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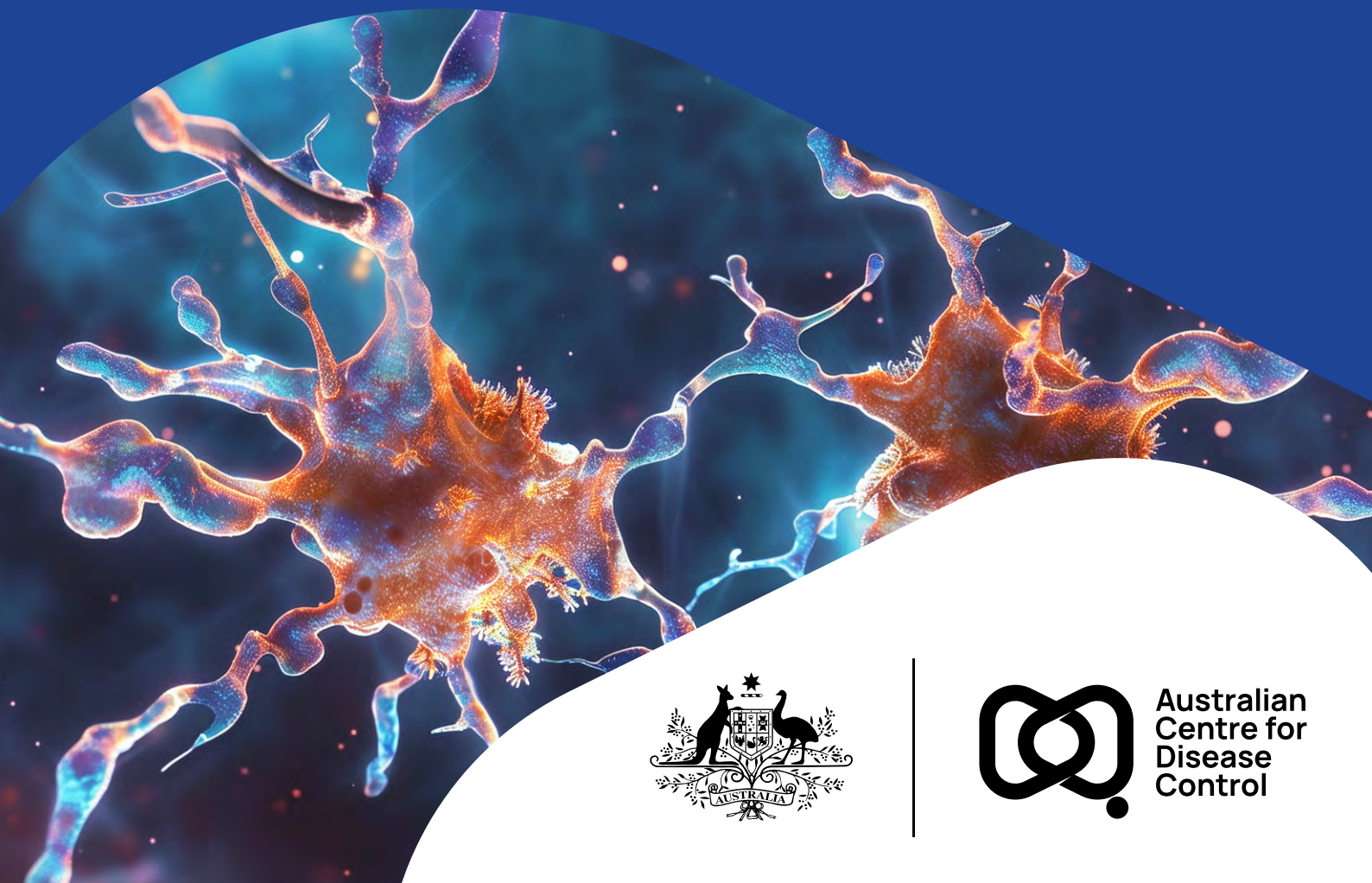
Creutzfeldt-Jakob disease surveillance in Australia: update to 31 December 2025

Christiane Stehmann, Matteo Senesi, Shannon Sarros, Amelia McGlade, Victoria Lewis, Genevieve Klug, Sarah Holper, Catriona McLean, Colin L Masters, Steven Collins



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Email: **cdi.editor@cdc.gov.au**

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Abstract

Nationwide surveillance of Creutzfeldt-Jakob disease (CJD) and other human prion diseases is performed by the Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR). National surveillance encompasses the period since 1 January 1970, with prospective surveillance occurring from 1 October 1993. Over this prospective surveillance period, considerable improvements have been developed in pre-mortem diagnostics in parallel with the delineation of new disease subtypes and heightened awareness of prion diseases in healthcare settings. Surveillance practices of the ANCJDR have evolved and adapted accordingly. This report summarises the activities of the ANCJDR during 2025.

Since the ANCJDR began offering diagnostic cerebrospinal fluid (CSF) 14-3-3 protein testing in Australia in September 1997, the annual number of diagnostic test referrals has steadily increased. In 2025, there were 788 domestic CSF specimens referred for diagnostic testing; 92 persons with suspected human prion disease were formally added to the national register. As of 31 December 2025, more than half of the 84 initial case notifications for 2025 (44/84) remain classified as 'incomplete'; 35 cases have been confirmed as 'definite' or 'probable' prion disease; five cases were excluded. In 2025, most suspected human-prion-disease-related deaths in Australia (56%) underwent neuropathological examination. No cases of variant or iatrogenic CJD were identified in Australia during 2025.

