Development of a Statewide Registry of Amyotrophic Lateral Sclerosis

A Final Report on Planning and Implementation Efforts

December 2007

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I. Introduction

This report is a compilation of work conducted by the Bureau of Environmental Health (BEH), Massachusetts Department of Public Health (MDPH) on the surveillance of amyotrophic lateral sclerosis (ALS) and the necessary components of a state-wide ALS registry. The work presented in this report should prove useful in determining the requirements for implementing a state-wide registry.

Section 26 of Chapter 140 of the Acts of 2003 included language relative to the establishment of a surveillance system or registry for ALS. Specifically, the legislative directive stated, "the Department of Public Health may establish an ALS registry, by areas and regions in the Commonwealth, with specific data to be obtained from urban, low and median income communities, and minority communities of the Commonwealth." The department worked with ALS patients and their families, neurologists, and patient advocacy groups to conduct a series of activities thought necessary in order to develop a system that would meet the needs and expectations of the ranges of parties interested in this disease, particularly in light of resources that may be required to sustain a registry in the long term.

A registry would allow for identifying all persons with ALS in order to establish incidence and prevalence of the disease. In addition to identifying confirmed cases of the disease, a state registry would provide complete, higher quality data that allows for follow-up with patients, physicians, and caregivers for additional data collection. The term "registry" in this report is defined as a minimum data set that will achieve the purpose of identifying all confirmed

ALS cases in Massachusetts. The term "database" is used to refer to a dataset that is more extensive and detailed and can be used as a tool for analyzing data to test a specific research hypothesis.

A well designed, efficient ALS registry would allow for timely population-based incidence and prevalence estimates of the disease as well as provide a basis for research studies related to the causes and cures for ALS. Regulations that ensure the protection of privacy already exist to allow researchers access to data for studies that could not easily be conducted otherwise. A well functioning ALS registry might also be an important support for future decision-making related to the identifying the causes as well as prevention and treatment of ALS.

There are currently no other state-wide population-based ALS registries in the United States. Massachusetts would be the first state in the United States to establish a population-based registry and therefore would likely become the prototype for the establishment of such registries in other states. Although there are no population-based ALS registries in the United States, there are several clinical ALS databases. The Department of Veterans Affairs in Durham, N.C. has developed a nation-wide voluntary registry of living veterans who have ALS. The University of Massachusetts (UMass) ALS C.A.R.E. Program has a voluntary, physician-directed database of outcomes for UMass ALS patients designed to be a mechanism for evaluating the impact of diagnostic and therapeutic decisions. The Australian ALS Registry is a national, observational database for outcomes of patients with motor neuron disease.

The recommendations included in this report are based on five projects conducted either by the BEH or in collaboration with a contractor, ABT Associates, under the direction of the BEH. These include determining the Prevalence of Amyotrophic Lateral Sclerosis in Southeastern Massachusetts; a feasibility study evaluating various options for the surveillance of ALS statewide; an ALS Pilot Registry in Essex County, Massachusetts; an ALS Pilot Registry in Boston, Massachusetts; and focus group feedback regarding the implementation of an ALS Registry in Massachusetts. State funds provided through annual allocation under S.26, c.140 provided support for the majority of these activities, while federal funds provided the large part of funding to carry out activities in Southeastern, MA.

II. Background on Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis, also commonly known as Lou Gehrig's disease, is a chronic and progressive neurodegenerative motor neuron disease affecting some 30,000 people in the United States at any given time. About 5,600 people are diagnosed each year in the U.S. Therefore, the estimate for the number of new cases in Massachusetts each year is 127, based on the 2000 census for Massachusetts (6, 349,000 population) (US Census, 2000). Based on an average life expectancy of 3 years from diagnosis, we would expect about 381 cases in the registry at any one time. If the average life expectancy were 4 years, there would be an anticipated 508 cases at one time. Proctor et al. (1992) report a prevalence of ALS of approximately 4 to 6 cases per 100,000 individuals per year in the U.S. population. A review of prevalence of ALS worldwide showed a range of 0.8 to 8.5 per 100,000, with US prevalence (from several studies) at 6.4 per 100,000 (Roman, 1996). It is estimated that ALS is responsible

for nearly two deaths per hundred thousand of the population annually. While some report that the incidence of ALS appears to be increasing over time, others feel that factors such as fewer competing risks, improved life expectancy, and/or improved case ascertainment may explain the trend (McGuire et al., 1996). The lack of an ALS registry to keep track of disease trends over time makes it difficult to determine whether the occurrence of the disease is increasing and why.

