HIGH LIGHT
CME

Prospective study of military service and mortality from ALS

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Abstract—*Background:* Two recent studies suggest that the risk of ALS is increased among Gulf War veterans. It is not known whether military service outside of the Gulf War is associated with increased risk of ALS. *Methods:* The authors prospectively assessed the relation between service in the military and ALS mortality among participants in the Cancer Prevention Study II cohort of the American Cancer Society, a cohort that includes over 500,000 men from the 50 states, Washington, DC, and Puerto Rico. Participant follow-up was conducted from 1989 through 1998 for ALS mortality. There were a total of 280 deaths from ALS among 126,414 men who did not serve in the military and 281,874 who did. Adjusted relative risks (RRs) were calculated using Mantel–Haenszel weights and Cox proportional hazards. *Results:* Men who served in the military had an increased death rate from ALS (RR = 1.53; 95% CI: 1.12 to 2.09; $p = 0.007$) compared with those who did not serve. The increase in ALS mortality was observed among men who served in the Army or National Guard (RR = 1.54), Navy (RR = 1.87), Air Force (RR = 1.54), and Coast Guard (RR = 2.24); no increase in risk was found in men who served in the Marine Corps, although there were only 13,670 men in this group. The risk of ALS among men who served was elevated in every 5-year birth cohort from 1915 through 1939. *Conclusions:* Military personnel have an increased risk of ALS. This increase appeared to be largely independent of the branch of service and the time period served.

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The median survival time from diagnosis with ALS is an estimated 1.5 to 3 years.[1-5] In the United States, >5,500 people are newly diagnosed with ALS each year, with an incidence rate that increases with age and is higher in men than women.[6] Although there are familial cases of ALS and both autosomal dominant and autosomal recessive transmission has been documented,[7] about 90% of cases are sporadic[8] and of unknown etiology.

Two recent reports have focused attention on the possible link between military service in the first Gulf War and risk of ALS.[9,10] It remains unclear whether this link is due to exposure to toxic or infectious agents specific to the Gulf War or to some more general aspect of military life.[11,12] To address this question, we assessed the relation between military service in different time periods and ALS mortality among men who participated in the Cancer Prevention Study II (CPS II) cohort of the American Cancer Society (questions on military service were not included in the women's questionnaire). This cohort comprises over a half-million American men[13] and includes data on military service up to 1982.

Methods. *Study population.* The CPS II is a prospective cohort study of nearly 1.2 million US men and women, begun in 1982. Participants were recruited by American Cancer Society volunteers in 50 states, the District of Columbia, and Puerto Rico.[13] Families with at least one member over age 45 and other family members over age 30 were invited to participate. In total, 508,334 men completed a 4-page questionnaire. The median age of the men at cohort entry in 1982 was 57 years. Because deaths from ALS before January 1, 1989, were not coded separately, we excluded follow-up time and 48,974 deaths that occurred before this date. In the baseline self-administered questionnaire, participants were asked whether they had a diagnosis of selected diseases (not including ALS) or "any other serious disease." We excluded the 44,218 (about 10% of the cohort) who reported "any other serious disease" because they may have had ALS at the time of completing the questionnaire and 6,854 men with missing military service data. The final population analyzed thus comprised 408,288 men who had survived until January 1, 1989, and who were followed for ALS mortality from January 1, 1989, to December 31, 1998. There were 284 ALS deaths among those men not reporting any other serious illness at baseline, among which 4 were men who had missing military data, leaving a total of 280 ALS deaths in our study. All aspects of the CPS II study are approved by the Emory University School of Medicine Human Investigations Committee. The study of military service and ALS was additionally approved by the Institutional Review Board of the Harvard School of Public Health.