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

Introduction

Of the human prion diseases (also known as transmissible spongiform encephalopathies), the most common phenotype is Creutzfeldt-Jakob disease (CJD). As described previously,[1] human prion disease mostly arises sporadically (~85%) but can occur through horizontal transmission or from a genetic aetiology due to pathogenic sequence variations in the prion protein gene (*PRNP*). The Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR) was established in 1993 as part of the response to four people dying from medically-acquired (iatrogenic) CJD (iCJD) related to fertility treatment utilising cadaveric pituitary hormones. In the following year,[2] the Allars inquiry released its findings into the use of cadaver-derived pituitary hormones under the Australian Human Pituitary Hormone Program, recommending a broadening of the responsibilities of the then nascent ANCJDR. In addition to monitoring for further cases of iCJD in Australia – related to cadaveric pituitary hormone treatment for infertility or short stature, and contaminated dura mater grafts – the ANCJDR's activities have evolved to encompass the surveillance of all types of CJD, including sporadic, genetic, and variant CJD (vCJD: the zoonosis related to bovine spongiform encephalopathy [BSE]), as well as other prion diseases such as Gerstmann-Sträussler-Scheinker (GSS) syndrome and fatal sporadic or familial insomnia (FFI). Human prion disease became a notifiable disease in all Australian states and territories in June 2006.

Initial case awareness at the ANCJDR mostly arises through diagnostic testing requests; this occurs prior to Health Department notification. The ANCJDR's neurologist performs a preliminary review of referred cases. Cases with a high clinical suspicion for human prion disease are added to the national surveillance register for further evaluation. The diagnostic criteria endorsed by the Creutzfeldt-Jakob Disease International Surveillance Network are then applied to determine whether a case can be excluded from suspicion, or can be classified as 'definite', 'probable' or 'possible' prion disease, and to ascertain the aetiology of the illness.[3]

The incidence of sporadic CJD (sCJD) is commonly reported to be approximately one case per million per year; however, in most countries with longstanding national surveillance systems in place, annual incidence rates have consistently been reported above this quoted figure.[4] A multi-national surveillance study showed that intensity of surveillance correlates with reported incidence rates.[5] Temporally, human prion disease incidence rates have increased in most countries, including Australia, as surveillance mechanisms have been optimised and diagnostic testing capabilities improved, in parallel with a generally greater awareness of this rare disease in the healthcare setting.

In this report, updated national surveillance figures to 31 December 2025 are provided for all retrospective (to 1970) and prospective (from 1993) cases ascertained, including a discussion on case notifications, classifications and overall incidence.

Surveillance methods

Patients with suspected human prion disease have been prospectively notified to the ANCJDR since October 1993. From 1997, suspected cases have been increasingly notified through referral for diagnostic cerebrospinal fluid (CSF) biomarker (especially 14-3-3 protein) testing, which has become the predominant means by which the ANCJDR becomes aware of suspected CJD cases. Other ascertainment mechanisms include, or have included, personal communications from clinicians, families, hospitals and CJD-related groups, as well as health record searches through hospitals and health departments.

Once referred to the ANCJDR, referrals undergo a *prima facie* assessment and, if the suspicion of prion disease is supported, the case is notified to the appropriate health department. Such cases are added to the ANCJDR register as a formal 'suspected case' for continued surveillance and evaluation, with the aim of exclusion or classification according to internationally endorsed diagnostic criteria. Investigation of registered cases can be prolonged, as the ANCJDR requires next-of-kin consent to access and compile the appropriate clinical information from various health information sources to facilitate a comprehensive review. Response times can vary, as the information can be extensive or sources numerous. Medico-demographic questionnaires offered and forwarded to families, if they are willing to contribute, provide valuable information for analysis and evaluation.

Classification of registered cases remains as 'incomplete' until all known available information is gathered and reviewed, or until a definitive result from neuropathological assessment is obtained. Cases may be excluded from the register based on non-supportive neuropathological examination or after thorough clinical evaluation. A 'definite' classification requires brain neuropathological examination, including immunochemical analysis; 'probable' and 'possible' cases are reliant on a specific clinical profile and diagnostic test outcomes as previously described.[3,6] As of 1 January 2017, the diagnostic criteria for 'probable sCJD' were amended to include a positive result in the real-time quaking-induced conversion (RT-QuIC) assay using CSF or other tissues in a person with a progressive neurological syndrome. The updated international diagnostic criteria for surveillance of sCJD are listed in Appendix A. As of 1 January 2026, the Communicable Diseases Network Australia (CDNA) updated the Australian surveillance case definitions to reflect these changes.[i] In keeping with previous reports, the total number of confirmed prion disease cases for 2025 included in the statistical analyses are those classified as either 'definite' or 'probable'.

To support surveillance responsibilities, the ANCJDR provides diagnostic platforms for ante- and post-mortem testing for human prion diseases. The testing of CSF for the presence of a family of low-molecular-weight proteins (14-3-3) has been performed weekly by the ANCJDR since 1997. This test has been readily utilised by clinicians. In 2023, the ANCJDR replaced the semi-quantitative 14-3-3 protein western blot analysis with a more accurate and quantitative technology involving the estimation of 14-3-3 protein concentrations using an Enzyme Linked Immunosorbent Assay (ELISA) (certified by the National Association of Testing Authorities [NATA]/International Laboratory Accreditation Cooperation [ILAC]).[7] The 14-3-3 ELISA has a sensitivity of 84%, specificity of 89%, positive predictive value (PPV) of 46% and negative predictive value (NPV) of 98%. The RT-QuIC assay, also NATA/ILAC certified, is routinely performed on all referred specimens with a sensitivity of 79%, a specificity approaching 100%, PPV of 98% and NPV of 97%. In optimal performance, using CSF from a well defined Australian cohort of neuropathologically confirmed sCJD and non-CJD controls, the sensitivity of the RT-QuIC is cited as 92.7%.[7]

