**Supplementary Table 1.** Studies reporting ALS incidence and/or prevalence\* estimates: location, time period† and study design

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| **Location Time Period** | **Study Design and Data Sources** | | **Case Ascertainment and Diagnostic Criteria** | **Incidence/Prevalence Calculations** | **ALS Cases Identified** |
| ***Europe*** |  | |  |  |  |
| Ferrara, Italy 1964-199838 | Retrospective review of data in clinical files and medical records from: archives of neurological ward, University Hospital; clinical neurophysiology in- and out-patient services; hospital-based consultant neurologists; rehabilitation facilities; area GPs; archives of same sources in bordering health districts | | WFN criteria for definite or probable ALS | Crude incidence (1964-98) calculated using population of Ferrara; rates age-adjusted to 1981 population of Italy for: gender; age cohort (10-y intervals); 1964-75, 1976-87, 1988-98 | 91 |
| 5 Piemonte Provinces, Italy 1971-199033 | Retrospective review of data from: (1) archives of neurological/geriatric departments (1960-90); (2) computerized archive of hospital discharges (1976-90); (3) Social Security archives (1970-90); (4) death certificates; (5) archives of EMG labs | | LMN involvement at spinal and/or bulbar level; UMN involvement; absence of sphincter, ocular, and sensory abnormalities; familial cases of ALS excluded | Crude incidence (1971-90); rates age-adjusted to 1981 population of Italy; SIRs for: gender; age cohort; area of birth; 1971-80; 1981-90 | 962 |
| Reggio Emilia, Italy 1980-199240 | Retrospective review of data from: records in Neurological Division (Reggio Emilia) and Neurological Clinics (Parma, Modena); request for files on patients with MND from all practitioners in hospitals, nursing homes, and member of Italian Neuromuscular Disease Foundation; death certificates with ICD-9 code 335.2 | | Signs of spinal motor neuron involvement, pyramidal tract lesions, and bulbar involvement; progressive failure of body muscles; EMG and neuroradiologic exams performed on all patients; absence of sphincter, ocular, and sensory abnormalities | Crude incidence (1980-92) and crude prevalence (31-Dec-92) calculated using 1992 population of Reggio Emilia; rates age- and gender-standardized to 1991 Italian population for: ALS variant, age cohort, public health district | 87 |
| Canton of Zurich, Switzerland 1981-199042 | Retrospective review of data from: (1) patient histories at the Neurology Department, Zurich University Hospital; (2) correspondence with practicing neurologists; (3) mortality information from Federal Office of Statistics | | Scottish Motor Neuron Disease Research Group criteria for “clinically definite motoneuron disease”: clinical signs unequivocal with muscular wasting and corticobulbar or corticospinal tract pathology; EMG evidence required to support/confirm diagnosis | Crude incidence (1981-90)  Point prevalence (30-Dec-90) | 104 |
| Belgrade, Yugoslavia 1985-199131 | Retrospective review of hospital registers at the Institute of Neurology and other neurology departments at 2 clinical centers and a Military Hospital | | Progressive UMN/LMN signs in bulbar and 2 spinal regions, or UMN/LMN signs in 3 spinal regions; X-rays, myelography, CAT scans and MRI used for differentials | Crude incidence (1985-91) and point prevalence (31-Dec-91) calculated using 1991 population of Belgrade; rates age-adjusted to world population (Segi); age-standardized to 1970 US population; cumulative incidence used to assess risk | 58 |
| South Estonia 1986-199539 | Retrospective review of hospital records from University Hospital of Tartu (only regional neurological center and only teaching neurological hospital in Estonia); other cases identified by contact with all neurologists and the National Society of Neuromuscular Disorders | | EEC for classical ALS; PBP and PMA included | Crude incidence (1986-95) calculated using 1996 population of South Estonia; rates age-adjusted to 1989 Estonian population for: gender, year (1986-95), age cohort (5-y intervals) | 50 |
| Faroe Islands 1987-200922 | Prospective evaluation of all patients suspected of having ALS who were referred to the Department of Medicine, National Hospital or to the investigator, a privately practicing neurologist | | EEC, including PBP, PMA or PLS; patients aged <18 y excluded | Crude incidence (1987-2009) calculated using mean population of Faroe Islands from 1987-2007 for: gender, 1987-97, 1998-2009, age cohort (10-y intervals); crude prevalence (31-Dec-09); calculated using population of Faroe Islands on estimate date | 28 |