Case ascertainment. Vital status of the study participants has been determined by automated linkage with the National Death Index (NDI) from January 1, 1989, through December 31, 1998.[14]

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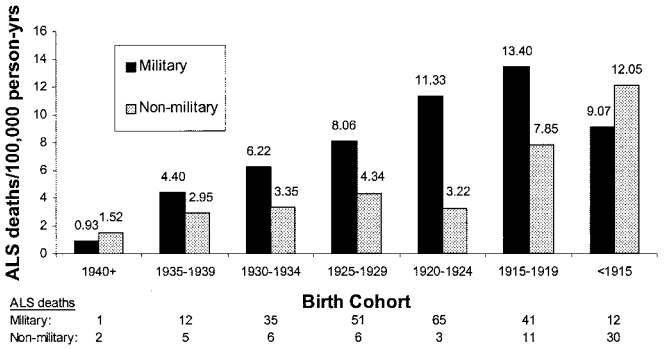

Figure. ALS mortality per 100,000 person-years by military service and birth cohort. The number of ALS deaths in each category is listed at the bottom.

The NDI began providing multiple cause-of-death codes for linked deaths in 1993. Death certificates (1989 to 1992) or multiple cause-of-death codes (1993 to 1998) have been obtained for >98% of known deaths. The underlying cause of death was coded according to the 9th revision of the International Classification of Disease (ICD-9).[15] Deaths from ALS are defined as ICD-9 code 335.2 (motor neuron disease) as either the underlying or a contributing cause of death. We had available for review 108 death certificates from men originally coded ICD-9 335.2 as underlying cause of death in CPS II (these certificates were obtained for deaths that occurred in 1989 to 1993; for later deaths, actual death certificates were not requested because NDI directly provided multiple cause-of-death codes). Among these 108 certificates, 93 (86.1%) were specified as ALS (ICD-9 = 335.20), whereas 12 (11.1%) were not specified beyond motor neuron disease (ICD-9 = 335.2). Of the remaining three (2.8%), one had a diagnosis of bulbar palsy, one had a diagnosis of progressive muscular dystrophy, and one (0.9%) had illegible text. These results suggest that few deaths with code 335.2 did not have a diagnosis of ALS.

Military service information. Military service was ascertained in 1982 by the question, "Were you in the US Armed Services?" Those who answered "yes" were also asked about the branch, location, and years of service. If the years of service included any portion of 1917 to 1918, the participant was considered to have served during World War I; if the years of service included any portion of 1942 to 1944, the participant was considered to have served during World War II; if the years of service included any portion of 1950 to 1953, the participant was considered to have served during the Korean War; and if the years of service included any portion of 1965 to 1973, the participant was considered to have served during the Vietnam War. The total number of years of service was categorized by quintile. The number of war periods during which personnel served was coded 0 to 4, the sum of the number of periods listed above during which the person served.

Statistical analyses. Participants contributed follow-up time from January 1, 1989, to the date of death from ALS or any other cause or December 31, 1998, whichever came first. Age-specific mortality rates were calculated as the number of ALS deaths divided by person-time of follow-up in each 5-year age group. Age-adjusted (in 5-year age groups) and smoking-adjusted (never, former, current) relative risks (RRs) were calculated by dividing the incidence of ALS among participants in each category of age, smoking, and military service by the corresponding incidence among those who never served in the military, using Mantel–Haenszel weights. We used Cox proportional hazards regression to estimate RR and 95% CIs when adjusting for additional variables. To obtain a better age adjustment, the Cox models were stratified by age in single years. The significance of trends was assessed using the method of Breslow and Day[16] or by including the variable as a continuous term to the Cox models. For total years served, this was done by assigning medians to each quintile and modeling the median values as a continuous variable. Alcohol intake was categorized into those who reported no intake and quartiles of intake for the others. The proportional hazards assumption was tested by adding a term to the Cox model for the interaction between military service and period of follow-up. SAS (version 8; Cary, NC) was used for all analyses.