The ANCJDR also undertakes western blot analysis for misfolded, protease-resistant prion protein in brain and tonsil tissue from biopsies or autopsies for supplementary immunochemical assessments, as required for diagnostic and sub-classification purposes. The ANCJDR recently developed RT-QuIC assays using frozen and fixed brain tissue, which can confirm minute amounts of PrP^{Sc} (prion protein: scrapie isoform) seeds, to aid in the classification of complex cases.[8] *PRNP* testing for sequence variations in the open reading frame, particularly for proven disease-causing mutations, is performed by an external independent provider as appropriate. Upon request, the ANCJDR performs DNA extractions from frozen post-mortem brain tissue, which can be used for *PRNP* testing. The ANCJDR actively promotes all diagnostic tests to clinicians and families to achieve the most accurate diagnosis and classification of persons with suspected prion disease.

i https://www.cdc.gov.au/resources/publications/surveillance-case-definition-creutzfeldt-jakob-disease.

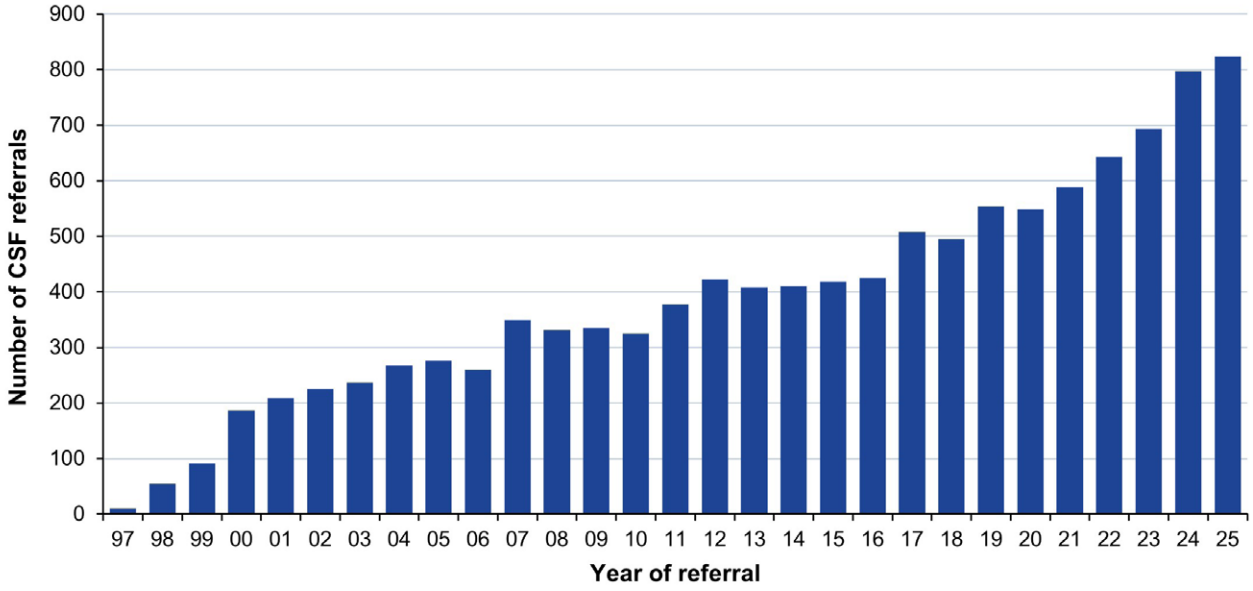
Annual human prion disease incidence rates are calculated using direct age-standardisation, based on the 1970–2025 Australian Bureau of Statistics estimated resident population data for Australia and for each state and territory.[ii] Health information is collected through a combination of public health and surveillance responsibilities, based on the national notification of communicable diseases in observance of the *National Health Security Act 2007* and *Privacy Act 1988* (Cth) 16B. ANCJDR surveillance activities for 2025 were approved by The University of Melbourne Human Research Ethics Committee (#20361).

ii https://www.abs.gov.au/statistics/people/population/national-state-and-territory-population/latest-release#data-downloads. (Accessed on 1 April 2026.)

Results

In 2025, the ANCJDR received 788 domestic CSF specimens for diagnostic testing. This number continues the enduring increase in annual CSF referral numbers, reflecting clinicians' increasing awareness of test availability and appreciation of its utility in patient management (Figure 1). In 2025, non-domestic CSF referrals made up 4% of the total diagnostic CSF specimens received by the ANCJDR. The majority of domestic CSF referrals come from the most populous states, from which there has been a noticeable steady increase in test referrals, while CSF referrals from the Australian Capital Territory, the Northern Territory and Tasmania have remained relatively unchanged over the last 10 years. Notably, diagnostic test referrals from New South Wales and South Australia have increased more rapidly over the last decade than those from other states, increasing from an average referral rate of 12/million/year (1997–2012) to 26/million/year (2013–2026) in New South Wales and from 9/million/year (1997–2015) to 25/million/year (2016–2025) in South Australia. The national average CSF referral rate for the period of 1997–2025 is 16/million/year; the Northern Territory has the lowest rate of CSF referrals (5/million/year), while all other jurisdictions range between 12/million/year (Western Australia) to 17/million/year (Tasmania).

Figure 1: Annual number of CSF specimens referred to the ANCJDR for diagnostic testing, from 1997 to 2025



During 2025, ninety-two persons with suspected human prion disease were formally added to the national CJD surveillance register following *prima facie* review. Of these, eight cases were known to the ANCJDR prior to 2025 through CSF referrals (n = 5), the CJD Support Group Network (n = 2), or the treating clinician (n = 1). At the time of their initial notification in 2020 (n = 1), 2022 (n = 1), and 2024 (n = 6), these cases were not added to the register due to a low level of suspicion for prion disease after initial case review. Further information ascertained in 2025 increased the likelihood of prion disease for these eight cases, resulting in their formal notification and the addition of these cases to the register. These cases therefore contribute to the total numbers of suspected case notifications arising in 2020, 2022 and 2024.

