instead, he talks about encouragement and ways to change one’s mindset to improve quality of life.
- Dr. Horton indicated that ATSDR is placing full page advertisements in clinical journals to target physicians and neurologists. ATSDR’s Director of Communications thinks the return on investment with advertisement is probably not the best way to spend money, but this is a much targeted approach. He asked whether any of the physicians or neurologists in the room had seen any of their advertisements.
- Dr. Sorenson responded that he does his entire journal reading on line, so he did not see any advertisements.
- Dr. Horton noted that on a comical note, when someone has an idea and wants to tweet about it, it is instantaneous. However, federal government tweets must go through an approval process that typically takes about two weeks. The same is true for tweeting responses. This is just one example of some of the obstacles ATSDR faces. While social media may not be the “be all, end all” it is cheap or free and lots of people are doing it. Thus, ATSDR is aggressively pursuing it.

Updates from Registry Partners

Amyotrophic Lateral Sclerosis Association

Steve Gibson
Chief Public Policy Officer
The Amyotrophic Lateral Sclerosis Association

Patrick Wildman
Director, Public Policy
The Amyotrophic Lateral Sclerosis Association

Mr. Gibson indicated that ALSA's Chief Scientist, Dr. Lucie Bruijn, was unable to attend because she was attending a research meeting in Paris. Dr. Bruijn has been very active in talking to her colleagues in the research field to engage with them about the registry, and to obtain suggestions about how the registry can be improved and made more useful. Mr. Gibson indicated that he has been involved in this project since the outset, and that early on they had the opportunity to build the "perfect" registry. If they had continued to try to build the "perfect" registry, he thought they would still be talking about it rather than implementing it. He is very happy that ATSDR moved forward to develop and deploy some type of infrastructure; particularly given that people with ALS do not have long lifespans. It is very important to collect the information that is available. Since the last annual meeting, ALSA has had very successful outreach on the Hill. In addition, ALSA convenes a conference each year that has over 800 participants who attend from 48 different states. The ATSDR team spoke during one of the plenary sessions, and helped people in the ALS Registry. While he agreed that social media is not the "be all, end all," he emphasized that this is a primary mechanism by which people with ALS communicate. Social media really is the next level of being able to engage the ALS community, and help that community understand the issues. Unfortunately, most people with ALS cannot speak toward the end stages of the disease. Therefore, social media has become a top priority for ALSA.

Mr. Wildman indicated that ALSA is working diligently to drive enrollment in the ALS Registry, and is employing a number of strategies to do so. One strategy is conducting outreach with chapters and clinics to stress the importance of the registry. ALSA provides a significant amount of information about what the registry does, what the benefits are, and what the potential outcomes are from enrolling. They are using social media much more frequently, and have discovered that people are highly responsive to videos and images from patients and researchers. Through Facebook and Twitter, they are finding people they have never reached before. The potential to reach people through social media is astounding. ALSA is also taking advantage of the hundreds of walks it has throughout the country each year. The walks are widely attended by members and patients, making these a great venue to reach audiences. They are exploring the idea of using mobile devices or other types of technology to allow people to enroll at a walk. ALSA convenes support group meetings throughout the country, and is trying to get technology into those meetings to allow people to enroll during these meetings. In all of its messaging, ALSA is attempting to take advantage of reaching out to veterans, because people pay a lot of attention to veterans. With all of these strategies, the ultimate "end game" is to achieve 100% ascertainment.

NEALS Biorepository

James D. Berry, MD, MPH
Neurology
Massachusetts General Hospital, East

Robert P. Bowser, PhD
Professor of Neurology
Director, Barrow Center for ALS Research
Barrow Neurological Institute
St. Joseph's Hospital and Medical Center

Dr. Berry reported on an example of one effort to forward the search for biomarkers in ALS, the Northeast ALS Consortium (NEALS). NEALS is a network for ALS clinical research that was formed in 1994, and has grown exponentially since then to include 92 investigators across the US and Canada. NEALS provides an infrastructure for multi-center clinical trials, as well as clinical studies that are not trials with any medication. Massachusetts General Hospital (MGH) serves the function of the NEALS Coordination Center for some of the trials and studies, while the State University of New York (SUNY) serves as the NEALS Outcomes Center. A Biorepository Committee oversees the growing sample repository.

The overall goal of the NEALS Biorepository is to create a large biorepository of samples collected using rigorous methods and linked to clinical information from patients with ALS, disease controls, and healthy volunteers to be used in the search for disease biomarkers. The principal aims are to reduce pre-analytical sample variation, link clinical data, identify and validate biomarkers, share samples with other investigators to expand these efforts, and maintain and expand the biorepository so that it is an on-going resource. This biorepository was designed to overcome shortcomings in biomarker discovery efforts, including small sample sizes, poor or non-uniform sample collection, inadequate sample storage, lack of adequate clinical information, lack of disease mimics as controls, and lack of validation studies. Study design solutions in the NEALS Biorepository to address these shortcomings include a multi-center study design to create a large biofluid repository; rigorous standard operating procedures (SOPs) for collection and processing, including medication washout; SOPs for storage; database clinical information with samples; inclusion of appropriate disease mimics; and sharing samples with ALS scientists.

During the first visit, demographic and disease data are collected in addition to ALS Functional Rating Scale (ALSFRS) data for patients who have motor neuron disease and samples of blood, urine, plasma, and DNA extraction. Similar data are collected for the disease mimics and healthy controls, with the exception of the ALSFRS. There are follow-up visits at 6, 12, and 18 months for the patients who have motor neuron disease. Telephone follow-ups are conducted at 24, 30, and 36 months to update ALSFRS to collect as much longitudinal data as possible.

For Aim 1, which is to reduce the pre-analytical sample variation, 30 centers have been included with formal SOPs for collection and storage. The study is run through the NEALS Coordination Center at MGH. The structure is similar to clinical trials, and there is yearly monitoring. There are study documents and procedure manuals just like clinical trials in order to bring rigor to the collection of these samples. Centralized supply management and storage at the MGH Coordination Center ensures conformity. All samples are prealiquoted and stored at -80C. In other words, they are collected in very small vials to be frozen so that those can be shared without thawing and refreezing, which can be harmful to samples.

For Aim 2, which is linking clinical data, the following clinical information is collected:

All Groups (ALS, Pure UMN/LMN, Disease Mimics, Healthy Volunteers)

- ☐ Demographics: Age, Sex, Ethnicity
 - Concomitant Medications/Washout Compliance (study drugs are recorded and placebo/active entered when study unblinds)
- ☐ Past Medical History
- ☐ Adverse Events

ALS Disease Information

- ☐ Date of symptom onset
- ☐ Date of diagnosis
- ☐ Symptom onset location
- ☐ El Escorial Criteria category (updated at each follow-up visit)
- ☐ ALSFRS-r

Dr. Bowser reported on Aims 3 through 4. Aim 3 is to identify and validate biomarkers. NEALS has NIH and ALSA funding to identify protein biomarkers in the CSF using mass spectrometry proteomics, as well as to identify metabolic signatures for ALS in the blood and CSF using mass spectrometry metabolomics. A multi-center study is being conducted to validate protein biomarkers in the blood and CSF using ELISA and 2-D gels. Longitudinal CSF and blood draws are utilized for prognostic indicators of disease progression. Results to date include identification of a proteomic signature by mass spectrometry in the CSF of ALS patients; validation of this signature using a separate cohort of CSF samples; validation that neurofilament is elevated early in disease; discovery of a signature containing neurofilament and complement c3 that can distinguish ALS from disease mimics; discovery that levels of cystatin C in the CSF may indicate rate of disease progression; and identification of a metabolic signature of ALS in blood.

In terms of Aim 4, which pertains to sharing samples, a number of efforts are being made with regard to tracking and sharing. Samples are housed in the central repository, and are tracked after collection using 3D bar code labels with redundant printed information. Samples and clinical information are stored de-identified, but all information is available for any investigator using NEALS samples. A potential future role is to have a virtual bio-repository, with each site maintaining samples locally. The NEALS Sample Sharing Committee oversees sample sharing policies and reviews sample requests. Novel approaches are valued, but scientific methods should be sound. Investigators must prove whether the methodologies and technologies they want to use with the samples are valid. If the committee is unsure of the methodologies / techniques, the investigators will be sent a blinded sample for which they must make predictions using their proposed methodologies / techniques. If the results submitted to the committee are accurate, the investigators will be provided with a much larger set of samples in order to conduct their actual experiment. Thus far, approximately 16 requests have been received. Of these, 8 investigators were provided with full samples and 5 were provided with "test sets" to validate their proposed methods.

Aim 5 regards maintaining and expanding the biorepository. The biorepository has potential to grow with future collection studies with equally rigorous pre-analytical variability controls, become a “virtual” repository, incorporate new sample types, and act as a resource to investigators worldwide. Expansion considerations include the following:

- ❑ Cerebrospinal Fluid
 - Longitudinally collected CSF
 - Linking of biofluid and imaging biomarker efforts
- ❑ Lumbar Puncture Education
 - Direct patient education
 - Webinars
 - Outreach to community providers
- ❑ Potential additional Sample Types
 - Skin
 - Saliva
 - Urine
 - RNA
 - Erythrocytes
 - Buffy Coat (WBC)

Discussion Points

- Dr. Horton noted that the ALSA chapters throughout the country have done a fantastic job of promoting the ALS Registry. Most chapter websites have the ALS Registry button, which ATSDR really appreciates. MDA has largely done the same thing, which speaks volumes about how important advocacy groups are to the registry effort.
- Dr. Sorenson noticed that NEALS had a higher CSF capture rate in the healthy population than the disease population. He asked what they are defining as “healthy” and where they are getting CSF.
- Dr. Berry responded that some preliminary goals were established that they were trying to achieve. The healthy controls are people who have no neurologic disease.
- Dr. Bowser added that it is difficult to define “healthy.” It is the non-neurologic control. Obviously, the disease mimics have been the most challenging to acquire.
- Dr. Berry said that was somewhat of a surprise, but part of this is in the presentation. This is set up as a motor neuron disease or ALS repository, which has been part of the difficulty.
- Mr. Tison said he thought he recognized the biomarker study in which he is a participant. He was surprised and disappointed about the 24 months from disease onset exclusion, with a median diagnostic delay between 1 and 1.5 years. He thought the study would be much swifter with relaxed inclusion criteria.