Table 1 *Baseline (1982) characteristics* according to service in the military*

	Never served, n = 126,414	Served, n = 281,874
Smoking status, %		
Never	32.4	23.2
Former	25.8	30.9
Current	18.8	21.5
Missing	23.1	24.4
Education, %		
Some high school or less	23.1	12.4
High school grad	23.1	19.5
Vocational/trade	5.8	6.8
Some college	16.2	22.3
College grad or more	31.7	39.0
Missing	1.1	0.8
Race, %		
White	91.6	94.8
Black	4.7	3.4
Other	3.8	1.9
Main lifetime occupation, %		
Electrical/welding	9.2	9.7
Farmer	12.1	3.5
Food preparation†	0.8	0.6
Self-reported regular work or daily life exposure to, %		
Chemicals/acids/solvents	19.2	18.7
Pesticides/herbicides	10.7	6.8
Vitamin E supplement use, %		
None	75.5	76.1
Occasional	6.4	6.3
Regular	7.6	7.9
Missing	10.6	9.7
Alcohol,‡ mean, g/d in 1982	15.9	18.4
Age, mean, y	64.7	62.8

* All variables, except age, are age adjusted by direct standardization to the entire cohort.
† Includes cook, chef, butcher, baker, waiter, and food service.
‡ Among those with nonmissing data.

Results. Between 1989 and 1998, we documented 280 deaths from ALS during 3,688,245 person-years. Sixty-three of these occurred among 126,414 men who did not serve in the military and 217 were among 281,874 men who did. Subjects' military service began as early as 1910 and as late as 1982. ALS mortality rates were higher in men who served in the military than those who did not in every 5-year birth cohort group except for those born before 1915 and those born after 1939 (figure). Selected characteristics of men included in the study by military service are shown in table 1; only variables proposed as putative risk factors for ALS have been included. Compared with men who did not serve in the military, men who served were more likely to have a college education and smoke

Table 2 *Adjusted relative risk (RR) of ALS by military service and branch, 1989–1998*

	No. of cases	Person-years	RR* (95% CI)	Multivariate† RR (95% CI)
Military service				
No	63	1,100,603	Ref.	Ref.
Yes	217	2,587,642	1.58 (1.14–2.19)	1.53 (1.12–2.09)
Branch of military service				
No military service	63	1,100,603	Ref.	Ref.
Army/National Guard	97	1,187,499	1.71 (1.18–2.47)	1.54 (1.09–2.17)
Navy	65	624,208	2.04 (1.33–3.13)	1.87 (1.28–2.74)
Air Force	34	414,923	1.85 (1.16–2.96)	1.54 (0.99–2.39)
Marines	4	126,890	0.78 (0.27–2.20)	0.64 (0.23–1.78)
Coast Guard	3	23,233	2.69 (0.80–8.98)	2.24 (0.70–7.18)
Branch not given	14	210,890	1.08 (0.56–2.08)	1.08 (0.60–1.94)

* Age and smoking adjusted.
† Also adjusted for education, alcohol intake, self-reported exposure to pesticides and herbicides, and main lifetime occupation as a farmer, in a job involving electrical work or welding, or food preparation.

and had a slightly higher alcohol intake. Other factors possibly related to risk of ALS, such as use of vitamin E supplements, occupation, and exposure to environmental pesticides and solvents, were similarly distributed in the two groups, except for a smaller proportion of farmers among men who served in the military.

The age- and smoking-adjusted RR for ALS mortality was 1.58 (95% CI: 1.14 to 2.19; $p = 0.005$) comparing those who served in the military with those who did not (table 2). These results were virtually identical if adjustment for smoking was made by quintile of pack-years of smoking (RR: 1.56; 95% CI: 1.13 to 2.16; $p = 0.007$). Mortality from ALS was higher among men who had served in nearly all branches of the military, including the Army and National Guard, Navy, Air Force, and Coast Guard (see table 2). The risk was not elevated for those who served in the Marines, although the number who reported serving in the Marines was small, as was the number serving in the Coast Guard. The increased risk of ALS was largely independent of the number of years served in the military (table 3). Results were similar after adjusting for education, alcohol consumption, self-reported exposure to pesticides and herbicides, and main lifetime occupation as a farmer, in a job involving electrical work or welding, or food preparation.

The increased risk of ALS mortality was similar among those who served in the military in World War II, Korea, or Vietnam compared with those who never served (table 4). The multivariate-adjusted RR of ALS among those who served increased steadily with an increasing number of periods of war during a person's military service, but the overall trend was significant only when including the reference category (see table 4).