| Møre and Romsdal county, Norway 1988-200741 | Retrospective review of discharge data for patients with an ICD-9 335/ICD-10 G12 code from Molde and Ålesund Hospitals; mortality data obtained from Cause of Death Registry in Norway | | Clinical history and exam consistent with ALS; presence of UMN/LMN signs, progressive symptoms spread and other signs consistent with ALS; patients aged ≤18 y excluded; patients classified using EEC/EEC-R with “suspected” category; PMA, PLS, SMA excluded | Crude incidence and prevalence (1988-2007) calculated using population of Norway for: gender, ALS variant, time period (5-year intervals), age cohort (10-y intervals);[point prevalence based on patients alive on 31-Dec-07 | 105 |
| Scotland  1989-199819 | Prospective, population-based evaluation of data from: (1) referrals from consultant neurologists and neurophysiologists; (2) referrals from Family Care Officers/Nurse Specialists of the Scottish Motor Neuron Disease Association; (3) Scottish Morbidity Records of discharges; (4) Mortality coding from the Office of the Registrar General | | EEC and EEC-R; autopsies performed to verify our epidemiologic diagnoses; ascertainment accuracy estimated using capture-recapture method | Crude incidence (1989-98) and  Point prevalence (31-Dec-98) calculated using mid-year 1994 Scottish population; SIR for age group 45-74 y using US 1990 Census population | 1226 |
| Modena, Italy 1990-199944 | Retrospective review of data from: all hospitals/neurologic centers using ICD-9 code 335.2 checked against ICD-9 codes: 335.0-335.9, 336.0-336.9, 344.0-344.9, 356.0-356.9; Laboratory of Neurophysiology, University of Modena; ALS Italian Association; Rehabilitation Medical Center of Veruno; death certificates; private neurologists, GPs, and families of patients not identified by other sources | | EEC-R for definite or probable ALS; resident of Modena for ≥1 y | Crude incidence (1989-99) and prevalence (1989-99) calculated using 1999 population of Modena; rates age- and gender adjusted using 1995 Italian population for: 1990-94, 1995-99, year (1990-99); point prevalence based on patients alive on 31-Dec for each year (1990-99) | 132 |
| Southwestern Greece 1990-200313 | Prospective review of medical records at the Department of Neurology, University Hospital of Patras (only tertiary centre providing medical care for neurological diseases in southwestern Greece) | | EEC for definite or probable ALS, including PBP and PSMA; patients aged <18 y excluded | Crude incidence (1990-2003) calculated using mean population for the region; rates age- and gender-adjusted to 2001 Greek population and standardized to 2001 European population | 133 |
| Sweden 1991-200535 | Retrospective, population-based evaluation of hospital discharge data from the Swedish Inpatient Register and Causes of Death Register between 1 Jan 91 and 31 Dec 05 | | ICD-9 code 355C or ICD-10 code G12.2 as primary or secondary diagnosis; ALS as cause of death on death certificates | Age-specific incidence (1991-2005) rates by age and gender (100,000 PYs); rates age-standardized using 1991 Swedish population for age cohorts and 3-year periods | 3481 |
| Padova, Italy 1992-200534 | Retrospective review of all neurological wards’ archives for all patients with a discharge diagnosis of ALS or MND | | EEC for possible ALS included PBP, PLS, UMN-ALS and Flail Arm Syndrome; suspected ALS included PMA | Crude incidence (1992-2005) calculated using 2001 population of Padova district; rates age- and gender-adjusted and standardized | 182 |
| Piemonte and Valle d’Aosta, Italy 1995-200416 | Prospective, population-based registry: (1) regional neurologic departments; (2) hospital discharge data (ICD-9 codes 335.20, 335.21, and 335.22) from Piemonte Central Regional Archive and Valle d’Aosta Central Regional Archive; (3) death certificates | | EEC and EEC-R for definite or probable ALS; unobserved cases estimated using capture-recapture method | Crude incidence (1995-2004) and crude prevalence (31-Dec-04); rates standardized and age- and gender-adjusted to 2001 Italian population for gender, age cohort, site of onset, and periods 1995-99 vs 2000-04 | 1260 |
| Reggio Emilia Province, Italy 1996-200532 | Retrospective review of data from: inpatients/ outpatients discharged from public/private hospitals with ICD-9 code 335.2 (1996-2006); death certificates with code 335.2 (1996-2007); riluzole prescriptions from Local Health Unit (2001-06) | | EEC-R for probable or definite ALS; Reggio Emilia resident at diagnosis; when diagnosis was uncertain or data were missing, patient’s GP was contacted | Age- and gender-adjusted incidence standardized to 2001 Italian population and world population for: gender, age cohort (5-y intervals), and year (1996-2005) | 94 |
