Final Summary Report

State-Based ALS Surveillance Project

Contract No. 200-2009-32577

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1. Background

A bill to amend the Public Health Service Act to provide for the establishment of an Amyotrophic Lateral Sclerosis Registry (S. 1382: ALS Registry Act) was signed into law on October 10, 2008 by President Bush and became Public Law No: 110-373. The purposes of the registry, as described in the bill, are to: (1) better describe the incidence and prevalence of ALS in the United States; (2) examine appropriate factors, such as environmental and occupational, that might be associated with the disease; (3) better outline key demographic factors (such as age, race or ethnicity, gender, and family history of individuals who are diagnosed with the disease) associated with the disease; and (4) better examine the connection between ALS and other motor neuron disorders that can be confused with ALS, misdiagnosed as ALS, and in some cases progress to ALS.

Although many traditional surveillance systems and registries have relied on physician reporting, physicians have historically been poor reporters, which results in the development of surveillance systems/registries that require reporting from numerous different sources including laboratories. The Agency for Toxic Substances and Disease Registry (ATSDR) conducted pilot projects to access the feasibility of developing a National ALS Registry using existing data. It was determined that it was feasible to use existing data, and the National ALS Registry was developed using existing national administrative data from the Centers for Medicare and Medicaid Services (CMS), Veterans Health Administration (VHA), and Veterans Benefits Administration (VBA). In addition, a self-registration component was deployed in October 2010, which allows persons with ALS (PALS) to self-register into the National ALS Registry through a secure web portal.

The National ALS Registry needs to be evaluated for completeness. Given that there are limited sources for information on cases of ALS, there is no definitive test for ALS, and ALS can be difficult to diagnose, it is important to develop focused state-based surveillance for ALS. In September 2009, McKing was awarded a 3-year contract to conduct ALS surveillance in two or more states in the U.S. The purpose of this contract was to develop datasets of all ALS cases in specific geographic locations (states) over a 3-year period (2009 – 2011). For this project, McKing and its partners developed state-based surveillance projects through a more traditional approach for surveillance, case identification and reporting by physicians. A comparison between the surveillance project dataset and the National ALS Registry dataset will identify gaps in the National ALS Registry. Once these gaps, if any, are identified, additional methods for encouraging self-registration into the National ALS Registry can be developed.

2. Selection and Management of State Subcontractors

To effectively implement this project, McKing partnered with state health departments to design and implement ALS surveillance projects in their state. After contacting several states to determine their interest and negotiating with a handful of states, McKing selected the Florida Department of Health, the New Jersey Department of Health and the Texas Department of State Health Services.

McKing provided oversight and monitoring of the state projects, as well as provided staff and additional resources to support the projects in the states. In addition to regular emails and phone calls with state health departments and their staff, we held formal monthly conference calls with the project sites. McKing also conducted quarterly site visits with each project site and held annual project meetings during

which all three state health department projects' staff came together for a 1-2 day meeting in Atlanta with McKing and ATSDR.

3. Methods

3.1. Recruitment of Neurologists

Each project site employed a number of methods to identify and recruit neurologists to the project. Prior to IRB and OMB approval of the project, states began to build a mailing list to identify neurologists and developed promotional materials. Following IRB approval, the project sites began contacting neurologists through mass mailing letters, phone calls and attending neurology focused conferences and events. Upon OMB approval, the states began data collection activities.

Identifying Neurologists in Each State

All project sites began the process of identifying neurologists in their state by building a mailing list of all neurologists in their state. They then removed neurology specialists from the mailing list that were unlikely to diagnose or treat ALS patients; these specialists included Pediatric Neurologists, Neuroradiologists, Neuropathologists, Neurophysiologists, Neuropsychiatrists, and Neurosurgeons in urban areas. The specific activities completed by each state to develop their mailing list are discussed in the following sections.

In addition, the project's Consulting Neurologist identified all ALS Specialists treating or diagnosing patients in Florida, Texas, New Jersey, Philadelphia, and New York City.

Recruitment Tracking Database

A contact tracking database was built to track communication with neurologists throughout the recruitment and data collection period. Linked tables and corresponding data entry forms were created to enter and store information associated with neurologists that would be contacted for the project. The database was developed and modified according to input from all three project sites. Each site maintained a separate database with individual state mailing list information. Modifications were made by each site based on needs and preferences of state personnel.

Promotional Materials

In preparation for recruitment activities, McKing coordinated the development of common promotional materials with all three state health departments. The goal of the coordinated development was to ensure a consistent identity, branding, and messaging across all three project sites. All materials distributed to neurologists for this project were cleared and approved by ATSDR. Examples of these materials can be found in Appendix A.