- Dr. Berry replied that this is a good point, and it is one of the studies they plan to add to the repository. That criterion has been removed. Dr. Bowser added that historically, they were taking all-comers. For this particular study, the goal was to look early in the disease process.
- Dr. Gubitz said that NINDS often receives inquiries from ALS patients who want to donate biofluids. The NINDS Division of Extramural Research cannot accept samples, so she usually directs patients to ALSA or MDA to acquire further information about clinicians who would be interested in such samples who are close by. NEALS would also be a great place for these patients to contact. NINDS does want to be more inclusive rather than directing patients who wish to donate only to a few specific investigators. She wondered whether there was a web link to which she could refer patients that explains how to donate biofluids. She thought a similar scenario would play out for the ATSDR biorepository.
- Dr. Berry replied that there is a web link for the NEALS webpage, which is nealsconsortium.com. There is a button within the NEALS website specifically for biofluid donations. There is also contact information to reach people by telephone and email.
- Dr. Horton inquired as to how NEALS was obtaining tissues. Are they advertising? Are people coming in to say they want to donate?
- Dr. Berry replied that one reason so many centers were included was to try to have as broad a reach as possible. The centers do their own recruitment, and NEALS tries to provide an easy way for patients to find the study on the website. Most of the participants are found through the researchers, who are also clinicians who have contact with patients in the clinics. Enrollment is always a major challenge for any study.
- Dr. Bowser added that most participants come from directors of the sites.
- Dr. Horton inquired as to what the average turnaround time is from the time the sample is obtained to the time it is distributed to a researcher.
- Dr. Bowser responded that while he did not have an exact number for a turnaround time, an on-going process is evolving. As noted earlier, they have received 16 applications for samples in little over a year. A large number of samples were collected during that same timeframe for this particular study. Using SOPs across sites has allowed for particular analyses, and they have not really noted a difference in sites thus far in terms of signatures or proteins. It appears that the methodology for collecting samples is working, and that the samples will be valuable to investigators.
- Dr. Berry added that there are two turnaround times. The first is from the time a sample is collected to the time it arrives at the central repository. The second is the time from a request being granted to shipping the samples. Shipments are batched from the sites unless there is an urgent need to have more samples, which has not occurred. Typically, samples are batched and sent to the central repository every two or three months. The turnaround time to send samples to investigators once they are approved depends upon how many requests are made simultaneously, how much clinical information needs to be

gathered, and how many / what type of samples need to be pulled. This could take up to a few weeks.

- Dr. Heywood noted that PatientsLikeMe engaged in some co-promotion that drove some patients to this study, although he did not know the exact number. Dr. Berry agreed that this was an important recruitment resource.
- Dr. Brady asked whether consideration had been given to developing SOPs for some of the future tissue that they hope to include in the NEALS Biorepository.
- Dr. Bowser responded that they are still developing some SOPs based on internal experience, as well as experiences other groups have had with other diseases. They are working with groups within the NEALS network to determine what is feasible for their populations in the participating centers.

Massachusetts Department of Public Health

Robert Knorr, PhD
Director, Environmental Epidemiology Program
Bureau of Environmental Health
Massachusetts Department of Public Health

Dr. Knorr emphasized that while Massachusetts is not part of the national registry effort, they share the same goals. When the Massachusetts registry was begun, there was only a dream of a national registry. Massachusetts has limitations as a state registry because they are state-funded.

As of 2003, there were no statewide population-based registries for ALS in the US. As a result of collaborative efforts of the Massachusetts Department of Public Health (MDPH) and patient advocacy groups, the authority to establish a Massachusetts ALS patient registry was granted by the Massachusetts Legislature in 2003 and further granted by Massachusetts General Laws. Chapter 111, Section 25A. MDPH regulations were amended in 2004 to clarify that the reporting by health providers of environmentally related diseases, which included ALS, was required. The surveillance of ALS using registry data and the protection of privacy is, in part, assured by Massachusetts General Laws. Because reporting is legally mandated for the purpose of public health surveillance, the reporting of ALS cases to the registry is in compliance with HIPAA and does not require patient consent.

Beginning in 2005, a series of feasibility, focus group, and pilot group studies were conducted to develop the registry methodology. Efforts were made to ensure that the data collection methods were minimally disruptive to neurologists and that the registry would meet realistic expectations of patients and advocacy groups. Statewide implementation began in January 2008, in order to identify all patients with ALS who resided in Massachusetts in 2007. For the first year of data collection, the goal was to identify all prevalent cases. Subsequent years have focused on identifying incident cases and in evaluating possible disease progression among cases previously classified as possible or suspected cases of ALS.

MDPH obtains data from primary and secondary data sources. Primary sources are neurologists and large hospitals. Primary sources are contacted once annually in January to report to MDPH the names, medical record number, and basic identifying information of cases who were Massachusetts residents and who had an office/hospital visit during the previous year. Secondary sources include death certificates, nursing homes/hospices, discharge diagnoses at all Massachusetts hospitals, and patient advocacy groups. Lists of ALS cases are requested from these secondary sources in order to assess the completeness of case ascertainment through the primary sources.

Following the comparison of reported cases between sources, unique cases are identified. The pertinent medical records of these cases are abstracted at the sources by trained nurses using an abstract form. Key source documentation is photocopied. The clinical information collected is that determined necessary to classify cases according to the revised El Escorial criteria. The classification of cases is made by one of two ALS neurology specialists. The category of "suspected ALS," which has been deleted from the revised El Escorial criteria, was retained for the purpose of the registry and sub-classified. The registry maintains the records of all reported cases. "Registered" cases are those that meet the registry eligibility criteria.

Analyses are conducted to estimate incidence and prevalence and also include capture/recapture analyses to evaluate the pattern and completeness of case ascertainment and analyses of the demographic characteristics of the registry population, location of residence, veteran status, usual occupation, family history, the site of onset, and time from onset to diagnosis. Incidence and prevalence is primarily calculated to include any patient whose diagnosis of ALS was classified as Clinically Definite, Clinically Probable, or Clinically Probable—Laboratory Supported. For the purpose of this registry, date of diagnosis was defined as the earliest month/year the medical record reflected that a diagnosis of ALS had been mentioned. Date of disease onset was defined as the month/year of first documented weakness that subsequently progressed to be part of ALS. Time to diagnosis was the interval between month of onset and month of diagnosis. All registered cases are geocoded to facilitate analyses by geography.

The registry is presently abstracting and classifying 2010 cases. MDPH receives reports from approximately 88% of the neurologists contacted. Preliminary evaluation suggests that non-participating neurologists are mostly neurologists who did not see ALS patients or who were no longer in practice. Hospital reporting is 100%. For the 2007-2009 period of registry operation, approximately 2000 reports were received for about 1400 unique cases. About 65% of those cases were subsequently registered. The difference between the reported and registered numbers is primarily due to the ineligible cases, and also because some cases had been registered in an earlier year. Overall, about 80% of cases are reported from primary sources. Multiple types of sources report about half of the cases (e.g., neurologists + hospital + advocacy groups).

While they do not have access to Medicaid and Medicare datasets, they have been negotiating to try to obtain these data. However, the bureaucracy is incredible to try to get through. Fortunately, Massachusetts currently has and is developing another database that many other states have known as the All-Payer Claims Database (APCD). The APCD includes medical, pharmacy, and dental claims, and information from the member eligibility, provider, and product files encompassing fully-insured, self-insured, Medicare, and Medicaid data. They expect to have access to the database for private insurers by the end of 2011 and the public insurance by 2012.

Massachusetts has very limited resources that have been further cut. They are currently running the registry with a budget of about \$70,000 per year. Therefore, it is not possible to conduct many analyses. Using secondary sources permits them to determine whether some cases are not being captured by contacting the neurologists directly. An important goal is to identify where the gaps are so that they can target their best sources most efficiently. This evaluation is currently being conducted.

Discussion Points

- Dr. Boylan inquired as to what percentage of Massachusetts cases are being directly validated by reviewing the medical records. Dr. Knorr replied that 65% of cases are validated in this manner.
- Dr. Brooks noted that one of the goals of having a state or any registry is being able to determine what is occurring in a population in terms of chronic exposure. He wondered whether any modeling had been done in terms of a source exposure that would lead to a certain number of cases.
- Dr. Knorr replied that they have not considered this too much, but it is certainly what they want to be able to do and is why they have not been sharing data with some researchers who have approached them with environmental hypotheses. He has mixed feelings about whether they should be sharing the data. While eventually the data will be shared, they are somewhat concerned because this is a new dataset. As with other new registries, there is always some caution about the comfort level with the data quality. They merely want to be certain. They have an excellent relationship with their healthcare communities, which are on board with the information they are providing. Based on the assessment of secondary sources, they do not believe they are missing cases and are feeling pretty good about completeness. The verification process is aggressive, so they feel confident that the cases being registered are actual ALS cases. Massachusetts uses a somewhat broader definition of ALS than what is being used in the national registry. They are attempting to reach out as broadly as possible to capture cases efficiently so that this will serve as a good model, and so that they will feel prepared to respond to concerns about certain exposures.
- Dr. Brooks inquired as to whether those who are not confirmed to have ALS would fit into Possible ALS or Suspected ALS under the original criteria and to what degree they are losing some capability in that regard. As a clinician, he would say that 16% or more of his patients in the secondary level of ALS are questionable ALS.
- Dr. Knorr responded that they try to be as inclusive as possible. Questionable ALS cases are currently entered into a category of Suspected ALS. This is generally not consistent with the revised criteria, so they are trying to include those. However, he is sure they are missing some cases. Possible and suspected cases are registered, but are not a part of the core dataset to be counted in incidence and prevalence. Possible and Suspected cases are followed yearly to determine whether the disease has progressed. If they are still Massachusetts residents seeing a neurologist, progression would be noted in the registry database. They are trying to be all-inclusive, but there is no way to be perfect.