| Limousin, France 1997-200724 | Prospective evaluation of data from the referral ALS center of the Department of Neurology, Regional University Hospital of Limousin | | EEC-R for definite, probable, probable supported by laboratory investigations, or possible ALS; Limousin resident | Crude incidence (1997-2007); rates age-standardized to 1999 French and 2000 US populations | 201 |
| Puglia, Italy 1998-199923 | Prospective, population-based evaluation of data in the Puglia ALS Registry, with information collected from: 23 neurology departments; ALS referral center, University of Bari; Italian ALS Lay Association; hospital discharge data bank for ICD-10-CM diagnosis code 335.2 | | EEC for definite, probable, possible, and suspected ALS, including PBP, PMA or PLS; all patients had EMG and were reclassified using EEC-R; patients aged <18 y excluded | Crude incidence (1998-99) calculated using 2001 Puglia population; rates age- and gender-adjusted using 2001 Italian population for cases aged 45-74 y; rates standardized to 1990 US population | 130 |
| England, Ireland, Italy, Scotland 1998-199949 | Retrospective review of data pooled from 6 population-based, European ALS registries: (1) Irish ALS Register; (2) Scottish MND Register; (3) Lancashire register; (4) Piemonte register; (5) Lombardy register and (6) Puglia register  Registry data collected from: clinics, neurologists, neurophysiologists, neuropathologists, neurosurgeons, GPs, local charitable organizations, hospital discharge databases, and/or mortality databases | | EEC for suspected, possible, probable or definite ALS, including PBP, PMA or PLS; patients aged <18 y excluded | Crude incidence (1998-99); rates age- and gender-adjusted for European population calculated from observed cases for all 6 registers combined, divided by the combined age- and gender-specific PYs from census data for each geographic region | 1028 |
| 9 Lombardy provinces, Italy 1998-200214 | Prospective, population-based evaluation of data from a regional registry with information from: Regional Archive of Discharges (ICD-9 CM code 335.2); archives of Italian ALS Lay Association; all ALS regional outpatient services and Veruno Medical Center; hospital and ambulatory consultations | | EEC and reclassified using EEC-R | Crude incidence (1998-2002); rates age- and gender-standardized using 2001 Italian and 1990 US populations for: year of diagnosis, province, site of onset, EEC category | 517 |
| Modena, Italy 2000-200920 | Prospective, population-based evaluation of data froma registry with information from: ALS Centre, S. Agostino-Estense Hospital, neurology departments, GPs, neurophysiology units, outpatient consultants, death certificates | | Hospital discharge or death certificate with ICD-9 code 335.2; only cases with definite or probable ALS included | Crude incidence (2000-2009) calculated using province population in a given year; crude prevalence calculated using population on 31-Dec of each year; rates age- and gender-adjusted to 2001 Italian population for: gender, year of diagnosis, site of onset | 193 |
| Republic of Ireland  2002-200427 | Prospective, population-based evaluation of the Irish ALS Register with data from: consultant neurologists, neurophysiologists, neuropathologists, neurosurgeons, and the Irish Motor Neuron Disease Association; GP referrals from the National Neuromuscular Clinic | | EEC for definite, probable, possible, or suspected ALS (case ascertainment has been 100% since 1 Jan 1995) | Crude incidence (2002-2004) calculated using Irish population; crude prevalence calculated based on Irish population on 31-Dec-03; rates age- and gender-adjusted to 1996 Irish population | 234 |
| England and Wales 2002-200630 | Retrospective review of population-based ALS registry with data from: Motor Neuron Disease Care and Research Centre; neurological and neurorehabilitation departments in specialist/general hospitals; clinicians involved in all aspects of ALS patient management; Motor Neurone Disease Association | | Differential diagnosis of ALS made by 2 consultant neurologists; cases classified using EEC; patients aged <15 y excluded | Crude incidence (2002-2006) calculated using 2001 census for England/Wales; crude prevalence date was 30-Jun-06; rates age- and gender-adjusted using direct method of standardization | 138 |
| Northern Ireland (NI), Republic of Ireland (ROI)  2004-200518 | Prospective, population-based evaluation of MND registers in NI and ROI with data from: (1) neurology departments, (b) MNDA, (3) acute hospital trust coding system lists, (4) regional pharmacy unit, (5) GPs, (6) neurophysiology departments; medical records reviewed to confirm MND diagnosis | | EEC for definite, probable, possible, and suspected MND/ALS; PBP and PLS included; cases aged ≤15 y excluded | Crude incidence (2004-05) and crude prevalence (30-Jun-05) calculated using 2004 mid-year populations of NI/ROI; rates age- and gender-standardized to 1990 US population | 109 |