Comorbidities might lead to some underascertainment of ALS on death certificates. Because comorbidities would be more likely at older ages, we repeated the analyses with follow-up only until age 75. These analyses included 183 deaths attributed to ALS. Compared with those who never served in the military, the RR for those who did serve was 1.77 (95% CI: 1.14 to 2.74). The association was somewhat

Table 3 *Adjusted relative risk (RR) of ALS by years of military service, 1989–1998*

Years of military service	Median years	No. of cases	Person-years	RR* (95% CI)	Multivariate† RR (95% CI)
No military service	0	63	1,100,603	Ref.	Ref.
1st quintile	2	21	238,780	1.95 (1.15–3.33)	1.60 (0.95–2.70)
2nd quintile	3	65	743,585	2.16 (1.43–3.27)	1.80 (1.23–2.63)
3rd quintile	4	54	589,926	1.62 (1.03–2.54)	1.49 (1.01–2.21)
4th quintile	5	37	443,019	1.71 (1.09–2.70)	1.47 (0.95–2.25)
5th quintile	9	36	460,386	1.57 (0.99–2.50)	1.47 (0.95–2.27)
p trend‡				0.06	0.26
p trend§				0.41	0.58

* Age and smoking adjusted.
† Also adjusted for education, alcohol intake, self-reported exposure to pesticides and herbicides, and main lifetime occupation as a farmer, in a job involving electrical work or welding, or food preparation.
‡ Trend including reference category and weighted by the median of each category.
§ Trend excluding reference category and weighted by the median of each category.

Table 4 *Adjusted relative risk (RR) of ALS by service during war periods, 1989–1998*

	No. of cases	Person-years	RR* (95% CI)	Multivariate† RR (95% CI)
No. of wars during period of service				
No military service	63	1,100,603	Ref.	Ref.
0 (no wartime service)	36	536,294	1.83 (1.11–3.00)	1.34 (0.87–2.06)
1 war‡	156	1,746,733	1.63 (1.15–2.30)	1.57 (1.14–2.17)
2 wars‡	15	149,775	2.04 (1.10–3.82)	1.74 (0.97–3.14)
>2 wars‡	6	46,072	2.24 (0.90–5.61)	1.97 (0.83–0.70)
p trend§			0.002	0.004
p trend‖			0.74	0.29
Service during only 1 war¶				
World War II	116	1,054,010	1.62 (1.09–2.42)	1.60 (1.12–2.30)
Korea	36	550,031	1.77 (0.95–3.30)	1.54 (0.92–2.60)
Vietnam	4	139,635	1.35 (0.41–4.46)	1.44 (0.47–4.47)

* Age and smoking adjusted.
† Also adjusted for education, alcohol intake, self-reported exposure to pesticides and herbicides, and main lifetime occupation as a farmer, in a job involving electrical work or welding, or food preparation.
‡ Total military service may include nonwartime periods.
§ Trend including reference category and weighted by the median of each category.
‖ Trend excluding reference category and weighted by the median of each category.
¶ Only 592 people reported service during World War I.

stronger across all categories of military service. For example, the RR of ALS increased among those in the Army or National Guard (RR: 1.67; 95% CI: 1.04 to 2.67), Navy (RR: 2.33; 95% CI: 1.41 to 3.84), Air Force (RR: 1.71; 95% CI: 0.96 to 3.04), and Coast Guard (RR: 3.93; 95% CI: 1.18 to 13.13). The results were similar for the trends over years of service and over the number of war periods of service.

