# Creutzfeldt-Jakob disease: Australian surveillance update to 31 December 2004

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## Abstract

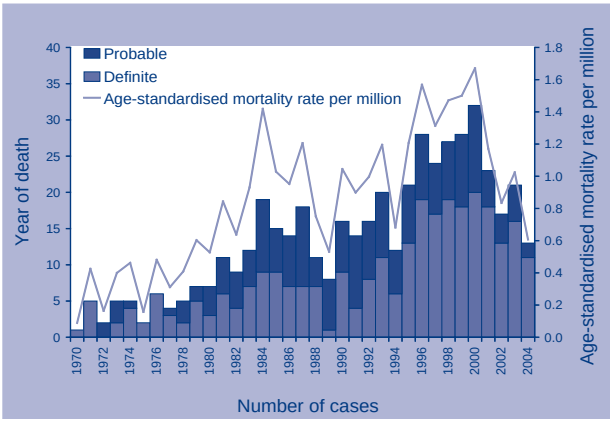
**The Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR) was established in October 1993 after the identification of probable iatrogenic CJD in recipients of human pituitary hormones. Since this time and with the recommendations of the Allars inquiry into CJD in Australia,[1] the registry has performed surveillance of CJD in Australia with retrospective ascertainment to 1970 and ongoing prospective ascertainment of all human prion diseases or transmissible spongiform encephalopathies (TSEs). Prion diseases include CJD, Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia and Kuru. This brief summary presents the epidemiological findings of the ANCJDR based on data from 1970 to 31 December, 2004. *Commun Dis Intell* 2005;29:269–271.**

*Keywords: Creutzfeldt-Jakob disease; disease surveillance; transmissible spongiform encephalopathy*

From 1 October 1993 to 31 December 2004, 1,004 suspected transmissible spongiform encephalopathy (TSE) cases acquired between 1970 and 2004, have been notified to the Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR) for investigation. Of these, 293 definite cases and 186 probable cases have been classified (Table 1) and comprise of 434 sporadic (91.0%), 36 familial (7.3%) and 9 iatrogenic cases (1.7%). Seven cases of possible CJD have been identified of which six were sporadic and one iatrogenic and a total of 86 cases were still under investigation with 47 of these cases still alive. After detailed follow-up and investigation, 432 suspect cases (43%) were excluded from the registry as non-TSE cases. As of December 2004, no further cases of iatrogenic CJD have been detected since the last identified case in 2000. Australia remains free of variant CJD (vCJD).

Between 1970 and 2000, a steady increase in the annual incidence of spongiform encephalopathies can be observed (Figure). This is consistent with, and analogous to, the experience of other CJD surveillance programs, with the increase probably reflecting case ascertainment bias stemming from improved recognition, reporting, investigation and case confirmation.[2] Since 2000, a decline in numbers, in particular probable cases, has been apparent. This may relate to a number of issues, including broadened surveillance responsibilities and difficulties encountered following changes to privacy legislation. The average annual age-adjusted mortality rate during the period from 1970 to 2004 is 0.84 deaths per million per year. During the prospective period of ANCJDR surveillance from 1993 to 2004, the average annual rate of mortality was 1.19 deaths per million persons. The rate for this prospective ascertainment epoch is considered to be a more robust representation of Australian CJD incidence as during this period standardised approaches to case classification and ascertainment were implemented nationally.[3]

**Figure. Australian National Creutzfeldt-Jakob Disease Registry definite and probable cases: number and age-standardised mortality rate, 1970 to 2004**




Mortality rates were calculated using the Australian Bureau of Statistics 2000 resident population estimates for Australia

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**Table 1. Classification of cases on the Australian National Creutzfeldt-Jakob Disease Registry, 1 January 1970 to 31 December 2004**

| Classification | Sporadic | Familial | Iatrogenic | Variant CJD | Unclassified | Total | Cases classified during 2004* |
|---|---|---|---|---|---|---|---|
| Definite | 260 | 28 | 5† | 0 | 0 | 293 | +19 |
| Probable | 174 | 8 | 4 | 0 | 0 | 186 | +6 |
| Possible | 6 | 0 | 1 | 0 | 0 | 7 | +1 |
| Incomplete | 0 | 0 | 0 | 0 | 86‡ | 86 | +27 |
| Total | 440 | 36 | 10 | 0 | 86 | 572 | +53 |

* Describes the classifications made during the 2004 surveillance year (includes cases notified in 2004 or previous years).

† Includes one definite iatrogenic case who received pituitary hormone treatment in Australia but disease onset and death occurred while a resident of the United Kingdom. This case is not included in the statistical analysis since morbidity and mortality did not occur within Australia.

‡ Includes 47 living cases.

The duration of illness for CJD cases varies depending on aetiology and other determinants. The median length of illness duration for all CJD cases was four months. For sporadic cases, the median duration was found to be four months (range, 0.9-60 months), for iatrogenic cases 6.25 months (range, 2-25 months) and for familial cases eight months (range, 1.5-192 months). Familial CJD was found to be associated with a significantly greater survival time in comparison to sporadic CJD ($p<0.0001$ by Log Rank Test).