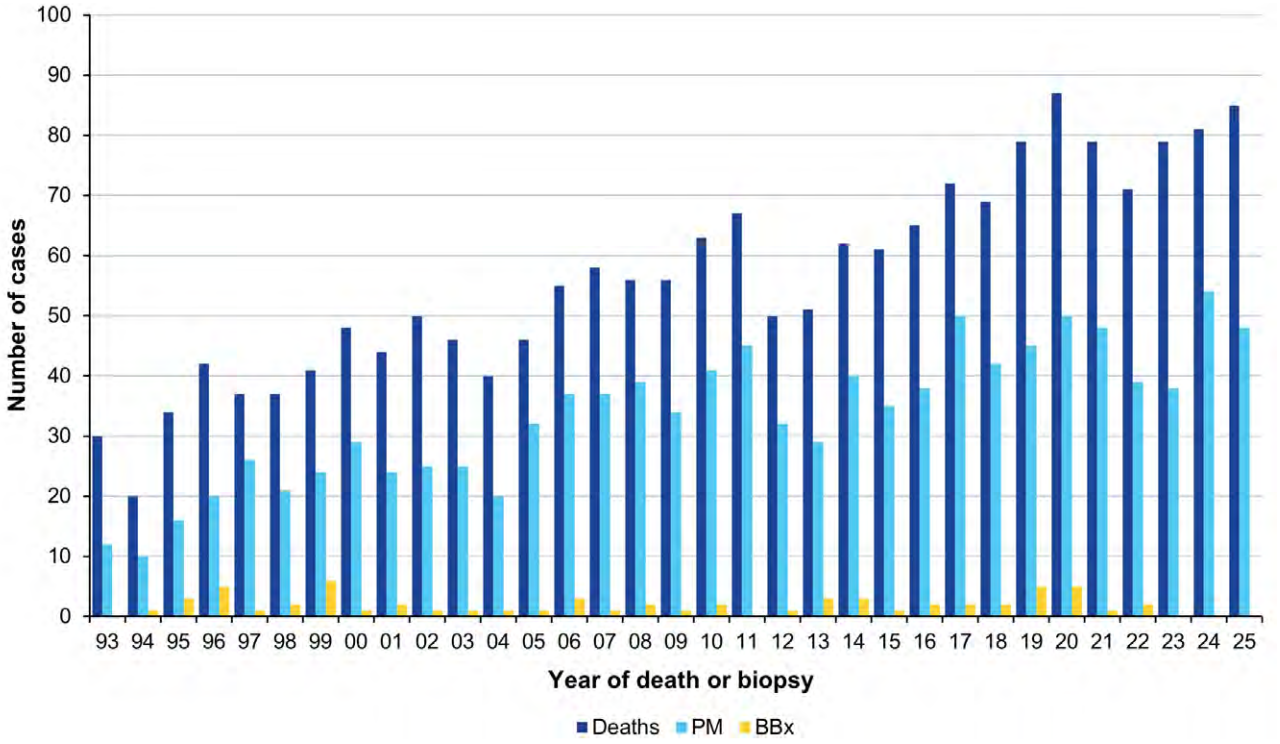
The remaining 84 suspected cases for 2025 were initially notified through various sources: requests for CSF diagnostic testing (n = 48); communications from treating clinicians (n= 19); neuropathology services (n = 9); the CJD Support Group Network (n = 3); health departments (n = 2); a family member (n = 1); a funeral director (n = 1); and a genetic counselling service (n = 1). While there is still a predominance of initial case awareness through referrals for CSF diagnostic testing, there has been in recent years a noticeable increase in case notifications through treating clinicians, neuropathologists, health departments and families seeking expert advice and guidance from the ANCJDR. Some previous proactive ANCJDR surveillance mechanisms (e.g. mortality database searches and reply-paid mailouts to clinicians) have been discontinued over time due to human resource constraints.

The number of suspected cases added to the ANCJDR register in 2025 continues the trend of increasing case notification rates. The average annual number of prospective, formal suspected prion disease cases notified to the ANCJDR for the period 1997–2025 (i.e. since the introduction of diagnostic testing of CSF) is 75. States and territories exhibited modest fluctuations in the annual number of suspected case notifications for 2025, compared to both the previous year and the longer-term average.

Of the 84 formal suspected case notifications added for 2025, twelve cases were confirmed as 'definite' by neuropathological examination; 23 cases were classified as 'probable' following detailed review of clinical information; four cases were confirmed as non-prion disease following neuropathological assessment, one case was removed following detailed case review; and 44 cases were considered 'incomplete' at the end of 2025 (twenty cases were still alive, while neuropathology reports were pending for 22 deceased suspected cases with two further deceased cases requiring case review and classification). It is typical for several months to elapse between performance of a post-mortem examination and completion of the neuropathology report.

Since 1993, there has been an overall positive trend in the annual number of suspected cases of human prion disease undergoing post-mortem brain examination, or less commonly brain biopsies, albeit with relative plateauing over the last 15 years. Beginning with twelve post-mortem brain examinations in 1993, numbers for the period from 2005 to 2025 increased to ranging between 30 and 50 brain autopsy referrals per year (Figure 2). In 2025, forty-eight of the 85 suspected CJD-related deaths were referred for a brain post-mortem examination.