Discussion. In this prospective study among US men, we found a positive association between military service and an increased death rate from ALS. The military service reported by participants in our cohort was all before the first Gulf War. Less than 2% of those who served in the military in our cohort were under age 45 in 1990 in contrast with 98% of military personnel deployed during the first Gulf War.[10] Thus, our results are effectively independent of Gulf War military service and suggest that the association reported[9,10] between ALS and service in the Gulf War may extend to other military conflicts. Increased risk appeared largely independent of the branch of military service, the years when service occurred, or the number of years served but had some association with birth cohort and with military service during war periods. A strength of our study is the availability of information on aspects of lifestyle that could potentially affect the death rates from ALS. The facts that there was little difference between those who served in the military and those who did not in race, vitamin E intake, or self-reported exposure to chemicals, acids, and solvents and that the observed increase in death rate from ALS among men who served in the military was virtually unchanged after adjustment for cigarette smoking, alcohol consumption, education, self-reported exposure to pesticides and herbicides, and specific occupations that have been suggested to be associated with risk of ALS[17-23] suggest that the excess in ALS deaths among men who served in the military is not explained by these factors. As in all observational studies, however, confounding by other unknown factors cannot be excluded.

Soon after the end of the first Gulf War, numerous neurologic symptoms were reported by deployed military personnel.[24-27] Early reports of increased ALS were inconclusive,[26,28] but an increased risk of ALS among Gulf War veterans was found in two recent studies.[9,10] An overall 10-year cumulative incidence RR of 1.92 (95% CI: 1.29 to 2.84) for ALS comparing personnel deployed with those not deployed using Department of Defense data on deployment status was found.[10] The RR was elevated for all branches of service, with the lowest RR found among those in the Marine Corps. In a separate study,[9] ALS diagnosed before age 45 was investigated, and 17 ALS cases among deployed Gulf War veterans were identified. The number of observed ALS cases was compared with the number expected based on ALS mortality rates in the US population, adjusting for age. The standardized morbidity ratio increased over the period 1991 to 1998 and was 2.27 from 1995 to 1998.

An important difference between the Gulf War studies[9,10] and our investigation is that we did not have information on deployment during wartime, which was the principal exposure considered in the previous reports. Thus, a possible adverse effect of deployment on ALS mortality in our study would

have been diluted by the inclusion of deployed and nondeployed men in the same category. The lower RR in our study compared with the previous investigations is consistent with this explanation, but further studies with more detailed data on deployment of military personnel regardless of their period of service will be needed to resolve this issue. Our results were somewhat stronger when we excluded deaths after age 75, which are probably more prone to misclassification of disease. This suggests that diagnostic errors at older ages might also partially contribute to the reduced association compared with the previous reports.

Another limitation of our study is that follow-up of the CPS II cohort was limited to mortality and did not directly measure ALS incidence. Bias from this source is, however, likely to be small because the median survival with ALS is short (1.5 to 3 years),[1-5] and mortality is thus a good surrogate for incidence. An additional question is the validity of the ALS diagnosis reported in death certificates. Although the diagnosis of ALS may be difficult early in the disease course and standardized criteria have been developed for selection of patients in clinical trials,[29] the diagnosis becomes manifest with the progression of the disease, and it is unlikely that a diagnosis of ALS would be made on the death certificate in patients who did not have the disease. In contrast, death certificates have been estimated to accurately identify only 70 to 90% of ALS or motor neuron disease cases.[30-33] Thus, a small number of ALS deaths will have been attributed to other causes in CPS II. This will not materially bias the RR estimates unless the misclassification of the cause of death was strongly related to military service. Finally, it should be mentioned that our cohort comprised healthy volunteers rather than a representative sample of the US population. This fact does not affect the validity of the findings, but generalization to the entire US veteran population should be done cautiously, although the overall and age-specific ALS mortality in our cohort, as previously reported,[34] is similar to that in other US-based studies.

The large number of environmental factors to which Gulf War veterans were exposed has led to skepticism that a particular etiologic agent could be identified from analyses of ALS among these veterans.[11,12] Our data suggest that the search for etiologic agents may be aided by considering exposures that are not specific to a particular time period or conflict. Among these are use of the insect repellant DEET (*N*,*N*-diethyl-*m*-toluamide; discovered in the 1930s) and inhalation of aerosolized lead, which can be generated by, for example, firing of weapons or military vehicle-finishing operations.[35-38] Exposure to other chemicals,[39,40] traumatic injury,[40-42] some viral infections,[40,41,43] and intense physical activity,[44,45] which have been—with varying degrees of consistency—associated with ALS in civilian populations, may also be more common for military personnel.