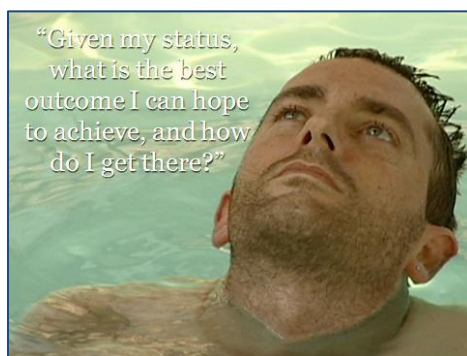
- Mr. Gibson asked how much is currently being spent on registry on an annual basis and what the forecast is for the future. Before writing a bill for the national registry, they assessed state models before states were going through a crisis. Thus, he was interested in knowing how the budget crisis would impact moving forward.
- Dr. Knorr responded that some activities in Massachusetts may not work in other states, which applies to costs as well. They began with the help of the ALS Association in Massachusetts. The bill that mandated the registry was a result of efforts by patient advocacy groups, like the ALS Association, that have been helpful in garnering funding. Initially, Massachusetts did not receive any actual money. There was a mandate by the legislature, but they did not allocate any funds to support the mandate. Eventually, funding became available at a level of about \$150,000 per year in the early years of development. However, that was cut to about \$70,000 which they operate with currently. What that means is that they can continue to collect the data, but cannot do very much with it. Therefore, to him, the registry is not successful. If there are any further cuts, the registry will not be sustainable at all and would cease to exist.
- Dr. Kasarskis requested clarification regarding the 65% case validation, and whether the first cut is Massachusetts residents versus non-residents, followed by determining which of the Massachusetts cases are ALS.
- Dr. Knorr replied that if they began with 100 that represent all reports from all sources, the first cut would be reduced to 80 or so unique individuals. Those 80 are then abstracted and go through verification. Of those 80, 20 to 40 will be eliminated. Of those, about half will be eliminated because they are not ALS cases or they are not residents of Massachusetts. Ostensibly, some patients who may have ALS will be eliminated because they are not Massachusetts residents.
- Mr. Dumas shared pieces of shelf paper and the product information that a friend of his, who is an Occupational Therapist, shared with him. The paper is excellent for gripping keys to turn on the ignition, open the dryer, open doors, et cetera. This is an inexpensive product that can help those with gripping problems. He requested that everyone encourage their patients or loved ones who have gripping problems to try the product. The product is called Non-Slip Shelf Liner and it is distributed by Greenbrier International, Inc. out of Chesapeake, Virginia.

PatientsLikeMe

Benjamin Heywood, MBA President and Director PatientsLikeMe

Mr. Heywood indicated that the mission of PatientsLikeMe is to improve the lives of patients through new knowledge derived from shared real-world experiences and outcomes.

PatientsLikeMe was founded in 2004 by MIT engineers Ben Heywood, Jamie Heywood, and Jeff Cole. The impetus behind this was that Ben and Jamie Heywood's brother, Stephen Heywood, shown in the following photograph, had ALS:

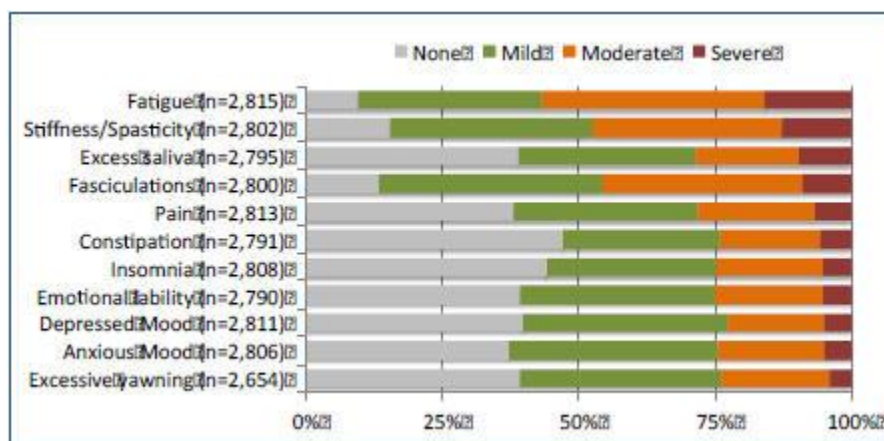


A lot of the work being done by PatientsLikeMe echoes what ATSDR is attempting to do with the National ALS Registry in terms of improving clinical research and improving clinical care. However, PatientsLikeMe has the very direct perspective of giving the tools to the patients first and then trying to balance the other two priorities of improving clinical research and clinical care. PatientsLikeMe was launched in the ALS community in 2005, and has expanded to over 1000 conditions and over 100,000 patients. PatientsLikeMe is an open, patient-facing community by patients for patients focused on specific, life-changing disease states. The business model is built around the aggregation, analysis, and syndication of patient data that is de-identified for partner companies (e.g., payers, pharma, pharmacy, PBMs). Financing to date totals approximately \$20 million. Investors include Invus Capital, Omidyar Network, CommerceNet, and other institutional investors.

With permission, Mr. Heywood shared a live version of Mr. Tison's profile on the system. For ALS, the system includes a basic measure of activities of daily living (ADL). Functional rating scales permit patients to assess their own disease progression mapped against the context of all of the other patients in the community and their standard progressions. Also included are forced vital capacity (FVC), medication / side effects lists, primary symptomology, additional symptoms, et cetera. This is all mapped back to Systematized Nomenclature of Medicine (SNOMED)® ICD-9 coding. In the system, one can look at any individual patient's profile. All of the data is aggregated. For the Rilutek® treatment report, PatientsLikeMe has data on over 1200 patients who are on the drugs (e.g., side effects, dosing, stop reasons, duration of treatment, and burden of costs). There is a search function for patients, which can be done by a variety of variables (e.g., all variables, ALSFRS score, years since onset of symptoms, male/female, et cetera) and the system will automatically filter an update. Mr. Tison is included in a Phase 3 study, which is a challenge that PatientsLikeMe is just beginning to encounter,

particularly in ALS, because they are co-tracking data from clinical trials and may or may not be able to observe signals sooner than the companies. As a company, PatientsLikeMe is ethically and legally assessing how to proceed with such information. They want to do what is right for their individual patients, as well as collectively for patients as a whole.

PatientsLikeMe has an ALS forum that has had over 100,000 forum posts since its inception, so they have a fair amount of qualitative and quantitative data. The ALS community started in 2005 and currently has a total of about 4600 patients, with 100 plus new patients signing up monthly. Roughly calculated, that amounts to approximately 8% to 9% of the newly diagnosed patients in the US joining. The system includes significant data on ALS symptomology, with the Ns reflected in the following table:



This is a longitudinal database, so it is possible to analyze how severity changes through time. PatientsLikeMe does not conduct double-blind, clinical trials, but has produced and published clinical research studies in ALS such as the following:

- ☐ Patients' use of off-label medication
- ☐ Excessive yawning in ALS (published in *Acta Psychiatrica Scandinavica*)
- ☐ What patients want to know and learn about cognitive dysfunction in ALS (published in *European Journal of Neurology*)
- ☐ Use of the ALS community as a control group to assess gambling compulsions in Parkinson's Disease patients (published in *Movement Disorders*)
- ☐ Whether handedness is important in predicting site of ALS onset
- ☐ Patient-led research to measure function in advanced ALS (published in *European Journal of Neurology*)
- ☐ Pilot collecting genetic mutation [When working with Parkinson's genetic mutations, approximately 50 patients voluntarily uploaded their full genome single nucleotide polymorphisms (SNPs)]
- ☐ Whether Lithium delays progression of ALS; the study included a matching algorithm to properly compare PatientsLikeMe ALS patients to those in the Italian study; this study showed that in the real-world there was a null effect, with significantly higher power than the original study [published in *Nature Biotechnology* in April, 2011]

PatientsLikeMe is partnering with national and regional non-profits to increase access to disease resources in ALS and beyond. This is a small company of 40 people, which has limited

resources. Therefore, they try to conduct research that they believe can truly make an impact, and then encourage the ALS community to participate. They recently launched some basic non-profit functionality to allow partners to engage and have a conversation in the site. They are looking to expand this into actually giving non-profits research tools and potentially an open registry—not of the ilk and rigor that ATSDR has, but for organizations with disease states that cannot get to that level or will not be able to fund that type of effort to have the ability to enroll and track patients in a meaningful way. There are currently a number of non-profits in the system across a number of diseases. PatientsLikeMe recently completed a full integration with clinicaltrials.gov so patients can be matched up to a clinical trial relevant for them.

Discussion Points

- Dr. Antao inquired as to how often they update the system. Mr. Heywood replied that he thought they take it down nightly.
- Dr. Brooks asked whether they had modeled a sense of when they lose patients (e.g., those who stop entering data who have entered data), and whether they had any sense of a Monte Carlo event.
- Mr. Heywood responded that in terms of calculated disease states, they had an intern assess the registry in terms of disease and captured a few that way. He thinks they have a few hundred deceased patients officially in the system, which they learn of from a family member, or another patient and which they verify. This has not been done actively.
- Dr. Brooks clarified that he was thinking more along the lines of having 100 in per month and a certain number out per month. He wondered how many were out per month.
- Mr. Heywood replied that they have not assessed this, but his estimate is that approximately 1500 of 4500 are deceased at this point.
- Dr. Horton inquired as to how PatientsLikeMe is marketing this effort.
- Mr. Heywood responded that they started out with standard marketing (SEO, clinical research publishing, PR, et cetera) but it is 100% word of mouth at this time. The lithium study really drove and sustained enrollment. They went from some amount of money to get some amount of ALS patients to basically spending zero and getting the 100 per month by conducting research in which ALS patients were engaged. That is not just people who are taking lithium. It included people who knew their data would be utilized as a control. ALS is the disease for which they capture the highest percentage of the newly diagnosed patients with the condition. The next best one is MS for which they have about 25,000 patients and probably capture about 5% of the newly diagnosed patients.
- Dr. Bowser asked what percent of patients decide they no longer want to be part of the system and request that their data be removed, or after they have passed whether their families request that they be removed from the database.
- Mr. Heywood replied that out of 100,000 registry users, half of them really never engage. About 50,000 have given them some data and about 30,000 have given them a decent amount of data, and about 10,000 have given them an amazing amount of data. They receive about 100 close account requests per month; however, the delete question is challenging because once something is placed on the Internet it really cannot be deleted.