Additionally, two of the project sites – Florida and New Jersey – prepared content and received approval for an ALS Surveillance Project website on their respective state health department websites.

Promotional Materials Developed e.g.,

- Tri-fold Brochures
- 4x6 Informational Cards
- El Escorial Educational Cards
- Customized 2-Pocket Folders
- Electronic 1-Page Factsheet
- Reporting Procedures
- Conference Exhibit
- Promotional Items (Pens and Mousepads)

Outreach to Patient and Provider Groups

In order to connect with neurologists and promote the project, all three project sites made contact with local ALS Association (ALSA) Chapters and state-level neurological societies. The ALS Association Chapters are primarily patient support groups; however, local chapters have existing relationships with neurologists that treat ALS. Through the ALSA National Office, we facilitated introductions between the state health departments and the local ALSA chapters' staff to introduce the project to them and solicit their support and assistance through Letters of Support and identifications of neurologists that treat ALS in their areas. All the state project sites also made contact with state-level neurological societies and arranged to exhibit at the societies' Annual Meetings in order to make contact with neurologists outside of their office settings. State project staff also attended other training conferences and national conferences that were attended by neurologists. Conferences provided an opportunity for state project staff to network with physicians whom they may have had difficulty in contacting.

Contacting Neurologists

Prior to contacting neurologists in their state, state project staff were trained on phone contact methods by McKing's Public Health Advisors. All three project sites followed a similar protocol in contacting neurologists in their state. In the fall of 2010, each state began distributing mass mailing letters introducing the project and asking if the neurologist diagnosed or treated ALS patients. Following the mass mailing, each project site began contacting neurologists by phone to determine if they did or did not diagnose or treat ALS patients. If the neurology office responded positively, that they did diagnose or treat ALS patients, the project was explained to them, a point of contact in the office was identified (usually an office manager or nurse), and they were asked to estimate the number of patients seen in the previous 12 months. By April 2011, the initial round of contact and phone calls was completed and each project site had a reduced contact list for recruitment to the project once the data collection period began.

In April 2011, the project received OMB approval and data collection efforts began in late April - early May 2011. Each project site prioritized contacting ALS Treatment Centers which saw hundreds of cases each year and large academic institutions or medical centers. These practices had the highest number of patients to report and would often require institutional review board (IRB) approval prior to reporting cases.

To contact the small and medium size practices, each project site employed a regional approach by dividing their state into districts and contacting all neurologists in the district before moving on to the next district. At the beginning of the data collection period, each project site began follow-up contacts with all neurologists that had previously been identified as "Yes, has seen an ALS patient during the project period (2009-2011)" or "No, does not currently see ALS patients, but would if one visited their office". While contact with these practices began in mid-2011, if a practice reported their cases or stated they had no cases to report, there were still several months left in the reporting period for a new ALS case to visit their office. For this reason, these practices had to be re-contacted after January 2012 to confirm that they had not seen a new ALS case since their last contact with the state health department.

Participation of VA Centers

Attempts to bring various Department of Veterans Affairs (VA) hospitals and clinics on board were met with mixed results. Often VA Neurology staff members were enthusiastic about the project and wanted to participate and report their cases. However, due to VA regulations regarding the sharing of identifiable

patient information, approval to participate in the surveillance project had to come from each individual VA medical center's Privacy Officer. VA Privacy Officers operate independently and there is not a national, regional, or state-level Privacy Officer that could grant approval for all VA medical centers. To facilitate this process, ATSDR signed a letter addressed to VA facilities requesting that they report their cases from one federal agency (the VA) to another federal agency (ATSDR). In the end, only one VA facility in Florida reported their cases.

3.2. Case Reporting

Development of Data Collection Tools

Data collection tools were initially developed by McKing's Project Director/Senior Epidemiologist and the Consulting Neurologist. Input was also gathered from ATSDR and each of the state health departments. Two data collection forms were used in this project: 1) the ALS Case Reporting Form and 2) the Medical Records Verification Form. The purpose of the ALS Case Reporting Form was to collect identifiable information about each ALS cases in the reporting areas. The purpose of the Medical Records Verification Form was to serve as a quality assurance activity by confirming the diagnosis of a sample of all cases reported. The final IRB and OMB-approved ALS Case Reporting Form gathered identification information, demographic information, diagnosis information, and form of payment. The final Medical Records Verification Form gathered information on various symptoms, prescriptions, date of death (if applicable), and EMG results (if available). Copies of the final forms can be found in Appendix B.

Data Collection Procedures

All recruited neurologists and office staff members, as applicable, were trained to complete the case reporting form and how to submit completed forms. Reports were returned to state health departments either by secure fax or transmitted via insured, traceable carrier (e.g., FedEx and LoneStarOvernight), provided that packages were identified as confidential, double enveloped, and the sender notified project staff prior to sending.

Once case reports were received, project staff reviewed the forms within 24 hours and contacted the reporting practice to obtain answers to missing fields or clarify any unreadable or confusing information. Clarifications and revisions to the case reports were done in red and initialed to identify changes made by the project staff. Once case reports were considered complete, the practice would be notified of receipt of the case and the case reports were then entered into the data collection database. Hard copies of the data collection forms were kept in locked filing cabinets in a secure area of each of the state health departments.

Compensation of Physicians

To encourage participation in the project, compensation for the completion of case reporting forms and the medical records verification form was provided. With input from the Consulting Neurologist and each of the state health departments, the compensation plan was $100 per case report and $50 per medical records verification form. The compensation amount was included in the final protocol and received both IRB and OMB approval.

3.3. Quality Assurance

Quality assurance was composed of different aspects: the data quality (quarterly data reviews), the accuracy of the diagnosis (medical records verification), and the completeness of case ascertainment (review of death and hospital discharge data).

Data Quality

On a quarterly basis, each site sent their case reporting database overnight via secure flash drive to McKing. Once the data arrived at McKing, it was transferred to a secure data laptop for storage and review. Every field/variable was sorted in ascending or descending order then viewed for discrepancies, misspelled words, missing and conflicting data. In addition, McKing verified that duplicates were identified.

Data Completeness

State and local health department staff evaluated the completeness of their case ascertainment prior to submitting their final dataset. Death data held by the state health departments were searched for all cause of death codes for International Classification of Diseases (ICD)-10, G12.2, the code for motor neuron disease (MND) for January 1, 2009 – December 31, 2011. These data were compared with those obtained from active reporting sources, i.e., reports from medical providers. Because the ICD-10 code is not specific for ALS, the hardcopy death certificates or electronic file was examined for anyone not already identified. If the cause of death was ALS and not one of the other MNDs, the provider signing the death certificate was identified and specialty of the provider was determined. If the individual signing the death certificate was a coroner or nursing home, the coroner or nursing home was contacted to obtain information on the treating physician. Because of the limited time to conduct follow-up, neurologists and those providers signing more than one death certificate were contacted first. Each provider contacted was asked for additional information about the individual to determine if the individual had ALS between January 1, 2009 and December 31, 2011. If yes, the provider was asked to complete a case reporting form.

Uniform hospital billing data was searched for ICD-9, 335.20, the specific code for ALS. These data were compared with those cases obtained from active reporting sources. In New Jersey, for those cases not already identified, attempts were made to identify the medical care provider and contacted him/her to determine why the case was not reported to the health department and to determine if there were additional cases that had not been reported. States worked with the medical personnel to complete the reporting form and/or abstracted the reporting forms. In the other states, hospital billing data was matched only and no follow-up activity was conducted.

Diagnosis Accuracy

ALS can be difficult to diagnose because there is no definitive test for the disease. Neurologists do not always agree on the diagnosis, therefore, a sample of case reports was reviewed by the Consulting Neurologist who is an expert in the diagnosis and treatment of ALS. Completed medical records verification forms were obtained from 11.5% of reported cases.

Selection of cases for verification was weighted towards smaller practices because of the concern for misdiagnosis among providers who rarely cared for or treated ALS patients.

Practice Size	Number of Patients Per Year	Percentage of Cases Selected
Small	<5	100%
Medium	5 – 20	10%
Large	21 – 49	5%
Super-Sized	≥50	3%

Upon review of the forms, the Consulting Neurologist would indicate the medical determination of the diagnosis using a numerical scale: 1 for Definite to 5 for Not ALS. Once the determination was received from the Consulting Neurologist, it was marked on the form, entered into the database and the verification was re-filed with the case report.

For any cases that the Consulting Neurologist selected a '5 – Not ALS', follow-up actions with the state health department were required to confirm the diagnosis. If the reporting practice had selected 'Not Classifiable' as the El Escorial Criteria, no further follow-up activity was completed. If the reporting practice had selected one of the other El Escorial Criteria ratings, state health department staff would re-abstract both the case reporting form and the medical records verification form. Where applicable, they would also gather additional pages from the patient's medical record. In some cases, when practices were contacted with the request for re-abstraction, they would notify us that the case was not ALS and should not have been reported. At this point, the Consulting Neurologist's determination of '5 – Not ALS' remained. Most often, the re-abstraction and additional medical records provided enough additional information for the Consulting Neurologist to assign the case to an El Escorial criterion. In the few cases where additional data was not available or when the re-abstraction did not result in the case being assigned an El Escorial Criteria, the Consulting Neurologist's determination of '5 – Not ALS' remained.

4. Results

The results are divided into three sections correlating with the different aspects of the project including recruiting neurologists, case reports, and quality assurance.

4.1. Recruitment of Neurologists

We attempted to contact approximately 2400 neurologists in the three participating states to determine if they diagnosed and or cared for persons with ALS.

Classification of Neurologists by Who Treats ALS Patients

	Total	
	#	%
All Neurologists	2367	100.0
Diagnosed/treated ALS Patient	628	26.5
Reported Cases	408	17.2
Did not report cases	220	9.3
Did not diagnose/treat ALS Patient January 1, 2009 – December 31, 2011, but would	371	15.7
Does not diagnose/treat ALS Patients	1307	55.2
Unknown	61	2.6

Of those neurologists who diagnosed/or treated persons with ALS during the project time period, 65% reported their cases. Of the neurologists that reported their cases, 50% were from practices treating less than 5 patients with ALS during the reporting period and 14% were from practices treating 50 or more ALS patients.

4.2. Case Reporting

Once data were collected, entered and cleaned by the states, the final datasets were sent to McKing. Every field was sorted in ascending or descending order then viewed for discrepancies, misspelled words, missing and conflicting data. A summary of data conflicts was emailed to the states followed by a conference call to resolve remaining conflicts.

Once the data conflicts were resolved, McKing sorted the data by name, social security number, and date of birth to determine which cases were the same person. The matching records were viewed and compared to each other and the record with the most information filled out became the composite record. Using the matching records, obituaries, death data, and Internet searches, missing information was filled into the composite record. Case reports that were reviewed by the Consulting Neurologist and determined not to be ALS were removed. Cases reported in error were also removed.

From the three states, we received 4,519 case reports. There were 708 cases reported more than one time, 65 cases received in error (not ALS, outside of timeframe, or outside of project area) for a total of 3,640 unique cases. We had estimated the expected number of cases to by 4,215 based on published literature[1], therefore we received reports for approximately 87% of the expected cases. Two of the three states identified more than 95% of the expected cases. Of the cases reported more than once, 613 cases were reported twice, 86 reported were three times, and 9 were cases reported four or more times.

Percent of cases reported by year of diagnosis for the reported cases was very similar between years, 2009 (21%), 2010 (23%), and 2011 (24%). The remaining cases were diagnosed before 2009 and alive during the surveillance time period. Approximately 84% of the cases reported were given an El Escorial Criteria Rating of "Definite", "Probable", or "Probable (lab supported)". There was no dementia or family (parent, sibling, child) history of ALS in most cases reported. Many ALS cases had more than one type of insurance. Approximately 63% of the reported cases had some type of federal benefit (Medicare, Medicaid, VA).

4.3. Quality Assurance

As discussed in the methods section, a sample of reported cases was selected to be verified by the Consulting Neurologist. A total of 622 cases were selected for verification and 520 completed forms were received. Of those received, approximately 80% were given an El Escorial Criteria of "Definite", "Probable" or "Probable (lab supported)" by the Consulting Neurologist. Only 2% were determined to be "not ALS".

Each state obtained death certificate and hospital billing data from appropriate state agencies offices. Although a large number of potential cases were identified through the use of these data only 115 cases were reported because of this effort. See the limitations section for more information.

[1] Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, and Zalutsky R. How common are the "common" neurologic disorders? *Neurology* 2007;68;326-337.

5. Discussion

In this section, we present a discussion of the unique experience of each state, operational problems incurred and solutions employed, and limitations of the project.

5.1. Unique Experience per State

The local culture and geography of each state shaped how the project was implemented.

Florida

At the beginning of this project, Florida had the dubious distinction of being the 'pill mill capital' of the United States. In an effort to curb this type of activity, the legislature enacted a series of laws and statutory regulations that affected various groups of physicians in adverse ways. Physicians who were targeted as part of this project were particularly aware of these laws and regulations, as Pain Management is a subspecialty of neurology. Consequently, project staff encountered a few physicians who were mistrustful of the state's request to collect patient data for surveillance purposes, despite efforts to educate the doctor's on the purpose of the project.

New Jersey

New Jersey is the fifth smallest state in land mass, but has the eleventh largest population. With an estimated population of almost 8.8 million, it is the most densely populated state in the United States. Proportionate to the population, a very large number of healthcare providers, including neurologists, practice in the state. Additionally, two of the most populated cities in the United States, New York City and Philadelphia, lie on New Jersey's state border. It is not uncommon for New Jersey residents to travel into these two cities to seek medical care; therefore, recruitment of neurologists had to extend past New Jersey state borders to the Philadelphia and New York City metropolitan areas.

Texas

The geography of Texas made recruitment and case ascertainment a challenging task. Texas is 268,820 square miles and its population is over 25 million. Although the major metropolitan areas have large specialty centers, there are many rural providers who see a small number of patients spread throughout the state. Many of these rural areas are not within close proximity of an airport, so conducting office visits was challenging.

The neurology group at one large hospital in Central Texas which initially indicated their willingness to participate did not provide a definitive response until close to the end of data collection. At this point, additional staff members at the hospital became involved and the process was started for internal IRB approval, which was never completed. That practice had a substantial number of cases, which would have increased total case ascertainment by 100 – 150 cases assuming those cases had not been reported by another provider.

5.2. Limitations

The major limitation was not getting all neurologists to report their cases. Because reporting was not mandatory, some neurologists declined to participate even when asked by a state health department. There were varying reasons for the lack of participation including practices that were converting to electronic medical records and could not use the system while those using paper records had no way to

search for ALS patients. The data from the death certificate and hospital billing data quality assurance activities support that not all cases were reported. Additional limitations include:

- There was not one source to identify all neurologists within a state and a variety of sources had to be used to create a master list. Although every effort was made to ensure neurologists' contact information remained accurate and current, it is possible that some neurologists may have moved into or out of the state, changed practices, or otherwise became unavailable to contact.
- Conducting surveillance throughout entire states requires a significant amount of time to be spent traveling throughout the state and visiting physician offices. In geographically large states such as Florida and Texas, this can have significant impact on the resources required to support the project.
- VA facilities (hospitals/clinics), except for one in Florida, did not participate because of VA specific privacy rules.
- Providers were instructed to consider if patients with PLS or PMA fit the El Escorial criteria and thus should be reported to the project. Although some providers did indeed treat PLS or PMA patients, it is not clear that these patients were reported.
- Death Certificate and hospital billing data were difficult to obtain and use. There was not sufficient time to complete follow-up on the death certificate data because there were so many signed by non neurologists. Much of the hospital discharge data did not include information on treating physician or state rules prohibited using data for follow-up to physicians.

6. Recommendations

Based on our experience in conducting this project, as well as the experience of our state health department subcontractors, we are providing the following recommendations if this project is undertaken again in the future.

- This type of surveillance should only be used as an evaluation component and not as a mechanism to create a national system because it is extremely time and resource intensive.
- Data collection was divided into to two distinct activities, recruiting neurologists and case reporting, because OMB approval had not been obtained at the time the project started. This required multiple calls to physicians to determine if he/she cared for ALS patients and then to receive case reports, increasing the work load. Therefore, it is recommended that data collection be designed to allow collection of case reports as soon as a neurologist is identified. In addition, it is best that cases be collected retrospectively to eliminate follow-up calls to determine if new cases have been diagnosed.
- Promotional materials should be faxed to practices prior to calling the office to provide a reference for the office staff and providers. When a fax did not precede a phone call, often office staff would request a fax and then any status determination would be delayed. Faxed materials should be followed-up with a phone call within a day.
- Direct faxes, which could be filled out and immediately faxed back, were helpful in cases where a simple 'yes' or 'no' was sufficient to answer a question (i.e. Would you diagnose or treat a patient with ALS?). Faxes of this sort were particularly helpful in removing a physician from the contact list, though it was not easy to determine if the respondent was the physician or office staff (who may not have a clear understanding of what ALS is).

- Strategies to circumvent "gate-keepers" to speak to the neurologists should be developed including a hard push for face-to-face appointments with the staff and neurologists.
- Reports should be reviewed as they are received and reporting providers contacted immediately to resolve questionable information or to provide further training on how to complete the forms prior to assigning a case number to each case report and entering it into the Case Reporting Database.
- Ensure adequate staffing levels necessary to develop a comprehensive list of neurologists, along with complete and accurate contact information, and contacting physicians to determine if he/she cares for ALS patients are provided.
- The ability to travel with little notice is crucial because physicians may not be able to schedule meetings far in advance. The ability to travel separate from the state's often cumbersome approval process was critical in ensuring that meetings were at the physician's availability.