ALS is about 20% more common in males than in females and most often diagnosed among Caucasians (Armon, 2001). Age at onset may vary from 40 to 70 years old, although other people at other ages may develop the disease as well (ALS, 2000). The duration of the disease can vary from 2 to 5 years after which most cases die from the disease or other complications. There have, however, been individuals who have lived as little as one year and as long as 20 years (ALS, 2000).

Although recent advances in ALS research have resulted in the development of some drug therapies, the primary approach to management of the disease is symptomatic treatment. The most common form of ALS is called Sporadic ALS. About 5-10% of cases are the inherited variety known as Familial ALS.

While the exact cause of ALS is not fully understood, both genetic and environmental factors are believed to contribute to the etiology of the disease. In addition to the genetic link, working theories on the cause of motor neuron degeneration in ALS include exposure to an environmental toxin, a viral infection, an inflammatory response, and other abnormalities in neurotransmission. There is a national and international movement by ALS clinicians, patients

and families to develop standards and procedures for patient registries and follow-up studies that will facilitate understanding of the causes and cures for the devastating disease.

Middleborough was the focus of one Massachusetts study of ALS that arose from community concern about a perceived cluster of the disease (Proctor et al., 1992). In 1987, town officials identified 11 possible cases of ALS in Middleborough (1980 population: 16,404). Proctor et al. investigated further to find a total of 17 ALS cases that had been Middleborough residents at some time over a 50-year period (1938-1988). Based upon death certificate data, the researchers estimated the ALS death rate in Middleborough for the period 1969-1985 to be 2.5 deaths per 100,000 person years, compared to the statewide rate of 1.26 per 100,000 person years. Although Proctor et al concluded that the increase was not statistically significant (at the 95% confidence level) they also recognized the difficulties in evaluating possible neurological disease clusters, particularly in the absence of a population based registry.

III. The Massachusetts ALS Registry-development Projects

Five projects to direct ALS surveillance in Massachusetts were carried out having the overall goal of identifying possible design and implementation strategies, implications for reporting, appropriate data elements, resource needs in terms of information technology (IT) and staffing, and regulatory and privacy requirements appropriate and essential for a successful ALS registry in Massachusetts. The five projects were: (a) The Prevalence of Amyotrophic Lateral Sclerosis in Southeastern Massachusetts; (b) A feasibility study evaluating various options for surveillance; (c) An ALS Pilot Registry in Essex County, Massachusetts; (d) An ALS Pilot

Registry in Boston, Massachusetts; and (e) Focus group feedback regarding the implementation of an ALS Registry in Massachusetts.

The model for state-wide population-based registries is the cancer registry that exists in most states, including Massachusetts. Cancer registries have well-established and standardized methodologies and a long, successful experience from which to draw information for the development of an ALS registry. However, ALS is a very different disease from cancer. In particular, the specific information required for establishing a diagnosis is much more complicated and less standardized. Most importantly, cancer registries obtain reports on patients with cancer from tumor registries within individual hospitals or regional hospital associations. Neurological diseases, such as ALS, have no such existing infrastructure upon which to build a registry. Consequently, different data sources, different data collection methodologies, and different approaches to diagnostic verification must be developed.

a. Prevalence of Amyotrophic Lateral Sclerosis and Multiple Sclerosis in Southeastern Massachusetts

This project was largely funded by the U.S. Agency for Toxic Substances and Disease Registry (ATSDR) a branch of the U.S. Centers for Disease Control and Prevention (CDC). While its specific goals were for determining the prevalence of ALS (and Multiple Sclerosis) in Southeastern Massachusetts (i.e., Plymouth County plus the towns of Raynham and Weymouth) and to evaluate disease occurrence near selected hazardous waste sites, the scientific methods

that evolved were instrumental in establishing the basic foundation for the subsequent pilot registry efforts.

The medical records of suspected ALS patients who were diagnosed prior to 2003 and were residents of Southeastern Massachusetts between 1998 to 2003 were reviewed for inclusion in the project. To identify those patients, methods were used to establish where cases could be found. For example, it was initially unknown whether all individuals diagnosed with ALS could be identified through the offices of neurologists or whether cases might also be identified through the offices of general practice physicians, outpatient clinics, or patient advocacy organizations. If we include the cases reported from patient advocacy groups, then the total number of ALS cases in Southeastern, Massachusetts for individuals residing in the surveillance area between 1998 and 2003 was 49 or about 9 cases/100,000.