PatientsLikeMe is very specific about this in its privacy policy. A patient can remove their information from the active data themselves, but PatientsLikeMe cannot delete it. It is in the company's back-up, logs, and drug safety database.

- Mr. Tison said he became aware of PatientsLikeMe from his clinic as part of the NEALS trial. He was requested to join.
- Mr. Heywood responded that particularly with ALS, they try to help as many as they are able to if they believe it is good work.
- Dr. Horton said he would be curious to compare the PatientsLikeMe database with ATSDR's database, and he wondered whether there is a way they could download the data and somehow do a cross-reference. This would be helpful, almost like a state / metro surveillance, to determine who they are missing and whether there are gaps in their surveillance system or registry. There could be IRB / OMB issues.
- Mr. Heywood thought this project could certainly be done. They would have to think about how to do the matching. In terms of co-marketing, they could certainly work together. PatientsLikeMe has had to do IRB work for other projects.
- Mr. Tison requested that PatientsLikeMe add an ALS Registry button to their website.
- Mr. Heywood replied that there is definitely an opportunity to do some work in that respect.
- Dr. Bruijn joined via telephone.

New Survey Modules

Lorene Nelson, PhD, MS
Associate Professor
Division of Epidemiology
Stanford University

Dr. Nelson reported on the new web-based modules being developed since last year's meeting. This work is being done at Stanford University School of Medicine. They have been working with Drs. Kaye, Muravov, and Horton over the past year to develop 10 new web-based modules that can be added to the registry for self-administered, web-based questionnaires for patients to complete. This work is based in her group, which with the support of ALSA, founded the ALS Consortium of Epidemiologic Studies (ACES). ACES now has greater than 100 multi-disciplinary members (e.g., epidemiologists, geneticists, neurologists, toxicologists, statisticians).

The aspect of their work that is registry-related has three major aims, which are to 1) develop short, web-based versions of risk factor questionnaires appropriate for self-administration; 2) use a modular format so that patients can answer the questions module by module; and 3) pilot test the web-based modules with patients across a range of ALS severity and make revisions

accordingly. The first and second aims have been completed for the 10 new modules, and they are soon to embark on the pilot testing phase.

In developing these modules, they had the goal of not only making them very easy to understand and self-administer, but also they were concerned about respondent burden. Thus, they tried to design the modules such that they could be administered in less than five minutes per domain. There are a couple of domains for which this simply could not be done because they are just too long. The OMB, from which ATSDR must acquire approval for the modules, will be much more willing to approve them if the respondent burden collectively is limited.

The epidemiology modules already in use in the ATSDR National ALS Registry include the following:

- ☐ Sociodemographic characteristics
- ☐ Occupational history
- ☐ Military history
- ☐ Lifestyle factors: alcohol intake, smoking
- ☐ Physical activity
- ☐ Family history of neurodegenerative disease

As noted earlier, approximately 40% to 47% of those registered in the National ALS Registry have completed one or more of the existing modules.

The epidemiology modules in development for use in the ATSDR National ALS Registry include the following:

- ☐ Residential history, pesticide exposures
- ☐ Toxicant exposures via occupations and hobbies
- ☐ Trauma (traumatic brain injury; electrical shocks)
- ☐ Caffeine consumption
- ☐ Reproductive history (women)
- ☐ Health insurance
- ☐ Open-ended questions

In addition to making the modules user-friendly, the developers tried to take the questions from already existing national data sources because if they were able to do this, there would be a possible comparison group. While this registry has people with ALS, it does not have controls and it is almost unheard of that such a registry would have a control group. By using questions from existing sources such as the National Health and Nutrition Examination Survey (NHANES), there will be a comparative data source when the time comes to analyze the data. There are few examples of registries that incorporate the collection of factor data. Certainly, Surveillance, Epidemiology and End Results (SEER) registries do not, other than the usual age, sex, race, and so forth. HIV registries do because they need these data for sub-classification of HIV by type. They were not able to come up with any other examples of where this is being attempted, and Dr. Nelson thought it was wonderful that this group had the foresight to do this at the outset. She then reviewed the new modules domain by domain, pointing out those modules for which a validated question set was used and noting that for modules that do not have a national data source for the questions, many are modules that are being used in epidemiologic studies throughout the US. Therefore, there are data in specific geographic regions for control populations for many of the questions.

The residential history module is by far the most burdensome because it requests all residences of > 6 months. While questions cannot be asked about specific addresses, the developers are hoping to link with objective data sources that will have people's specific addresses. Information will be asked for every residence, even if someone moved within the same city or town.

Residential pesticide exposure is of interest including insecticide use, herbicide use, and fungicide use. For each area of pesticide use, information on the number of years used and average uses per year is collected.

The most complex after residential history is the occupation module that asks about toxic exposures for the classes of substances that potentially have neurotoxic properties (e.g., metals, solvents, and pesticides).

The next domain is hobbies that involve toxic exposures, with a particular emphasis on lead or solvent exposure. There is a list of 12 to 14 hobbies that potentially involve lead or solvent exposure.

The questions in the traumatic brain injury (TBI) module come from the Ohio State University Traumatic Brain Injury Identification Method Short Form (OSU TBI-ID), which is a validated, published source. The OSU TBI-ID was developed based on the case definition for TBI used by CDC's National Center for Injury Prevention and Control (NCIPC). NINDS has endorsed this instrument for use for their TBI data element selection. It has high inter-rater and test / retest reliability, and has had a predictive validation in terms of correlating the measures obtained from this with cognitive and affective status.

While electrical injuries are much less frequent, they are of interest due to past studies that have suggested that there might be an increased risk of ALS associated with electrical shocks. In this module, questions are asked about the severity of the electrical shock.

The caffeine consumption instrument was chosen from the Fred Hutchinson Cancer Research Center Caffeine Questionnaire, which asks about the source of caffeine, years of exposure, and frequency of consumption.

The reproductive history questions were taken directly from NHANES to address the age at menarche and menopause, and number of pregnancies.

Also from NHANES is a single question about the type of health care insurance the individual has. There are two open-ended questions, the first of which asks the person's thoughts about factors that may have caused his or her ALS. Obviously people who develop a condition like this think a lot about what may have caused it in their own particular situation, so it will be very interesting to hear what insights they have about this. The second question pertains to what individuals think might be risk factors for ALS in general.

There are no requirements for joining ACES. Joining permits access to all of the ACES resources, including a soon to be updated literature review of all of the epidemiologic studies conducted on ALS with links to the actual literature. The ACES site can be accessed at aces.stanford.edu.

Discussion Points

- Mr. Heywood asked whether all of the items are open source and are free licenses, whether it is easy to gain access to the questions, and whether there are any calculations.
- Dr. Nelson responded that each has the potential for calculation of the composite variables that represent a person's exposure. These are still being developed and pre-tested. She deferred to Drs. Horton and Kaye regarding the open source question.
- Dr. Horton replied that he had not really thought about having this integrated into other sources.
- Dr. Kaye added that the questions that came from other sources would have to be obtained directly from those sources.
- Mr. Heywood said he could get them 10,000 controls in two weeks if they want data.
- Dr. Horton clarified that the risk factors were selected based on literature reviews and other considerations.
- Dr. Nelson replied that considerable thought went into what the next set of modules would encompass. Those who are reading the ALS literature on a regular basis could understand why there is an interest in neurotoxicant exposures, pesticide exposures, lead exposures, et cetera. TBI is a particularly hot topic currently in ALS, so they definitely wanted to include something about this. There has been little data and few reports regarding whether there is any association whatsoever between caffeine consumption and ALS, but caffeine is actually protective in the case of Parkinson's disease. Reproductive history probably has not received as much investigation as it should.
- Dr. Kaye added that the health insurance question was included to help evaluate why individuals may not have been found in the national databases, that is, they did not have Medicare or VA benefits. ALS is a compensated VA disability and once someone is diagnosed with ALS, they should be able to obtain Medicare benefits fairly quickly. Asking the insurance question is another way to evaluate whether people are taking advantage of the benefits for which they may be eligible.
- Dr. Horton noted that on the open-ended question, they have received some criticism from some PALS and others that these risk factors being developed are way too short and they want to offer more information about their history. Because OMB requires that burden on participants for completing these surveys is minimized, they must be kept brief and to the point. The open-ended questions offer people an additional opportunity to provide whatever information they wish. While it will be somewhat difficult to analyze this information, it is good to give people the chance to put down what they are thinking.
- Mr. Dumas inquired as to whether these modules are currently available for him to complete.
- Dr. Nelson responded that these modules are not yet available. Development is complete, but they must now be pilot tested with human subject committee approval.

- Mr. Dumas asked whether people could volunteer to be included in the pilot testing of these questions.
- Dr. Kaye replied that the pilot test is being designed at Stanford, and they already have two or three different groups they will evaluate for these surveys. Once the surveys have been evaluated and blessed, the IRB, OMB, and CNA computer security must be amended to get these modules added. Best case for a projected date when the modules will be available is 2013.
- Dr. Horton emphasized that while this is not as rapid as they would prefer, they must follow protocol. There are currently seven surveys already on the portal that people can take.
- Mr. Johnson indicated that ATSDR would notify registered PALS when the new modules are available via social media, email, the website, and ALS support groups.
- Mr. Tison acknowledged that there are approval requirements; however, he emphasized that the patient community is very interested in these additional modules and he wondered whether anyone could estimate timing for any of these new modules to become available.
- Dr. Kaye indicated that they are engaged in discussions with OMB to determine whether there is a subset that they would allow under a minor modification rather than a full application. It is possible that a few of these could be available sooner.
- Regarding the open-ended question, Mr. Gibson said that probably the largest community is comprised of families who have lost a loved one to ALS. Because they are not the patient, they cannot enter information. He wondered whether there is a way to set the open-ended questions up for non-patients to enter their information.
- Dr. Horton thought this was a good idea. Although the modules are currently open only to PALS, ATSDR can look into making them accessible to family members. Many people use ATSDR's feedback mechanism as a way to express their feelings, concerns, et cetera. While he could not make any promises, he thought it was worth pursuing.
- Dr. Brooks commended the developers on using modules that might have external control groups. Moving forward he thought they might want to consider publishing these for a number of reasons, not the least of which is that the American Academy of Neurology (AAN) and other organizations are working on performance measures for ALS clinics as part of disease-specific certification. It would be very beneficial to have an epidemiological capture of performance measures.
- Mr. Dumas pointed out that while they talked about the burden of the questions, the burden is really the ailment. It seemed to him that if loved ones / caregivers had the log-in and password, they would be able to help facilitate correct answers. Many people with ALS may not be able to make keystrokes or recall what happened in 1958. Loved ones / caregivers should be encouraged to be involved, with the approval of the patient.
- Dr. Horton replied that there are currently two accounts: PALS and Public. They can look at including some type of open text field.

