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Amyotrophic lateral sclerosis in an urban setting

A population based study of inner city London

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Sirs: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease primarily affecting cortical and spinal motor neurons. There have been several previous population studies, reporting incidences between 0.44 and 3.2 per 100,000 person-years [1, 2].

As a preliminary step in establishing a population register for ALS in South-East England, we have identified all prevalent cases in the London Boroughs of Lambeth, Southwark and Lewisham (LSL) between 1 January 1997 and 31 July 2004. Cases were identified from multiple sources to ensure ascertainment was as complete as possible, but it is important to recognise that this register covers a relatively small population, with a high rate of migration in and out of the area.

Seventy-three individuals with ALS were identified, of whom 56 were newly diagnosed (23 female, 33 male). Crude incidence was 1.20 per 100,000 person-years and prevalence 4.06 per 100,000 (Table 1). For England and Wales, the projected age-adjusted incidence rate was 1.66 per 100,000 person-years (95% CI 1.30–2.03), (females 1.34 (95% CI 0.95–1.72), males 2.04 (95% CI 1.50–2.58)). The cumulative lifetime risk of ALS in LSL was 0.15% for males and 0.08% for females by age 75, (for comparison, it ranges as high as 0.43% by age 90 in the Irish register) (Table 2). The median age of onset was 63 years (males 59.7, females 66.8). Sixty individuals described themselves as White (83%), 11 Black (15%), one Asian (1%), and one declined. For comparison, 25% of the LSL population is Black and 4% Asian according to the 2001 census[3]. A binomial test for observing 11 or fewer events out of 73 when the event probability is 0.25 has p=0.03, suggesting ALS may be less common in those with African ancestry.

To standardize the clinical definition of ALS, the World Federation of Neurology (WFN) has devised and subsequently revised diagnostic criteria. To examine the effect of this on incidence and prevalence rates, we used three alternative case definitions: the original WFN criteria (El Escorial), the revised WFN criteria, and only cases classified as clinically probable or definite by the original criteria [4, 5]. Not surprisingly, we found nearly two-fold variation in the calculated rates, with the lowest when including only probable and definite cases, and the highest when the original criteria were used (Table 1). The seven-fold variation in worldwide incidence may therefore partly be explained by the inclusion methods of different studies, even though most use WFN criteria.

Our incidence rates are within previously reported ranges, but are at the lower end for most large studies, as can also be seen from the lifetime cumulative risk rates. In addition, in the Italian and Irish registers, the risk continues to climb with age, whereas in our data, this is not seen for those aged 85 years or over. This reflects the size of this register and the population structure in LSL, for example having only 5% "elderly" residents compared with 7.6% for the national average[3]. There are fewer cases to ascertain, under-ascertainment is more likely, and even with complete ascertainment, rates depend on population structure [6]. (Table 2)

Comparative studies using large scale population registers are necessary to determine the true variation in the worldwide incidence of ALS, to confirm if the lifetime risk continues to increase with age as suggested by the Irish and Italian data, and to explore in a larger sample the possible lower risk for those with African ancestry that we have identified. To this end, it is timely that there is now a European

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Table 1 Variation in calculated incidence and prevalence according to how World Federation of Neurology criteria are used for case definition

Criteria used for case definition	Number of new diagnoses in study period	Number alive on 31st July 2004	Crude incidence (per 100,000 person-years)	Point prevalence (per 100,000)
Original El Escorial	56	25	1.20	4.06
Revised Airlie House	50	23	1.07	3.74
Probable or Definite Cases only	37	13	0.79	2.11

Table 2 The cumulative lifetime risk of ALS estimated using the cumulative distribution function of an exponential distribution, and expressed as a percentage. The Italian data are calculated from the Piemonte and Valle d'Aosta register; the Irish risk is calculated from data kindly provided by Drs Bryan Traynor and Orla Hardiman

By Age	Italy		Ireland		LSL	
	Male risk (%)	Female risk (%)	Male risk (%)	Female risk (%)	Male risk (%)	Female risk (%)
20	0.00	0.00	0.00	0.00	0.00	0.00
25	0.00	0.00	0.00	0.00	0.00	0.00
30	0.00	0.00	0.00	0.00	0.00	0.00
35	0.00	0.00	0.00	0.00	0.00	0.00
40	0.01	0.00	0.01	0.00	0.00	0.00
45	0.01	0.01	0.02	0.01	0.01	0.01
50	0.02	0.02	0.03	0.02	0.02	0.01
55	0.03	0.03	0.05	0.03	0.03	0.01
60	0.07	0.04	0.09	0.05	0.06	0.01
65	0.11	0.07	0.14	0.08	0.08	0.03
70	0.16	0.11	0.19	0.13	0.11	0.04
75	0.21	0.16	0.25	0.18	0.15	0.08
80	0.27	0.18	0.31	0.22	0.17	0.12
85	0.30	0.19	0.38	0.24	0.17	0.13
90	0.32	0.20	0.43	0.26	0.17	0.13

initiative to pool epidemiological resources, EURALS. The South-East London register will be expanded to include other regions of South-East England, with the aim of establishing a comprehensive register for the whole UK.

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