References

1. del Aguila MA, Longstreth WT Jr, McGuire V, Koepsell TD, van Belle G. Prognosis in amyotrophic lateral sclerosis: a population-based study. Neurology 2003;60:813–819.
2. Drory VE, Birnbaum M, Korczyn AD, Chapman J. Association of APOE epsilon4 allele with survival in amyotrophic lateral sclerosis. J Neurol Sci 2001;190:17–20.
3. Louwerse ES, Visser CE, Bossuyt PM, Weverling GJ. Amyotrophic lateral sclerosis: mortality risk during the course of the disease and prognostic factors. The Netherlands ALS Consortium. J Neurol Sci 1997; 152(suppl 1):S10–S17.
4. Magnus T, Beck M, Giess R, Puls I, Naumann M, Toyka KV. Disease progression in amyotrophic lateral sclerosis: predictors of survival. Muscle Nerve 2002;25:709–714.
5. Sorenson EJ, Stalker AP, Kurland LT, Windebank AJ. Amyotrophic lateral sclerosis in Olmsted County, Minnesota, 1925 to 1998. Neurology 2002;59:280–282.
6. Walling AD. Amyotrophic lateral sclerosis: Lou Gehrig's disease. Am Fam Physician 1999;59:1489–1496.
7. Siddique T, Nijhawan D, Hentati A. Familial amyotrophic lateral sclerosis. J Neural Transm [Suppl] 1997;49:219–233.
8. Armon C. Motor neuron disease. In: Gorelick PB, Alter M, eds. Handbook of neuroepidemiology. New York: Dekker, 1994:407–456.
9. Haley RW. Excess incidence of ALS in young Gulf War veterans. Neurology 2003;61:750–756.
10. Horner RD, Kamins KG, Feussner JR, et al. Occurrence of amyotrophic lateral sclerosis among Gulf War veterans. Neurology 2003;61:742–749.
11. Armon C. Occurrence of amyotrophic lateral sclerosis among Gulf War veterans. Neurology 2004;62:1027–1029.
12. Rose MR. Gulf War service is an uncertain trigger for ALS. Neurology 2003;61:730–731.
13. Thun MJ, Calle EE, Rodriguez C, Wingo PA. Epidemiological research at the American Cancer Society. Cancer Epidemiol Biomarkers Prev 2000;9:861–868.
14. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. Am J Epidemiol 1993;137:235–241.
15. World Health Organization. International classification of diseases for oncology. 2nd ed. Geneva: World Health Organization, 1990.
16. Breslow NE, Day NE. Statistical methods in cancer res, vol 2: the design and analysis of cohort studies. New York: Oxford University Press, 1987:114.
17. Deapen DM, Henderson BE. A case-control study of amyotrophic lateral sclerosis. Am J Epidemiol 1986;123:790–799.
18. Granieri E, Carreras M, Tola R, et al. Motor neuron disease in the province of Ferrara, Italy, in 1964–1982. Neurology 1988;38:1604–1608.
19. Gunnarsson LG, Bodin L, Soderfeldt B, Axelson O. A case-control study of motor neurone disease: its relation to heritability, and occupational exposures, particularly to solvents. Br J Ind Med 1992;49:791–798.
20. Holloway SM, Mitchell JD. Motor neurone disease in the Lothian Region of Scotland 1961–81. J Epidemiol Community Health 1986;40: 344–350.
21. McGuire V, Longstreth WT Jr, Nelson LM, et al. Occupational exposures and amyotrophic lateral sclerosis. A population-based case-control study. Am J Epidemiol 1997;145:1076–1088.
22. Rosati G, Pinna L, Granieri E, et al. Studies on epidemiological, clinical, and etiological aspects of ALS disease in Sardinia, Southern Italy. Acta Neurol Scand 1977;55:231–244.
23. Strickland D, Smith SA, Dolliff G, Goldman L, Roelofs RI. Amyotrophic lateral sclerosis and occupational history. A pilot case-control study. Arch Neurol 1996;53:730–733.
24. Haley RW, Hom J, Roland PS, et al. Evaluation of neurologic function in Gulf War veterans. A blinded case-control study. JAMA 1997;277: 223–230.
25. Self-reported illness and health status among Gulf War veterans. A population-based study. The Iowa Persian Gulf Study Group. JAMA 1997;277:238–245.
26. Kang HK, Mahan CM, Lee KY, Magee CA, Murphy FM. Illnesses among United States veterans of the Gulf War: a population-based survey of 30,000 veterans. J Occup Environ Med 2000;42:491–501.
27. Kang HK, Mahan CM, Lee KY, et al. Evidence for a deployment-related Gulf War syndrome by factor analysis. Arch Environ Health 2002;57: 61–68.
28. Smith TC, Gray GC, Knoke JD. Is systemic lupus erythematosus, amyotrophic lateral sclerosis, or fibromyalgia associated with Persian Gulf War service? An examination of Department of Defense hospitalization data. Am J Epidemiol 2000;151:1053–1059.
29. Brooks BR, Miller RG, Swash M, Munsat TL. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler 2000;1:293–299.
30. Buckley J, Warlow C, Smith P, Hilton-Jones D, Irvine S, Tew JR. Motor