- Mr. Johnson added that they would have to work out inclusion of a text field with IRB and OMB, but they do encourage family members to assist PALS in completing surveys if needed. There is a statement on the website about this being allowable.
- Dr. Kaye indicated that they have received permission to assist people on-line. If someone does not have anyone to assist him/her, ATSDR now has the approval to take their information. While they obviously cannot interview everybody, they can facilitate registration for someone who cannot complete the information by themselves.
- Dr. Horton invited feedback on risk factors not shown that people thought should be included.
- Dr. Gubitzi noted that for a number of degenerative diseases, researchers have started to mine for exposure data along with genetic risk factor data from patients. The existing modules ask about family history, but she wondered whether that module captures any disease mutations.
- Dr. Nelson responded that it does not. The existing family history module asks about history of ALS, Parkinson's, and Alzheimer's.
- Dr. Brooks requested that someone go through the flow chart of "blessing" the modules. He assumed that the modules would pass from Stanford to McKing, but he wondered what procedure followed (e.g., public comment, et cetera).
- Dr. Horton replied that they receive the modules from Stanford, they have to amend the IRB package and submit it to OMB, and usually OMB takes the longest time. OMB is in place for checks and balances. The IRB typically weighs in on scientific issues, while OMB addresses burden issues. They have a good relationship with the IRB, which is very familiar with this project. For the new modules, they cannot simply submit an amendment. They have to submit a new OMB package, which will take some time.
- Dr. Kaye added that the original protocol and all of the original surveys went through external peer review at ATSDR and then to the IRB. Once everything was approved, they went to OMB and then had to have computer clearance. There were four reviews, including all of the annual meetings during which ATSDR accepted input.
- Dr. Brooks asked whether there was ever any on-line public comment aspect to the approval process.
- Dr. Kaye replied that there was not an on-line public comment aspect. However, there is a 60-day public comment period when an announcement is made that something is going to OMB, and there is another 30-day comment period once it arrives at OMB. They tried via these meetings and working with colleagues to acquire people's input in advance rather than waiting for the OMB comment periods.
- Dr. Williamson said that it was worth noting that these are all different hurdles that ATSDR has to overcome that are controlled by different groups, some of which are within CDC / ATSDR and some of which are outside. The external peer review is an ATSDR process; however, it is controlled by the external peer reviewers in terms of the timing. The IT and

IRB processes are controlled by ATSDR / CDC, although Stanford may have an IRB process as well (Dr. Nelson confirmed that they do). OMB is a federal government entity that is entirely separate from ATSDR / CDC. They are told that the typical average length of time from submission to OMB through clearance is 6 to 9 months.

- Dr. Brooks said he was thinking more along the lines of giving the patient community a larger input into this than they currently have with only two members in this meeting. He suggested that PatientsLikeMe, ALSA, and MDA should announce when the new modules will be up for public comment. The patient voice must be heard.
- Dr. Nelson replied that patients at the ALS clinic at Stanford are included. A year ago, they were told by the Stanford IRB that they did not need approval to pilot test these modules. Then they wanted to use a research subject source called researchmatch.org, which CTSA-funded organizations can use. There are 31 patients in that source that Stanford could access, but the site requires an IRB approval number. When they requested a formal waiver from the Stanford IRB, a higher level person indicated that they would have to have IRB approval for the pilot. This pilot information has been submitted to the Stanford IRB for approval.
- Mr. Tison asked why PLS and PMA were excluded from registration.
- Dr. Kaye responded that ATSDR is assessing whether they can add PLS. The algorithm that was built to use the national data does not accurately identify any MND except for ALS. They think they may be able to develop an algorithm for PLS as well, but nothing else. The ICD-9 codes for other MNDs did not reliably identify the specific diseases they represented.
- Dr. Boylan inquired as to whether the existing modules are published anywhere so that people could see them, in terms of the results.
- Dr. Horton replied that this is a somewhat touchy issue in terms of the actual questions, given that publishing the questions could bias the results. For that reason, they have shared only the module names.
- Dr. Kaye added that there was also some concern that some people may not take a module because they know what the questions are, or that some people knowing the question ahead of time would provide a different answer if they had a week to think about it versus someone who just went on-line to take the module. To try to decrease that type of bias over which they have no control, they have not published the specific questions.
- Dr. Horton pointed out that the smoking module is a good example. If someone knows the question ahead of time but does not smoke, there is a chance that they would not complete the smoking module because they do not believe it relates to them. However, it is also important to know if someone does not smoke.
- Dr. Boylan clarified that he was not asking so much in regard to public access, but instead was asking about access for health professionals or others in the field who are interested in knowing what is actually being asked in the registry in terms of either offering comments or making suggestions about additional information that might be included or activities they may be engaged in separately that might run parallel with it.

- Dr. Horton replied that they could potentially discuss this, but if they do something like this, it would have to be strictly limited to a small subset of people (ALSRG, ALSA, and MDA). As mentioned before, once something gets out, it can take on a life of its own. ATSDR is simply trying to be cautious.
- Mr. Dumas suggested that the people in the room who are interested in the information Dr. Boylan was talking about certainly have his trust. He would not be at all reluctant to share the questions, especially if a doctor or specialist could enhance those questions, help to dig deeper, or better analyze the responses.

Kevin Boylan, MD
Director, ALS Center
Department of Neurology
Mayo Clinic

Dr. Boylan reported that ATSDR has invited the ALS Research Group (ALSRG) to contribute a clinical module to the national registry. The ALSRG is an organization comprised of approximately 200 basic and clinical investigators and clinicians who are involved in ALS care, as well as representatives from ALSA and MDA. It is primarily North American, but others from nations outside the US are involved. About a year ago, ALSRG established a registry subcommittee to act as a conduit to or liaison with ATSDR to learn more about the national registry and offer to contribute in any way that they can. The clinical module has been reviewed by the registry subcommittee at a level at which there is an exchange of ideas, but not a formal outline—certainly nothing on the order which Dr. Nelson discussed. He thought in part the interest of the subcommittee at this point is to try to inform the process to the extent possible, and they chose to convene at the international meeting in Tarrytown to be held the week after this meeting because it will follow a clinical data elements meeting that will address the status of development of the clinical data elements for ALS. There is a general feeling that this will be highly relevant to any contribution the group tries to offer.

One question regarding what optimally should be included in a clinical module is impacted by what is already being asked. Dr. Boylan's understanding is that there are some elements regarding ALS, for example physical region of the body where the disease began that are not asked in the existing demographics. This would be of interest to the ALSRG group, and there are potentially other elements of ALS that would be of interest to them in terms of long-term and large-scale data collection as part of the registry. An important starting point is a clear sense of what is presently being collected in order to do that. There are some key questions: Ideally, what should the objective of a new module be? Are we looking for clinical information to augment the existing modules? Is it intended to stand alone and collect data on milestones for a person with ALS? There are also questions regarding the content that could potentially "bump up against" some of the things on which Dr. Nelson is working in terms of epidemiology. The objective certainly is not to be redundant, and certainly is not to include things that are already being addressed. One thing that has given the group some pause is that this is like a large machine that is moving forward, but there are some questions about the direction and how best to contribute to it. To the extent possible, it is important to know what information is currently being collected and what information will be collected in the future so that they can be confident in the end that it will not be duplicative or result in something that will not be an optimal contribution. A corollary question regards whether there is any potential for existing modules to have questions added. The frequency of the longitudinal survey every six months and whether

there is any potential for increasing the frequency to quarterly has also been raised as an issue. Quarterly completion would align better with the typical cycle of patient follow-up in ALS centers.

Discussion Points

- Regarding the potential for existing modules to have questions added, Dr. Kaye pointed out that once modules have been completed, they are grayed out and the registrant can no longer access them. Any new questions must be contained in a separate module. There are also some questions about existing registrants versus new registrants. Creating a new module is beneficial from a mechanistic as well as an epidemiologist point of view, because some people may be deceased by the time the new question is included, and having to keep track of which version they saw could be problematic as well. It may be easier to simply note the date at which certain modules came on line, which could help with some analysis issues. Regarding the frequency of the longitudinal survey, this has been discussed internally and can be done. Obviously, completing the survey every quarter rather than every six months increases the burden, which raises a number of issues.
- Dr. Brooks pointed out that they could be missing incident cases and important information about those by not having registrants complete the longitudinal survey more frequently.
- Dr. Horton indicated that they would provide a list of the questions, particularly if it would help guide ASLRG about what is included in the potential clinical module. He cautioned that all of the surveys on line and those that are being created are patient-answered surveys. Thus, even though it may be referred to as a "clinical module," it needs to be developed such that a patient can answer the questions without having to seek the answers from their physician or neurologist to acquire the information to enter into the system.
- Dr. Nelson added that she would be happy to assist as well, and indicated that there are no real clinical questions in the risk factor modules. Other than the family history question that asks about ALS, Parkinson's, and Alzheimer's, there is no clinical content.
- Dr. Kaye clarified that the quality of life module and the ALS functional ratings self-administration have some clinical content, and they have added a few questions that are related to emergency room use and hospitalizations. In demographics, the only clinical item is the weight at age 40 and current weight. This was included in demographics because they simply did not know where else to place it.
- Dr. Sorenson requested further information about the OMB guidelines so that those who are working on the module can triage what they believe to be most important.
- Dr. Horton responded that a general rule of thumb is the shorter the better.
- Dr. Kaye added that they are averaging the burden to some extent in that the burden is for the entire process. Currently, they are saying that the burden is approximately 45 minutes from start to finish. That includes 10 minutes to complete registration and 5 minutes for each module. There are 7 modules, as well as the additional burden of completing the functional rating scale every 6 months. Regarding OMB, her rule of thumb is that they do not want to exceed 1.5 hours of total burden. With 45 minutes currently, there are approximately 45 minutes to spare. Dr. Nelson is in the process of developing 8 modules at

5 minutes each, which basically leaves 5 to 7 minutes. With simple Yes / No or point / click responses, this would allow for approximately 14 to 15 questions.