Figure 2: Number of brain-only post-mortem (PM) examinations and brain biopsies (BBx) completed relative to suspected case deaths from 1993 to 2025, by year



The average annual proportion of suspected prion disease cases added to the register between 1993 and 2025 undergoing post-mortem brain examination is 59% (range 40–70%); the provisional proportion for 2025 is 56%. Annual suspected prion disease brain autopsy referrals by states and territories over the period 1993–2025 display considerable fluctuation in each jurisdiction. In the more populous states, there has generally been an overall temporal increase in brain autopsy referrals. In regions with smaller populations, this positive trend is also present but less robust due to the relative impact of variation in the annual brain autopsy referrals caused by small population sizes and case numbers.

As of 31 December 2025, there were 1,721 cases on the ANCJDR register, with 1,493 of these classified as 'probable' or 'definite' prion disease cases. An additional 'definite' iatrogenic case, who was treated in Australia but died in the United Kingdom (UK), is included in Table 1; this case is not classified as an Australian case due to their location at death and is thereby excluded from the overall statistical analysis of Australian prion disease cases. Since the start of prospective surveillance in 1993, a total of 911 suspected prion disease cases have been removed from the register following non-supportive neuropathological assessment or after detailed clinical review.

In 2025, twenty-nine cases were re-classified from 'incomplete' to 'definite' prion disease and 46 cases to 'probable' prion disease. In 2025, the total number of 'incomplete' cases under evaluation was slightly higher than in 2024. Seven cases were assigned the label of 'indeterminate', as they could not be classified confidently using the international diagnostic criteria after detailed clinical review. Impediments to timely and complete access to all clinical information, especially magnetic resonance brain imaging (MRI), can limit confident case classifications.

Table 1: Overall summary of Australian human prion disease, 1 January 1970 to 31 December 2025

Classification	Sporadic	Familial	Iatrogenic	Variant CJD	Incomplete or Indeterminate	Total
Definite	812	78	5[a]	0	0	894
Probable	552	43	4	0	0	599
Possible	15	2	1	0	0	18
Incomplete		7	0	0	203	210
Total	**1,379**	**130**	**9**	**0**	**203**	**1721**

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

The age-standardised mortality rate (ASMR) for prion disease for 2025 was 1.39 deaths per million per year. This figure is provisional and almost certainly an underestimate, as 26 neuropathology reports and one case review are pending. Annual ASMR values for human prion disease in Australia during the period of 1970 to 2025 have generally increased. The mean annual ASMR during the period from 1970 to 2025 is 1.17 death per million (range 0.1–2.3). For the prospective surveillance period of 1993 to 2025, the annual mean ASMR is 1.52 deaths per million (range 0.7–2.3). By state and territory, most regions in Australia have an annual mean ASMR equivalent to or above one case per million per year between 1993 and 2025 (Table 2), except for the Northern Territory. The lower rates of ascertainment in the Northern Territory may be partly explained by geographical challenges relating to proximity to specialised health care and post-mortem services, as illustrated by CSF diagnostic test referral rates and autopsy referral rates being well below the national average.

A breakdown of annual case numbers and mortality rates is shown in Figure 3 and Table 2. The highest annual number of 'probable' and 'definite' prion disease cases reported, since surveillance commenced in 1993, was 73 in 2020, resulting in an ASMR for that year of 2.28 deaths per million. Higher mortality rates, ranging between 1.7 and 2.3, have been recorded since 2016; this coincides with the introduction of new diagnostic tools, such as CSF total-tau protein assay, the RT-QuIC assay, and improved understanding of supportive brain MRI findings.

The proportions of human prion disease aetiologies on the ANCJDR register for 2025 remains similar to previous years (Figure 4). The vast majority of the 1,493 statistical cases of human prion disease are sporadic (91.4%), while genetic and iatrogenic cases represent 8.1% and < 1%, respectively, of all 'definite' and 'probable' cases. No case of vCJD has ever been confirmed in Australia, including during 2025.

There are currently 1,364 'definite' and 'probable' sporadic prion disease cases on the ANCJDR register. The distribution is almost equal between males (49%) and females (51%). The average age at death is 67.7 years, with a median of 69 years, ranging in age from 19 to 91 years. The average duration of illness is 6.6 months, with a median of 4 months, ranging from 0.7 to 84 months.

Table 2: 'Definite' and 'probable' cases of human prion disease from 1993 to 2025, by year and state or territory