neuron disease in England and Wales, 1959–1979. J Neurol Neurosurg Psychiatry 1983;46:197–205.
31. Chio A, Magnani C, Oddenino E, Tolardo G, Schiffer D. Accuracy of death certificate diagnosis of amyotrophic lateral sclerosis. J Epidemiol Community Health 1992;46:517–518.
32. Hoffman PM, Brody JA. The reliability of death certificate reporting for amyotrophic lateral sclerosis. J Chronic Dis 1971;24:5–8.
33. O'Malley F, Dean G, Elian M. Multiple sclerosis and motor neurone disease: survival and how certified after death. J Epidemiol Community Health 1987;41:14–17.
34. Weisskopf MG, McCullough ML, Calle EE, Thun MJ, Cudkowicz M, Ascherio A. Prospective study of cigarette smoking and amyotrophic lateral sclerosis. Am J Epidemiol 2004;160:26–33.
35. Brantley LC, Hammond JR. Assessment of airborne exposures to lead during military vehicle finishing operations. Mil Med 1982;147:49–50.
36. Lofstedt H, Selden A, Storeus L, Bodin L. Blood lead in Swedish police officers. Am J Ind Med 1999;35:519–522.
37. Ozonoff D. Lead on the range. Lancet 1994;343:6–7.
38. Valway SE, Martyny JW, Miller JR, Cook M, Mangione EJ. Lead absorption in indoor firing range users. Am J Public Health 1989;79: 1029–1032.
39. Armon C. Environmental risk factors for amyotrophic lateral sclerosis. Neuroepidemiology 2001;20:2–6.
40. Nelson LM. Epidemiology of ALS. Clin Neurosci 1996;3:327–331.
41. Mitchell JD. Amyotrophic lateral sclerosis: toxins and environment. Amyotroph Lateral Scler 2000;1:235–250.
42. Riggs JE. Trauma, axonal injury, and amyotrophic lateral sclerosis: a clinical correlate of a neuropharmacologic model. Clin Neuropharmacol 1995;18:273–276.
43. Cermelli C, Vinceti M, Beretti F, et al. Risk of sporadic amyotrophic lateral sclerosis associated with seropositivity for herpesviruses and echovirus-7. Eur J Epidemiol 2003;18:123–127.
44. Strickland D, Smith SA, Dolliff G, Goldman L, Roelofs RI. Physical activity, trauma, and ALS: a case-control study. Acta Neurol Scand 1996;94:45–50.
45. Longstreth WT, McGuire V, Koepsell TD, Wang Y, van Belle G. Risk of amyotrophic lateral sclerosis and history of physical activity: a population-based case-control study. Arch Neurol 1998;55:201–206.