- Dr. Boylan inquired as to which existing module is the longest.
- Dr. Kaye responded that the longest would be family history for those with large families. The most complicated to answer is the module pertaining to physical activity, given that people must recall the age at which they engaged in certain activities and to what extent (e.g., per day, per week, per month).
- Dr. Horton requested input about further questions people thought would be important to add now. For example, there are no questions currently that ask about Rilutek® use.
- Dr. Kaye clarified that it is not asking additional questions—it is one or two of the modules that have already been proposed.
- Dr. Kasarskis pointed out that if he was a patient confronted with all of this web-based information and surveys, the cumulative burden of the existing modules, the modules being developed by Dr. Nelson, and the PatientsLikeMe questions, he would think, “I have already answered that somewhere else.” He could understand why patients might want to bail out of the entire process because of that. This speaks to the importance of using validated, standardized instruments so that they can request permission from patients to acquire this information from other groups, such as PatientsLikeMe.
- While Mr. Dumas agreed that respondents could become frustrated, as long as he knows someone is actually assessing his responses and they are not going into a “black hole,” he is fine with answering the questions. He could understand how people might be concerned if they did not know whether their responses were being read, especially those who do not have the privilege of being involved to the extent that he is.
- Dr. Kasarskis inquired as to whether ATSDR had considered downloading standardized instruments onto a patient’s computer so that they could complete the modules at their leisure off-line, and then upload a completed packet so that all of the fields would be in the register and ATSDR would be able to acquire the data. That way, the responder would not have to be concerned about losing all of their data due to power failure, time-out, et cetera. However, this would open the possibility of people sharing the questions.
- Dr. Horton replied that this has not been discussed.
- Dr. Kaye added that the major issue regards whether they would ever be able to acquire the security to do this. This would mean transferring personal identifiers through time and space, which is a major red flag. She liked the idea because people could work on it in their own time. They can certainly float the idea with their security representatives to determine whether this is feasible.
- Mr. Johnson clarified that the way the system currently works, people can take the modules at their leisure. They do not have to complete everything at one time. They can save what they have completed and return a week later to complete additional surveys. They can take one survey at a time. There is no requisite to complete all of the surveys at once. While

ATSDR would like for people to get as much done as possible, they do not want to place that burden on anyone as a requirement.

- Dr. Boylan requested clarification about adding a small number of questions and how that would work, given that they could not be added to existing modules. He also wondered what the timeline would be.
- Dr. Horton replied that they could not insert questions into existing modules. A new module would have to be developed.
- Dr. Kaye responded that the timeline would depend upon whether something was considered to be a minor modification. She knows what a minor modification would be for the IRB; however, she is not clear what OMB means by minor modification. A major modification is the same as an initial application, which can take 12 to 18 months.
- Dr. Horton added that there is no reason why a good clinical module could not be part of the minor amendment. It never hurts to ask, and they always do.
- Dr. Nelson pointed out that one or two of the risk factor modules being developed may take on a lower priority compared to obtaining more clinical information. To her, acquiring more clinical information on a patient is a very high priority.
- Mr. Tison said he realized that another generation added to the family history adds a lot of people, but he wondered about a simple question pertaining to a grandchild or grandparent who is also affected by ALS. His grandfather also had sporadic ALS. The current registry misses this data. His parents and siblings are unaffected.
- Regarding Mr. Tison's earlier question about why they only ask for one generation rather than going two or deeper, Dr. Horton asked whether there was some reason this was decided.
- Dr. Nelson replied that it had to do with the difficulty of recalling this information, even with interview-based surveys. Perhaps this could be a minor modification to the family history component. While it will be a small percentage of people, those who have multi-generations affected is an important group.

Biorepository for ALS Specimens

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Agency for Toxic Substances and Disease Registry

Dr. Antao reminded everyone that very little is known about the role genetics plays in ALS. Given that there is familial ALS, it is believed that genetics plays a major role in this disease. There are other biorepositories that contain specimens from persons with ALS and other neurological diseases, such as Traumatic Brain Injury (TBI). The problem is that some of these biorepositories are often limited to select groups (e.g., military veterans with ALS).

The purpose of the proposed biorepository component of the National ALS Registry is to evaluate the feasibility of establishing a biorepository open to all US residents with ALS enrolled in the National ALS Registry. The objectives are to establish a protocol for the creation of a biorepository of specimens (e.g., blood, tissue, spinal fluid) from persons with ALS enrolled in the National ALS Registry; and conduct a small pilot project to collect biological samples from the ALS Registry enrollees based upon the protocol developed.

Regarding the methods, beginning October 1, 2011, ATSDR will provide funding to prepare such a protocol. ATSDR is particularly interested in establishing a blood and brain tissue bank. The selected contractor will work closely with the VA to determine how registry enrollees with military experience can become part of the VA's Brain Banking program.

The expected outcomes of the pilot project are as follows:

- ☐ Evaluation of the feasibility of a biorepository of persons with ALS enrolled in the National ALS Registry;
- ☐ Identification of the most efficient sample collection strategies (e.g., blood spots, buccal swabs, blood draws) for patients with ALS;
- ☐ Provision of guidance on the type of molecular analyses that can be conducted;
- ☐ Recommendations about appropriate location(s) to house the repository specimens;
- ☐ Description of quality assessment/quality control procedures for sample collection; and
- ☐ Development of a protocol for evaluating requests and releasing specimens to qualified scientists/researchers.

The value of the proposed repository is the ability to connect the biological material to information about demographics, potential risk factors, and medical treatment. This will make the biorepository especially valuable to ALS researchers.

In conclusion, Dr. Antao indicated that the purpose of his presentation was to obtain input from the meeting participants regarding what more ATSDR can do to make the biorepository a reality like the National ALS Registry.

Discussion Points

- Dr. Horton pointed out that while ATSDR knows a great deal about creating registries, they are not necessarily experts at creating a bioregistry. Any bioregistry is going to be expensive, but the hope is that two to three years from now the economy will have improved and the climate will be such that ATSDR can start a bioregistry. The first goal is to determine whether doing so is feasible, how a registry can be constructed that does not necessarily compete with other existing bioregistries. The ATSDR bioregistry would truly be national in scope, and the data from the National ALS Registry could be leveraged in terms of marketing to PALS to find out whether they are interested in providing biological samples. This would be a win for ATSDR and could help the scientific community at large. ATSDR is interested in blood, tissue, brain banking, et cetera.
- Dr. Sorenson inquired as to whether ATSDR has experience with bioregistries and what the rationale is for moving into this area.
- Dr. Horton replied that in his personal opinion, the bioregistry would make this a more complete, world class registry because not only does ATSDR have epidemiological data, but also they would have biological samples that could make the epidemiological data that much stronger.
- Dr. Sorenson pointed out that NIH funds a number of bioregistries, including NEALS. Given that there are many large, funded biorepositories already in existence, he wondered why ATSDR would want to do this.
- Dr. Horton said he was not saying that ATSDR was necessarily going to do this, but he thought they owed it to themselves and people like Mr. Tison and Mr. Dumas to determine whether a bioregistry can be incorporated into the National ALS Registry. The contractor who is awarded the funding will be asked to evaluate all of the existing bioregistries to determine whether there is room for a national bioregistry and whether it makes sense for ATSDR to pursue this.
- Dr. Kasarskis said that one experience he had was with the sample gathering endeavors for the NINDS Coriell Cell Repositories. He thought that was a successful effort because the physicians and their teams were paid \$100 per sample to complete the small common data element form and draw the blood and ship it, which was very easy to do. Almost 2000 samples were collected in 15 to 18 months. Almost without a doubt patients are very concerned about DNA sequencing. When patients present in the clinic, they have reviewed the web page and other media and are very focused on this question and appreciate what ATSDR is trying to do. The VA registry included a blood sample DNA banking component. As he recalled, 95% or more of the participants in the registry agreed to donate a blood sample for DNA banking. What operationalized that in a highly successful manner was that the registry had funding to pay a nurse to visit homes to collect and ship the samples. There was a great deal of regulatory training involved with that. This effort made the process user-friendly and effortless, so the only reason to opt out of making a sample donation of that type was that they did not want to. There were no excuses. No one had to make an extra trip to

the medical center or extend their scheduled clinic visits. The samples were collected at their convenience in their own homes. That was a major selling point, but everything has a dollar sign attached to it. There is interest and there are mechanisms in place for collecting DNA samples, so he thought that people would gravitate to this, especially since they have invested so much of their time completing the modules.