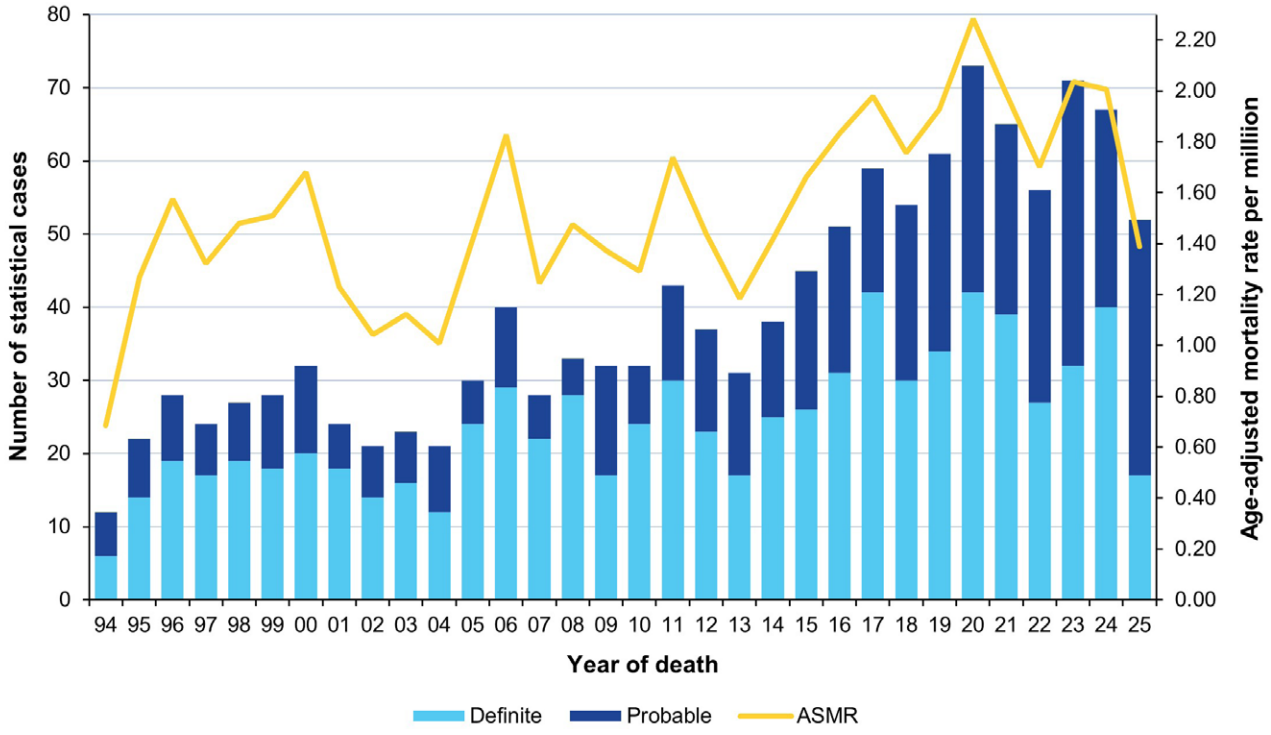
Jurisdiction[b]	2025[a]		1993–2025		
	Definite/ probable cases	ASMR[c] (dths/mill/yr)	Total cases	Long term average cases	Average ASMR[c] (dths/mill/yr)
ACT	0	0	18	0.6	1.25
NSW	20	1.47	413	12.5	1.51
NT	1	1.49	9	0.3	0.83
Qld	10	1.30	228	6.9	1.29
SA	2	0.74	106	3.2	1.70
Tas.	2	2.08	31	0.9	1.32
Vic.	13	1.42	319	9.7	1.60
WA	4	0.91	156	4.7	1.76
Australia	**52**	**1.39**	**1,280**	**38.8**	**1.52**

a The figures for 2025 are provisional and almost certainly an underestimate, as 26 neuropathology reports and one case review are pending.

b ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld.: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.

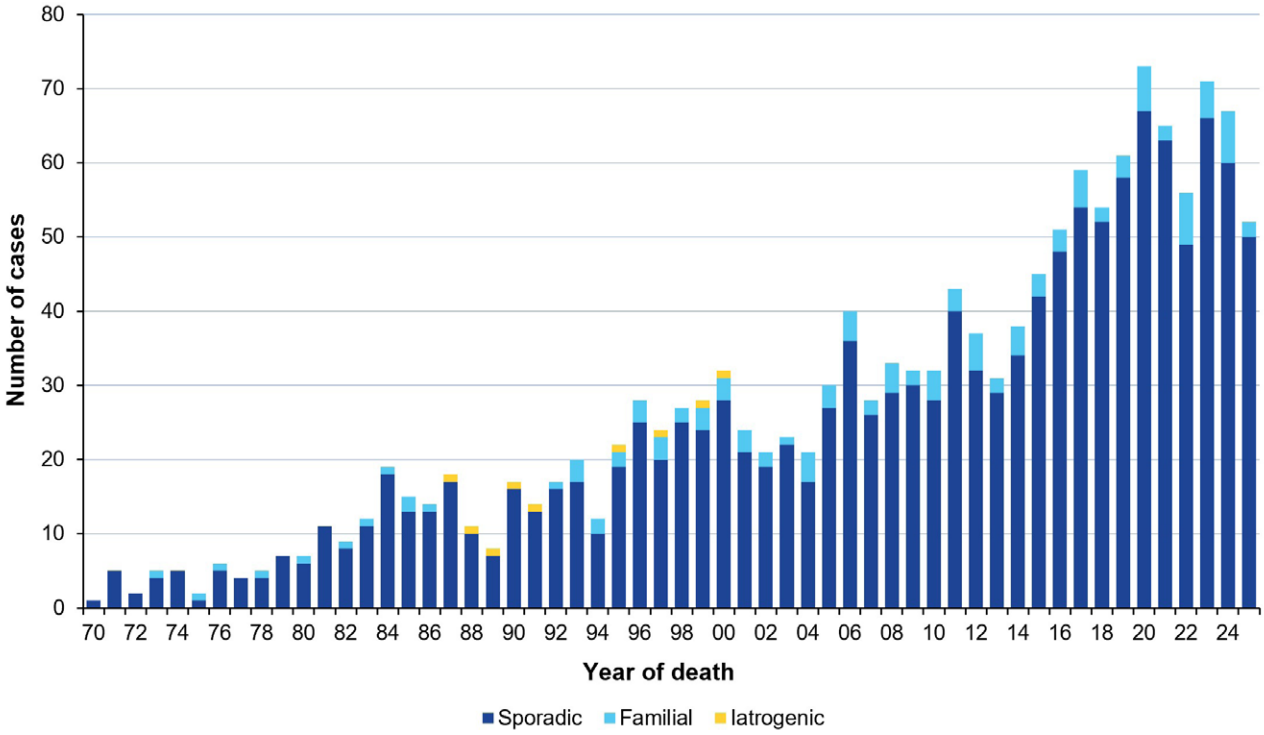
c ASMR: age-standardised mortality rate, in deaths per million population per year.

