BMJ Open   Results of Florida's Amyotrophic Lateral Sclerosis Surveillance Project, 2009–2011

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ABSTRACT

Objective: Studies to determine the incidence and prevalence of amyotrophic lateral sclerosis (ALS) in defined geographic areas in the USA are needed. The Florida Department of Health received funding from the federal Agency for Toxic Substances and Disease Registry to implement a state-wide ALS Surveillance Project. The objectives of the project were to describe the demographic characteristics of ALS cases and to calculate the incidence and prevalence of ALS in Florida.

Setting/participants: All neurologists were asked to submit case reports for persons with ALS diagnosed and/or under their care during 1 January 2009 through 31 December 2011. A medical record verification form and an electromyogram (EMG) report were requested for a sample of cases and reviewed by an independent consulting neurologist to confirm ALS diagnosis. Death data were used to aid with case report collection.

Primary and secondary outcome measures: Demographics, relevant history and clinical characteristics, El Escorial classifications, time from symptom onset to diagnosis, crude annual incidence rates and 2009 period prevalence are presented.

Results: The 1450 reported ALS cases were more likely to be older, male, white and non-Hispanic. Slightly more than 4% of cases were reported as also having dementia, and 4.8% were reported to have an immediate family member diagnosed with ALS. Incidence rates ranged from 1.7 to 1.9 per 100 000 person-years during the project period and the 2009 period prevalence was 4.0 per 100 000 persons.

Conclusions: Project findings are generally consistent with findings of population-based studies in Europe, as well as geographically limited studies in the USA. Our findings add to the growing body of epidemiological literature about ALS in the USA. Future epidemiological studies in the USA should focus on identifying cases from minority groups and those that may have limited access to healthcare, and should consider conducting capture–recapture analysis to assess case ascertainment.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease affecting the central nervous system resulting in loss of

Strengths and limitations of this study

- This is the first state-wide report on the incidence, prevalence and demographic characteristics of amyotrophic lateral sclerosis (ALS) in Florida. All neurologists, including those at ALS specialty centres and those at general neurology practices, were asked to submit case reports for all patients with ALS under their care in order to obtain as many case reports as possible.
- Successful working relationships were developed with reporting providers and their staff, particularly with specialty centres in the region that diagnose and care for patients with ALS.
- Some physicians refused to report cases, citing concerns for patient confidentiality or the desire to obtain patient consent even though the study had a waiver of informed consent approved by the Institutional Review Board. Despite these limitations, 96.7% of the expected cases were reported.
- Hospital discharge and death certificate data were examined and attempts were made to collect case reports for decedents that were not reported to the project; 962 unique names were identified in the two databases and 11 of them were reported to the project. It is uncertain what portion of the remaining 951 may actually have been true ALS cases.

motor function. ALS is difficult to diagnose and requires a combination of clinical examinations and a series of diagnostic tests to rule out diseases that mimic ALS.[1] According to the revised El Escorial Criteria, patients are classified as Definite, Probable, Probable-Lab Supported, Possible and Not Classifiable using information gathered from clinical examinations and electromyography.[2]

Little is known about the aetiology of ALS; fewer than 10% of cases are genetic.[3] In their systematic review of 19 studies conducted worldwide, Hirtz et al[4] found a median annual incidence rate of 1.6 per 100 000 person-years (range of 0.7–2.5), the median point prevalence was 4.0 per 100 000 persons, and there was a strong association with increased age. More recently, Chio et al[5]

reported a worldwide median incidence rate of 2.1 per 100 000 person-years and a point prevalence of 5.4 per 100 000 persons.

Few studies have been conducted to determine the incidence and prevalence of ALS in the USA. Most that have been conducted are within limited geographic areas, such as a study conducted in Rochester, Minnesota, which found an incidence rate of 1.7 per 100 000 person-years[6] and a study conducted in selected areas of Texas which found a point prevalence of 1.6 per 100 000 persons.[7] There is a lack of large-scale surveillance efforts to understand the incidence and prevalence of ALS in the USA.

In 2008, President George W Bush signed Public Law No. 110-373, authorising the National ALS Registry.[8] This population-based Registry, maintained by the Agency for Toxic Substances and Disease Registry (ATSDR), gathers information on patients with ALS through an algorithm that searches existing national databases, including Medicare, Medicaid, Veterans Health Administration and Veterans Benefits Administration.[8 9] Patients diagnosed with ALS also self-enroll through a secure web portal.

In 2010, ATSDR funded state and metropolitan area ALS surveillance projects. The Florida Department of Health (FDOH) received funding to implement a state-wide ALS surveillance project. The Florida ALS Surveillance Project served two purposes: (1) to help determine the completeness of the Registry; and (2) to describe the incidence, prevalence and demographic characteristics of ALS in Florida. This paper describes the data collection methodology, the incidence and prevalence of ALS in Florida, and the demographic characteristics of Floridians diagnosed with ALS.

METHODS

Project staff worked with FDOH's Medical Quality Assurance Board (MQA) to provide a list of all physicians practising in Florida with neurology listed as a specialty during each year of the Project. We then removed physicians that specialised in areas such as vascular neurology, paediatric neurology and neurosurgery in urban areas. Physicians who were found to be retired, to have moved out of state or to be deceased were also removed.

The identified neurologists were contacted via telephone, letter and fax to determine if they diagnosed and/or cared for patients with ALS during the three-year Project period (1 January 2009 through 31 December 2011). Neurologist who indicated that they had diagnosed and/or provided care during the Project period were provided information about the Project, including a brief summary of the Project's goals, authority of FDOH to collect the requested patient information, and a list of frequently asked questions. Special emphasis was placed on contacting academic centres and ALS specialty clinics, typically seeing more than 50 patients per year, and in-person meetings were conducted with these sites to encourage their participation.

A point of contact was identified at each practice to help facilitate participation in the Project.

Based on population data for each year of the Project, an expected incidence of 2.0 per 100 000 person-years, and an expected prevalence of 4.0 per 100 000 persons, we expected to collect 1505 unique cases.[4 10] Neurologists were asked to report persons diagnosed and/or under their care for ALS from 1 January 2009 through 31 December 2011. Persons with ALS that were diagnosed before 2009 were reported as long as they were under the neurologists' care on or after 1 January 2009. Incident and prevalent cases were collected. Patient data were captured through Case Reporting Forms completed by neurologists and their office staff after a review of the patient's medical chart. The Case Reporting Form, consisting of 15 questions, collected demographic data, date of diagnosis and date of symptom onset, revised El Escorial criteria classification, if an immediate family member (ie, parent, sibling, child) had been diagnosed with ALS, if the patient had a dementia diagnosis and payer type (eg, insurance type, self-pay). Physicians were provided compensation to offset expenses related to case reporting.

To ensure accuracy of diagnosis, a sample of cases was selected for further review. Cases were selected for verification using both a systematic sample of all cases and targeted selection of unusual cases, for example, those <40 years of age or those with a diagnosis before 1999. Smaller neurology practices, defined as those diagnosing and/or caring for five or fewer patients with ALS during the Project period, were asked to submit a Medical Records Verification Form on all reported patients, while larger practices and ALS specialty clinics submitted forms for a small percentage of their reported cases. The Medical Record Verification Form collected data on the patient's symptoms and whether or not the patient was prescribed Rilutek, the only drug approved for the treatment of ALS. A copy of the patient's most recent electromyogram (EMG) report was also requested. These were reviewed by the Project's consulting neurologist who is an expert in the diagnosis and care of ALS. The consulting neurologist classified each case according to the revised El Escorial criteria[2] based on this information. Cases determined not to have ALS by the consulting neurologist were removed from the data set.

The state's hospital discharge database (HD) and death certificate database (DC) were also reviewed to help identify possible cases of ALS that neurologists may not have reported. For the HD database, records were searched using the International Classification of Diseases (ICD), Revision 9 code for ALS (335.20).[11] For the DC database, records were searched using ICD-10 code for motor neuron disease (G12.2).[12] Attempts were made to collect case reports for decedents that were not already reported by neurologists.

Incidence was calculated for each Project year. The state's population for the specific year was used as the denominator[10] and the number of new ALS patients

reported by year was used as the numerator. Average annual incidence rates were calculated by adding the incidence rates for the 3 years and then dividing by three. A Poisson distribution was assumed in the calculation of the 95% CI and differences in incidence rates between subgroups were considered significant if the CIs did not overlap. Period prevalence was calculated for 2009 only by using the state's population as the denominator and the number of ALS cases alive in 2009 regardless of the year of diagnosis.

No patients were contacted. The Project was approved by the Centers for Disease Control and Prevention Institutional Review Board (IRB) and determined to be public health practice not requiring review by the FDOH IRB.

RESULTS

The MQA provided the names of more than 2500 physicians in Florida who indicated neurology as a specialty. After removing those not likely to diagnose or treat patients with ALS, there were 862 neurologists to be contacted. Of these 862 neurologists, (29.9%) acknowledged that they had diagnosed and/or cared for patients with ALS during the Project period. Of these, 57.4% submitted case reports. These 148 physicians represented 96 practices located throughout the state. All ALS specialty centres in the state reported cases.

A review of the state's HD and DC databases yielded a total of 962 unique names that had not been reported; 390 in the HD database only, 338 in the DC database only, and 234 listed in the HD and DC databases. Follow-up with neurologists that could be identified via a review of death certificates resulted in 11 additional case reports.

A total of 1843 case reports were received. Of these reports, 20.9% were duplicate cases reported by more than one neurologist at different practices. Fifteen per cent of submitted case reports were selected for verification. Medical records verification forms were received for 70.4% of those requested, and 10.2% of all case reports received. Seven cases were removed because of case verification process when the diagnosis could not be confirmed, resulting in 1450 unique case reports, which was 96.7% of the expected cases.[4 10]

Of the 1450 cases that were reported, 82.7% were diagnosed after age 50 years, 57.9% were male, 73.0% were white, 74.8% were non-Hispanic (table 1).

The ratio of men to women who were reported to have ALS was 1.4:1. An immediate family member with ALS was reported for 4.8% of the cases. A dementia diagnosis was reported for 4.3% of the cases.

The neurologists' reported revised El Escorial classification for 79.1% of all reported cases and for 79.6% of incident cases diagnosed in 2009–2011 was Definite, Probable or Probable-Lab Supported (table 2).

Data on time from symptom onset to diagnosis were available for 82.3% of the cases. Fifty per cent of the cases experiences symptoms for 11 months or less

Table 1 Demographic characteristics of all reported ALS cases in Florida, 2009–2011 (n=1450)

Demographic characteristic	2010 Florida population*		ALS cases	
	N	% †	N	% †
Age (in years)				
<40	9 209 760	50.0	80	5.5
40–49	2 653 989	14.1	161	11.1
50–59	2 542 709	13.5	309	21.3
60–69	2 094 483	11.1	450	31.0
70–79	1 384 221	7.4	337	23.2
≥80	916 148	4.9	104	7.2
Unknown	NA	NA	9	0.6
Sex				
Male	9 189 355	48.9	839	57.9
Female	9 611 955	51.1	611	42.1
Race				
White	14 109 162	75.0	1058	73.0
Black	2 999 862	16.0	89	6.1
Asian	454 821	2.4	17	1.1
Other	1 237 465	6.6	5	0.3
Unknown	NA	NA	281	19.4
Ethnicity				
Hispanic	4 223 806	22.5	155	10.7
Non-hispanic	14 577 504	77.5	1085	74.8
Unknown	NA	NA	210	14.5
Total	18 801 310	100.0	1450	100.0

*US Census Bureau, 2011.
†May not add up to 100% due to rounding.

before diagnosis and 90% of the cases were diagnosed within 3 years of symptom onset.

There were 1021 cases diagnosed in 2009–2011. The incidence rates were 1.71, 1.79, and 1.93 per 100 000 person-years for 2009, 2010, and 2011, respectively. The average annual incidence rate was 1.81 per 100 000 person-years. The average annual incidence rates between males (2.13 per 100 000 person-years; 95% CI 1.83 to 2.42) and females (1.51 per 100 000 person-years; 95% CI 1.26 to 1.75), between whites (1.77 per 100 000 person-years; 95% CI 1.55 to 1.99) and blacks (0.68 per 100 000 person-years; 95% CI 0.38 to 0.97),

Table 2 El Escorial criteria classification of reported ALS cases in Florida, 2009–2011

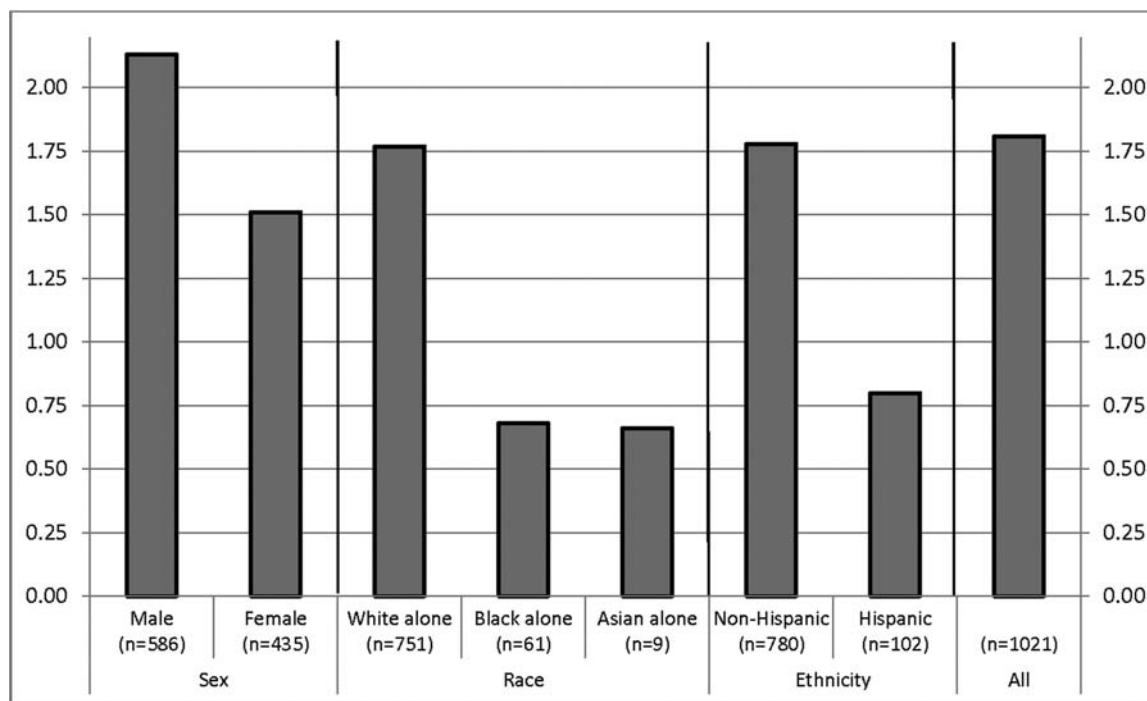| Reported El Escorial criteria classification	All reported cases		Incident cases diagnosed 2009–2011	
	N	%	N	%
Definite	664	45.8	441	43.2
Probable	338	23.3	254	24.9
Probable-lab supported	145	10.0	117	11.5
Possible	193	13.3	131	12.8
Not classifiable	110	7.6	78	7.6
Total	1450	100.0	1021	100.0

Figure 1 Stratified average annual incidence rates (per 100 000 person-years) for ALS cases diagnosed 1 January 2009 through 31 December 2011 in Florida (n=1021). Y axis: average annual incidence rates (per 100 000 person-years). X axis: sex (male and female), race (White, Black and Asian), ethnicity (Non-Hispanic and Hispanic) and all.

between whites (1.77 per 100 000 person-years; 95% CI 1.55 to 1.99) and Asians (0.66 per 100 000 person-years; 95% CI 0.00 to 1.41) and between Hispanics (0.80 per 100 000 person-years; 95% CI 0.53 to 1.08) and non-Hispanics (1.78 per 100 000 person-years; 95% CI 1.57 to 2.00) were significantly different (figure 1). There were 742 cases with a diagnosis by 31 December 2009; the period prevalence for 2009 was 3.95 per 100 000 persons.

DISCUSSION

The Florida ALS Surveillance Project was the FDOH's first effort at conducting surveillance on a non-reportable disease. A total of 148 neurologists representing 96 practices throughout the state submitted 1843 case reports. After deduplication, 96.7% of the expected cases were retained in the final data set. Therefore, we are confident that we collected the majority of eligible cases.

This distribution of demographic characteristics is similar to other published data.[4 5 7 13 14] The incidence rates for each year of the project period ranged from 1.71 to 1.93 per 100 000 person-years, which are within the range described in the USA and around the world.[4 5 13 14] Our findings with regard to differences in incidence rates between males and females, between whites and blacks, between whites and Asians, and between Hispanics and non-Hispanics are similar to previous reports.[5 14–18]

In addition, the 12-month period prevalence for 2009 was 3.95 per 100 000 persons which is consistent with the recently published Morbidity and Mortality Weekly Report (MMWR).[9] The MMWR noted a nation-wide 14-month period prevalence of 3.90 per 100 000 persons using a multiple sources to determine case eligibility. Specifically, ATSDR applies an algorithm to national administrative data sets and examined patient self-enrollment in the National ALS Registry to determine eligible ALS cases. While the Florida ALS Surveillance Project conducted case ascertainment activities among neurologists, the national approach conducted by ATSDR uses multiple sources is consistent with other population-based prospective registries in Europe.[19] Although the reported period prevalence in Florida was found to be consistent with the nation-wide report, it is possible that some ALS cases were not seen by neurologists and thus may not have been reported. A comparison of the Florida data set and the national data set is warranted to understand potential gaps in case reporting, such as certain subgroups, that is, the elderly. Further, the current study was not able to determine survival status of reported cases, therefore reporting point prevalence was not appropriate. Caution is advised when comparing our estimates of period prevalence to point prevalence estimates reported in the literature.

More than 22% of Florida's population is Hispanic, compared with 11% of reported cases. This discrepancy may be explained by nearly 15% of cases listing the patient's ethnicity as unknown. Several physicians noted that the patient's chart did not contain information regarding ethnicity, and a few large ALS clinics noted that their electronic medical record systems did not have

a field to gather this information. The lower percentage of Hispanic cases could reflect a true discrepancy; recent studies have suggested that the true rate of ALS in the Hispanic population is lower than in the non-Hispanic population.[17] [18] It is also possible the Hispanics are less likely to seek or have access to specialty care.[20]

The percentage of cases reported with either a family history of ALS (4.8%) or having a dementia diagnosis (4.3%) was lower in our project compared with previous reports.[21–24] Our findings may be due to a high percentage of missing data for these two questions. These data may not have been available in the patient's chart, or there may have been a misunderstanding of 'immediate family' (some case reports were returned with notes stating that a patient's aunt, uncle or cousin had ALS). Further, diagnosis of early frontotemporal lobe dementia is difficult and many patients with dementia may go undiagnosed, including those who are no longer verbal or those whose physicians do not specifically screen for dementia.[19]

There is currently no clinical test to determine if a patient has ALS. Disease progression, as well as tests ruling out other conditions, is often used to make a diagnosis.[2] Given this limitation, there is a concern that ALS can be misdiagnosed. To assess the completeness of the project's case ascertainment, the state's DC data set was reviewed to help identify cases of ALS that were not reported. A study in South Carolina found that on inspection of medical records of patients identified in the state's morbidity data with the ICD-10 code of G12.2 85% had information in their medical charts that would support an ALS diagnosis according to the El Escorial Criteria.[25] Only 65% of death certificates coded with ICD-10 code G12.2 had medical documentation that supported an ALS diagnosis and 18% had an 'alternative neurological diagnosis'. We were only able to obtain 2.3% of the potential cases identified from the DC database reported to the project because of the difficulty in identifying a neurologist who could report the case. However, based on the experience in South Carolina, many of these potential cases may not actually have had a diagnosis of ALS.

Of the seven cases that were removed due to inability to confirm the diagnosis with information gathered from the Medical Records Verification Form, over half were patients seen by the reporting neurologist after having received a diagnosis elsewhere. The patient's symptom history may not have been available, and in at least one case, the diagnosing physician was located at an ALS specialty clinic outside of Florida. In at least two cases, physicians reported patients for whom they had ordered medical devices (eg, walkers), but had not completed a medical history or completed tests to confirm the ALS diagnosis. In these cases, the patients were seen by the reporting physician after receiving an ALS diagnosis and after the disease had progressed. It is likely that these cases would not have been removed from the final data set if the diagnosing physician could have

been contacted for further information, and is not an indication of error in the diagnosis.

This surveillance project relied on neurologists' reporting of patients with ALS within a defined time frame. Despite a lengthy process of contacting physicians numerous times through letters, phone calls, faxes, office visits and conference attendance, only 57% of physicians who acknowledged providing care for patients with ALS reported cases. Some physicians refused to report cases, citing concerns for patient confidentiality or desiring to obtain patient consent despite having a waiver of informed consent. In many cases, physicians and office staff had to be educated about the role of the FDOH in gathering data to calculate the incidence and prevalence of diseases. However, all ALS specialty centres in the state participated and reported the majority of cases, and 96.4% of the expected unique case reports were collected.

Another obstacle was the lack of participation by all but one Veterans Affairs (VA) hospital in the state. The process for obtaining approval from each VA hospital to provide patient information is not centralised; therefore, it was necessary to identify, contact and persuade a neurologist on staff to complete the lengthy approval process with each location's privacy officer. It is likely that some unique cases were not reported due to the lack of participation by VA hospitals.

Data gathered from the review of hospital discharge and death certificate data were to be used to identify a neurologist for each patient, who would then be contacted and encouraged to report eligible cases. Death certificates were often signed by physicians who were unfamiliar with the decedent, or the only physician identified with the patient was a family physician, therefore locating a treating neurologist for the decedent was difficult. Similar issues arose with identifying patients from hospital discharge records; in most cases the physician listed for the patient was a hospitalist, or a physician who otherwise had no record of the patient beyond their hospital visit. Hospitalists were unable to report ALS cases because patient records are the property of the hospital, not the physician. There were a total of 962 unique names identified in the two databases and 11 of them were reported to the project. It is uncertain what portion of the remaining 951 may actually have been true ALS cases. It is possible that some of the patients that appeared in the HD database did not have a Florida residence, which was a requirement for case eligibility.

Some physicians admitted that reporting was not worth their time, due to the low number of cases seen, and the belief that their patients would be reported by larger practices where a patient may have sought second opinions or for comprehensive care. Despite these limitations, 96.7% of the expected cases in Florida that were diagnosed and/or under a neurologist's care for the period 1 January 2009 through 31 December 2011 were collected.

CONCLUSIONS

Conducting surveillance for a non-reportable disease, such as ALS, is a time-consuming effort. Despite the limitations of this project, 96.7% of expected cases were reported. The data collected by the Florida ALS Surveillance project were consistent with previously published data and add to the epidemiological literature in the US. These findings can be used by neurologists, other healthcare providers and patient services groups to better understand the number and demographic characteristics of persons with ALS in Florida.

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