- Ms. Bledsoe inquired as to what scientific questions ATSDR anticipates such a repository would answer. She emphasized that this is important to keep in mind when building a repository because they are expensive. There are other resources, so it is important to determine what those resources are and what the gaps are in the science and resources.
- Dr. Horton responded that while ATSDR knows how to build disease registries, they are not as familiar with biorepositories. Therefore, they needed a contractor with experience to help answer these questions. The contractor will help to identify the resources and gaps.
- Dr. Antao added that while there are several existing registries, they are limited to certain specific populations. In his mind, what would differentiate the ATSDR registry from other registries is that it would be national in scope and would not be limited to certain types of populations. ATSDR's primary contribution would be to make the samples available to other scientists in the future.
- Ms. Bledsoe indicated that the VA is very interested in ways that they can partner with ATSDR on this effort with regard to the VA brain collections, and will be speaking with the ATSDR contractor as soon as the contract is awarded.
- Dr. Horton responded that the VA is set up for this and ATSDR is not. They do not want to "reinvent the wheel," so the goal is to leverage what already exists.
- Ms. Bledsoe added that the details such as the scope, feasibility, and resource requirements will need to be addressed before the VA and ATSDR can decide how they might best work together on this effort. Certainly, it is a great opportunity to explore.
- Dr. Gubitzi stressed that thinking about the gaps and needs of the ALS community will be very important as this project is developed. She said she was less concerned about duplications at this point. For example, the NINDS Repository is a multi-disease biobank that focuses on genomic DNA and lymphoblastoid cell lines with associated de-identified clinical data. They are currently expanding the scope of biomaterials they are accepting, and have begun to bank stem cells that can be reprogrammed for several neurological diseases. However, in general, the NINDS Repository does not accept patient autopsy material. So at least from the NINDS perspective, there is a need in this area.
- Dr. Bowser reiterated that there are other biorepositories and that these are very costly. The scope and magnitude of what can be done is obviously driven by the amount of funding behind any effort. The NEALS Repository work was driven by NIH funding he received for that project for a finite time. If that funding disappears, their ability to collect samples also disappears. The scope and magnitude of being able to marry a biorepository with a national registry, collect clinical information, obtain samples from living patients, and register them for post-mortem assessment offers an opportunity to evaluate clinical information and samples throughout the entire disease course. This is unique, and the ability to collect all of the neurologic information after the fact would be an incredible resource and one for which he

could not dream of obtaining enough funding to conduct. There are currently a number of individuals and groups that can piecemeal together portions of the information, but cannot bring it together into one larger effort. That is really the major dream and goal. That is to be applauded in something that in the future will be incredibly valuable. They must think big, but carefully. For example, the one week washout period is critical because some of the high end instruments detect metabolites of drugs that ALS patients take. That is a meaningless biomarker, so careful thought must be given to how to eliminate some of the noise in the samples in order to dig deep, address questions, and use high end technologies. Bringing in individuals and groups from some of the other neurodegenerative diseases, which are in some ways ahead of them, would be beneficial. For example, the Alzheimer's Consortium has a lot of nice guidelines and Parkinson's is soon to publish their guidelines. Using the best case scenarios from those efforts and merging them into the ALS initiative would be advantageous.

- Dr. Brooks indicated that the Canadians, the Dutch, the Italians, New York University, and the University of North Carolina School Of Medicine have RNA-based registries. He highly recommended taking a more modern look at this from the point of view of adding RNA to the things that should be considered for collection. That would differ from any existing registry, with the exception of potential autopsy tissue that could have RNA, though it may not be the way it is needed for processing. With regard to process, he suggested that ATSDR convene those who are already engaged in biorepository efforts to try to outline the processes that will be evaluated with the repository moving forward. He did not think all of the representatives were in the room that would be necessary to formulate that. Several repositories at different levels have suggested what types of items should be collected. Some of their European colleagues may be ahead of them with regard to this. It might be helpful to convene a separate meeting to address this issue.
- Dr. Horton indicated that one of the first things the contractor will be required to do is assemble a group of experts, such as those Dr. Brooks mentioned, to deliberate what would make a good bioregistry.
- Dr. Pentz applauded ATSDR's effort to work with the VA. She is a consultant on the Genotype-Tissue Expression (GTEx) that is funded by NIH. She emphasized that starting a brain collection program is incredibly difficult, and RNA must be collected. She suggested that ATSDR speak with the GTEx investigators about all of the difficulties they experienced setting up that program.
- Dr. Horton acknowledged that there is no question that setting up a bioregistry will be incredibly expensive. It was his understanding from Dr. Brady that the cost of one brain is \$5,000 minimum.
- Dr. Brady responded that if they receive a brain that required only collection, processing, storage, and conducting the neuropathological diagnosis, the cost is approximately \$5,000. If they enroll the individual, conduct the follow-up, complete the ALS function rating scales every six months, and develop a recovery portfolio, the cost is approximately \$10,000 per patient. That does not include the cost of the equipment, which is approximately \$1.5 million.
- Dr. Bowser noted that with ALS, it would be important to collect spinal cord and muscle samples. This is something that the expert panel would define, but it is clearly more involved than just the brain.

- Dr. Horton indicated that ATSDR does not intend to limit it to just brain and tissue, but wants to determine the feasibility of collecting everything possible (e.g., blood, saliva, tissue).
- Dr. Bruijn said she was very interested in and excited about this opportunity, and would support the importance of the bioregistry and the need for it in the community in collaboration with what is already being done with Coriell and the VA Registry.
- Dr. Horton indicated that ATSDR hoped to make the award within a couple of weeks. This has been an on-going process that required the announcement to be published in the *Federal Register* and follow the application process.
- Dr. Williamson added that the process for selecting a contractor is strictly regulated, and is out of their hands. The CDC Procurement and Grants Office (PGO) is in charge of the process of overseeing a panel of experts who review the proposals that are submitted. While the team can offer input into the request for proposals, they do not necessarily have control on the back-end of that process.

Connecting PALS with Clinical Research

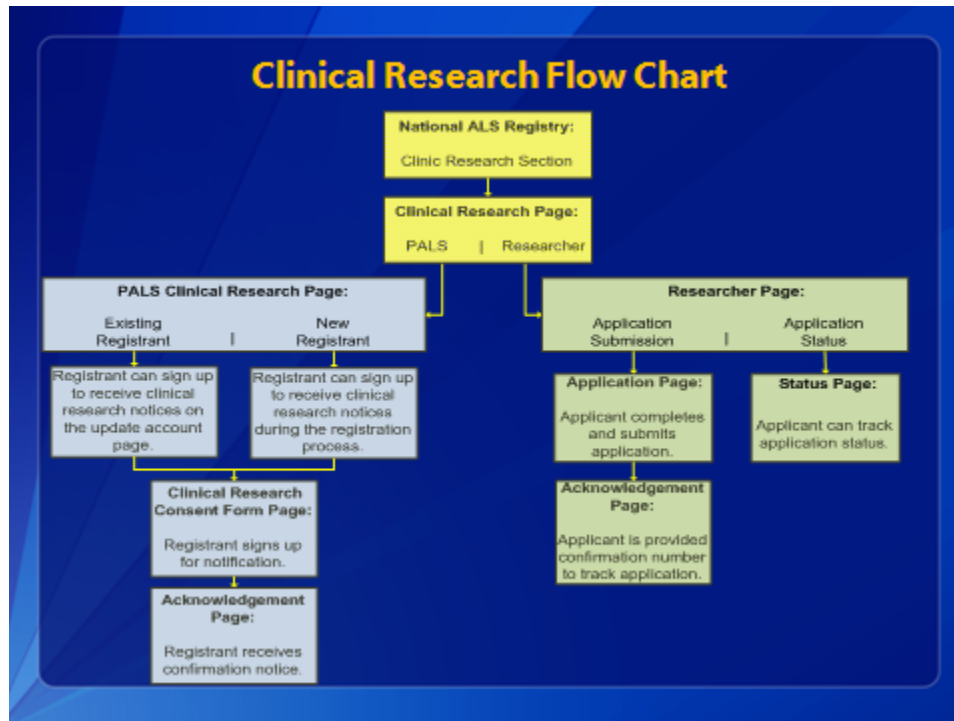
Wendy E. Kaye, PhD
Senior Epidemiologist
McKing Consulting Corporation

Greco Johnson
Business Analyst
Emergint

Dr. Kaye emphasized that recruiting patients for a clinical trial is challenging. ALS researchers have expressed interest in using the National ALS Registry for recruitment purposes. However, under the current arrangement, ATSDR cannot release identifiable data. ATSDR spoke with a group who were attending the American Academy of Neurology meeting in April 2011, as well as others, and determined that people were interested in ATSDR pursuing a way to identify registry participants interested in participating in clinical studies. In order to link interested PALS enrolled in the National ALS Registry with researchers conducting clinical trials, the Clinical Research Notification Purpose was created. This system will notify eligible ALS Registry participants about ALS-related clinical research being conducted throughout the US.

The process will be that a researcher will submit an application to ATSDR. The proposed study has to be IRB-approved and the researcher will have to provide documentation of IRB approval of the study and of any recruitment materials. The submission will be reviewed to determine the appropriateness of the study, and will then submit an IRB amendment to allow notification for approved studies. After IRB approval, ATSDR would then notify the investigator of approval, send an email to eligible participants, and notify the investigator of the email being sent and the number receiving the email. ATSDR will develop a tracking tool for researchers that will be accessible via the web portal, which will update the status of the request. ATSDR received IRB approval to add consent for contact into the registry. Consent to contact has been added for new registrants, and ATSDR is working on re-consenting current registrants so that they can also participate. That component is expected to be deployed in October or November 2011.

Dr. Kaye shared the following clinical flow chart, explaining that ATSDR would not be able to do as fine a screening as in a clinical setting, but if a researcher requests certain age ranges or subjects who ATSDR has heard about in the last 6 months, those can be subsetted and the emails sent only to those who meet the requested eligibility criteria:



The following is an example of the Consent for Clinical Trials Notification page on the website, which is now up and live:

The screenshot shows the ATSDR website for the National Amyotrophic Lateral Sclerosis (ALS) Registry. The header includes the ATSDR logo and the text "Agency for Toxic Substances & Disease Registry". A navigation bar lists letters A-Z and a search icon. The main heading is "National Amyotrophic Lateral Sclerosis (ALS) Registry". On the left is a sidebar menu with links like "About", "Frequently Asked Questions", "News", "Resources and Links", "Publications and Reports", "Order Registry Materials", "Conferences and Events", "ALS Clinical Research", "State-Metro ALS Surveillance", "ALS Bioregistry", and "Contact the System Administrator". The main content area is titled "Consent Form - ALS Clinical Research Notification". It contains text explaining the purpose of the registry and the research, and a section for users to agree to the terms. At the bottom, there are links for "Email", "Print", and "Share", along with page review and update dates (June 16, 2010) and the content source (Centers for Disease Control and Prevention). The footer includes links to "ATSDR Home", "Privacy Policy", "Disclaimer", "Accessibility", "e-Government", "CDC FOIA", and "Contact Us", as well as the ATSDR address and contact information.

ATSDR Agency for Toxic Substances & Disease Registry

A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

National Amyotrophic Lateral Sclerosis (ALS) Registry

ALS Registry Home

About

Frequently Asked Questions

News

Resources and Links

Publications and Reports

Order Registry Materials

Conferences and Events

ALS Clinical Research

State-Metro ALS Surveillance

ALS Bioregistry

Contact the System Administrator

ATSDR

Text size: S M L XL

Create Account | Login

Consent Form - ALS Clinical Research Notification

Research is an important part of the National ALS Registry. Not all research is done by ATSDR. Sometimes other ALS researchers would like to contact people in the National ALS Registry to ask them to take part in clinical research. If you want to receive emails from ATSDR about clinical research, please check the "I Agree" box below

We will not give the researchers your name or contact information. If you want to be part of a project, you will have to contact the researcher listed in the email.