Figure 3: Human prion disease in Australia from 1993 to 2025; number of cases and age-standardised mortality rates (ASMR), by year



There are currently 71 families affected by genetic prion disease on the ANCJDR register, comprising 121 individuals (78 'definite' and 43 'probable' cases) with a confirmed genetic aetiology, 54% of whom are female. The average age at death for genetic prion disease is approximately a decade younger than in sporadic prion disease, at 57.8 years, with a median of 59 years (range 18 to 83 years). The average duration of illness is approximately 10 months longer than in sporadic prion disease, at 17.1 months, with a median of 6.2 months (range 1.3 to 192 months). Age of onset and duration of illness depend on the mutation present and its resulting phenotype: FFI and GSS are often associated with younger age of onset and longer durations than mutations resulting in CJD-like presentations, for example.

Figure 4: 'Definite' and 'probable' human prion disease cases from 1970 to 2025,[a] by year and aetiology



a 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.

The range of *PRNP* mutations in Australian genetic prion disease cases is shown in Table 3. In 2025, five cases of genetic prion disease were confirmed neuropathologically or by clinical case evaluation. To date, three *PRNP* mutation carriers have been excluded from the register after brain autopsy. They died without symptoms of prion disease aged 70, 88, and 91 years old: well above the average age at death of symptomatic members of their pedigrees. Seven incomplete cases, in which there is concern for genetic prion disease due to a pathogenic *PRNP* mutation, remain under investigation on the register without a neuropathological or clinical case classification outcome; the individuals are still alive or neuropathology reports are pending. Four families are of unspecified *PRNP* status, although there is a recorded family history of prion disease. The utility of diagnostic biomarkers for genetic prion disease, especially those found in CSF, continues to be defined.[9]

Previously misdiagnosed cases, displaying very subtle or negligible neuropathological changes of spongiform encephalopathy, were demonstrated to harbour *PRNP* mutations and were confirmed as prion disease using a combination of techniques centred on an adapted RT-QuIC methodology.[8] These cases highlight the crucial importance of comprehensive diagnostic evaluation, including genetic testing and brain tissue analysis, to accurately diagnose the aetiology of neurodegenerative diseases presenting with less typical clinical phenotypes.[10,11]

Table 3: Prion protein gene (PRNP) sequence variations/mutations identified in Australian cases

Mutation/polymorphism	Definite/probable cases	Cases post-mortem proven not CJD[a]
E200K	56	3
D178N	21	0
V210I	9	0
P105T	6	0
P102L	7	0
Insert mutations/OPRI[b]	7	0
Other mutations[c]	8	0
Not determined	7	0
Total	**121**	**3**

a In known mutation carrier.

b OPRI - abbreviation for octapeptide repeat insertion.

c A133V, E200D, E211D, G131V, T188A, V176G, V180I, V189I.

Discussion

In 2025, the number of suspected prion disease referrals and confirmed cases broadly matched the long-term prospective surveillance period (1993–2025) averages. Australia continued to be free of vCJD and no further cases of iCJD were detected in Australia in 2025. By state and territory, the numbers of suspected case referrals showed modest fluctuations during 2025 compared to previous years and were within previously observed ranges.

Globally, long-term national surveillance units report differing annual prion disease mortality rates, ranging from 0.24 to 4.56 per million population.[4] The underlying basis for fluctuations and differences in national mortality rates is uncertain, although variation in case ascertainment is one potentially contributing factor.[5] Periods of higher rates of human prion disease over short time frames have been recognised and investigated in various global settings with inconclusive outcomes.[12] For example, such spatio-temporal clustering of CJD has been previously recognised in New South Wales and Victoria.[13,14] Detailed epidemiological assessment by the ANCJDR did not identify any likely horizontal transmission event but instead uncovered a heightened intensity of surveillance. This more intense level of surveillance was reflected by the significantly higher rates of referrals of suspected prion disease cases for evaluation and diagnostic testing to the ANCJDR, as well as higher neuropathological examination rates in suspected patients. Monitoring of the geographical distribution of suspected case referrals and confirmed cases remains an important facet of ANCJDR national surveillance. The overall increase in sCJD cases observed in Australia is most likely due to a combination of an ageing population, improved case ascertainment and diagnostic capacity, and greater awareness of prion disease in the healthcare sector. The gradual increase in the incidence of sCJD, but not that of genetic prion disease, has also been reported in other countries with longstanding national prion disease surveillance programmes, supporting the notion that it is at least partly a result of the globally ageing population, as well as enhanced diagnostics and awareness.[15,16]

Ascertainment mechanisms in 2025 remained unchanged compared to recent years, with a majority of initial referrals coming through requests for diagnostic CSF testing. Some proactive ascertainment mechanisms (such as state health department and tertiary hospital mortality database searches) have ceased, while other case detection methods have increased. The number of CSF referrals to the ANCJDR for diagnostic testing remained high for 2025. A 20% increase in diagnostic test referrals in 2017 coincided with the introduction of CSF total-tau protein assay and the detection of misfolded prion protein in CSF by RT-QuIC assay. Since 2021, the ANCJDR, as per an amended contract with the Commonwealth Department of Health, ceased its cost recovery for CSF diagnostic testing for domestic specimens, which may have contributed to a maintained increase in domestic test referrals. The ANCJDR continues to evaluate emerging diagnostic tools and criteria; with a recent publication confirming that the suggested amendments to the MRI diagnostic criteria, supportive of a diagnosis of sCJD, being at least as good as extant criteria.[17]