In sporadic CJD, no significant sex differences have been observed. Overall, 47.2 per cent of cases were male and 52.8 per cent were female. The average age of death in sporadic cases by sex was 65 years (range, 25-89) for males and 66 years (range, 33-89) for females. Over the period of 1970 to 2004, there was no difference between the average age-specific mortality rates of males (0.62 deaths/million/year) and females (0.68 deaths/million/year). In males, the peak mortality rate occurred between 70-74 years (4.0 deaths/million/year) and in females between 65-69 years (4.6 deaths/million/year).

In comparison to sporadic cases, the average death age of familial cases was 51 years (range, 20-82 years) in males and 62.5 years (range, 42-82 years) in females. Peak mortality rates occurred in the 65-69 year age group in both males (0.26 deaths/million/year) and females (0.41 deaths/million/year) and in iatrogenic cases, the average death age was 45 years (range, 27-62 years) for males and 39 (range, 26-50 years) for females.

Analysis of the geographical distribution of sporadic CJD cases showed no significantly increased risk for any individual Australian state or territory. The number of total TSE deaths by state or territory between 1993 to 2004 is shown in Table 2 and reflects geographical population distributions. Crude incidence rates show little variability in the larger regions of Australia and are similar to international rates where similar surveillance mechanisms are in place. The lowest rates were observed in Tasmania and the Northern Territory and may suggest lower ascertainment. No geographical birth region of sporadic CJD cases demonstrated a significantly increased or decreased rate of sporadic CJD incidence.

The notification of suspect cases to the ANCJDR initially peaked (132 cases) during the first year of the registry's surveillance. This was the result of the investigation of the Australian Institute Health and Welfare (AIHW) death certificate searches, which ascertained cases retrospectively to 1988. Further peaks of referrals were observed in 1995-1996 (129 and 125 cases respectively) and again in 1999 (103 cases). The 1995-1996 consecutive peaks were a direct result of AIHW death certificate and hospital and State Morbidity data searches while the 1999 peak was representative of an increased level of acceptance and utilisation of the 14-3-3 cerebrospinal fluid (CSF) diagnostic test by clinicians. More recently, referrals have plateaued with around 60–70 cases referred to the registry each year for evaluation. Overall, the large majority of notifications of suspect cases have been obtained by personal communication from clinicians (34.5%), CSF 14–3–3 protein test request

**Table 2. Transmissible spongiform encephalopathy deaths, 1993 to 2004, by state and territory**

| State/ territory | TSE cases by year of death | | | | | | | | | | | | Total | Mean crude mortality rate (deaths/ million/yr) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | | |
| ACT | | 1 | | | | | 1 | | | 1 | | | 3 | 0.80 |
| NSW | 2 | 3 | 7 | 6 | 10 | 10 | 13 | 12 | 9 | 4 | 7 | 7 | 90 | 1.17 |
| NT | | | | | | 1 | | | | | | | 1 | 0.44 |
| Qld | 5 | 2 | 5 | 6 | 3 | 3 | 7 | 7 | 3 | 3 | 3 | | 47 | 1.14 |
| SA | 1 | 3 | 2 | 3 | 3 | 1 | 3 | 2 | | | 1 | 1 | 20 | 1.12 |
| Tas | | | | 1 | | | | | | 2 | | | 3 | 0.53 |
| Vic | 10 | | 4 | 8 | 5 | 9 | 3 | 9 | 10 | 5 | 8 | 3 | 74 | 1.32 |
| WA | 2 | 3 | 3 | 4 | 3 | 3 | 1 | 2 | 1 | 2 | 2 | 2 | 28 | 1.29 |

(34.1%), death certificates (13.3%) and hospital and health department searches (12.2%). Since 1998, the diagnostic CSF test has been the most dominant initial notification source of definite and probable cases (45–86%) of CJD cases. Compulsory notification of suspect CJD cases has been implemented in four Australian states and territories since 2003–2004. The effect of scheduling CJD as a notifiable disease will be closely monitored by the ANCJDR. At present, there has been no demonstrable change to the number of referrals.

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## *References*

1. Allars M. *Inquiry into the use of pituitary derived hormones in Australia and Creutzfeldt-Jakob disease. Report* – June 1994. Australian Government Publishing Service, 1994.

2. Ladogana A, Puopolo M, Croes EA, Budka H, Jarius C, Collins S, *et al.* Mortality from Creutzfeldt-Jakob disease and related disorders in Europe, Australia, and Canada. *Neurology* 2005;64:1586–1591.

3. Collins S, Boyd A, Lee JS, Lewis V, Fletcher A, McLean CA, *et al.* Creutzfeldt-Jakob disease in Australia 1970–1999 *Neurology* 2002;59:1365–1371.