☐ I Agree

Next

Contact Us:

Agency for Toxic Substances and Disease Registry
4770 Buford Hwy NE
Atlanta, GA 30341

(800) 232-4636
TTY: (888) 232-6348
24 Hours/Every Day

cdcinfo@cdc.gov

Email Print Share

Page last reviewed: June 16, 2010
Page last updated: June 16, 2010
Content source: Centers for Disease Control and Prevention

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Agency for Toxic Substances and Disease Registry, 4770 Buford Hwy NE, Atlanta, GA 30341, USA
Contact CDC: 800-232-4636 / TTY: 888-232-6348

USA.gov Government Made Easy

Discussion Points

- Dr. Sorenson emphasized that this a tremendous step forward for researchers in terms of seeking out participants, as well as a great step toward receiving buy-in from the academic community and patients.
- Dr. Horton stressed that they wanted to make it easy. While people can go to clinicaltrials.gov, they have to spend a considerable amount of time sorting through all of the clinical trials. ATSDR's system will electronically notify patients via email of new studies for which they meet the criteria.
- Dr. Kaye clarified that the system has already been launched for new registrants, and existing registrants should have access by October or November. While they have not tested it yet, she estimated that it would be three months from submission to final approval to access participants.
- Dr. Sorenson encouraged ATSDR to highlight this capability at Columbia University's ALS Conference in Tarrytown, New York, September 6-9, 2011. Dr. Horton confirmed that this topic is on the agenda for Tarrytown.
- Mr. Tison said he did not recall a registry question regarding date of disease onset. Possibly the most restrictive criteria for trial inclusion is time since disease onset. This may be very frustrating to PALS, some of whom who are already excluded on the day of diagnosis should an onset question be added.

- Dr. Horton replied that he and Dr. Boylan recently spoke about this. There is a question that asks date of diagnosis, but there is not a question regarding date of onset. That is somewhat tricky, but this may be something that can be incorporated into the clinical module that perhaps will satisfy PALS.
- Dr. Boylan asked whether the investigators would be able to convey this to the patient.
- Dr. Kaye replied that ATSDR is assuming that the investigators would submit IRB-approved recruitment material, which would include eligibility criteria. This way ATSDR can pre-screen and will not send information to those who are ineligible.
- Dr. Bowser noted that they are consenting for clinical trials notification, but the consent form is for clinical research notification. He conducts a lot of clinical research that does not fit under clinical trials, so he thought this might be somewhat confusing.
- Dr. Kaye responded that all types of clinical research will be considered, not just trials. The title of her slide was merely mislabeled.
- Dr. Williamson added that ATSDR is deliberating what the process would be for epidemiological studies.
- Dr. Horton emphasized that obviously it is up to the patient themselves to make contact with the researcher once they are notified about a clinical trial or study. ATSDR's role is to link the researchers and PALS, so that PALS have an opportunity to participate in research they may not have otherwise known about.
- Dr. Boylan asked what is actually sent to PALS (e.g., whatever the investigator submits or a standard ATSDR email).
- Dr. Kaye said she anticipated sending out the researcher's actual IRB-approved recruitment materials once it was approved by ATSDR's IRB. It may include a standardized ATSDR email header, but it would be the investigator's recruitment materials as received.
- Dr. Horton added that they would have a place on the web portal to upload the information rather than emailing it directly to ATSDR so that it could be logged in and the status could be tracked.
- Mr. Johnson added that the investigator would upload the information into the database, which would then be forwarded to the registry team to review. The email going to PALS will have an email header with ATSDR information and the researcher's description of the research in a PDF format.
- Mr. Dumas wondered what PALS could do proactively to say they are interested in this research mechanism.
- Dr. Kaye responded that those registering now would be able to enroll immediately. Beginning in October / November, an email will be sent to everyone who is already registered informing them of this opportunity so that they can then enroll if they are interested. At this time ATSDR is not ready to notify existing or new enrollees about any

studies, so no one will be behind. They could easily begin this process with new registrants, but it is somewhat more complicated with existing registrants.

- Mr. Heyward reported that PatientsLikeMe has found that being able to email proactively is a very effective way to drive something. The upper left-hand corner of a person's PatientsLikeMe profile lists all of the trials for which that individual is eligible that are in clinicaltrials.gov. When they are added to clinicaltrials.gov, the left-hand bottom corner of their profile reflects the update. He encouraged researchers to ensure that they are included in clinicaltrials.gov as well. He wondered whether ATSDR was thinking about the Continuity of Care Record or other locations they or patients might be able to upload data proactively.
- Dr. Horton responded that this has been discussed, but that was about the extent to which this has been pursued at this point. He emphasized that ATSDR must be careful that what they house on the registry is pre-approved by IRB/OMB. That is not to say that they cannot make modifications, but they have to think things through carefully. Other patients have asked whether there is a data repository where they can upload their charts, files, et cetera. While that would be interesting, ATSDR does not currently have this capability.
- Dr. Nelson requested an email indicating when everyone planned to meet during the Tarrytown meeting. Dr. Boylan responded affirmatively.
- Mr. Dumas thanked everyone in the room for showing interests in PALS, and for working so hard to try to help them. There are not words to describe the appreciation and interest that everyone involved shows to try to help PALS. In return, he would like to try to help future generations through his tissue donation and anything else he can do to help with early diagnosis to a point where ALS might be resolved in the next generation.
- Mr. Tison expressed his sincere thanks for being invited, and said he was honored to participate amongst this group. He further thanked everyone for their efforts to solve ALS.
- Mr. Gibson offered his gratitude to Mr. Tison and Mr. Dumas, thanking them for sharing what people with ALS must endure. He really appreciated them taking the time to attend the meeting and share their information to help make this work better. ATSDR had a vision and set out on a journey 7 years ago to put this infrastructure in place. They could not have done this without the active participation of everyone involved. PALS are ATSDR's most powerful messengers, and the agency continues to need their support and the registry is for PALS.
- Dr. Brooks pointed out that one of the uncovered aspects of ALS is the fact that there are susceptibility genes within a genetic pool that may define people who might interact with an environmental toxin and get ALS. He proposed that somewhere in the minutes a small space should be reserved to state that the future of this registry might include assessing the children of people who have ALS who are registered in this registry, and at a time when it can be afforded, develop a comparable registry. This is already being done as a practice in Alzheimer's disease to examine risk factors that might help to identify disease earlier. From the point of view of the VA, where it is already known that there are diseases and environmental impacts for veterans that will affect generations after them, the VA should be at the table because the children of veterans who are at risk environmentally/genetically represent an important aspect of this work. The 10-, 20-, 30-year view of this may change, so he would recommend that this at least be taken into consideration.

Next Steps and Closing Remarks

G. David Williamson, PhD
Director, Division of Health Studies
Agency for Toxic Substances and Disease Registry

Dr. Williamson said he was always impressed by the depth and breadth of the questions, the comments, and the clarity that each participant brought to the table. They asked some very difficult questions throughout the day, some of which ATSDR had answers for but many of which they did not. They will eventually provide answers for those questions they could not answer. He assured everyone that each and every one of the ideas and suggestions would be carefully weighed and reviewed. Hopefully, ATSDR can incorporate as many of these as possible to strengthen the registry effort. He thoroughly enjoyed meeting new faces and renewing existing friendships. He thanked everyone for all of their efforts and for the time they took to attend and participate. He invited everyone to continue to provide suggestions, guidance, questions, comments, et cetera any time via telephone and email. He thanked everyone very much for their commitment to this tremendous effort that he believes will be a model for other surveillance systems for other registry efforts. One thing that makes this effort unique is that it is a different type of registry than ATSDR is used to in terms of disease and exposure registries in the sense that the agency has almost always relied on the healthcare or medical provider. This model does not rely 100% on the provider, which is unique to public health surveillance, for which he also offered his gratitude.

D. Kevin Horton, DrPH, MSPH
Chief, Surveillance and Registries Branch
Division of Health Studies
Agency for Toxic Substances and Disease Registry

Dr. Horton thanked everyone for their attendance, and expressed his hope that they found it interesting and knew a little more about the direction ATSDR would like the registry to proceed. He stressed that they were all sitting there for PALS—like Rob and for Rick. As a quick aside, ATSDR is engaged in many different activities. One of the activities that his and other branches are engaged in is community studies around hazardous waste sites. While some community members may not always view the federal government in a positive light, the National ALS Registry project is different because of the positive nature of PALS. He could not count how many times PALS, like Rick, said to him, “Hey, when this bioregistry is up and running I want to be the first person to contribute tissue or blood.” Every person with ALS he has ever met has that same positive attitude, which is very refreshing and makes their team work that much harder.

Dr. Horton also reemphasized that the National ALS Registry is a collaboration—not an ATSDR initiative. ATSDR cannot do this alone. Each and every person in the room was invited because of his or her ALS expertise. ATSDR must rely on experts, PALS, physicians, researchers, and advocacy partners for input. Without everyone providing their experience and guidance, this registry would not be up and running right now. ATSDR appreciates everyone’s collaborative spirit, and hopes that it will continue. It is no secret that the economy is “in the tank.” Without a crystal ball, it is not possible to predict when the economy will improve. ATSDR is constantly asked how the economic crisis will impact the registry. At this point, there

is no indication that this project is going to come to an end anytime soon. While he could not make any promises, it is currently “full steam ahead” and ATSDR will simply keep moving. They plan to pursue the bioregistry and the clinical link for PALS and researchers. There are a number of good initiatives on the horizon for this registry. ATSDR is happy that everyone in the room is a part of it, and any feedback is welcomed at any time. He thanked everyone again for their attendance and wished them safe travels.

Jim Sacco, Facilitator
Atlanta, Georgia

Mr. Sacco thanked everyone for letting him be the traffic cop, and said that he was truly impressed by everyone he had met there. He concluded that people living with ALS, people coming from altruism, and people trying to collaborate with the federal government to solve a problem is really the best part of what public health should be, and he wished everyone the best.

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