| Northern Ireland 2004-200617 | Prospective, population-based evaluation of MND register in NI with data from: (1) neurology department, (b) MNDA, (3) acute hospital trust coding system lists, (4) regional pharmacy unit, (5) GPs, (6) EMG records | | No further details regarding case ascertainment were provided; capture-recapture analysis used to estimate unobserved cases | Crude incidence (2004-06) and crude prevalence (30-Jun-05) calculated using 2004 mid-year populations of NI; rates adjusted to European standard population | 67 |
| the Netherlands 2006-200921 | Prospective, population-based evaluation of data from: University Medical Centres, 30 largest general hospitals; ALS-focused rehabilitation centres; mail to all neurologists and rehabilitation consultants; patient recruitment via Dutch Association for Neuromuscular Diseases and study Web site | | EEC for definite, probable, possible, or suspected ALS, including PBP, PMA or PLS; residents aged <15 y excluded; capture-recapture methods used to estimate unobserved cases by age and gender | Crude incidence (2006-2009) calculated by dividing number of observed cases by PYs of observation; crude prevalence calculated as number of patients alive on 31-Dec-08; rates age- and gender-adjusted to Netherlands census data and US 1990 census | 1217 |
| ***North America*** |  | |  |  |  |
| Olmstead County, MN, USA 1925-199846 | Retrospective, population-based review of medical records from the Mayo Clinic, which provides virtually all specialty care for Olmsted County residents | | Np further details regarding case ascertainment were provided | Crude incidence (1925-1998) calculated using census data (10-y intervals); rates age-adjusted for historical (diagnosed pre-1990) and contemporary (diagnosed in or after 1990) cohorts | 77 |
| King, Pierce, Snohomish counties, WA, USA 1990-199525 | Prospective, population-based evaluation of data from: clinicians (neurologists, physiatrists, neurosurgeons, neuroradiologists); hospices; ALS support services; Muscular Dystrophy Association; medical examiners | | County residents aged ≥18 y diagnosed by a neurologist as having ALS; patients with PMA, PBP were included, and those with PLS were excluded | Crude incidence (1990-2005) calculated using 1990 US census data; age-specific rates based on Poisson distribution; age-adjusted rates calculated using direct method of standardization | 235 |
| Jefferson County, Missouri, USA 1998-200248 | Retrospective, population-based review of data from: Missouri Department of Health and Senior Services (primary); hospital, ED and outpatient data; neurologists, GPs, nursing home administrators; self-referral; rehabilitation facilities; death certificates; regional ALS Association | | ICD-9 code 335.20 or ICD-10 G12.2; classified using EEC-R for definite or probable ALS; case ascertainment verified using capture-recapture method, and missing cases estimated | Crude prevalence calculated using patients alive and residing in Jefferson county on 31-Dec-02; rates age-adjusted using 2002 US population | 36 |
| South Carolina, USA 2001-200547 | Retrospective review of discharge data from all 63 acute care hospitals; verified using in-patient records and emergency department visits when former not available | | Primary or secondary MND diagnosis (ICD-9-CM 335.2–335.29; non-residents and patients aged <18 y at first MND encounter excluded | Annual prevalence (2001-2005)  (South Carolina population ≥18 y each year) | 94-104 |
| Nova Scotia, Canada 2003-200415 | Prospective survey of all physiatrists and neurologists practicing in Nova Scotia | | ICD-9-CM code 335.20 as primary diagnosis; EEC for proven, definite, or probable ALS; patients aged <18 y excluded | Crude incidence (2003-2004)  Rates age-adjusted to 2001 Canadian standardized population | 21 |
| ***Asia/Pacific*** |  | |  |  |  |
| North & Central Canterbury Health Districts, New Zealand  1985-200626 | Prospective evaluation of the data from: (1) Christchurch Public Hospital neurology department database; (2) hospital discharge data from Canterbury District Health Board centers; (3) neurologists' private practice records | | Diagnosis of MND by neurologist; classified using EEC for definite or probable ALS via chart review; patients with PBP included; capture-recapture method used to estimate missing cases | Crude incidence (1985-2006) calculated using population census data from 1986, 1991, 1996, 2001, 2006; rates age- and gender-adjusted for each year referenced to the European population | 244 |
| Hong Kong, China 1989-199237 | Retrospective review of data from: (1) medical records (ICD code 335.2) from 4 regional hospitals serving as tertiary referral centers for neurological diseases; (2) survey sent to other internists, geriatricians, all neurologists/ neurosurgeons; 3) Hong Kong Medical Association newsletter announcement; (4) death certificates with ICD code 335.2 was the direct/contributory cause | | WFN recommendations: UMN/LMN sign in brainstem and ≥1 spinal region; if only 1 spinal region, UMN and LMN signs required in that region or probable MND (included ALS, PBP, PMA, PLS)  Cases sub-classified based on Scottish Motor Neuron Disease Research Group criteria | Average annual crude incidence and age- and gender adjusted rates calculated using the 1991 population of Hong Kong | 84 |
| Wakayama Prefecture, Kii Peninsula, Japan 1989-199329 | Prospective, population -based study using data from: (1) clinical records from Division of Neurological Diseases, Wakayama Medical College; (2) List of Patients with Intractable Diseases; (3) surveys sent to 85 general hospitals | | Age of onset >20 y; relentless progression; weakness, wasting, and fasciculation of bulbar (PBP) or spinal muscles (SPMA) with cortico-spinal or cortico-bulbar tract involvement (ALS) in the absence of sensory defect, sphincter dysfunction, and ocular disturbances | Average annual incidence calculated using 1990 Japanese population; rates age- and gender-adjusted to 1990 Japanese population for gender, year of onset, region | 77 |
| Hong Kong, China 1997-200236 | Retrospective review of Clinical Management System database (serves 94% of population) using ICD-9 codes 335.xx; identified cases validated by neurologists | | EEC-R for definite, probable, probable laboratory supported, possible and suspected ALS/MND; classified using ICD-9 codes for ALS (335.20), PMA (335.21), PBP (335.22), pseudobulbar palsy (335.23), PLS (335.24) | Crude incidence (1997-2001) calculated using 2001 Hong Kong population; crude prevalence based on patients alive on 31-Jan-02; rates were age- and gender-adjusted to HKSAR and 1990 US census | 98 |
| Wakayama prefecture, Japan 1998-200243 | | Retrospective review of data from: (1) two sequential mail surveys (589 clinics/ hospitals; (2) Wakayama Prefecture's List of Patients with Intractable Disease | EEC-R; PBP and PLS included, familial PMA excluded | Crude incidence (1998-2002); crude prevalence estimated on 31-Dec-02; rates age- and gender-adjusted to 1990 and 2000 Japan population | 134 |
| Isfahan, Iran 2002-200645 | | Retrospective review of medical records from 6 neurology departments and neurologists practicing in outpatient clinics using ICD-10 code G12; duplicates removed; missing data collected by telephone with patient, family members, or appointment with their neurologist | EEC for definite, probable, or possible ALS; PBP and PLS excluded; only confirmed diagnoses included; residents aged <15 y excluded | Age- and gender-adjusted incidence (Iran, 2006); age- and gender standardized incidence (US 2000 census); age- and gender-adjusted prevalence (21-Mar-06) | 98 |
| ***South America*** | |  |  |  |  |
| Republic of Uruguay 2002-200328 | | Prospective, population-based study using data from: hospital records; death certificates; company distributing riluzole; contact with specialists and GPs (combined sources ensured complete case ascertainment) | EEC for MND; only definite or probable ALS patients included in analysis (PMA, PBP, PLS excluded); capture-recapture method used to estimate missing cases | Crude incidence (2002-2003) calculated using Uruguayan population estimates; crude prevalence based on patients alive on 31-Dec-03; rates age- and gender adjusted to 2004 Uruguayan population and 1990 US Census | 89 |

\*Overall incidence or prevalence rates; studies reporting rates by gender or age cohort only were excluded.  
†Ranked chronologically by study period.  
ALS=amyotrophic lateral sclerosis; CAT=computer-assisted tomography; EEC=El Escorial Criteria; EEC-R=El Escorial Criteria-Revised; EMG=electromyography; GP=general practitioner; ICD-9=International Classification of Diseases-9th Revision; ICD-9-CM=International Classification of Diseases-9th Revision-Clinical Modification; ICD-10=International Classification of Diseases-10th Revision; I=incidence; LMN=lower motor neuron; MND=motor neuron disease; MNDA=Motor Neurone Disease Association; MRI=magnetic resonance imaging; NI=Northern Ireland; NR=not reported; P=prevalence; PBP=progressive bulbar palsy; PLS=primary lateral sclerosis; PMA=progressive muscular atrophy; PSMA=progressive spinal muscular atrophy; ROI=Republic of Ireland; PY=person years; SIR=standardized incidence rate; SMA=spinal muscular atrophy; UMN=upper motor neuron; WFN=World Federation of Neurology.