The proportion of post-mortem examinations being performed in suspected prion disease cases remains high and aligns with the long-term mean brain autopsy percentage of 59% (of suspected case deaths) between 1993 and 2024. This contrasts with the findings of an Australian healthcare setting survey where the national hospital post-mortem rate was 12% in 2002–2003.[18] More recently, a major Australian tertiary centre audit of hospital autopsy data described an even lower autopsy rate of 6.6% in 2011–2013.[19] A high rate of post-mortem examinations over the more recent prospective surveillance period has supported the consistently high number of confirmed human prion disease cases in Australia recorded and has also allowed for confident determination of alternate causes of death in suspected cases ultimately determined as non-prion disease. Neuropathologists occasionally request that the ANCJDR test for the presence of PrP^{Sc} to confirm or rule out prion disease in neuropathologically challenging or atypical cases. Historically, the ANCJDR relied on performing increased sensitivity (sodium phosphotungstate [NaPTA]) western blotting, which required fresh/ frozen brain tissue.[20] More recently, the adoption of an RT-QuIC assay compatible with fixed, fresh/ frozen brain tissue has expanded the ANCJDR's ability to assist in more complex or historical cases.[8]

A study by the ANCJDR of prion disease in Indigenous Australians has confirmed that sCJD occurs in Indigenous Australians throughout Australia with a phenotype and incidence rate equivalent to non-Indigenous Australians, supporting the representativeness and reliability of national human prion disease surveillance.[21]

No further iCJD cases were confirmed in Australia during 2025. The most recent human cadaveric pituitary gonadotrophin-related iCJD death occurred in 1991, while the most recent Lyodura-related iCJD death occurred in 2000. Globally, iCJD is still being detected. The most recent cases occurred in 2023; the USA and UK each reported one iCJD death associated with growth hormone treatment,[iii,iv] while Japan reported in 2023 one Lyodura-related case of iCJD.[v]

Since vCJD was first reported in 1996, a total of 233 patients from 12 countries have been diagnosed with this disease. The most recent three vCJD cases, who died in France in 2019 and 2021 and Italy in 2016, are plausibly related to accidental occupational exposure incidents in laboratory settings.[16,22] Case 178 from the UK was methionine-valine heterozygous at codon 129 of the *PRNP* gene;[23] all previous vCJD cases had been methionine homozygous at codon 129. The patient was 36 years old when he presented with psychiatric symptoms, went on to develop cognitive decline, ataxia and myoclonus, and died after an illness duration of 20 months. CSF 14-3-3 and RT-QuIC were negative. Brain MRI revealed features more typical of sCJD (i.e. bilateral high signal in the basal ganglia) without the posterior thalamic high signal ('pulvinar sign') classically seen in vCJD. The patient did not meet the epidemiologic diagnostic surveillance criteria for 'probable' or 'possible' vCJD, although fulfilled criteria for 'probable' sCJD. Neuropathology, including western blot glycotyping, was typical of vCJD. It remains uncertain whether this case marks the start of a second wave of vCJD affecting those heterozygous for methionine-valine at codon 129. This case underscores the vital importance of performing brain autopsy examinations in suspected CJD cases and emphasises the ongoing need to maintain high-level surveillance within Australia.

iii Personal communication, Centers for Disease Control and Prevention (United States Government Department of Health and Human Services, Atlanta, Georgia, United States of America).

iv Personal communication, National Creutzfeldt-Jakob Disease Research and Surveillance Unit (Western General Hospital; Edinburgh, Scotland, United Kingdom).

v Personal communication, Utsunomiya City Public Health Centre (Utsunomiya, Togichi, Japan).

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Author details

Dr Christiane Stehmann – Coordinator, Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR)[1]

Dr Matteo Senesi – Research Fellow, ANCJDR[2]

Ms Shannon Sarros – Research Assistant, ANCJDR[1]

Ms Amelia McGlade – Research Assistant, ANCJDR[1]

Dr Victoria Lewis – Research Fellow, ANCJDR[2]

Ms Genevieve Klug – Research Assistant, ANCJDR[2]

Dr Sarah Holper – Neurologist, ANCJDR[1]

Professor Catriona A McLean – Neuropathologist, ANCJDR[1,3]

Professor Colin L Masters – Director, ANCJDR[1]

Professor Steven J Collins – Director, ANCJDR[1,2]

1. The Florey Institute, The University of Melbourne, Victoria, 3010, Australia
2. Department of Medicine, The University of Melbourne, Victoria, 3010, Australia
3. The Alfred Hospital, Department of Anatomical Pathology, 55 Commercial Rd, Melbourne Vic 3004 Australia

Corresponding author

Prof. Steven Collins

Australian National Creutzfeldt-Jakob Disease Registry, Department of Medicine, The University of Melbourne, Victoria, 3010, Australia

Telephone: +61 8344 1949

Facsimile: +61 9349 5105

Email: s.collins@unimelb.edu.au

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Appendix A

EUROCJD diagnostic criteria for surveillance of sporadic CJD from 1 January 2017

1.1: Definite

Progressive neurological syndrome AND neuropathologically or immunohistochemically or biochemically confirmed

1.2: Probable

1.2.1: I + two of II and typical EEG[a]

OR

1.2.2: I + two of II and typical MRI brain scan[b]

OR

1.2.3: I + two of II and positive CSF 14-3-3

OR

1.2.4: Progressive neurological syndrome and positive RT-QuIC in CSF or other tissues

1.3: Possible

I + two of II + duration < 2 years

I Rapid progressive cognitive impairment

II A Myoclonus

B Visual or cerebellar problems

C Pyramidal or extrapyramidal features

D Akinetic mutism

a EEG: electroencephalogram; generalised periodic complexes.

b High signal in caudate/putamen and MRI brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR).