



Epidemiology of ALS and Suspected Clusters

Definition - What is epidemiology?

“Epidemiology is the study of factors determining and influencing the frequency and distribution of disease, injury and other health-related events and their causes in a defined human population for the purpose of establishing programs to prevent and control their development and spread.”¹ Epidemiologic studies in ALS have contributed to a better understanding of the incidence, prevalence, mortality rate and clinical expression of ALS as well as the patterns of occurrence in relation to age, gender, race and geographic distribution. The association of ALS with specific factors such as genetics, occupations and toxic exposures has been studied using case control^a and cohort^b studies.^{2,6}

a “...subjects are classified on the basis of the presence or absence of the outcome of interest, and then their prior exposures are determined. Case control studies are often used to study rare diseases provided a mechanism exists to identify an ample number of subjects within the disease.”

b “... subjects are classified on the basis of the presence or absence of exposure to a particular factor and then followed forward in time to ascertain the development of the disease in each (group).”

Background

In order to determine and describe the frequency, distribution patterns of occurrence and/or to evaluate whether a specific group or geographic area can be associated with a greater than expected incidence of ALS (suspected cluster), rigorous epidemiologic studies must be conducted.

Descriptions of disease characteristics come from population studies that investigate ALS in specific geographic areas. Such studies make significant effort to identify all of the people with ALS within the specific geographic area. Results from scientifically rigorous and well-conducted research can be applied with confidence to the general population.

When evaluating whether the incidence of ALS is higher than predicted in any certain group or locale, it is often important to include a comparison group. The effort to identify ALS cases must be as intensive in this comparison group as it is in the group which is suspected to have given rise to the cluster report. In order to conclude that the incidence of ALS is higher in a group than would be expected, it is not unusual to require a two-fold increase in incidence over the expected rate to conclude a statistically significant finding. The results must demonstrate statistically that the likelihood of the actual observed incidence cannot be explained by chance alone. It is necessary to take into consideration that there are numerous opportunities for clusters to arise in the community by chance alone.

If a higher than predicted incidence of ALS is concluded, additional investigation would be necessary to determine why the incidence of ALS is higher in a particular group of people or in a specific geographic area. “To establish risk factors for ALS, a statistical association must be





demonstrated between a specific event and the subsequent occurrence of the disease.”²

Confirmation of an increased incidence of ALS is of limited value alone. True scientific and clinical usefulness comes from determining why the incidence is elevated.

Accurate epidemiologic studies begin with case ascertainment, which in turn depends on correct disease diagnosis. A number of rigorous studies in the U.S. over recent decades all indicate fairly stable ALS incidence and prevalence both geographically and over time. There are some data suggesting a small increased incidence of ALS, but it is not clear if the data reflect an actual increase in the frequency of ALS, improved case ascertainment or a better understanding of how to make the diagnosis. In general, the incidence and prevalence of ALS worldwide are uniform.

What is the incidence of ALS?

The incidence of ALS (number of new cases per year) is two cases per 100,000 population per year.

ALS is a disease of upper middle age with a mean age of onset between 55 and 65 years of age.¹

The incidence of the disease varies by decade of age with an incidence of three to four cases per 100,000 population (per year) in the sixth decade.² While the incidence of ALS increases with age up until the eighth decade, ALS does occur in the second and third decades of life. Observational reports from clinicians of seeing “increasing number of younger ALS patients” need further epidemiological investigation.

What is the prevalence of ALS?

The prevalence of ALS is said to be between six and eight cases per 100,000 population. Using the higher prevalence estimate and data from the 2000 U.S. census, nearly 22,600 Americans are living with ALS at any one time. Since ALS is a disease of aging, as the U.S. population increases and ages, an increase in the prevalence of ALS can be anticipated.

Is ALS more prevalent in men or women?

ALS occurs more frequently in men than women with a ratio of approximately “... 1.5:1 to 2.0:1. With increasing age at disease onset, however, this ratio decreases and approaches 1:1 over the age of 70.”¹

Is there a racial predisposition in ALS?

“There is evidence that the frequency of non-Western Pacific ALS is higher in whites than in nonwhites in the United States.”² It is not clear whether the lower frequency (as compared with the racial proportion in the general U.S. population) of ALS in nonwhites is due to incomplete case identification or a lower susceptibility in nonwhite populations.

Are there known risk factors for ALS?





Despite numerous studies and a number of positive correlations, only age and gender have been consistently and conclusively found to be risk factors in sporadic ALS. Several studies have suggested an association between some specific environmental factors and ALS. The nature of these associations is unproven and no environmental factor has yet to be conclusively determined to be a risk factor for developing ALS. More research in this area is needed.

Is there a mandatory reporting requirement for ALS?

No, there is no requirement for physicians to report cases of ALS. Without mandatory reporting, it is difficult and costly to investigate and describe the incidence, prevalence, risk factors and clinical course of ALS. A number of epidemiologic studies have and are currently being conducted in the United States. (Refer to the “ALS Statistical Data” *Talking Points* for a listing of these studies.) The ALS CARE database is a longitudinal, North American database of ALS patients and caregivers.

Over 2,500 patients have enrolled in the database over the past five years. Although this is not a population database and its goal is to track clinical outcomes and improve clinical management of ALS, some interesting trends have been observed that have led to epidemiologic inquiry. Despite lack of mandatory reporting for ALS, mortality rates by state and local communities can be calculated using data from death certificates. “Studies have shown that 70% to 90% of patients diagnosed as having ALS had this condition recorded on their death certificate.”²

From time to time, patients, their family members and friends establish registries for people with ALS to record their own family, medical, occupational and community histories in an attempt to identify trends in exposure or other shared circumstances. While usually not scientifically designed or controlled, such voluntary registries may have some potential to identify trends and provide information that could lead to epidemiological studies and then to a better understanding of the disease and factors that may play a role in the cause.

What is The Association’s response to reports of suspected clusters?

Despite a number of studies investigating suspected clusters in the U.S., the only confirmed cluster of ALS was described in the Western Pacific in the 1940’s. Although history has not provided clues to the cause of ALS through investigation of suspected clusters, this is a potentially significant area of inquiry if it can be shown that an ALS cluster results from an epidemiologic factor and not chance alone. In order for a community report of a suspected ALS cluster to warrant the expenditure of clinical and public health resources, there must be reasonable certainty that the cluster occurred due to an underlying specific cause rather than chance alone.¹ Community investigations take into account the geographic location of each individual with ALS when the disease was diagnosed, age at time of diagnosis, population of the geographic area and familial cases.

From time to time The Association is notified of a number of ALS patients from the same community or work environment that may be higher than the expected number of cases in the





area. The National Office of The ALS Association maintains a file of suspected clusters from reports received. When there is a question of a higher than expected number of people with ALS in one geographic or occupational area, The Association recommends that its local chapters raise their questions of an increased incidence of ALS to one or more of the following:

- Local community and state public health agencies, community and academic medical center neuromuscular neurologists, epidemiologists and toxicologists, university school of public health or medicine.
- Epidemiology staff at one or more of these agencies is best equipped to conduct an initial exploration to determine if the number of (incident) cases reaches a threshold to prompt case ascertainment and a full investigation.⁵

The ALS Association has been actively involved over several years with a number of ALS environmental studies and has established relationships with the country's leading ALS epidemiologists. The Association's Research Program includes exploration of the possible role environmental toxicants can play in learning more about, the cause(s), frequency and distribution of ALS. The Association welcomes the submission of abstracts for epidemiological studies that would be considered for funding through The Association's Research Program.

When scientists determine that an epidemiologic investigation will be conducted, The ALS Association's National Office and local chapters can assist the investigators with case ascertainment by raising public awareness and media interest. Additionally, in selected situations, The Association's local chapters can assist in data collection, promoting communication between patients and the investigators and providing education about ALS and living with the disease to the investigators, legislators and the public.

Although inquiry into community-reported clusters of ALS has not historically been fruitful in identifying the underlying cause of ALS, each new report should be evaluated and, if indicated, scientifically investigated.

References

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