It was known from the start of the project that name and residential address would be needed in order to ensure that duplicate cases were not counted and to enable environmental epidemiologic investigations to be conducted. Shortly before the project was initiated, Congress passed the Health Insurance Portability and Accountability Act (HIPAA). This act -- intended to protect the privacy of an individual's medical records -- permits the surveillance of disease by public health departments where surveillance is authorized by law. Initially however, HIPAA created barriers in access to medical records/patient information. To best clarify the state's authority, it was necessary to amend the Department's existing regulations to more explicitly authorize the surveillance of ALS and other selected environment-related diseases. The citation for these regulations is 105 Code of Massachusetts Regulations (CMR) 300.000 – Reportable

Diseases, Surveillance, and Isolation and Quarantine Requirements. Clarifying the regulations helped assure health providers that providing the names of ALS patients was in compliance with federal and state laws designed to protect privacy. With these amended regulations, health providers, under HIPAA, were permitted to disclose protected health information to the MDPH without obtaining written authorization from the data subject. A public health authority is authorized by law to receive such information (see 45 CFR 164.512(b)).

MDPH staff also worked with various health care providers to clarify another state regulation that governs collection of surveillance data. Under MGL c.111, §24A, all information collected for public health investigations approved by the Commissioner of Public Health is strictly confidential and is not admissible as evidence in any legal proceeding. The statute also states that anyone providing information to a researcher approved by the Commissioner of Public Health shall not be liable for any damages related to that disclosure.

As mentioned, since there is no central source for identifying ALS patients in a hospital, similar to that for identifying individuals diagnosed with cancer, it was determined that MDPH nursing staff be trained in abstracting neurological clinical information. For this study, as well as for the other pilot registry efforts described in this report, only cases with a definite or probable diagnosis of ALS are included. This requires employing a two staged data abstraction process to first establish eligibility of a case (based upon residence, date of diagnosis, and certainty of diagnosis) and to subsequently obtain detailed clinical information. The abstracted clinical information was then reviewed by an independent neurologist.

The principal information gained from this project that was applied in the development of a registry included:

(a) The identification of different sources of ALS patients (i.e., hospitals, private neurologists, patient advocacy groups).

(b) The need for specialized neurological training of nurses for record abstraction.

(c) The adaptation of standardized diagnostic criteria (i.e., El Escorial diagnostic criteria – see table 2).

(d) The development of a two stage data collection process.

(e) The selection of essential clinical data for abstraction.

(f) The requirement for independent diagnostic verification before a case is considered eligible.

(g) The need to amend state regulations to encourage the reporting of cases and ensure the protection of privacy and compliance with HIPAA.

All hospitals and neurology practices contacted participated in the surveillance, except the Veterans Administration (VA) Hospital. The prevalence estimates for each of the three areas evaluated are shown in Table 1.

b. The ALS Feasibility Study

The sole purpose of this project was to assess the necessary components for a successful state-wide ALS registry (Abt, 2005). The Southeastern Massachusetts ALS/MS study helped to establish the basic methodology that would be useful for a registry, but that study involved a

one-time surveillance of ALS, whereas a comprehensive surveillance will require the ongoing reporting of cases. This presents issues such as timely reporting, ongoing compliance with regulations, changes in patient clinical status over time (e.g., possible ALS progressing to definite ALS), and costs to sustain a registry. Notably, this effort also highlighted the importance of evaluating data from advocacy organizations.

To address these and other practical issues, the literature on ALS was reviewed and patient advocacy and health professionals were interviewed. It was established that the specific criteria that an ALS registry must satisfy should include the following:

- The registry must be population-based and assure complete ascertainment of all new ALS cases in Massachusetts.

- The basic data of the registry to be provided publicly should contain only the information required for the calculation of community specific and statewide prevalence and incidence rates.

- The registry must have mechanisms in place to confirm the diagnosis of ALS cases reported.

- The registry should be designed for close collaboration with the research interests of providers, patients and their families.

- The registry must provide strict confidentiality of all information about ALS patients.

- The registry should be flexible enough to facilitate modifications and extensions as needed.

The important conclusions regarding feasibility issues and specific registry recommendations include:

- Regulatory Requirements While the Southeastern Massachusetts ALS study found the need to amend state regulations in order to allow MDPH to request and receive case information, the regulations do not require the routine reporting of cases. Rather, physicians are required to do so upon request of the department. For purposes of establishing a statewide registry to be feasible, regulatory amendments may be necessary to require reporting with specific timelines and penalties for non-reporting.

- Identification of Cases ALS clinical specialists participating in the March 2005 ALS Database Workshop in Cambridge, Massachusetts, expressed concern about the accuracy and confirmation of the ALS diagnosis in this type of mandated state registry. The workshop participants noted that physicians might use a low threshold to register patients. Consequently, the registry might include all forms of motor neuron disease, some cases of which may end up not being ALS at all (Traynor et al., 2000). Therefore, the national and international ALS experts suggest instituting a process of confirmation of diagnosis for each registered patient by a third party record

review or patient exam, using the World Federation of Neurology (1998) criteria. At the very least, follow-up with physicians every 6 months to obtain additional diagnostic and clinical data will establish greater certainty of the diagnosis.

- Sources of Cases The goal for the registry would be a complete capture of all Massachusetts residents diagnosed with ALS. Consideration must be given to those patients in Massachusetts who may receive their care in surrounding states (e.g., Connecticut, New York, Rhode Island, etc.). Although Massachusetts's legislation cannot mandate reporting by these out-of-state physicians, it is recommended that Massachusetts develop reciprocal agreements with other states as they develop similar registries. In the absence of these agreements, Massachusetts could work with both neurologists and ALS patients in Massachusetts who could encourage participation by colleagues in other states. In all cases, however, because of the requirements of HIPAA and the lack of reporting requirements in the other states, Massachusetts patients would need to give informed consent to MDPH in order for the department to access their medical records **in other states**.

  Secondary sources of data are recommended to verify the completeness of the Massachusetts registry. Secondary sources include hospital discharge data, pharmacy records (tracking Riluzole® prescriptions), Veterans Administration records, and databases maintained by the ALS Association and other patient advocacy groups.

- Linkage with Vital Statistics In order to ensure that the registry consists of active "living" cases, linkages with the death records will be needed at various intervals to identify the cases that are deceased. Identification of the "live" cases at any one time will be important for assuring accurate prevalence estimates of ALS.

- Access to Data by Researchers Policies and procedures for using the registry to conduct follow-up research studies should follow Departmental processes for acquiring data from other registries and data sets. Researchers would apply for access to data using the Section 24A "Authorization for Public Health Research" requirements of MGL Chapter 111. Section 24A authorizes the Commissioner of Public Health to approve "scientific studies and research which have for their purpose the reduction of morbidity and mortality with the Commonwealth" (MDPH, 2004). It is recommended that the regulations developed for an ALS registry include a statement about the authorization or disclosure of data from the ALS registry for research purposes. Under these conditions, the Commissioner can allow researchers to have personal health information from the registry without each individual's informed active consent. Accessing active informed consent has become a major barrier in some recent epidemiologic investigations with response rates as low as 30-40%.

- Electronic File Requirements It was found to be preferable for the registry to be electronic and accessible via a secure web portal, however, it was also acknowledged that it may not be a realistic expectation for physician offices to be electronically

linked with the Department. Therefore, it was recommended that the registry begin with options for paper reporting via fax and mail (Hummel, 2000).

- Data Elements Case definition was recommended to be based on ICD-9 codes 335.2, 335.20, 335.21, and 335.22. At the ALS Database Workshop held in March 2005 in Cambridge, MA, ALS clinicians discussed the question of a minimum data set, and their consensus opinion is presented in Table 2 (supplemented by Tables 3 and 4). The identification of standard data elements will facilitate merging Massachusetts state data with other national and international health data sets for future analyses and comparisons.

- Registry Reports It was determined that a report on the number of cases and their characteristics should be made available to the public via printed publications and the DPH website. This report should include an estimate of the prevalence and incidence of ALS for a given calendar year, ideally by community of residence. The report should include reports of cases by the most finite level of geography that will not compromise confidentiality.

- Advisory Committee It was concluded that the Department should create an Advisory Committee to support the operations of the registry once it has been implemented and to assist with further development of the regulations. The Advisory Committee should include neurologists from ALS centers, representatives from the

ALS advocacy organizations, patients, their caretakers and others determined by the Department.

Resources Required

- Staffing The staffing needs of the basic registry was estimated to include one full time scientist/manager for the registry with research support including nurse abstractors, administrative support and a consulting neurologist. The manager would direct the operations of the registry and interact with all the constituent groups involved. As mentioned, staffing would also include a number of temporary data abstractors to collect the information initially and then subsequently through on site record abstraction. Research studies that may evolve from such a surveillance system may be supported by federal funding agencies and others that support academic research, clinical trails and/or the MDPH in public health investigations.

c. Pilot ALS Registries in Essex County and Boston

Based upon the experience gained from the southeastern Massachusetts ALS/MS study and the feasibility project, two additional pilot registry projects were undertaken (Abt, 2006) in different areas of the state. The two different geographic areas were chosen in order to assess differences in applying the surveillance methods in an urban area and a suburban area. Their methodologies were similar to each other and generally followed the case ascertainment and data collection methods of the southeastern ALS/MS Massachusetts study. The numbers of cases identified and prevalence estimates for these areas as can be found in Table 1. The difference in

the total number of cases abstracted and cases identified definite or probable diagnoses was primarily due to a greater number of duplicate reports for individuals with ALS living outside of Boston, but obtaining services from private neurology practices in Essex county as well as ALS clinics in Boston. Boston residents with a diagnosis of ALS generally received all services at an ALS clinic in Boston.

Most cases residing in the urban area (i.e., Boston) were provided a confirmatory diagnosis and were/are being followed in one of the Boston ALS clinics. While many of the Essex County cases also were seen in the Boston clinics, the Essex County project provided greater experience working with private practice neurology offices.

The pilot surveillance efforts allowed for a number of observations to be made regarding factors potentially impacting the successful implementation of a comprehensive statewide registry. These included:

(a) the data abstraction form required several additional, and important, modifications (in particular, to note the presence or absence of disease progression) (see Appendix);

(b) the registry process flow chart from the southeastern Massachusetts project was revised to include additional data collection steps (Figure 1).

(c) medical record abstraction required 1-3 hours per record (not including travel time);

(d) multiple records from different institutions were required for abstraction in about 20% of the cases;

(e) several calls were required to arrange for case reporting and record abstraction for most of the physician offices contacted;

(f) practice managers were found to be the best contact for data requests;

(g) the initial response rate of physicians was very low thereby requiring follow-up letters and telephone calls;

(h) for neurologists practicing within hospitals, either the abstractor was often referred to the central medical record department or it was found to be generally more efficient for the abstractor to request and review records at the medical record department;

(i) staff at private neurology offices often felt that the request for cases was burdensome; mainly because of busy workloads and recordkeeping organization that sometimes made it difficult to select cases by specific criteria like ICD diagnostic codes;

(k) privacy or regulatory authority was rarely raised by physicians as a concern.

d. Focus Group Findings on Implementation of an ALS Registry in Massachusetts

This project represented a comprehensive and formal approach to obtaining the input of ALS patients, families, and advocates as well as those of neurologists and researchers regarding the important components of a registry (Abt, 2007). Questions were discussed with each group based upon information obtained from the four activities described previously in this report. Three focus groups were selected to include key stakeholder groups:

- Advocates/People Living with ALS

- ALS Specialists/Researchers

- General Practice Neurologists

The focus group approach was taken to confirm some of the observations previously made, but, importantly, to ensure that expectations for the components and capabilities of a registry are realistic and responsive to those with the greatest interest in establishing a statewide surveillance system. The key questions asked of these focus groups related to patients' clinical experiences and their implications for the registry and recommendations for the operation of the ALS Registry. The recommendations made by the focus groups were:

- ***Cases of ALS should be reported to the registry from community-based neurologists as well as ALS specialty clinics.*** It is important that all neurologists, regardless of the frequency of cases of ALS in their practices, be included as the major source of reports to the ALS registry. Primary care physicians do not make a diagnosis of ALS and therefore do not need to be asked to report cases.

- ***Many mechanisms should be used to ensure that all neurologists participate in the registry.*** Suggestions for these mechanisms include regular reminders, prominent web links on frequently accessed websites, and development of ongoing relationships with neurologists to explain the public health importance of the registry. Marketing to all groups should emphasize that reporting is mandatory and that removal of duplicate reports is simple. On going communication about the registry plans and reports of data from the registry should be maintained with the advocacy, research and medical community working with ALS patients and their families

- ***Patients may play an important role in ensuring that the registry is complete.*** If ALS advocacy organizations publicize the existence of the registry and patients remind their doctors, there could be a more complete capture of ALS patients—especially by physicians who see very few ALS patients and may forget about their obligation to register.

- ***The broadest possible criteria should be used in reporting patients to the registry, followed by an initial verification of diagnosis using a review of secondary materials.*** All suspected and probable cases of ALS should be prospectively reported to the registry by neurologists, either in community practice and/or in ALS specialty clinics. Even though follow up after initial verification may only be required in 'suspect' cases of ALS, there are differences of opinion on the need to continue to track patients until they have definitive ALS based on the El Escorial criteria. Additional input from physicians may be needed to clarify the optimal verification parameters and schedule.

- ***Death certificates, pharmacy records, insurance claims, hospital discharge data and patient advocacy files are all potential sources of auxiliary or confirmatory registry data.*** Vital record death certificates can be used to regularly check the accuracy and completeness of information on ALS patients. Identification of ALS cases can be potentially improved by checking pharmacy records since Rilutek, the

only drug approved for treatment of ALS, is taken by a majority of patients at some point during their treatment.

- ***A scientific and ethical review process should be in place to determine who should have access to the registry data for further studies.*** MDPH should use an IRB and an expert advisory board to determine the appropriateness of requests for the data, and whether or not identifying information is included. Patients reported to the registry should have an option for no further contact.

- ***MDPH should make regular public reports on the aggregate data in the ALS registry.*** Clinicians, researchers and advocates expressed a desire for having an ongoing accurate snapshot of ALS in Massachusetts. Reports should be available on the MDPH website and discussed in regular communication with the ALS community.

- ***Advocates feel that there is an immediate need to move on with the ALS registry and that further accountability of the ALS allocations should be a priority of MDPH.***

IV. Summary

The five registry-development projects have provided the essential components of a state-wide ALS registry that has the endorsement of the neurology medical community and of the

ALS patients and advocates who participated in one or more of the projects. Figure 1 illustrates the recommended registry data flow. Tables 2-4 list the recommended registry data elements to be collected and the Appendix shows the recommended data collection form.

The basic methods have been field tested. These were largely successful, with the exception of initial private physician response. Greater outreach to physicians, as recommended, might improve the response rate. If the response rate remains low, it would increase the cost of a registry at a minimum and, if the initial response later results in no response over the long-term, it would raise concerns regarding complete case ascertainment.

The essential registry methods of semi-annual updating of patient status and annual reporting of new cases could not be tested during the pilot efforts, so it is not known if this will affect reporting compliance. In addition, it is not known if the new amendments to state regulations directed at requiring reporting will help to improve compliance.

The focus group recommendation that suspected (not only definite or probable) cases be included would increase the number of cases to be abstracted if this recommendation is implemented. However, the number of suspected cases is unknown; therefore, the true impact on registry implementation is also unknown. It is important to note, however that results of the pilot projects suggested that outside of Boston up to half of the records abstracted were not classified as definite or probable after the charts were reviewed. Although some were classified as possible ALS diagnoses, a number were identified as duplicate records or not ALS cases. Therefore, a registry design must incorporate the need to abstract an equal number of ineligible

records in order to ascertain the number of ALS cases considered eligible for estimating incidence and prevalence.

The most immediate next step for the implementation of a state-wide registry includes the hiring of a full time epidemiologist data manager. As of the preparation of this report, this position has been advertised and hiring of an individual is likely to be in November 2007. Following that, requests for data will be forwarded to all neurologists in MA, beginning in January 2008. During 2008, an advisory committee will be established. Among the initial discussions with this group will be the need to amend state reporting regulations, develop a registry database that incorporates case tracking methods and quality control methods for handling multiple and duplicate reports.

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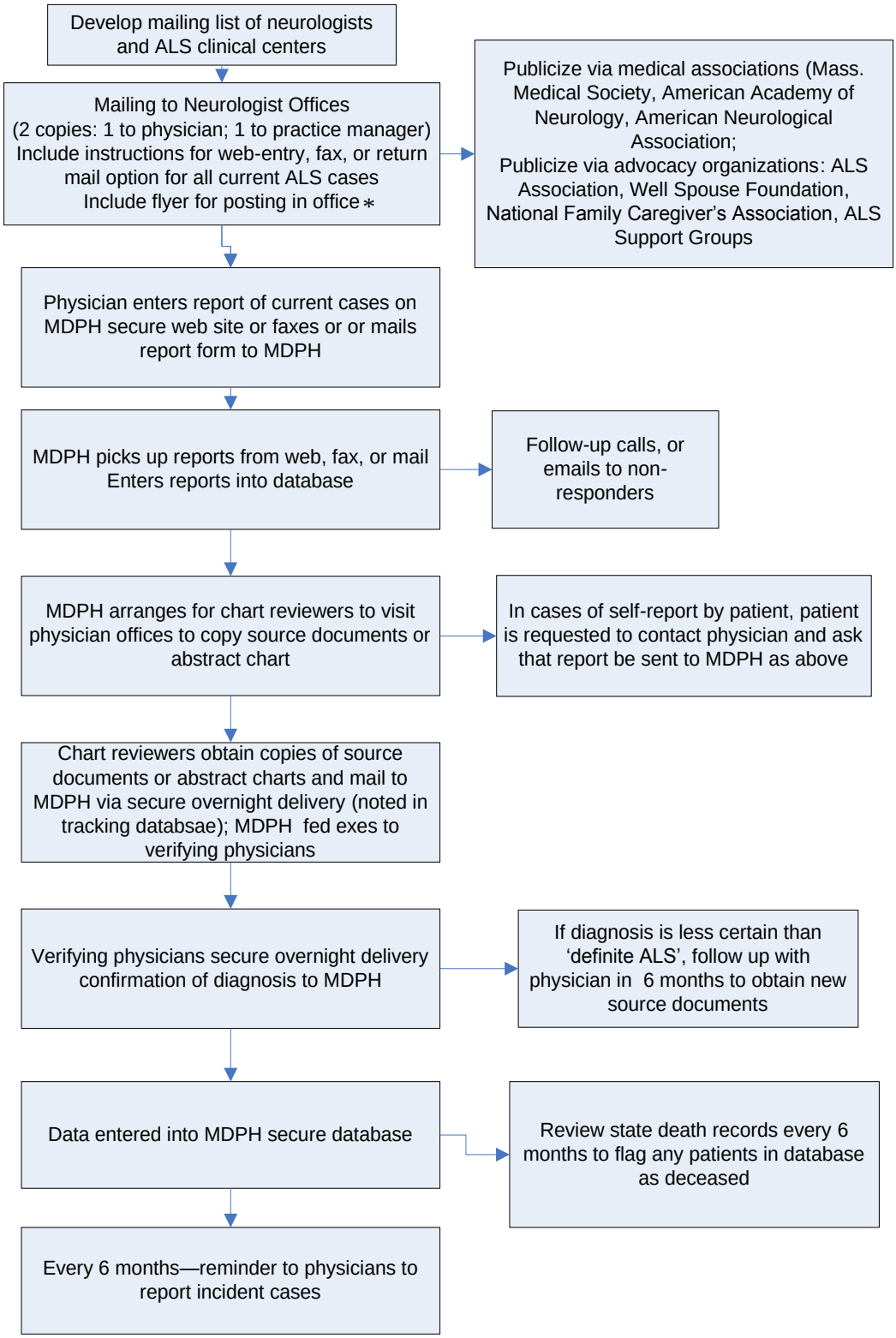
Figure 1: ALS Registry Process Flow Chart



* Concurrent with this effort contact with patient advocacy organizations should be made to ensure data completeness

Table 1: Records abstracted in the ALS Registry-development Projects

Project	Total Records Abstracted	Number of Cases	Prevalence estimates
Southeastern Massachusetts ALS (1998-2003)	54	49	9/100,000
Essex County (2006)	59	44	6.1/100,000
Boston (2007)	44	38	5.5/100,000

Table 2: Minimum Data Set: ALS Registry	
Data Element	**Comments**
Patient Name	Basic demographic/locator information
Patient Date of Birth	Basic demographic/locator information
Patient Gender	Basic demographic/locator information
Patient Social Security Number	This will facilitate matching with other state records, e.g. death records
Patient Address	Basic demographic/locator information
Patient Phone	Basic demographic/locator information
Patient E-Mail	Basic demographic/locator information
Physician Name	Reporter contact information
Physician Address	Reporter contact information
Physician Phone	Reporter contact information
Physician E-mail	Reporter contact information
Date of Diagnosis	Establishes incidence in a given year
Certainty of Diagnosis	**The El Escorial** criteria for the diagnosis of ALS have been widely accepted. The criteria described below represent the result of a workshop convened in 1998 by the World Federation of Neurology **(WFN)** Research Committee on Motor Neuron Diseases to update and revise these diagnostic criteria. (World Federation of Neurology 1998) The diagnosis of Amyotrophic Lateral Sclerosis [ALS] requires: **A - The presence of:** (A: 1) evidence of *lower motor neuron (LMN) degeneration* by clinical,

	electrophysiological or neuropathologic examination, (A: 2) evidence of *upper motor neuron (UMN) degeneration* by clinical examination, and (A: 3) *progressive spread of symptoms or signs* within a region or to other regions, as determined by history or examination **AND** **B - The absence of:** (B: 1) *electrophysiological and pathological evidence of other disease processes* that might explain the signs of LMN and/or UMN degeneration, and (B: 2) *neuroimaging evidence of other disease processes* that might explain the observed clinical and electrophysiological signs. **Levels of Diagnostic Certainty:** **Clinically Definite ALS** is defined on clinical evidence alone by the presence of UMN, as well as LMN signs, in three regions. **Clinically Probable ALS**: is defined on clinical evidence alone by UMN and LMN signs in at least two regions with some UMN signs necessarily rostral to (above) the LMN signs. **Clinically Probable/Laboratory-supported ALS**: is defined when clinical signs of UMN and LMN dysfunction are in only one region, or when UMN signs alone are present in one region, and LMN signs defined by EMG criteria are present in at least two limbs, with proper application of neuroimaging and clinical laboratory protocols to exclude other causes.

	Clinically Possible ALS: is defined when clinical signs of UMN and LMN dysfunction are found together in only one region or UMN signs are found alone in two or more regions; or LMN signs are found rostral to UMN signs and the diagnosis of Clinically Probable - Laboratory-supported ALS cannot be proven by evidence on clinical grounds in conjunction with electrodiagnostic, neurophysiologic, neuroimaging or clinical laboratory studies. Other diagnoses must have been excluded to accept a diagnosis of Clinically possible ALS.
Region of Onset	Brainstem, Cervical, Thoracic, Lumbosacral
Signs by region	See Table 3 below. Clinical evidence of upper and lower motor neuron degeneration must exist in four anatomical regions (bulbar, cervical, thoracic, and lumbosacral)
Atypical Features	Helps to establish certainty of diagnosis
Family History of ALS	To distinguish between familial and sporadic ALS
Confirmation of Diagnosis by second opinion (using WFN criteria)	"In order for the registry to be useful, it is necessary that a diagnosis of ALS be confirmed by an ALS expert, applying WFN criteria to determine the level of diagnostic certainty. This is the current "gold standard" for making a diagnosis of ALS while the patient is alive. It and has been used for enrollment into clinical trials, within the most recent high-quality population-based epidemiology studies coming out of Europe and within the current VA ALS patient registry. This can be accomplished if the expert examines the patient (as might happen, when patients obtain a second opinion), or by record review of the documents on which the diagnosis was based. We can discuss who can help with this effort in Massachusetts (Armon 2005)."
Date Moved to Mass.	Documentation that residence was established before disease onset is necessary

(if applicable)	for population-based epidemiology.
Race/Ethnicity	Basic demographic

Table 3: Signs by Region Matrix **(Indicate by ✔ whether signs are present)**				
	Brainstem	**Cervical**	**Thoracic**	**Lumbosacral**
Upper Motor Neuron Signs				
Lower Motor Neuron Signs				
EMG-Confirmed Lower Motor Neuron Signs				

Table 4: Possible Data Elements for State ALS Registry and other ALS Databases

Data Element	Basic Registry	Intermediate Database	Expanded Database	Data Source *
Patient Name	X	X	X	1
Patient DOB	X	X	X	1
Patient Gender	X	X	X	1
Patient Social Security Number	X	X	X	1, 2
Patient Address	X	X	X	1
Patient Phone	X	X	X	1
Patient E-Mail	X	X	X	1
Physician Name	X	X	X	1
Physician Address	X	X	X	1
Physician Phone	X	X	X	1
Physician E-mail	X	X	X	1
Date of Diagnosis	X	X	X	1
** Degree of Certainty of Diagnosis	X	X	X	1
Region of Onset	X	X	X	1
** Signs by region	X	X	X	1
** Atypical Features	X	X	X	1
Family Hx of ALS	X	X	X	1
** Confirmation of Diagnosis	X if	X record	X physical	1

Table 4: Possible Data Elements for State ALS Registry and other ALS Databases				
Data Element	**Basic Registry**	**Intermediate Database**	**Expanded Database**	**Data Source ***
by second physician using WFN criteria (name of physician; date)	available	review	exam	
Date Moved to Massachusetts (if applicable)	X	X	X	2
Race/Ethnicity	X	X	X	1, 2
Place of Birth		X	X	1, 2
Date other regions became involved		X	X	1
Use of Rilutek® (Riluzole)		X	X	1
Family Ancestry		X	X	2
Marital Status		X	X	1
Residential History (locations)		X	X	2
Employment History (locations)		X	X	2
Type of Work/ Employment Status		X	X	2
Military Service		X	X	2
Living Arrangement			X	2
Personal and Family Medical		X	X	2

Table 4: Possible Data Elements for State ALS Registry and other ALS Databases

Data Element	Basic Registry	Intermediate Database	Expanded Database	Data Source *
History				
Smoking History			X	2
Diet Information			X	2
Education Level			X	2
Electrophysiology Testing			X	1
Neuroimaging Studies			X	1
Laboratory Studies			X	1
Other Diagnostic Studies			X	1
Blood/Tissue Samples			X	1, 2
Disability Status			X	1
Functional Status			X	1
Health Status			X	1
Symptomatic Management/Medications			X	1
Adverse effects of Rx			X	1, 2
Income			X	2
Health Insurance			X	2
Health Care Expenditures			X	2
Health Care Utilization (Specialists/Therapists/			X	2

Table 4: Possible Data Elements for State ALS Registry and other ALS Databases				
Data Element	**Basic Registry**	**Intermediate Database**	**Expanded Database**	**Data Source ***
Hospitalizations/ Physician Visits, etc.				
Patient Satisfaction with Rx			X	2
Patient Compliance with Rx			X	2
Use of Alternative Therapies			X	2
Quality of Life Measures			X	2
Caregiver Information/Experience			X	3

*1=physician, 2=patient, 3=caregiver

**Repeated at 6-month follow-up intervals to confirm diagnosis