The CJD Review – Final Report

For the Australian Government
Department of Health

16 September 2021

pwc

Table of contents

Disclaimer

This Final Report has been prepared by PricewaterhouseCoopers Consulting (Australia) Pty Ltd (PwC) at the request of the Commonwealth of Australia, as represented by the Department of Health, in our capacity as advisors in accordance with the agreement executed 18 February 2021 between PwC and the Department of Health.

This report is not intended to be utilised or relied upon by any other persons other than the Department of Health, nor be used for any purpose other than that articulated above. Accordingly, PwC accepts no responsibility in any way whatsoever for the use of this report by any other persons or for any other purpose.

The information, statements, statistics and commentary (together the "information") contained in this report have been prepared by PwC from publicly available statements, peak and regulatory body publications, peer reviewed and grey literature, and consultation with Australian and international stakeholders. PwC has not sought an independent confirmation of the reliability, accuracy or completeness of this information. It should not be construed that PwC has carried out any form of audit of the information that has been relied upon.

Accordingly, whilst the statements made in this report are given in good faith, PwC accepts no responsibility for any errors in the information provided by the Department of Health or other parties nor the effect of any such error on our analysis, suggestions or report.

The information must not be relied on by third parties, copied, reproduced, distributed or used, in whole or in part, for any purpose other than detailed in our Agreement without the written permission of the Department of Health and PwC.

Liability limited by a scheme approved under Professional Standards legislation.

Acknowledgements

PwC would like to thank the CJDSGN, the ANCJDR, the international and national prion disease experts and AHPHP Participants who participated in this review and who provided access to materials and information to inform this report.

Executive summary

Project context

Creutzfeldt-Jakob disease (CJD) is a rare and fatal neurodegenerative prion disease that may develop sporadically or can be genetically inherited or acquired (via medical procedures or consuming contaminated food items).

Between 1967 and 1985, over 2,000 people were part of the Australian Human Pituitary Hormones Program (AHPHP) and received cadaver-derived pituitary hormones to treat infertility and short stature. Certain batches of the hormones were suspected to be contaminated with the infectious prion causing CJD and five people have been known to have died as a result in Australia.

The Commonwealth Government's investments in managing the public health risks posed by CJD (and other transmissible spongiform encephalopathies (TSE) diseases) have focused on funding support for the CJD Support Group Network Pty Ltd (CJDSGN) – a peak consumer advocacy and support group and the Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR) – a national surveillance registry of people with clinically suspected and diagnosed human prion disease.

Project background

The Australian Government Department of Health (the Department) engaged PwC to ***'review the CJDSGN and ANCJDR, and provide advice on the ongoing needs of participants of the AHPHP'*** (hereafter referred to as the CJD review). The objective of this review was to develop evidence-informed findings of how Australia should respond to the risk of CJD in the future. Specifically, it aimed to conduct an independent review of:

- **CJDSGN's support and advocacy services** for participants of the AHPHP and those at risk of prion disease, as well as the appropriateness and effectiveness of existing arrangements in meeting these needs
- **ANCJDR's services in providing national surveillance** and diagnosis of human prion diseases in Australia (noting CJD's status as a national Notifiable Disease)
- the needs of the AHPHP participant cohort following the cessation of the Special Account and any associated obligations for the Commonwealth Government
- the current evidence base and literature surrounding CJD and prion diseases in general.

Methodology

This project adopts a program evaluation methodology in undertaking this review which entails a comprehensive data and information process to enable a triangulation of findings and conclusions. An overview of our project methodology is as follows:

Review of documented evidence

Drawing on the available literature evidence including peer-reviewed and grey literature sources, we examined the evidence surrounding the risk landscape of CJD and prion diseases. This included:

- Best practice in communicating with and supporting those impacted by or at increased risk of prion diseases
- The transmission risk status of cadaveric human pituitary hormone recipients
- An assessment of international approaches to infection control.

Consultations with stakeholders

We undertook a total of 30 consultations with Australian and international stakeholders including:

- Overseas CJD surveillance units, research organisations and support groups
- Representatives from the Communicable Diseases Network Australia
- Clinical and consumer peak organisations
- Representatives from the ANCJDR and the CJDSGN (written submissions were also sought from these stakeholders)

AHPHP participant survey and consultations

We surveyed 19 AHPHP participants and interviewed 10 to understand their current and future needs as well as their experiences of engaging with the CJDSGN. Given the sensitivity and their status as 'vulnerable' under the National Statement on Ethical Conduct in Human Research, a human research ethics application was submitted and approved by Bellberry Limited (Ref. 2021-02-150)

Future needs projections

Drawing on available data, we modelled:

- The likely future prevalence of sporadic CJD
- The likely time for ongoing supports needed for the AHPHP Cohort

Executive summary

The role of the CJDSGN

The CJDSGN is a not-for-profit organisation established to support Australians affected by CJD and prion diseases. Their services, in accordance to their grant agreement with the Australian Government includes:

- providing and maintaining a national network of support groups through which AHPHP participants can interact with each other and provide mutual support, share information and discuss issues and concerns
- improving the wellbeing of AHPHP participants by assisting with the management of anxiety associated with the increased risk of contracting CJD
- acting as an advocate on behalf of recipients of hPH who are experiencing difficulties accessing medical treatment because of infection control issues
- providing a mechanism for the Department to receive comments from AHPHP participants and to represent the views of its members in other forums.

The CJDSGN also extends those services to a broader cohort of people who have been affected by CJD. In addition, the CJDSGN plays a role in supporting health care providers through the provision of infection control advice, education and information. Finally, the CJDSGN has a global footprint through its participation in international CJD conferences and through fundraising for research.

The organisation primarily relies on donations and bequests (making up 49 per cent of their revenue) followed closely by grants provided by the Australian Government (47 per cent). The CJDSGN is led by a salaried Director while support staff participate voluntarily.

Key findings regarding the CJDSGN

We note the following findings made of the CJDSGN in this evaluation:

The CJDSGN provides a range of supports for people impacted by CJD (including AHPHP participants). These supports are consistent with services provided by other disease-specific support groups. Given the rarity and uniqueness of this disease, there are no alternative support groups with CJD specific expertise.

The CJDSGN plays a unique role in Australia by drawing the attention of healthcare providers to infection control advice, education, and information. Overseas, this function is typically performed by CJD specific health services (for example in the UK, this is performed by the National CJD Research and Surveillance Unit at the University of Edinburgh). Currently, there is insufficient expertise for CJD in the broader Australian health system resulting in the role being performed by this support network. The jurisdictional public health units (PHU) and the ANCJDR also provide advice in these areas.

The CJDSGN is well regarded both within Australia and internationally. Feedback from stakeholders including the AHPHP participants indicate positive views of the organisation and the services they provide. Survey responses by the AHPHP participants indicate that the support meetings and the clinical advocacy (referred to as liaison services) were the most useful service offerings.

The organisation's operations are primarily funded through a grant from the Department. While they do engage in fundraising activities, these are directed towards research. The available financial statements indicate that the CJDSGN has no cash reserves or investments to draw on to continue operations in the absence of continued government funding.

The governance of the CJDSGN heavily relies on a group of volunteers. The organisation's Director is the sole salaried staff member and adequate succession planning is noted to be hindered by a lack of funding certainty.

Executive summary

The role of the ANCJDR

The ANCJDR is a public surveillance organisation established to provide:

- Research and monitoring of new cases of CJD in Australia and overseas
- An examination of risk factors for CJD such as blood transfusions
- Annual reports to *Communicable Disease Intelligence* and the Department
- On-demand advice to the Department and other health authorities regarding CJD (e.g. upcoming CJD risks to the public health system)
- Expertise, when required, to committees and working groups on prion diseases and infection control.

The services provided by the ANCJDR include:

- Undertaking national surveillance of CJD which includes developing annual reports to government
- Conducting public health risk assessments (i.e. the monitoring of overseas cases of CJD, working with Lifeblood to test blood samples, accepting and testing samples directly provided by clinicians) followed by notifying state health departments including VIC, QLD, NSW and WA (the remaining jurisdictions do not have any formal data sharing agreements with the ANCJDR to enable this).
- Ad-hoc expert advice provided to clinicians in public and private health care settings on infection control matters relating to surgery. We note that the CJDSGN also performs a similar role, resulting in an overlap of activities
- Expert advice to state and territory health departments in the event of an adverse event involving CJD (i.e. exposure of a patient to instruments or materials contaminated with CJD). This includes the provision of advice on look-back processes (which is a tracing and notification process when an incident is triggered e.g. a contamination of surgical equipment with CJD) as well as infection prevention and control
- The undertaking of specialist CJD diagnostic tests. It is understood that the nature of these tests (including the technical nature of tests like RT-QuIC and requirements for infection control) means that these cannot be readily undertaken by other laboratories
- Biobanking of infected tissue including cerebrospinal fluids, brain tissue and genetic material for national and international research
- Research collaborations and presentations at seminars locally and internationally.

Findings on the role of the ANCJDR

We note the following findings made of the ANCJDR in this evaluation:

The ANCJDR provides additional services beyond those defined in their grant agreement with the Department. This additional role includes attending family meetings where there is suspected CJD, participation in research working groups and the provision of neuropathology diagnostic services for the purpose of post-mortem testing for CJD. These additional roles are funded by the CJDSGN or through the National Health and Medical Research Council.

There has been a growing demand for the services provided by the ANCJDR over the past six years. This is particularly observable in the number of diagnostic tests (specifically the 14-3-3 protein test) performed e.g. there were 554 tests performed in 2019 compared to 410 in 2014.

A review of the ANCJDR's 2019-20 income and expenditures indicates that the registry primarily relies on grant funding provided by the Australian Government. The organisation also receives supplementary funding from the CJDSGN (which the network in turn, derives from fundraising) and through research grants.

International and Australian stakeholders value the ANCJDR both in terms of the public health surveillance functions, but also in their contributions towards advances in diagnostic processes and their contribution to the global CJD research and evidence base. New Zealand is also reliant on the ANCJDR for diagnosis, testing and advice on atypical CJD cases. These are funded by New Zealand.

The ANCJDR is currently awaiting accreditation for RT-QuIC testing and following a successful accreditation, the ANCJDR plans for every CSF sample to undergo RT-QuIC from 2021 onwards. RT-QuIC is currently the most advanced diagnostic tool as it is highly accurate (compared to other protein tests) and less invasive than brain biopsies. RT-QuIC is widely used overseas and the accreditation of this test will bring Australia's diagnostic testing in line with global best practice.

The ANCJDR is staffed by a small number of multidisciplinary experts in CJD. Succession planning for the ANCJDR is of concern. The registry had reported to this review that the supply of expertise in Victoria could adequately meet their future workforce requirements. However, a training pipeline for these specialists may take several years. In addition, the certainty and adequacy of funding are reported to be the key barriers.

Executive summary

There are several risks to public health associated with CJD

CJD is a transmissible disease which therefore, creates a known risk to the public health system of Australia. This known risk can be mitigated through an appropriate public health response. Through an analysis of data and projection modelling, we have identified possible issues for the public health system:

- The future risk profile and needs for the AHPHP participant cohort
- The growth in sporadic CJD in line with population growth and ageing
- Emerging concerns regarding potential iatrogenic or variant CJD.

The future needs of the AHPHP participants

The AHPHP participants remain at risk of developing CJD until the point at which there is evidence that conclusively proves that the risk no longer exists. A comparison of outcomes with other countries who provided similar hormone treatments cannot be undertaken due to a combination of factors including differences in treatment dosages, preparation methods and the types of hormones used.

The identification of the AHPHP participants future needs

The analysis shows that unless science can definitively prove that they are no longer at risk of CJD, the cohort could require support for their risk of developing CJD until 2065. As the participants advance in age they are expected to increase their interaction and engagement with the health system (as is common for older persons). As a result, the public health system will need to consider:

- How appropriate healthcare access can be provided based on their risk profile for CJD
- The plans and strategies to be put in place to minimise the transmission of CJD as participants increase their interaction with the health system.

A survey of AHPHP participants, indicates that some continue to need support from the CJDSGN and their responses indicate that they also expect that the government will continue the available support into the future i.e. support with medical or other costs should they develop CJD in future.

Sporadic Creutzfeldt-Jakob disease will grow in line with population growth and ageing

Despite its transmissibility, CJD is primarily acquired sporadically (the cause is unknown). Approximately 85 per cent of CJD cases are sporadic CJD (sCJD) cases. The available evidence shows that sCJD is correlated with age.

A projection modelling of future sCJD cases based on Australia's population growth rates show a notable increase in the number of cases over the next 20 years (consistent with the ageing of the Australian population).

Where there were 51 cases reported in 2020**, projections indicate that by 2041 this will increase to 99 cases. In addition to the impact to those directly affected and their families, this increase in prevalence becomes a further avenue for the risk of CJD transmission in healthcare settings.

There are emerging concerns regarding variant CJD

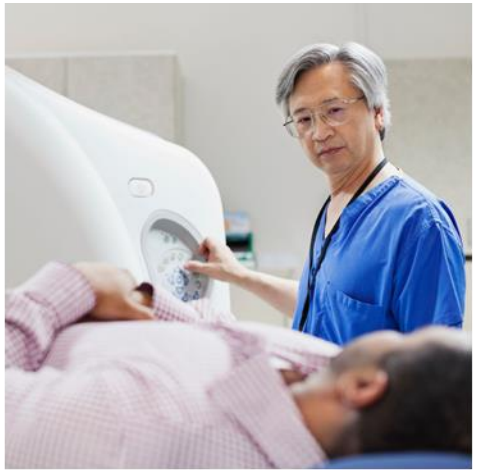
Variant CJD (vCJD was colloquially referred to as mad cow disease in the UK), is a type of CJD typically transmissible through the consumption of contaminated beef. Australia has never reported vCJD. Other than cattle, prion diseases also occur in other animals such as sheep, deer and elk. As such, the importation of these products within the food chain can pose an additional risk to human health. Despite this, however, Australia's biosecurity systems and processes have minimised the risk of transmission of animal prion diseases and by extension, the risk of transmission to humans.

There is also some historical evidence of vCJD being transmitted through blood transfusions and plasma products. To minimise these risks, blood donation guidelines have placed restrictions on individuals who have lived or travelled in the UK throughout the late 80s and early 90s. There is insufficient evidence of blood transfusion-related transmissions of sCJD or CJD. Despite this, guidelines have been established for those who may have been exposed to infectious agents to exclude them from blood or tissue donation.

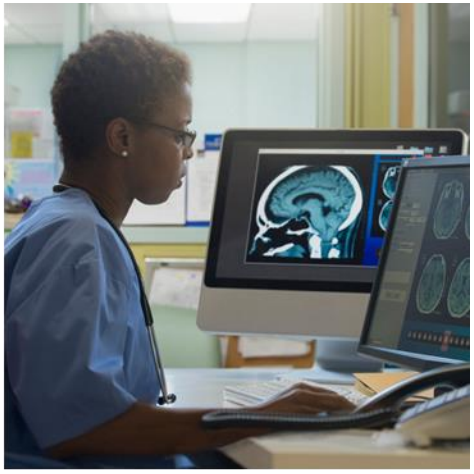
** Data courtesy of the ANCJDR and includes definite sCJD cases only.

Conclusions and recommendations

Both the ANCJDR and CJDSGN will require support to continue their operations in future. This should consider the projected additional increase in demand (e.g. growth in sCJD) and the realignment of roles and responsibilities through a formal agreement like a memorandum of understanding (MoU).

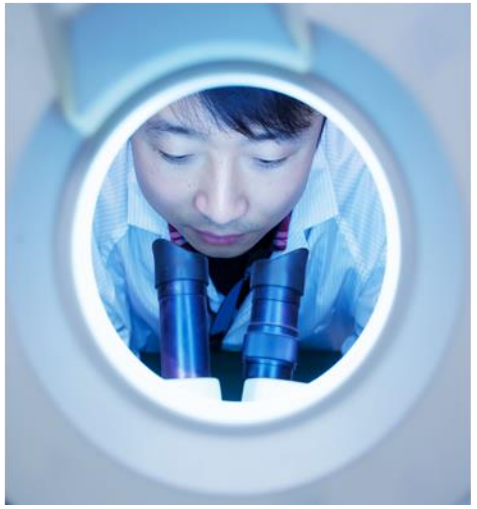


Adequate support to enable succession planning for both the ANCJDR and the CJDSGN is also required. The quantum of this support should consider the duration, and the amount, to enable an appropriate handover period of leadership in each organisation.



A review of the CJD Infection Control Guidelines is being considered by the Communicable Diseases Network Australia (CDNA). As part of this CDNA review, a review of the roles and responsibilities for the provision of advice and guidance on implementing the guidelines should be undertaken. This review should consider the increase in future needs (in particular the increase in sCJD cases and the AHPHP participants use of the health system).

Following successful NATA accreditation, the implementation of RT-QuIC as a standard diagnostic tool would be aligned with international practice. Implementation and funding through existing government processes could be considered.



Historically, support to the AHPHP participant cohort was provided through a Special Account. Feedback indicates that certainty of continued support is important but the funding mechanism itself is not critical. Other mechanisms of funding support could be considered by the Department.

Introduction and background

In this section, we present the context for this project and a summary of the project's objectives and method

Overview of the project and this report

About this project

The Australian Government Department of Health (the Department) engaged PwC to ***'review the CJDSGN and ANCJDR, and provide advice on the ongoing needs of participants of the AHPHP'*** (hereafter referred to as the CJD review). The objective of this review was to develop evidence-informed findings of how Australia should respond to the risk of CJD in the future. Specifically, it aimed to conduct an independent review of:

- **CJDSGN's support and advocacy services** for participants of the AHPHP and those at risk of prion disease, as well as the appropriateness and effectiveness of existing arrangements in meeting these needs
- **ANCJDR's services in providing national surveillance** and diagnosis of human prion diseases in Australia (noting CJD's status as a national Notifiable Disease)
- the needs of the AHPHP participant cohort following the cessation of the Special Account and any associated obligations for the Commonwealth Government
- the current evidence base and literature surrounding CJD and prion diseases in general.

This document is the final report and presents a consolidation of findings to date in particular from:

- a review of evidence which synthesises the current literature evidence about the risk landscape of CJD and prion diseases both in Australia and internationally
- consultations with local stakeholders and international experts in CJD and prion diseases
- a survey and interviews with a sample of AHPHP participants to understand their current and future needs.

This report does not present the policy implications or recommendations for the Department's consideration.

Overview of project methodology

This project adopts a program evaluation methodology in undertaking this review. It was guided by a structured evaluation framework which in turn was supported by several approaches to data collection, analysis and synthesis. Figure 1 provides an illustrative overview of the review methodology. A more detailed description of the methodology can be found in Appendix E.

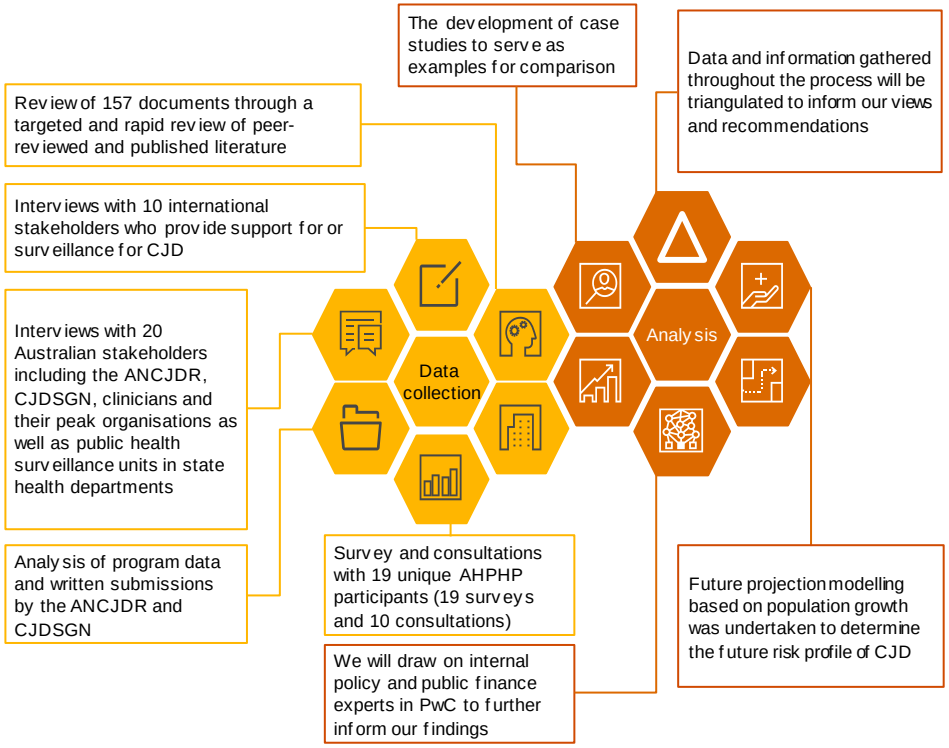
The key review questions addressed are:

1 Does the CJDSGN meet the current and future needs of people impacted by CJD?

2 Does the ANCJDR meet the current and future needs of Australia in responding to the risk of CJD?

3 What are the policy implications and government obligations for meeting the future needs of Australia in responding to CJD?

Figure 1: Overview of the CJD review evaluation methodology



Introduction to prion diseases and CJD

Prion diseases

Prion diseases or TSEs are rare neurodegenerative diseases that result in approximately 1 to 2 cases per million (people) per annum throughout the world each year.[1] Prion protein occurs normally, however, the disease occurs when the prion aggregates in the brain causing tissue damage and death. Prion diseases can occur in humans and animals.

Creutzfeldt-Jakob disease (CJD)

CJD is the most common and well-known of the human prion diseases. Like others, it is a fatal neurodegenerative brain disorder. People directly affected by CJD experience a rapid progression of the disease starting with early symptoms of memory loss, behavioural changes, confusion and disorientation leading to more severe symptoms such as dementia, blindness, coma and ultimately death.[2] CJD has a 100 per cent mortality rate and most people die within 12 months of symptom onset. To date, there is no known cure or treatment for CJD.

CJD can be caused by multiple means, these include:

- **Sporadic** CJD (sCJD) is where spontaneous changes occur to prions resulting in the disease. This form is the most common and accounts for approximately 85 per cent of CJD cases globally.[1]
- **Genetic** CJD (gCJD) which is where certain families are more susceptible to the genetic mutation that results in changes to the prion protein. This is relatively rare and accounts for 10 to 15 per cent of CJD cases globally.[2]
- **Iatrogenic** CJD (iCJD) is caused by the cross-contamination of materials that came into contact with people with CJD. It is typically a result of medical procedures. Documented cases of iatrogenic diseases include corneal transplants, dura mater grafts, and hormone treatments where hormones were derived from human pituitary glands.[2]
- **Variant** CJD (vCJD) is caused by the consumption of meat contaminated with animal prion disease or through a blood transfusion from someone who contracted vCJD. There is a risk of a new vCJD through Chronic Wasting Disease (CWD) or Scrapie.[2]

Consistent with global prevalence rates, sCJD is the most common variant in Australia. Table 1 provides the most recent breakdown of the number of cases of CJD by their types. Figure 2 separately shows the trends in prevalence rates (measured as the number of cases per million population) over the past ten years.

We note that there have not been any documented historical cases of vCJD in Australia and the last case of iCJD was reported in the year 2000.

Table 1: Overview of human prion diseases in Australia

Type of CJD	Number of cases in 2020
sCJD	51*
gCJD	2*
vCJD	0#
iCJD	0~

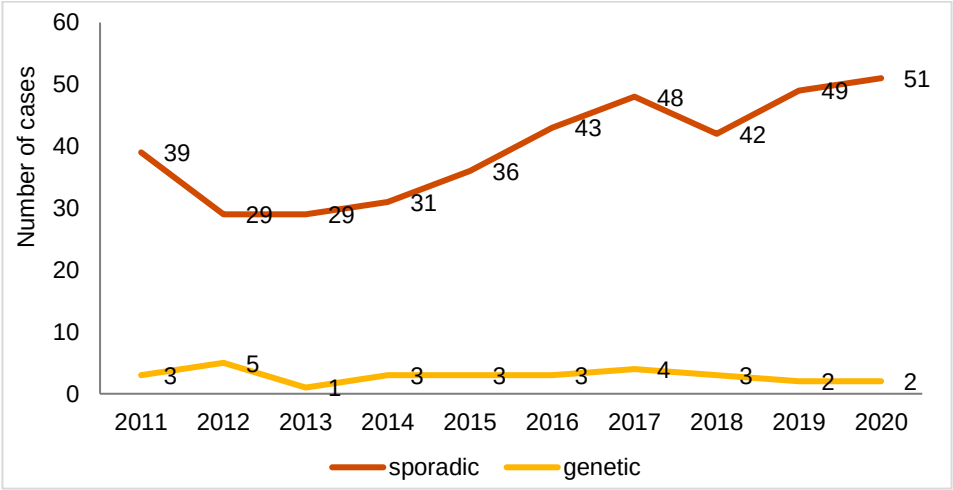
*Definite cases only

No cases ever reported in Australia

~ Last known case was reported in 2000

Source: Data provided by the ANCJDR to PwC, 12 May 2021

Figure 2: Trends in the incidence of CJD in Australia (2011-2020)*



*Definite CJD cases only

Source: Data provided by the ANCJDR to PwC

The historical use of human derived hormone treatments and iCJD in Australia

Hormone treatment and the risk of iCJD

Beginning in 1967, new medical treatments were made available using cadaver-derived human pituitary gland hormones (hPG) and human growth hormones (hGH). hPG was used for infertility while hGH was a treatment for short stature. In Australia, human pituitary hormones were supplied as a Commonwealth approved and subsidised Pharmaceutical Benefit and manufactured by the Commonwealth Serum Laboratories (CSL). Around 2,100 Australians were treated with hGH or hPG as part of the Australian Human Pituitary Hormone Program (AHPHP).[3]

Reports of overseas deaths of cadaver-derived hormone recipients by CJD emerged in 1985. As this occurred, the AHPHP was suspended and treatments were halted in Australia in the same year. The collection of human pituitary glands by CSL were also ceased the year after.

In 1988, Australia reported its first case and death by CJD for an AHPHP participant. Out of the five participants that died in Australia, four participants (3 definite and 1 probable case of CJD) were treated with hPG and one participant (possible CJD case) was treated with hGH, though globally more deaths were reported for those who received hGH.[3, 4]

The *Report of the Inquiry into the Use of Pituitary Derived Hormones in Australia and Creutzfeldt-Jakob Disease* (the Allars Inquiry Report, 1994) found that there were known dangerous side effects for participants before 1985 and that the Government did not properly disclose the risks under the "right to know".

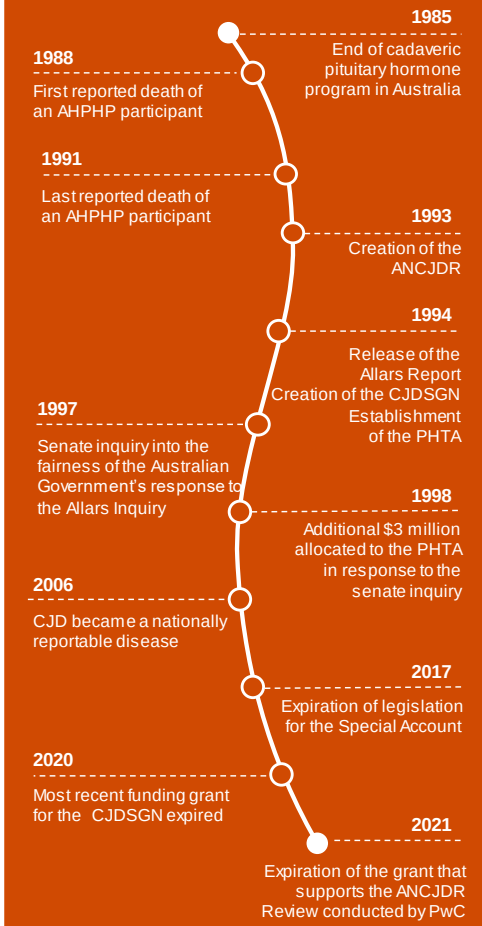
In response to the Allars Inquiry Report, the Australian Government announced a $10 million package of measures to implement the recommendations. This package included $5 million for the establishment of the Pituitary Hormones Trust Account (PHTA) in 1994 to fund the medical and other care costs of pituitary hormone recipients who would contract CJD as well as continuing the provision of counselling services and support groups including the CJD Support Group Network (CJDSGN).

The Australian National CJD Registry (ANCJDR) was established in 1993 and has received funding from the Commonwealth, separate from the PHTA and subsequent special accounts. The Government maintained a trust/special account continuously since 1994, which evolved with various legislative arrangements, as required. Most recently, the Human Pituitary Hormones Special Account was established under the *Public Governance, Performance and Accountability Act (PGPA Act)* between 2015 and 2017.

Subsequently, a 1997 Senate Inquiry into the fairness of the Australian Government's response published the Report on the CJD Settlement Offer and in 1998, the Australian Government allocated an additional $3 million to the PHTA to allow payments to be made to recipients who could demonstrate that, before 1 January 1998 they suffered, a recognised psychiatric injury due to having been informed that they are at a greater risk of contracting CJD. The PHTA guidelines established for access to funding were amended to facilitate "One-Off Payments for Psychiatric Illness" being made.

Timeline of key events

A brief overview of key events in Australia's public health response to the risk of Creutzfeldt-Jakob disease (CJD) from the AHPHP.



The risk profile for the AHPHP participant cohort

Iatrogenic exposure and risk for CJD

To date, the known methods of iatrogenic exposure to CJD include:

- neurosurgery equipment and deep Electroencephalography (EEG) electrodes
- corneal transplants
- dura mater grafts
- hormones derived from cadaveric pituitary hormones.[5]

Iatrogenic risk through cadaveric pituitary hormones

From the 1967 to 1985, an unknown global number of individuals were put at an increased risk for developing CJD by receiving CJD-infected batches of cadaveric pituitary hormones for either short stature or infertility.[5] Table 2 outlines the number of deaths around the world for those who had been a recipient of cadaveric human pituitary hormone treatments. Treatment duration and dosage of hormone received are the most predictive factors in determining the risk that someone who received cadaveric pituitary hormones will develop CJD.[5] However, poor record-keeping, differing case classifications based on available data and dosage differences across nations limit the ability to compare internationally.

Table 2: Comparison of CJD deaths in cadaveric pituitary hormone recipients

Country	Recipients	Received hGH	Received hPG	Last reported death
	Approximately 2,000	1*	4**	1991
	1,849	79	-	2019#
	7,700	35	-	2018#
	159	6!	-	2004
	1,700	122	-	2008

*1 death: a possible CJD case

**4 deaths include 3 definite and 1 probable case of CJD

The USA and the UK reported an iatrogenic case of CJD in 2020, but the source is not reported and thus not included

! cadaver-derived hormone was procured from the USA with varying quality control measures applied

Source: Stehmann et al 2020, the National Institute of Diabetes and Digestive and Kidney Diseases 2021, Boyd et al 2010, and the National Creutzfeldt-Jakob Disease Research and Surveillance Unit 2020

As such, it is not meaningful to compare the time from exposure to death from CJD in these groups across countries. So, whilst the UK may have the last death recorded over forty years after exposure, due to differences in the hormones, programs and doses, it can not be concluded with certainty whether the risk of developing CJD has reduced for AHPHP participants.[3]

It is also difficult to estimate the risk of developing CJD for individual recipients of human pituitary hormone treatments despite risk factors being known. While some countries, such as France, have been able to look back and identify which hormone batches carried the increased risk,[6] other countries experienced difficulty. A key reason for this is the differences in how these pituitary hormone treatments were prepared. In Australia, the use of multiple source tissues to make one batch of hormones and the re-use of certain batches increased the complexity in identifying and quantifying the risk. Australia is also the only country to have individuals die after treatment with hPG, which makes determining the risk posed to participants in the AHPHP particularly challenging.[7]

Some studies state an average latency period of 20-30 years, however, every new case documented represents the new longest latency period known with the case in the UK in 2019 with an over 40 year latency period.[3,7]

Key findings

- Differences in record keeping, diagnosis, and dosage across international comparisons limit the ability to directly compare risk
- From the evidence reviewed, there is no compelling evidence to conclude that the AHPHP participants remain at risk of developing CJD or to conclude that they are no longer at risk
- Until the latency period for CJD can be conclusively determined, it is likely that the possibility that AHPHP participants will have a lifetime risk of developing CJD can not be ruled out.

Issues and complexities associated with CJD

There are challenges to attain timely and definitive diagnosis of CJD

To date, there are still major challenges in conclusively and rapidly diagnosing CJD.[2] The only way to definitively determine CJD as a diagnosis is a post-mortem examination of the brain. While pre-mortem brain biopsy is possible, the inherent risks for the patient and for potential transmission as well as diagnostic confirmation not leading to any viable treatment means that this method is not widely used.[2]

Several premortem diagnostic tests are available and these are focused on identifying indicators of abnormalities commonly associated with CJD. These tests include:[2]

- Real Time-Quaking-Induced Conversion (RT-QuIC), a cerebrospinal fluid (CSF) based test that directly identifies misfolded prion proteins.
- CSF protein tests, including 14-3-3 protein, in which the CSF is tested to detect protein markers of prion diseases.
- Magnetic resonance imaging (MRI) is a brain scan that shows diseased tissue
- EEG is a non-invasive approach to measure brain wave frequencies.

Given the inherent difficulties in diagnosing CJD, diagnostic criteria were developed to guide and support clinicians in classifying CJD. Additionally, given the uncertainties around a definitive diagnosis, a case classification system was developed where a case can be defined in three ways (in brief):[8]

- **Definite** where there is confirmation by post-mortem examination and clinical symptoms
- **Probable** where there are clinical symptoms and supported by the positive results in the premortem tests outlined above
- **Possible** where clinical symptoms are observed at a specific duration.

As a result of these complexities, there are several challenges faced in achieving an accurate and rapid diagnosis of CJD:

- **Clinicians need to recognise symptoms of CJD before ordering tests.** As the disease is rare and can be mistaken for other neurological diseases (particularly dementias), this means that appropriate tests may be delayed or not conducted previously. The ANCJDR undertook active searches of individuals whose cause of death included unspecified dementia diagnosis. This would trigger further investigation to determine if CJD was the cause of death. Due to its time and resource intensity, this practice has been halted.
- **Reliance on post-mortems for a definitive diagnosis.** Due to extensive infection control requirements, the need for specialist neuropathologists and post-mortems being non-mandatory in Australia, limited post-mortem examinations occur in Australia to provide a definite diagnosis of CJD. Consultations with stakeholders for this review revealed that waiting times for post-mortems were reported to be up to years. As a result, some cases are never given a definite diagnosis and instead remain as 'probable' or 'possible'. As part of their surveillance activities, the ANCJDR counts these case definitions as part of their overall case counts of CJD.
- **Lack of utilisation of RT-QuIC technology**. Both the USA and the UK have integrated the use of RT-QuIC into their regular surveillance and diagnostic practice and procedures.[9,10] At this time in Australia, RT-QuIC is used by the ANCJDR in a research capacity.[7] The ANCJDR has begun the process of National Association of Testing Authorities (NATA) accreditation to authorise its use in Australia.

Stringent infection control processes must be applied in clinical settings to limit the spread and transmission of CJD

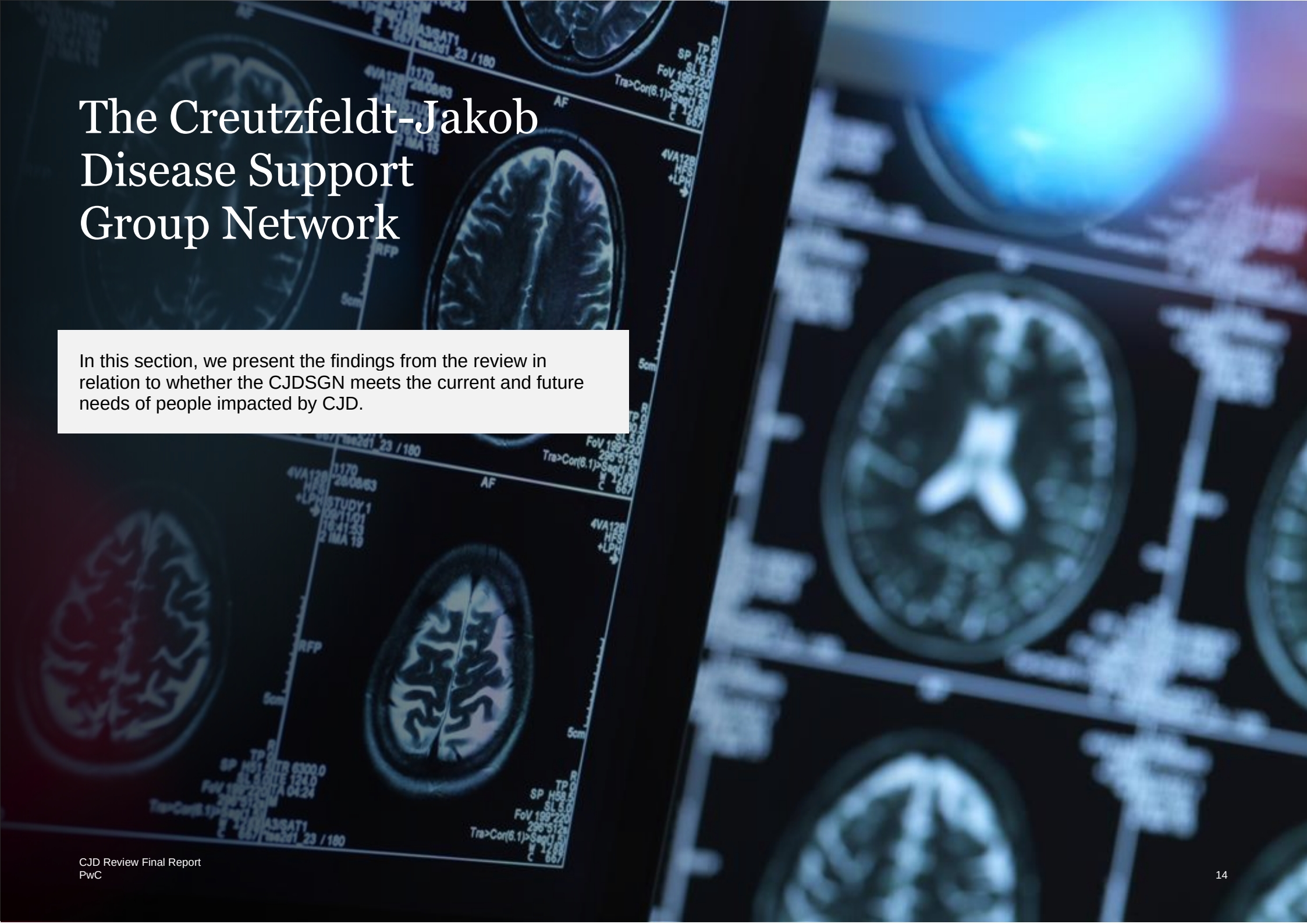
As noted earlier, CJD can be a transmissible disease. This can occur through the consumption of contaminated foods or via medical procedures. To limit transmission through the latter, processes are in place to systematically determine when and what appropriate infection control steps must take place in a clinical setting. In Australia, a standardised set of rules apply for infection control. They were developed by the CDNA and are known as the CJD Infection Control Guidelines.[8] They set out recommendations for infection prevention and control procedures to minimise CJD risks in a medical setting.

The guidelines support the assessment of risks for transmission, procedures for infection control and surveillance processes in the event that a clinician suspects CJD. They also guide specific practice settings including dentistry, post-mortem examinations and the funeral industry.

Contributions to the review reported that there is considerable variability in understanding within the health sector of how to consistently implement these guidelines.

The Creutzfeldt-Jakob Disease Support Group Network

In this section, we present the findings from the review in relation to whether the CJDSGN meets the current and future needs of people impacted by CJD.



CJD Support Group Network (CJDSGN)

The CJDSGN relies on government grants for core operational activities but is significantly dependent on pro bono volunteer support to conduct many of its activities.

The CJDSGN is a not-for-profit organisation established to support Australians affected by CJD and prion diseases.[11] Their services, in accordance with the grant provided by the Australian Government, include:

- *providing and maintaining a national network of support groups through which recipients of Human Pituitary Hormone (hPH) (now referred to as the AHPHP cohort) can interact with each other and provide mutual support, share information and discuss issues and concerns*
- *improving the wellbeing of recipients of hPH by assisting with the management of anxiety associated with the increased risk of contracting CJD*
- *acting as an advocate on behalf of recipients of hPH who are experiencing difficulties accessing medical treatment because of infection control issues*
- *providing a mechanism for the Department to receive comments from the hPH recipients and to represent the views of its members in other forums.*

The grant further outlines the following key objectives of the CJDSGN:

- *ensure membership and participation in support group activities is available to all recipients of hPH;*
- *arrange and hold meetings of hPH recipients and their family members as required;*
- *maintain the informative website www.cjdsupport.org.au;*
- *provide a national toll free number for the recipients and the general community;*
- *produce and distribute the CJDSGN newsletter; and*
- *provide the Department in writing or by electronic mail within five working days, information regarding any changes in the status of the support group and any ad hoc changes to the management of the support group.*

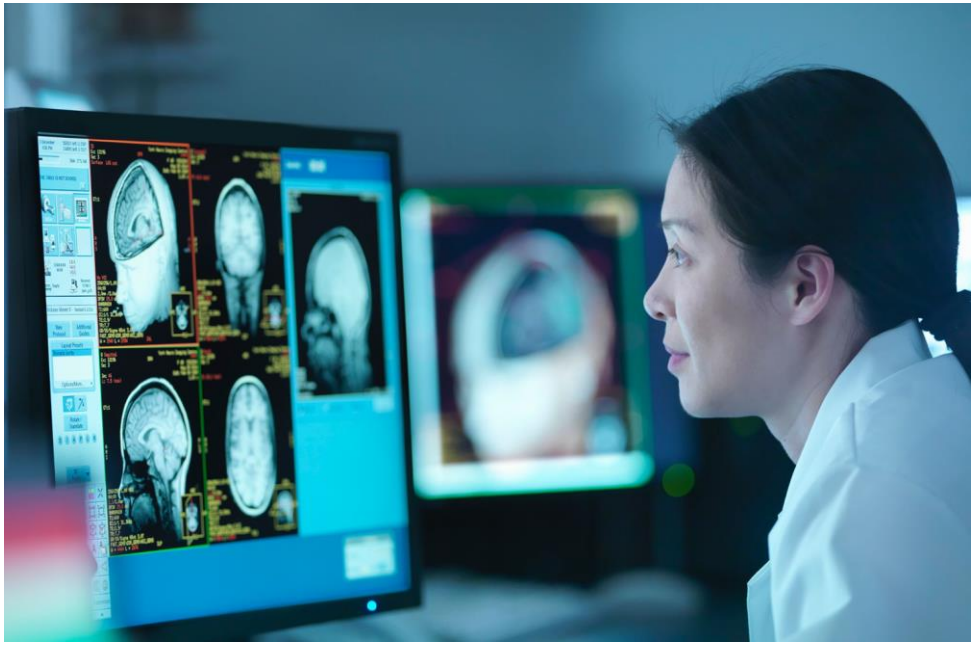
The CJDSGN meets the above requirements of the grant which is focussed on supporting AHPHP participants. However, we also note that its services extend to people affected by other forms of CJD such as sCJD, gCJD and iCJD (contracted by means other than hPH).

Finally, the CJDSGN presents at international conferences and this activity is supported by funding from the Department.

We also understand that the CJDSGN facilitates fundraising for research. Donations raised through the fundraising process are administered by the CJDSGN and entirely provided for research.

The CJDSGN also provides support for people affected by CJD in other countries and they present at medical facilities. These activities are conducted on a voluntary basis.

Since 2014, the three year budget provided by the Commonwealth has marginally increased from $486,000 (2014-2017) to $510,000 (2017-2020).[12] Available information from the CJDSGN financial statement indicates that the network has no cash reserves or investments to draw on to continue operations in the absence of continued government funding.



CJD Support Group Network (CJDSGN)

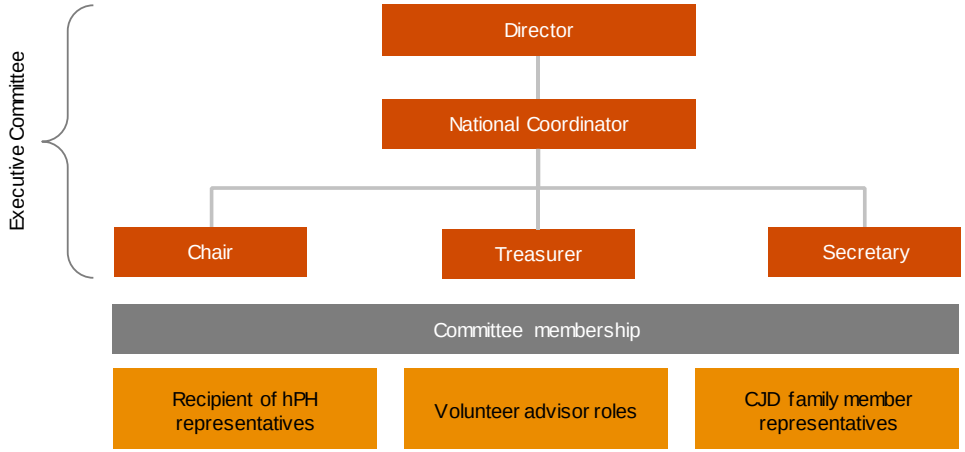
Governance structure of the CJDSGN relies on a small group of people who have lived experience of CJD

The CJDSGN has one full-time employee and primarily relies on volunteers for its operations. This employee functions as Director, National Coordinator and Treasurer of the CJDSGN (hereafter simply referred to as the Director). Supporting the Director are the members of the management committee (the Chair and the Secretary). Solely comprised of volunteers (except the National Coordinator who is funded for the role), the executive committee is responsible for:

- representing the interests of those affected by CJD and other prion diseases
- attending committee meetings and the National CJD Conference
- performing standard functions of their nominated governance role.

Committee members act as an advisory group and assist when requested by the executive committee. Members of the committee have themselves in various ways been affected directly or indirectly by CJD. Figure 3 presents the governance structure of the CJDSGN. This feature of the executive committee is reliant on few individuals. This has implications for the sustainability of the CJDSGN and succession planning.

Figure 3: Governance structure of the CJDSGN



Source: CJDSGN Business Plan

A review of the CJDSGN's 2019-20 income shows that the organisation relies significantly on the grant provided by the Australian Government.

Donations to the CJDSGN are primarily provided to support research and a small proportion is used to provide financial support for people to receive genetic testing. For example, fundraising by the CJDSGN was used to provide a research grant to the ANCJDR to support the development of Real-Time Quaking-Induced Conversion (RT-QuIC) diagnostic technology in Australia.

The CJDSGN spends relatively little on staffing expenses given the array of services provided. The remainder of staffing costs is provided pro bono by the staff member. This level of expenditure for a full time staff member would be insufficient in the open employment market for a role like this.

The remainder of the CJDGSN revenue is spent on operational costs including:

- National conference
- Volunteer expenditure
- Overseas conference expenses
- Education Awareness Programme
- Website and database maintenance.

CJD Support Group Network (CJDSGN)

The CJDSGN offers multiple supports and services

In 2021, the CJDSGN has reported that they have contact with approximately 721 people affected by CJD and their families. This network of contacts includes AHPHP participants as well as people impacted by sCJD or gCJD in Australia. Annually, the CJDSGN reports on various metrics and seeks feedback from its network to ensure that it is meeting its objectives to support those impacted by CJD.

Table 3: CJDSGN's website analytics, 2018 to 2020*

Year	Visits per month	Unique visitors per month	Pages visited per month	Pages per visit (monthly)**
2020	2,315.6	1,422.25	24,859.4	10.74
2019	3,043.75	1,946.17	32,341	10.63
2018	2,784	2,055	27,056.3	9.72

*CJDSGN website usage varies with conference and presentation attendance

**Pages per visit is the average number of pages visitors view on a site within a session, 3-4 pages per visit per month is considered "high" engagement

Source: NetVirtue analytics provided by the CJDSGN and Piersall & Armstrong n.d. Google analytics pages per visitor and average length of visit reports, dummies. 2021. Google Analytics Pages Per Visitor and Average Length of Visit Reports – Spinutech. [online] Available at: <https://www.spinutech.com/digital-marketing/analytics/analysis/7-website-analytics-that-matter-most/> [Accessed 28 May 2021].

Figure 4: Summary of services provided by the CJDSGN

Toll-free helpline
Available 24 hours a day, if a call was not answered immediately then they will be returned within 12 hours. The CJDSGN fields between 30 to 60 calls per month on a variety of topics.*

Informational website
Includes resources for participants and health care professionals. In 2021 the site has averaged 376 unique monthly visitors who visited three pages each. Table 3 reviews website analytics from 2018 to present.

Educational conferences
The annual CJDSGN conference is attended by between 110 to 120 individuals. Attendees include health care professionals, families impacted by CJD and AHPHP participants. These conferences allow AHPHP participants an opportunity to learn about new breakthroughs in research, diagnostics, or treatment.

Presentations
Representatives from the CJDSGN provide educational presentations to different healthcare facilities throughout the country. They provide between 15 to 20 presentations annually.

Support services
State-level support meetings are attended by representatives from the CJDSGN. They attend between two and four per year. In 2020, they attended two meetings before COVID-19 restrictions began.

Advocacy services
As per CJDSGN reports to the Department, on average the CJDSGN advocates for between 10 and 15 individuals (per year) who are interacting with the medical community.* They report between two and six cases of difficulty to access health care each year; noting six cases in their 2020 report.

*Reported through written communication with the director of the CJDSGN

CJD Support Group Network (CJDSGN)

The majority of people supported by the CJDSGN provided positive feedback on the services provided.

To review the CJDSGN's performance and feedback on the services provided by them, we analysed performance and monitoring data provided by the CJDSGN as well as the feedback provided by key international and Australian stakeholders and AHPHP participants.

Performance and monitoring data provided by the CJDSGN

The CJDSGN conducted a survey (April 2021) with their network and healthcare providers who had previously contacted them for support. A total of 249 survey recipients responded to the survey. The results from the CJDSGN member survey revealed that:

- 80 per cent of survey participants rated their experience and support provided by the CJDSGN as "extremely good"
- 96 per cent reported that they contacted the CJDSGN for support (time frame not specified)
- the top three most frequently used services were the information package (including video media and brochures about CJD and services available to support those affected), phone support, and the website.

The CJDSGN's healthcare provider survey (N=95) reported that:

- 67 per cent of survey participants had an "extremely good" experience with the information and assistance provided by the CJDSGN
- 61 per cent sought assistance from CJDSGN (unknown time frame)
- the top three most frequently used services were the website information and resources, the information package including a handbook on patient care and information or resources sent via email or mail.

The CJDSGN also conducts an annual evaluation of their National CJD Conference. Their most recent evaluation report (2018) showed that the conference was attended by health care professionals, hPH recipients, researchers or students and family members or friends of those affected by CJD. The majority of attendees rated the overall conference as "excellent".

There were over 65 testimonials provided to the Review by a broad group of people who received services from the CJDSGN between 2009 and 2021. These testimonials reported gratitude and positive feedback on the CJDSGN's services.

Consumer feedback from stakeholder consultations for the review

Stakeholders reported that the activities of the CJDSGN are not confined to supporting AHPHP participants, and are provided to any person impacted by CJD.

The CJDSGN was cited by several international stakeholders as playing an instrumental role in the establishment of CJD support networks in several countries as well as the CJD International Support Alliance (CJDISA – an international group of non-profit organisations that collaborate to help patients and families affected by prion diseases).

Clinical peak bodies consulted as part of this review also noted that the services provided by the CJDSGN meet the needs of people affected by CJD and their families. The CJDSGN was also reported to be "*very helpful"* to several peak body organisations as it is a key source of information for them.

> *"From my perspective, she [the Director] has been great, very helpful. Sometimes they [support groups] ask for information e.g. journal articles, etc. and it can take weeks but she won't do this and she doesn't take up a lot of our time. She makes things easier"* – Australian consumer representative

Like the other stakeholders, the majority of AHPHP participants who completed the survey for the Review (74 per cent) also reported that the CJDSGN is supporting them "extremely well". The survey also revealed that the CJDSGN is the most utilised support service for AHPHP participants. In addition, respondents find the support meetings and liaison services to be the most useful services offered by the CJDSGN, especially given that the majority of interviewees (60 per cent) reported that they had experienced what they believe is 'discrimination' when seeking medical care.

> *"It is important to know that CJDSGN 'has my back' with support and advice when and if I need it."* – AHPHP Participant

CJD Support Group Network (CJDSGN)

Improvement to the CJDSGN

Whilst stakeholders involved in the review (including AHPHP participants) indicated satisfaction with the services of the CJDSGN, some areas for improvement were identified by a small number of stakeholders (3 of 20 Australian stakeholders):

- The CJDSGN could be guided by a scientific or medical advisory committee.
- A review of the CJDSGN's fact sheets (summary documents of various CJD topics) on their website, means:
  - updating the fact sheets on the CJDSGN's website to be consistent with the most recent updates of CJD Infection Control Guidelines and expert opinion. The most recent update to the CJD Infection Control Guidelines was performed in 2013 however, the last update of the fact sheet was performed in 2009 and some fact sheets have no review dates
  - in one instance, providing clarity in the Inherited Prion Disease Fact Sheet as it pertains to dental practices. Specifically, clarity on what dental procedure constitutes as a high-risk procedure (in terms of CJD infection) and specifying a process of referring those procedures to a maxillofacial surgeon instead of a dental hospital.
- Provision of supporting literature or guidelines in conjunction with the verbal advice given to clinicians.

In the CJDSGN's document submission, they noted that:

- the committee members of the CJDSGN includes a medical director and medical advisor (a GP and palliative care registrar). The CJDSGN also liaises with the ANCJDR for expert and medical advice. As a member of the CJD International Support Alliance (CJDISA) the CJDSGN provides direct access to medical and scientific advice from international CJD experts, who are known as the Friends and Advisors group of the CJDISA.
- they will monitor and respond to the need for more face-to-face meetings.
- online educational information and a handbook on implementing the CJD Infection Control Guidelines are in the process of being developed.
- a review and update of the website is planned however the CJDSGN is limited by the contractual cost of IT assistance.

While it is unusual for support networks to provide clinical advice and information, this feature is frequently observed with rare disease support networks.

The importance of succession planning for sustainability

Feedback from a stakeholder indicates that the sustainability of rare disease support networks (like the CJDSGN) typically rely on robust succession planning arrangements which are themselves generally dependant on:

- adequate funding
- the support group leaders' willingness to train and provide opportunities to other members to lead the group
- the availability of willing individuals to devote time to training and carrying forward with the mission and vision of the organisation.

We note that the above relates to support networks broadly and is not specifically about the CJDSGN. When asked about succession planning, the CJDSGN reported that they have a short term and long term succession plan – however enacting this is dependent on funding certainty and adequacy to employ staff.

The CJDSGN also noted that, in the absence of their current director, the network will continue to function for a short period under a new governance structure with the assistance of the chair and secretary. However, the CJDSGN noted that this new governance structure cannot sustain its activities over the long term.

> *"It's [the CJDSGN] personality-driven. [The Director] works closely with [the Chair] and he's very involved but [the Director] is the driving force. If she retired it would be hard for someone to take over in the same way. It would be a huge loss if she is not there. The families think very highly of her."*

CJD Support Group Network (CJDSGN)

Additional or alternative support options

There is a paucity of evidence about the effectiveness of specific support interventions for those who are impacted by prion diseases and those at increased risk of CJD. Of note, because of the short duration of illness before CJD death, stakeholders reported that information comes 'too little too late'.[13] Due to the rarity of the disease, it is suggested that early communication and access to education is imperative.

Looking outside of CJD into other rare diseases and their support networks, evidence recommends supporting those impacted by rare diseases via:[14]

- meeting and befriending other people with the same rare disease and similar experiences
- learning about the disease and related treatments
- giving and receiving emotional support
- having a place to speak openly about the disease and their feelings
- learning coping skills
- feeling empowered and hopeful
- advocating to improve healthcare for other rare disease patients.

This is consistent with what AHPHP participants reported in surveys and interviews for the review. Respondents noted the importance of face to face meetings for both support and friendship, the ability to advocate for themselves and others through the CJDSGN, the importance of accurate information regarding diagnostic and treatment breakthroughs as well as updates on cases in Australia and worldwide.

A comparison of the CJDSGN and two support groups in Australia, the Mito Foundation and Dementia Australia, was completed using publicly available information and is summarised in Table 4. Please see Appendix B for more detailed case studies of these two support groups. Appendix F provides a comparison of other international CJD support groups.

Dementia Australia is a well established organisation that offers support, education, and research for dementia.[15] Dementia Australia is a useful comparison because of the heavy emphasis on research, international collaboration, symptom presentation, inclusion of medical professionals, and strong fundraising capabilities.

Table 4: Comparison of CJDSGN to the Mito foundation and Dementia Australia

Services	CJDSGN	The Mito Foundation	Dementia Australia
Face to face meetings	✓	✓	✓
Fundraising events	✓	✓	✓
Research support	• Memorial grants	• Scholarships • Clinical trials • International collaboration	• Dedicated research foundation
Advocacy services	✓	✓	✓
Educational resources for patients/families and health professionals	✓	✓	✓
Annual conference	✓	-	-
International collaboration with similar support networks	✓	✓	✓
24 hour toll free helpline	✓	✓	✓
Linking people and families affected by the disease	✓	✓	✓

Source: Publicly available documents from the CJDSGN, The Mito Foundation, and Dementia Australia

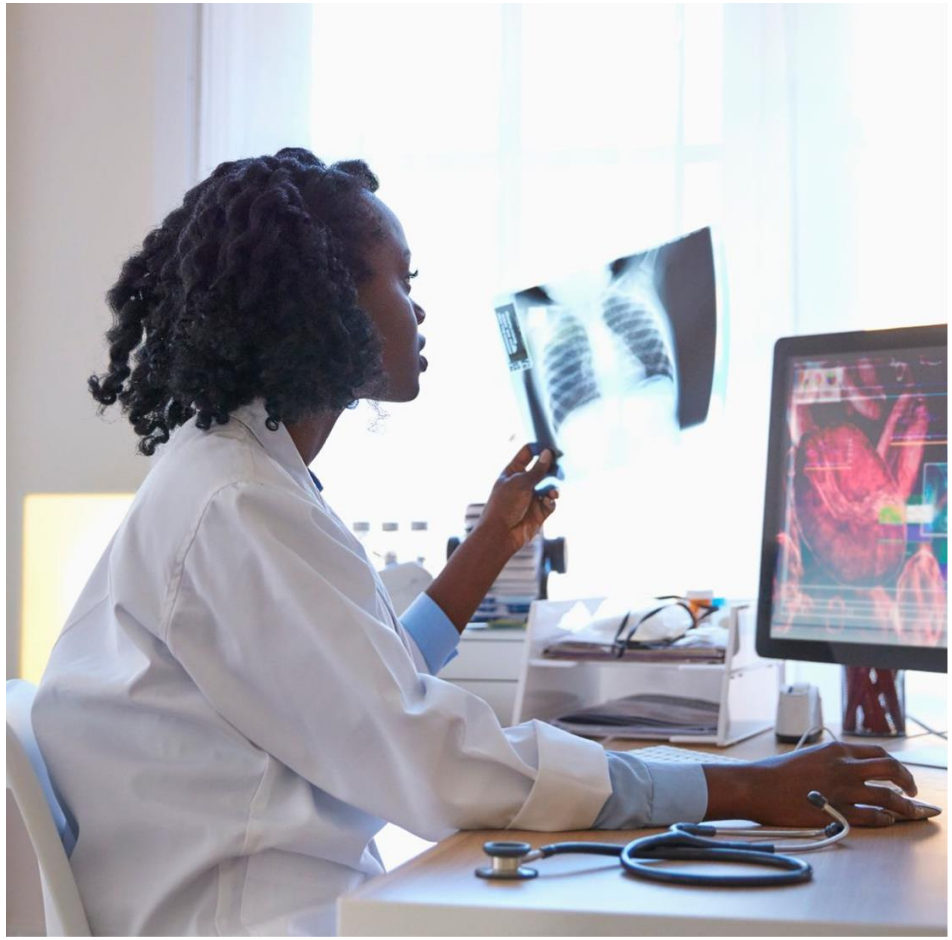
The Mito Foundation is a grassroots organisation that raises awareness for multiple genetic conditions that affect the mitochondria of the cell.[64]

The Mito Foundation is a useful comparison due to the rarity of the condition, grassroots origin, international collaboration, and emphasis on education for both families and medical professionals.

CJD Support Group Network (CJDSGN)

Key findings

- The CJDSGN provides a range of supports for people impacted by CJD (including AHPHP participants). These supports are the types of services provided by other disease-specific support groups. There is no alternative support group with CJD specific expertise if the CJDSGN ceases operations.
- The CJDSGN also draws the attention of health care providers to infection control advice, education and information. The provision of infection control information in other countries is facilitated by CJD specific health services. Although the ANCJDR and the PHUs generally provide this advice, the CJDSGN also plays this role in Australia as there is currently insufficient expertise relating to CJD within the broader Australian health system.
- The CJDSGN is well regarded both within Australia and internationally and there is evidence that their supports currently meet the needs of people impacted by CJD.
- CJDSGN operations are mostly funded through a grant from the Department. Fundraising revenue is directed to research. Available information from financial statements indicates that the network has no cash reserves or investments to draw on to continue operations in the absence of continued government funding.
- The governance of the CJDSGN relies heavily on a small group of individuals who provide significant pro-bono support. The provision of services through employed staff is paid for through a mix of government funding and pro bono contributions. Adequate succession planning is hindered by a lack of funding certainty.



The Australian National Creutzfeldt-Jakob Disease Registry

In this section, we present the findings on whether the ANCJDR meets the current and future needs of Australia in responding to the risk of CJD.

Australian National CJD Registry (ANCJDR)

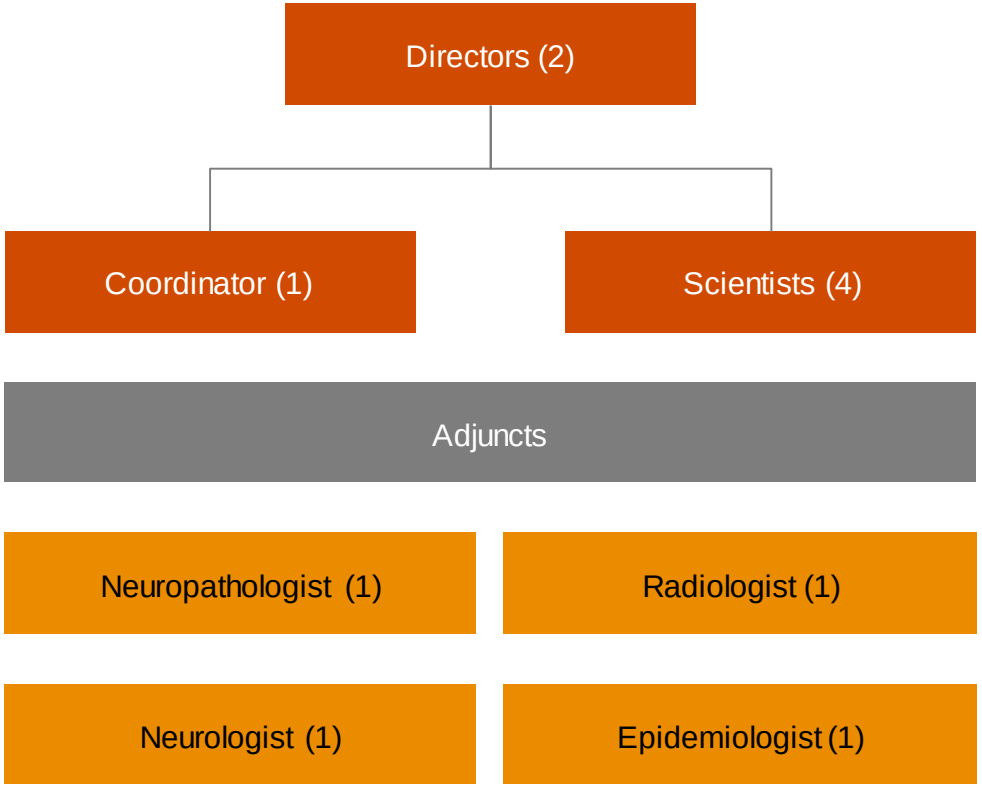
The ANCJDR was established to provide the following services under the grant provided by the Australian Government:

- to undertake research, monitor new cases of CJD in Australia and overseas
- to examine risk factors for CJD such as blood transfusions
- to produce annual reports to *Communicable Disease Intelligence* and the Department
- to provide advice (e.g. upcoming CJD risks to the public health system) to the Department and other health authorities on request
- to provide expertise, when required, to committees and working groups on TSEs and infection control.[17]

Figure 5 presents the governance structure of the ANCJDR. The expertise and functions of the ANCJDR primarily lie with its directors, comprising a neuropathologist and a neurologist. The ANCJDR holds monthly meetings that are attended by the members of the ANCJDR governance committee.

There have been reported concerns of sustainability and succession planning for the ANCJDR. This feedback will be elaborated upon further in this report.

Figure 5: Governance structure of the ANCJDR



Source: Numbers refer to headcount; Governance structure provided by the ANCJDR

Australian National CJD Registry (ANCJDR)

A review of the ANCJDR's 2019-20 income and expenditures indicates that the registry primarily relies on a three-year grant provided by the Australian Government. The recent grant's annual amount (financial years (FY) 2018-2021) has increased (+$24,126.50/year) when compared to the previous two grants (FY 2014-2018 and FY 2010-2014). However, the grant period has reduced from four years (FY 2014-2018) to three years (FY 2019-2021).

The Commonwealth's grant outlines the following activities to be undertaken by the ANCJDR:

- Ascertain all human cases of TSE occurring within Australia.
- Monitor the possible occurrence of the zoonotic vCJD related to Bovine Spongiform Encephalopathy (BSE).
- Perform detailed epidemiological analyses of the Australian surveillance data.
- Undertake comparative epidemiological studies from data generated by other national surveillance units.
- Provide a specialised national pre-mortem diagnostic services.
- Undertake research including through international collaborative studies, to improve the understanding of human prion diseases.
- Promote and maintain collaborations with similar national surveillance registries in Europe, Canada, and the US, to ensure optimal awareness of International developments in relation to human prion disease.
- Provide expert advice in relation to human prion disease to governments, agencies, and committees on a range of matters (e.g. participating in working groups such as the PRNP testing working group).
- Provide information and advice to families, clinicians and allied health workers on a range of issues, including infection control questions and management of potential contamination events and participate in activities such as the development of national infection control guidelines (we understand that the ANCJDR also attends family meetings with the CJDSGN).
- Offer formal advice at the national CJD Incidents Panel in relation to potential contamination events during the provision of health care.
- Assist states and territories with case classification and accurate diagnosis to facilitate formal notification of suspect human prion disease with the respective jurisdiction.
- Maintain a comprehensive and up-to-date bibliography of published literature in relation to prion disease.
- Continued comprehensive surveillance of all forms of human prion disease within Australia, including detection of possible vCJD.

Whilst the majority of funding for the ANCJDR comes from the grant, they also receive supplementary funding from the CJDSGN and National Health and Medical Research Council (NHMRC). From 2016 to 2020, the ANCJDR received donations of approximately $124,000 (in total across the four years) from the CJDSGN.

Supplementary funds from the CJDSGN and NHMRC are used to purchase equipment and establish diagnostics tools. It is also used to attend and present at international conferences and collaborate with international surveillance units to learn more about new technologies. For example, the ANCJDR used funds provided by the CJDSGN to visit The National CJD Research and Surveillance Unit at the University of Edinburgh to attend RT-QuIC training.

Besides meeting the requirements of the grant, the ANCJDR provides other services such as the provision of neuropathology diagnostic services. This service provided by the ANCJDR includes the provision of a dedicated CJD laboratory for brain tissue preparation and analysis and expert advice on autopsy and brain tissue biopsy results. A neuropathologist visits the ANCJDR approximately twice a month (on a 'on-call' basis) to perform autopsy and brain biopsy analysis for Victoria, South Australia and Tasmania.

Finally, we also understand that the ANCJDR maintains a biobank of tissue samples for national and international research. The services offered by the ANCJDR are commonly performed by CJD surveillance units in other countries. Refer to Appendix G for further information on services provided by international CJD surveillance units.

It is important to note that there is some overlap in services provided by the ANCJDR and CJDSGN. Advice is given to healthcare providers on infection control matters by both organisations. However, the ANCJDR provides the majority of this service.

Further details on the services provided by the ANCJDR are described on the next page.

Australian National CJD Registry (ANCJDR)

Figure 6: Description of services provided by the ANCJDR

Ad hoc infection control advice and guidance
Expert advice provided to Lifeblood and clinicians in public and private health care settings on infection control matters. In 2020, the ANCJDR addressed 22 infection control enquiries.

Incident panels
Expert advice provided to state and territory health departments if an adverse event involving CJD occurs, including advice on specific look-back and infection prevention and control issues. Three incident panels were convened in 2020.

CJD diagnostic tests
Diagnostic tests performed includes 14-3-3 protein and PrPSc detection via western blot, glycotyping of PrPSc, total tau protein estimation, RT-QuIC and DNA extraction from brain tissue.

Surveillance
National surveillance of suspected CJD cases including CJD case classification and reporting to government.

Public health risk assessments and notifications
Conducting public health risk assessments and notifying state and territory health departments (VIC, QLD, NSW, WA) of suspected CJD cases.

Biobanking
Biobanking of CSF, brain tissue and DNA for national and international research purposes. This includes preparation, packaging and transport of samples.

Research
Collaboration with various national and international research organisations to conduct research into CJD biomarkers, new diagnostic technology and treatments for CJD.

Presentations and educational sessions
The ANCJDR presents educational seminars to health care services, veterinary and legal students, PHUs and at national and international conferences.

There is a growing demand for the services provided by the ANCJDR over the past six years

Table 5 presents the ANCJDR's volume of activity from 2016 to 2019. The volume of services provided by the ANCJDR has steadily increased. This has been attributed to improvements in diagnostic technology and greater awareness of CJD within the health care community.

Table 5: Volume of activities performed by the ANCJDR from 2014 to 2019

Activities	2014	2015	2016	2017	2018	2019
No. of 14-3-3 protein tests	410	419	425	508	495	554
No. of total-tau protein tests	0	0	0	371	290	444
No. of RT-QuIC tests	0	0	0	17	44	33
No. of suspected CJD case notifications	74	67	72	70	89	89
No. of brain autopsy referrals	26	28	21	46	40	45
No. of brain biopsies	0	0	0	1	2	5
No. of case classifications	24	36	43	47	60	98
No. of National CJD incident panels convened	1	0	0	0	1	1
No. of infection control enquiries	3	8	8	11	22	23

Source: ANCJDR's Annual Reports 2014-2019, List of infection control enquiries provided by the ANCJDR

Abbreviations: RT-QuIC, Real-Time Quaking-Induced Conversion

Australian National CJD Registry (ANCJDR)

There will continue to be a public health need for the functions of the ANCJDR

The review found that there is an ongoing need for CJD and prion diseases surveillance in Australia because:

- CJD continues to be a notifiable disease by law in Australia and there are no other current registries or systems that could fulfil this requirement.
- Australia has a growing older-age population which will increase the number of sCJD cases in line with population trends.
- The emergence of new animal prion diseases such as seen in deer and elk in the US and Europe (these are consumed by humans thereby posting a risk of vCJD). There is the potential that these prion diseases will also occur in Australia.
- It is important for Australia to contribute to the global prevalence and trend statistics in CJD (as Australia's biosecurity system has contributed to an absence of vCJD, the surveillance system in Australia is reported to provide a valuable 'test case' for other countries in supporting the definitions of new forms of prion diseases).

Meeting these public health needs is currently completed by the ANCJDR.

> *"Australia has been a leader in the world in terms of their surveillance program"* – International stakeholder

> *"The Registry [ANCJDR] is doing very well. They distribute data to other surveillance centres and there are several epidemiological studies on risk factors which came from the Australian data set, which is a very important contribution that's coming from Australia. I think they are doing a very good job."* – International stakeholder

We also understand that the ANCJDR is being called upon to support differentiation between CJD and a transmissible Alzheimer's disease in symptomatic people with a history of dura mater graft. The latter is an emerging disease and (to date) there have been four cases.

International and Australian stakeholders value the ANCJDR

As CJD is a rare disease, key stakeholders reported to reviewers that they value the following functions of the ANCJDR:

- the provision of CJD-specific laboratories (equipped to manage appropriate infection controls) to undertake specialised diagnostic tests (CSF 14-3-3, total tau and RT-QuIC)
- support for clinicians and PHUs through advice for CJD diagnosis, risk management, and look back processes (a CJD risk management process undertaken by PHUs to determine iatrogenic exposure of CJD)
- the contribution of data and expertise to international and national research by providing CJD patient data, blood and CSF samples and collaborating with researchers
- support for smaller countries like New Zealand in diagnosis, testing and advice on atypical CJD cases

> *"Australia has been an incredible contributor to the surveillance of CJD data worldwide for the past 20+ years. They are a model country in many ways."*
> – International stakeholder

Testimonials (from people affected by the CJD and their families and clinicians), written feedback and customer satisfaction survey results provided to the Review, also indicates that the ANCJDR is highly valued by consumers and health professionals.

Australian National CJD Registry (ANCJDR)

Improvement to the ANCJDR

Whilst stakeholders involved in the review indicated satisfaction with the services of the ANCJDR, several areas for improvement were identified:

- increasing involvement and participation in clinical trials, such as treatments for CJD.
- developing a defined process and criteria for national autopsy coordination and genetic testing – currently, there is reported to be insufficient information on the logistics of transporting specimens or cadavers to neuropathology testing centres and criteria for genetic testing
- supporting the adoption of RT-QuIC testing as the gold standard CJD test routinely used in Australia
- sharing information of newly suspected or diagnosed CJD cases to jurisdictional PHUs via a monthly report
- formal agreements with the CJDSGN that define the respective roles of the organisations.

The ANCJDR's formal response to the review indicates that the ANCJDR is in the process of addressing most of the above-mentioned areas of improvement. The areas reported by the ANCJDR currently being addressed in their forward work plan include:

- participation in clinical trials for CJD treatments:
  - collaboration with the Massachusetts Institute of Technology and Harvard (US) who are developing the anti-sense oligonucleotide technology.
  - contributes to the monthly meetings with the CJD and Biofluids research groups where new treatments and/or diagnostic techniques are discussed.
- implementing RT-QuIC testing as the gold standard CJD test:
  - the ANCJDR is currently awaiting accreditation by NATA.
  - following a successful accreditation, the ANCJDR plans for every CSF sample to undergo RT-QuIC from 2021 onwards. Funding for this function has not been identified or confirmed.
  - RT-QuIC is also being investigated for use in diagnosing other neurodegenerative diseases such as Parkinson's disease.

Data sharing between jurisdictional PHUs and the ANCJDR

Currently, jurisdictional PHUs are notified about suspected or newly diagnosed CJD cases from various sources such as:

- the ANCJDR
- doctors via public health notification forms or emails
- regular reviews of the deaths registry.

Following notification, PHUs obtain further information about the CJD case from the hospital that diagnosed or referred the patient to diagnostic testing. Information is gathered on (but not limited to):

- what procedures were undertaken in the past: invasive procedures, surgical history
- where the patient is being treated
- who is the treating and reporting doctor
- history of blood donation or recipient travel to the UK
- genetic CJD

Obtaining this information was reported to be time-consuming and burdensome to the PHUs as the information is obtained from different sources.

Similar information is also collected by the ANCJDR who also reported similar challenges with accessing this information and the resource-intensive nature of following up. Incomplete data sets of CJD cases is an issue that is commonly faced with jurisdictions that do not have existing data sharing agreements with the ANCJDR. At present, there are data-sharing agreements with Victoria, Queensland, New South Wales and Western Australia. The remaining states and territories do not have a data sharing agreement with the ANCJDR.

Sustainability of the ANCJDR services requires succession planning

When asked about succession planning, the ANCJDR reported that the local supply of expertise (including neurologists, neuropathologists, scientists, etc.) in Victoria could adequately meet their future workforce requirements. However, a training pipeline for these specialists may take several years, and certainty and adequacy of funding are reported to be the key barrier to enable the appropriate workforce transition activities to begin.

Australian National CJD Registry (ANCJDR)

Comparing the ANCJDR to international surveillance systems

Comparison of the ANCJDR to the UK's National CJD Research and Surveillance Unit (NCJDRSU) and Canada's CJD Surveillance System (CJDSS) is outlined in Table 6. For more details on both of these international surveillance systems please refer to Appendix C. Both the NCJDRSU and the CJDSS were created as a response to the BSE outbreak in the UK whereas the ANCJDR was created as part of the Government response to the AHPHP.

All three systems are funded through their respective Governments and are housed in one central location for specimen testing. Both in Australia and Canada follow up with suspected cases of CJD is managed remotely, whereas in the UK, follow-ups to assess the clinical presentation and obtain consent are in person (until the COVID-19 pandemic where the UK found that conducting their surveillance via telemedicine was an effective strategy.)[18]

Learning from international comparisons

Canada has a population density similar to that of Australia. They have ongoing difficulties with ensuring that notifications of suspected CJD are happening through the local health departments and in ensuring proper diagnostic tests are performed due to availability and clinician knowledge of CJD symptoms.

Canada does not have a significant need to monitor the population for vCJD as there have been minimal cases of BSE and only two documented cases of vCJD (with the last in 2011 and thought to be acquired overseas). They do, however, field questions about Chronic Wasting Disease (CWD) that has been observed in deer and elk populations in Canada.

Due to the outbreak of BSE that originated in the UK, the UK developed a robust surveillance system that was first aimed at monitoring the emergence of vCJD in the population. Because of its origin in the BSE outbreak, the NCJDRSU includes a dedicated care team that, even in the absence of vCJD cases, helps the wider CJD community in the UK navigate the healthcare system. By comparison to Australia, the UK has a significantly denser geographic spread of its population which aide in completing in-person follow-ups.

Table 6: Comparison of the ANCJDR to two international surveillance systems

Function	ANCJDR	NCJDRSU	CJDSS
Surveillance began	1993	1990	1998
Cause for creation	AHPHP	BSE outbreak	BSE outbreak
Staff (headcount)	11	40	8
Annual referrals (2019)*	513	146	140
Total cases (2019)	51	135	78
Animal TSEs of interest	Scrapie, BSE	BSE	CWD, BSE
Monitoring of blood supply	-	✓	-
Funding	Australian Government & CJDSGN	UK Government	Canadian Government
Primary location	The Florey Institute/ University of Melbourne	University of Edinburgh	University of Ottawa

Source: Stakeholder consultation, Public Health Agency of Canada and The National Creutzfeldt-Jakob Disease Research & Surveillance Unit

Abbreviations: ANCJDR, Australian National CJD Registry; BSE, bovine spongiform encephalopathy; CJDSS, CJD Surveillance System; CWD, chronic wasting disease; NCJDRSU, National CJD Research & Surveillance Unit; TSE, transmissible spongiform encephalopathy

*Referrals are as classified in the most recent reporting from each country. The difference in the number of referrals between Australia and the UK and Canada likely stems from the differences in definitions.

Australian National CJD Registry (ANCJDR)

Key findings

- The ANCJDR provides services beyond those defined in the grant provided by the Department. The services offered by the ANCJDR are services commonly performed by CJD surveillance units in other countries.
- There is a growing demand for the services provided by the ANCJDR over the past six years
- A review of the ANCJDR's 2019-20 income and expenditures indicates that the registry primarily relies on a grant provided by the Australian Government
- International and Australian stakeholders value the ANCJDR both in terms of the public health surveillance functions, but also about progressing advances in diagnostic processes, the accuracy of cases and contribution to international CJD surveillance.
- The ANCJDR is currently awaiting accreditation of RT-QuIC testing and following a successful accreditation, the ANCJDR plans for every CSF sample to undergo RT-QuIC from 2021 onwards. This would bring Australia's diagnostic processes in line with best practice in other countries. Funding for this function has not been identified or confirmed.
- The ANCJDR is staffed by a small number of multidisciplinary experts in CJD. Succession planning for the ANCJDR is of concern. It was reported to the review that the supply of expertise in Victoria could adequately meet their future workforce requirements. However, a training pipeline for these specialists may take several years, and certainty and adequacy of funding are reported to be the key barrier to enable the appropriate workforce transition activities to begin.

Future public health needs

In this section, we present the findings from the review in relation to future public health needs of Australia in responding to the risk of CJD.

Future public health needs for CJD

There are several risks to public health associated with CJD, for which the public health system needs to respond.

The risk to the public health system of CJD relates specifically to the potential transmissibility of the condition. There are sources of risk that need to be considered:

1 AHPHP participants remains at risk of CJD until scientific advances can confirm a risk no longer exists.

2 The provision of surgical care to AHPHP participants could potentially expose others to the risk of CJD transmission if appropriate infection control procedures are not undertaken

3 Sporadic CJD incidences are expected to continue in line with prevalence trends. See page 32 for the projected incidence.

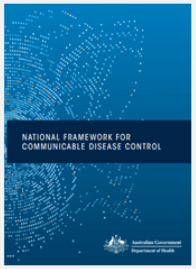
4 Emerging concerns regarding potential iatrogenic or variant CJD.

These risks cannot be eliminated and as such, public health measures need to be put in place to respond to these. The key measure is the use of appropriate and up to date infection control processes.

The National Framework for Communicable Disease Control

Australia has a framework within which public health responses to the risk of communicable disease are planned and managed. Whilst CJD is a transmissible rather than a communicable disease, the same principles of public health apply. The key functions outlined in this framework are:

1.	**Surveillance and laboratory testing**	Currently performed by the ANCJDR and jurisdictional PHUs.
2.	**Preparedness and response**	Relies on the appropriate application of the CJD Infection Control Guidelines and early detection of vCJD and animal prion diseases.
3.	**Evidence based prevention policy**	
4.	**Public health communications**	Health risk communications completed by the CJDSGN, jurisdictional PHUs and the ANCJDR.[19]



The requirements for appropriate infection control for CJD has unintended consequences

As noted earlier, CJD can be a transmissible disease. The CJD prion cannot be destroyed through usual infection control processes for medical procedures. Given the transmission risks of CJD, additional infection control procedures are needed for disposal of waste, reprocessing and incineration of medical equipment, cleaning of surgical areas and other measures health care providers can take to minimise iatrogenic transmission. Most comparable countries have CJD specific infection control guidelines – although they differ in a range of areas, including if people at elevated risk of CJD are able to donate blood. In Australia, a standardised set of rules apply for infection control. They were developed by the CDNA and are known as the CJD Infection Control Guidelines. The guidelines support the assessment of risks for transmission, procedures for infection control and surveillance processes if a clinician suspects CJD. They also provide guidance for specific practice settings including dentistry, post mortem examinations and the funeral industry.

New research is being conducted to determine alternative disinfection strategies for deactivating prion proteins including the use of ozone gas, however, findings must be validated, and there is limited evidence on the cost-effectiveness or barriers to uptake.

As a result of extensive infection control requirements, there have been situations where individuals with known risks of CJD (in particular AHPHP participants) have reported challenges in accessing surgical care in Australia. This is reported to be manifested as:

- Providers refusing to use certain procedures as these involve costly equipment that must be destroyed post-procedure (per the guidelines)
- Delays in procedures while clinicians familiarise themselves with the necessary infection control process
- In some instances, refusal of care.

A review of the CJD Infection Control Guidelines is being considered by the CDNA.

Projected CJD cases in the future

We have undertaken projection modelling to determine the possible epidemiological profile of sCJD in Australia over the next 20 years. The other subtypes were not projected due to:

- gCJD having no known risk factors other than being carried by a small number of families and that incidence of gCJD has remained stable and low (five or fewer cases annually) over the last few years.
- iCJD (specifically AHPHP participants) showing no evidence of increasing or decreasing risks of developing CJD.
- Other iCJD occurring due to surgical material contamination as there have not been any cases since approximately 2000.
- vCJD due to no cases ever being detected in Australia and no cases detected overseas since 2019 (i.e. there is not an active risk).

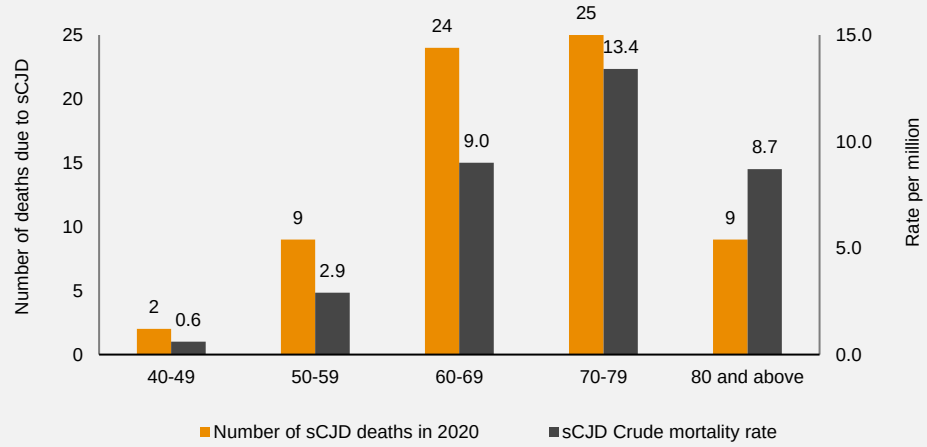
The incidence of sCJD however, is known to be associated with increasing age. Given that Australia's population (much like most of the world) is ageing, this suggests that the number of cases of CJD will similarly grow in the near future. This finding is consistent with the observed trends to date.[1,20]

We have projected the likely number of sCJD cases based on the number of cases (deaths) in 2020 and the estimated crude mortality rate ('crude' in this context refers to a statistical term where the rate has not been adjusted for age). See Figure 7. We then applied the 2020 crude mortality rate to the future population projections made by the Australian Bureau of Statistics (ABS). This assumes the 2020 mortality rates remains the same.

According to projections, by 2041 we would anticipate 99 cases of sCJD annually. There were 51 definite sCJD cases in 2020. However, we have opted to model probable and likely cases so as to not underestimate the possible impact of sCJD in the future. This raises the number of cases in 2020 to 69 sCJD cases. As shown in Figure 8, the large driver of this growth will come from those aged 70 to 79 years as well as those aged 80+ years. We note, however, minimal growth in CJD cases in the cohort of people aged between 60 to 69 years and younger. This trend is likely due to the ageing of the 'baby boomer' generation (born between 1946 to 1964), who by 2041 will be at least 77 years old.

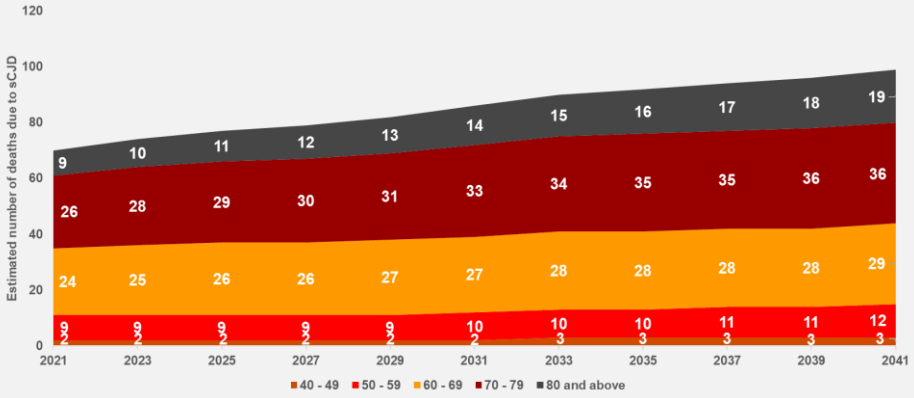
This modelling suggests that there will be an increased need for a CJD public health response and support, not only for people affected by CJD but for the healthcare system itself to be prepared for the increase in case numbers.

Figure 7: Number of deaths and the mortality rates due to sCJD in 2020



Source: PwC analysis of case data provided by ANCJDR. Crude mortality rate were estimated based on population data derived from the ABS. sCJD cases included those that were definite, probable and likely (69 total cases). There were 17 suspected cases but these were deemed unlikely or ultimately confirmed to not be CJD. These were not counted above.

Figure 8 Projected number of sCJD deaths 2020-2041, Australia



Source: PwC analysis based on ABS population projection data and 2020 sCJD mortality rates

Ongoing support needs for AHPHP participants

In our review of evidence, we noted that there is **no conclusive evidence to suggest that the risks of developing CJD for the cohort of AHPHP participants have either reduced, maintained or increased**. While the most recent death in Australia occurred in 1991, the more recent death of a hGH recipient occurred in the UK in 2019. A country by country parallel cannot be drawn due to various factors including differences in treatment dosages, preparation methods and hormones used. Poor record-keeping and case classifications further limit any ability to make comparisons and draw findings.

To identify future needs, we were unable to estimate or model any future likelihood of CJD disease manifestation for AHPHP participants. However, modelling indicates that the AHPHP may continue to require support for their risk of CJD until 2065.

Health issues are known to increase with age. We expect, therefore, that as the younger members of the AHPHP participant cohort age, they will increasingly experience health issues and interact with the health system. Evidence shows that people aged 65 years and older are more likely to engage with the health system. For example, 70 per cent of those aged 65 years and older reported seeing a medical specialist in the last 12 months in 2018 compared to 59 per cent of those under 65 years.[21]

Evidence indicates that a majority of AHPHP participants are hPG recipients.[22] While the oldest person in this cohort would be aged 95 years, the youngest person would be aged 58 years. As such, many are currently in their older age with the youngest person reaching age 65 years by 2028. Given that this cohort is now of the age group where they will increasingly use healthcare services, effort needs to be made to:

- Ensure appropriate healthcare access is provided regardless of their CJD risk
- Ensure that appropriate plans and strategies are in place to minimise the transmission of CJD as this cohort increasingly engages with the health system.

Those in the hGH group, while generally 'younger' than the hPG cohort will also eventually reach older age with the last person reaching age 65 years by 2048. Together this means that there could be two 'waves' of the different AHPHP participant cohorts who reach older age and will cumulatively place a demand on the health system.

Key findings

- While many in the cohort have already reached older age and are increasingly interacting with the health system, it is expected that the cohort will continue to require support for their risk of developing CJD until 2065.

Future needs – Emerging issues

New diagnostic methods are available and can enhance the future diagnostics capabilities in Australia

RT-QuIC is a more recent advancement in CSF based tests. Its benefits include increased sensitivity and better specificity in detecting CJD and can also be performed pre-mortem.[2] It does have limitations, however, in its ability to detect vCJD and rare genetic prion diseases.[2] It has the potential of greatly enhancing the overall diagnostic accuracy and therefore, reducing the need or reliance on other methods such as post-mortem brain examinations (which as discussed earlier require highly specialised personnel, equipment and there is currently an extensive waiting list).[2] This has the potential, therefore, of enhancing diagnostic and surveillance processes.

Importantly, RT-QuIC can provide an opportunity for differential diagnosis for people who may have dementia (not CJD) where access to treatment may be effective in improving their quality of life and prolonging their lives.

Currently, the United States and the United Kingdom have integrated the use of RT-QuIC into their standard diagnostic criteria. In Australia, RT-QuIC has not yet reached widespread adoption and is currently awaiting NATA accreditation to be able to be used for diagnostic purposes. The ANCJDR currently offers RT-QuIC testing as a research tool however it is not funded by the health system.

Evidence is emerging that CJD can be transmitted via blood transfusions but this is currently limited to one type of CJD

To date, there have been three cases of CJD being transmitted through blood transfusions and plasma products.[7] These, however, are specific to vCJD and have occurred only in the UK (and align with the outbreak of the disease in the 1990s). No cases of vCJD (regardless of transmission) have been detected in Australia. Consistent with international approaches, Australia has set out guidelines for individuals who lived in the UK or travelled for six months or longer between 1980 and 1996 to be prevented from donating blood and plasma.[23]

There is no evidence of blood transfusion-related transmissions for sCJD or iCJD.[24] For the latter type, it is possible that transmission would have been limited as people who were known to have been exposed to iCJD would have been discouraged from donating blood. The CJD Infection Control Guidelines recommend that AHPHP participants be excluded from any organ or tissue donation (including blood and plasma).[8] An exception can be made for organ donation if informed consent is given by the recipient.

Animal to human transmission of vCJD is another avenue for transmission but the risk is reduced by biosecurity measures

We note again that the consumption of contaminated meat forms the key method of vCJD transmission.[2] Other than cattle, prion diseases can also occur in animals such as sheep, deer and elk. This suggests that the import of live animals or prion disease contaminated animal products poses an additional risk to human health.

While this can present as an additional avenue of transmission of prion diseases to humans, Australia's biosecurity systems have (to date) successfully minimised the risk of animal prion diseases and by extension their transmission to humans in Australia.

Research and stakeholder consultation, however, does suggest that a future threat of prion diseases will come from animal to human transmissions. International CJD surveillance systems are currently focused on the threat of vCJD through prion diseases including CWD and scrapie, a prion disease of sheep. This highlights the importance of:

- Continued biosecurity and animal disease surveillance monitoring
- A system of communication and reporting between animal surveillance and the CJD surveillance processes.

Issues of animal disease surveillance were not included in the scope of this review. This issue may warrant further investigation in future.

Future needs – Emerging issues

Although neuropathologists play a key role in the definitive diagnosis of CJD, there are challenges in sustaining this service

The role of neuropathologists in CJD diagnosis

Definite diagnosis and subtyping of CJD can only be performed through the analysis of brain tissue obtained from post-mortem autopsy or brain biopsy. Preparing the brain tissue (from a suspected CJD case) for analysis is a highly specialised skill that can only be performed by a neuropathologist and a skilled team of scientists.

Given the small number of neuropathologists in Australia, stakeholders report that there is a heavy reliance on the small pool of professionals to perform these services across multiple jurisdictions.

> *"Currently all brain autopsy processing in Victoria, South Australia and Tasmania relies on one neuropathologist. I have offered to do ones [CJD brain tissue analysis] for South Australia and Tasmania but I don't get paid to do this. It's happening because of my goodwill."* – Neuropathologist

As a result of this arrangement, stakeholders reported incidences where brain samples are sent to another state for testing – resulting in delays. It was reported by stakeholders that waiting times for post-mortem test results can be between six months to two years.

Stakeholders also reported that neuropathologists across Australia are inconsistently funded for this service. For example, in NSW, the neuropathologist is reported to be funded by a local health district but in Victoria, a neuropathologist is not directly funded for this service. This inconsistency in funding raises concerns about of ongoing sustainability of post-mortem brain autopsies which in turn would impact the reliability of diagnosis for CJD in Australia (in particular if no reliable pre-mortem tests can be invented).

Further, the formal training for neuropathologists was reported to be inadequate for the specific needs of CJD diagnosis. Standard training is required to be completed over a short period – a stakeholder cited four years is the appropriate timeframe for training whereas current training is one year. The examination for neuropathology accreditation has a low pass rate resulting in a low pipeline of future neuropathologists. Additional training (not formal) is reported by stakeholders to be needed for a neuropathologist to have the requisite skills to safely perform CJD brain autopsy and diagnosis.

Key findings

- RT-QuIC is a highly sensitive and specific technique to undertake pre-mortem diagnosis of CJD. It is widely adopted overseas but is currently awaiting NATA accreditation and therefore, not yet widely used in Australia.
- There is evidence of vCJD transmission via blood transfusion but blood donation guidelines provide restrictions to reduce the risk of transmission in Australia. There is currently no evidence of transmission via blood of sCJD or iCJD.
- The importation of animals infected with prion diseases presents an area of risk for human transmission of the disease. However, Australia's biosecurity measures currently reduce this risk.
- Neuropathologists are essential for conducting definitive diagnostic tests of CJD. However, there are challenges in sustaining these services in Australia.

Appendices

Appendix A – References

1 Uttley, L., Carroll, C., Wong, R., Hilton, D. A. & Stevenson, M. 2020. Creutzfeldt-Jakob disease: a systematic review of global incidence, prevalence, infectivity, and incubation. Lancet Infect Dis, 20, e2-e10.

2 Pocchiari, M & Manson, J 2018, Human prion diseases: Clinical, epidemiology, neuropathological, biochemical, biomarkers, and genotypes, Handb Clin Neurol, 153.

3 Allars, M 1994, Report of the inquiry into the use of pituitary derived hormones and Creutzfeldt-Jakob disease, Australian Government Publishing Service.

4 National Institute of Diabetes and Digestive and Kidney Diseases 2021, National hormone and pituitary program (NHPP): Information for people treated with pituitary hormone growth hormone, viewed 9 March 2021, <https://www.niddk.nih.gov/health-information/endocrine-diseases/national-hormone-pituitary-program>

5 Peckeu, L., Brandel, J. P., Welaratne, A., Costagliola, D. & Haik, S. 2018. Susceptibility to Creutzfeldt-Jakob disease after human growth hormone treatment in France. Neurology, 91, e724-e731.

6 Abrams, J. Y., Schonberger, L. B., Belay, E. D., Maddox, R. A., Leschek, E. W., Mills, J.L., Wysowski, D. K. & Fradkin, J. E. 2011. Lower risk of Creutzfeldt-Jakob disease in pituitary growth hormone recipients initiating treatment after 1977. J Clin Endocrinol Metab, 96, E1666-9.

7 Stehmann, C., Sensi, M., Sarros, S., McGlade, A., Simpson, M., Klug, G., McLean, C., Masters, C. L. & Collins, S. 2020. Creutzfeldt-Jakob disease surveillance in Australia: update to 31 December 2019. Commun Dis Intell (2018), 44.

8 Communicable Diseases Network Australia 2013, Creutzfeldt-Jakob disease (CJD) control guidelines, viewed 9 March 2021, <https://www1.health.gov.au/internet/main/publishing.nsf/content/3A968399995CFCE5CA257BF000211E32/$File/CJDInfectionControlGuidelinesJan2013.pdf>

9 National Health Service 2017, Minimising transmission risk of CJD and vCJD in healthcare settings, viewed 9 March 2021, <https://www.gov.uk/government/publications/guidance-from-the-acdp-tse-risk-management-subgroup-formerly-tse-working-group>

10 World Health Organization 2000, WHO infection control guidelines for transmissible spongiform encephalopathies. Report of a WHO consultation, Geneva, Switzerland, 23-23 March 1999, viewed 30 March 2021, <https://www.who.int/csr/resources/publications/bse/WHO_CDS_CSR_APH_2000_3/en/>

11 Creutzfeldt-Jakob Disease Support Group Network 2021, The Creutzfeldt-Jakob Disease Support Group Network, viewed 9 March 2021, <https://www.cjdsupport.org.au/>

12 Australian Government Department of Health 2017, Commonwealth Grant Agreement between the Commonwealth represented by Department of Health and CJD Support Group Network Pty Ltd.

13 Appleby, B. S., Lu, M., Bizzi, A., Phillips, M. D., Berri, S. M., Harbison, M. D. & Schonberger, L. B. 2013. Iatrogenic Creutzfeldt-Jakob disease from commercial cadaveric human growth hormone. Emerg Infect Dis, 19, 682-4.

14 Delisle, V.C., Gumuchian, S.T., Rice, D.B., Levis, A.W., Kloda, L.A., Korner, A & Thombs, B.D 2016, Perceived benefits and factors that influence the ability to establish and maintain patient support groups in rare diseases: A scoping review, The Patient-Patient Centered Outcomes Research, 10,283-293

15 Dementia Australia n.d. Information, viewed 5 May 2021, <Delisle, V.C., Gumuchian, S.T., Rice, D.B., Levis, A.W., Kloda, L.A., Korner, A & Thombs, B.D 2016, Perceived benefits and factors that influence the ability to establish and maintain patient support groups in rare diseases: A scoping review, The Patient-Patient Centered Outcomes Research, 10,283-293>

16 The Mito Foundation, n.d., Vision and mission, viewed 5 May 2021, <https://www.mito.org.au/vision-mission/>

17 Australian Government Department of Health 2018, Commonwealth Standard Grant Agreement between the Commonwealth represented by The Department of Health and The Florey Institute of Neuroscience and Mental Health.

18 Watson, N., Kurudzhu, H., Green, A., Summers, D., SMITH, C. & PAL, S. 2021. Application of telehealth for comprehensive Creutzfeldt-Jakob disease surveillance in the United Kingdom. J Neurol Sci, 420, 117221.

19 Commonwealth of Australia 2014, National Framework for Communicable Disease Control

20 Nishimura, Y., Harada, K., Kayama, T., Hagiya, H. & Otsuka, F. 2020. A nationwide trend analysis in the incidence and mortality of Creutzfeldt-Jakob disease in Japan between 2005 and 2014. Sci Rep, 10, 15509.

Appendix A– References

21 Australian Institute for Health and Welfare 2020, Health of Older People, viewed 25 May 2021, <https://www.aihw.gov.au/reports/australias-health/health-of-older-people>

22 Parliament of Australia 2014, Report on the CJD Settlement Offer, Background, viewed 25 May 2021, <https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Completed_inquiries/1996-99/cjd/report/index>

23 Australian Red Cross: Lifeblood, n.d., More information about donating blood if you have lived in the U.K., viewed 22 April 2021, <https://www.donateblood.com.au/vcjd-blood-donation>

24 Food and Drug Administration (FDA) 2020, Recommendations to reduce the possible risk of transmission of Creutzfeldt-Jakob disease and variant Creutzfeldt-Jakob disease by blood and blood components: Guidance for industry, viewed 9 March 2021, <https://www.fda.gov/media/124156/download>

25 Australian Charities and Non-for-profits Commission n.d., Dementia & Alzheimer's Australia Ltd. viewed 5 May 2021, <https://www.acnc.gov.au/charity/ea8fc39d97f682a9cfffe220fd8f5ae5>

26 The National Creutzfeldt-Jakob Disease Research and Surveillance Unit 2017, Protocol: Surveillance of CJD in the UK, viewed 9 March 2021, <https://www.cjd.ed.ac.uk/sites/default/files/NCJDRSU%20surveillance%20protocol-april%202017%20rev2.pdf>

27 Public Health Agency of Canada n.d., Creutzfeldt-Jakob disease surveillance system, viewed 9 March 2021, <https://www.canada.ca/en/public-health/services/surveillance/blood-safety-contribution-program/creutzfeldt-jakob-disease.html>

Appendix B – Support network case studies
Case study of The Mito Foundation

What are mitochondrial diseases?

Mitochondrial diseases (mito diseases) are a group of diseases that are linked by the common feature of dysfunction of a cell's mitochondria. Mitochondria are the energy powerhouses of all cells in the human body and their inability to function properly can have symptoms across multiple organs and systems at varying degrees.[16]

It is estimated that as many as one in two hundred Australians carry the genetic risk for mito diseases, and serious disease impacts around one in five thousand Australians, making it the second most common genetic disease after cystic fibrosis. Mitochondrial disease has both a genetic and spontaneous component, there are few treatments available, but no cure. Diseases diagnosed in childhood have a poorer prognosis than those diagnosed later in life. Diagnosis can be confirmed with genetic testing, however, due to the complexities in testing so many potentially affected areas of the body, many patients never receive definitive diagnoses, and are treated based on clinical presentation.[16]

The Mito Foundation

The Mito Foundation is a registered charity and was created in 2009 by a family impacted by mitochondrial disease.[16] Since the inception, the Sydney based organisation has grown and has volunteers all over the country that help it function.

The Mito Foundation's vision is to be the "pre-eminent source of energy and hope for the mito community", and their mission is to "support the mito community while seeking a cure". To help do this they coordinate with many rare disease and genetic organisations throughout the country and provide education and support for this rare disease.

The Mito Foundation's objectives

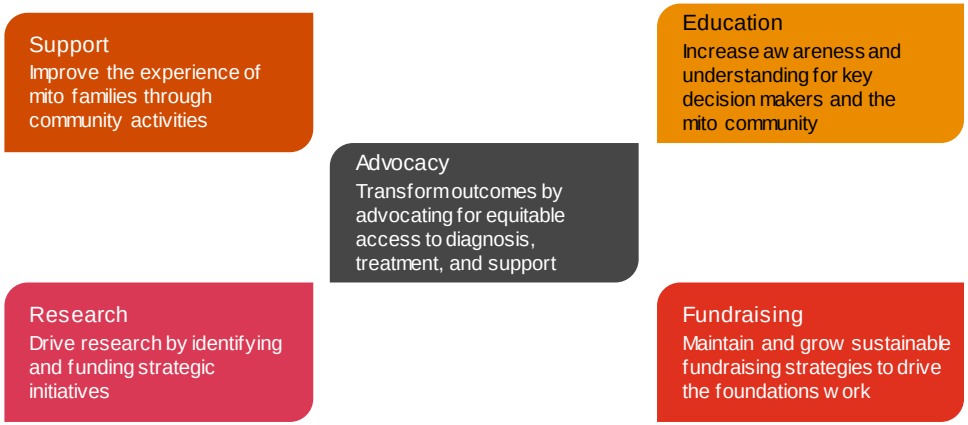
The Mito Foundation has three objectives.[16] Its primary objective is to "support sufferers of mito diseases and their families." The Foundation does this through:

- Assistance in identifying medical specialists
- Navigation of the National Disability Insurance Scheme (NDIS)
- Providing information about living with mito diseases
- Advocacy for the mito community

The secondary objective is finding effective methods of prevention, diagnosis, treatment, and a cure for mito diseases. It aims to do this via improving diagnosis rates, establishing connected centres of excellence, collaborating with international organisations to create a global registry of mito disease, and changing legislation to legalise mitochondrial donations and allow more reproductive options for families.

The third objective is to increase awareness and education about mito disease. It seeks to do this through the inclusion of mito disease in medical school curriculums, research grants, community events including fundraising and awareness events throughout the country. The Mito foundation also maintains a robust social media presence including Facebook, Twitter, Instagram, and a YouTube channel.

Strategies of the Mito Foundation



Case study of The Mito Foundation

Maybe it's Mito?

Due to the varying array of potential symptoms and organs that are involved in mito diseases, the Mito Foundation has developed a program called 'Maybe it's Mito?' This program is aimed at GPs which helps provide education for providers to make a rapid referral to the right specialists to speed up the diagnostic process.

Registry

The Mito Foundation offers an optional registry for patients and families to join. This registry gathers a database of patients for clinical trials due to the rarity of the disease, and the number of different individual diagnoses within the heading of mito diseases.

Family supports

Through their toll-free patient helpline, a patient pathway nurse helps guide patients through different support options and medical consultations.

Research grants

A large portion of the Mito Foundation's research is given through grants into treatment and diagnosis. These grants include international collaborations on large scale projects, fellowships, clinical trial funding, and PhD "top-up" scholarships for individuals studying different scientific avenues that can lead to breakthroughs in diagnosis or treatment for the varying syndromes and diseases that make up the umbrella of mito diseases.

Fundraising and support activities

Members of the mito foundation participate in multiple fundraising events throughout the year including a national stay in bed day and the Bloody Long Walk

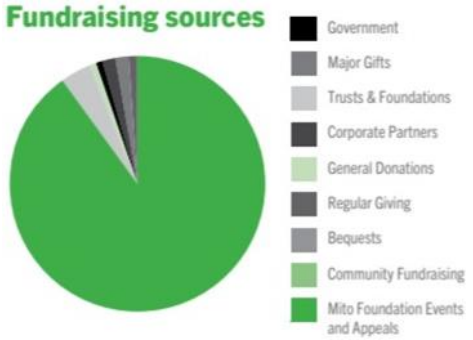
Members also participate in support groups tailored to either patients or parents called mito meetups, information days, and luncheons called Munch for Mito.

Financial information from the Mito Foundation

In 2019, the Mito Foundation accepted $4.7 million through donations and fundraising events, making up a significant proportion of their revenue. Their FY 2019-20 fundraising sources is provided in Figure B.1 and B.2.

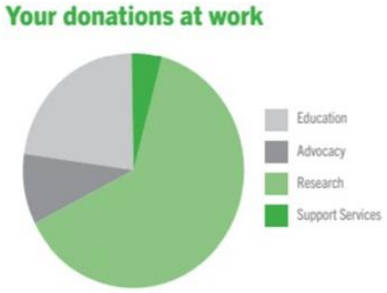
While not all 2019 data is available, the foundation has committed nearly $3 million to funding research grants and other foundation activities including their helpline and maintaining the Maybe it's Mito? Program. The Foundation has reported $1.047 million dollars in total salaries in 2020 with $182,053 aggregate paid to the director of the Mito Foundation.

Figure B.1: Fundraising sources for the Mito Foundation



Source: Mito Foundation 2020 Annual Report

FIgure B.2: Use of donations for the Mito Foundation



Source: Mito Foundation 2020 Annual Report

Case study of Dementia Australia

Dementia in Australia

Dementia is a group of diseases that involve a gradual loss of cognitive function. These losses are noticeable in memory, intellect, and social skills.

Some of the most common types of dementia include frontotemporal dementia, vascular dementia, Lewy body disease, and Alzheimer's disease. Alzheimer's disease makes up between 50-70 per cent of all dementia diagnoses.[15]

There is no cure for dementia, although there are medications that can help minimise or delay progression of symptoms including anxiety and depression. Numerous neuroprotective factors help prevent the onset of dementia including exercise and participating in cognitively stimulating activities.

Nearly half a million Australians are living with dementia, and approximately 1.6 million Australians are involved in their care. As of 2021, approximately 250 Australians are diagnosed with dementia every day and it is the single greatest cause of disability among Australians over the age of 65. It is estimated that over half of the residents in residential aged care facilities are individuals with dementia and there are 36 deaths per day in Australia where dementia is an underlying cause.

Dementia Australia

Dementia Australia was created over 35 years ago. They maintain offices in all states and territories and they are the national peak body for those impacted by dementia. Dementia Australia encompasses what was formerly known as Alzheimer's Australia and is a member of Alzheimer's Disease International.[15]

The organisation provides support, advocacy, education, and fundraising for those impacted by dementia in Australia with the vision of "an inclusive future where all people impacted by dementia receive the care and support they choose."

Priorities of Dementia Australia

Dementia Australia, with government and other stakeholder partnerships, has developed a five year strategic plan to address three stated priorities of the organisation which are described in Figure B.3.[15]

Figure B.3: Priorities of the strategic plan for Dementia Australia

Access to timely diagnosis and support for all people living with dementia.
To significantly reduce the time it takes to diagnose dementia and increase the number of people accessing support.

Quality of Dementia Care
Create baseline and best practice standards for quality dementia care. Advocate for the baseline standards which will include provisions for training, to be implemented into aged care facilities across Australia.

Reduce Discrimination
Tackle discrimination head on so that no one with dementia feels isolated.

Objectives of Dementia Australia

- Be a strong and credible voice for all Australians whose lives are touched by dementia and provide a means by which they can influence dementia related policy
- Drive quality in service provision and care for people living with dementia
- Facilitate and provide support for persons with dementia and related disorders and their families and friends
- Educate and inform the public and the medical and helping professions about dementia, related disorders and other relevant aspects
- Stimulate research and improve the management treatment and prevention of dementia and related disorders
- Advise the Australian Government and state or territory governments on policy development and programs concerning dementia and related disorders
- Do all other things as may seem incidental or conducive to the achievement of the above objectives.

Case study of Dementia Australia

Fundraising Activities

To support members and increase awareness, Dementia Australia organises and participates in fundraising activities. Their largest fundraising event is the annual Memory Walk which raises around one million dollars at events around the country.

Support Services

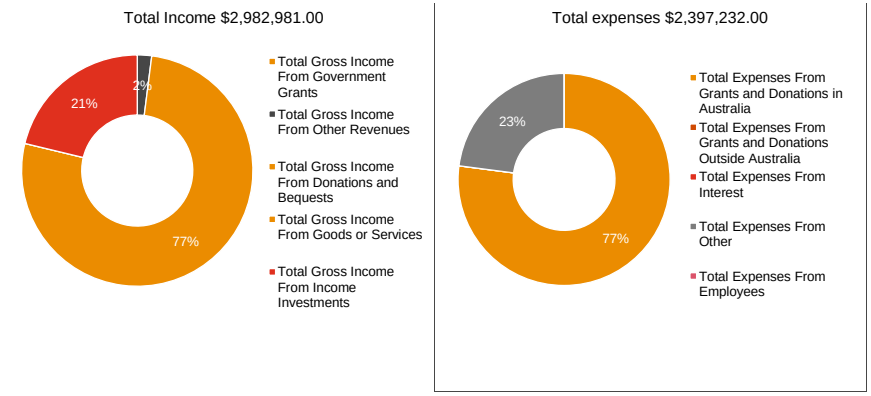
Direct services to individual impacted by dementia include services that range from young onset dementia information to palliative care programs. Selected offerings from Dementia Australia include:

- A national helpline
- Programs to keep the mind active
- Carer and family support services
- Counselling services

Dementia Australia Research Foundation

Dementia Australia has a dedicated research foundation. The primary purpose of the foundation is to fund research grants that will further the understanding of dementia diagnosis, treatment, and care. Publicly available financials for the Dementia Australia Research Foundation are in Figure B.4.

Figure B.4: Income and Expenditures for the Dementia Australia Research Foundation, July 2019-June 2020

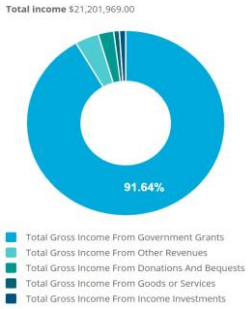


Source: Australian Charities and Not-for-profits Commission

Funding of Dementia Australia

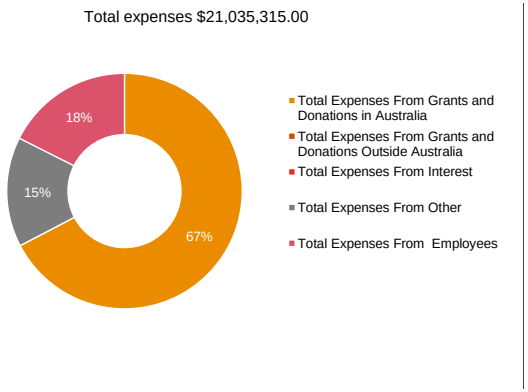
The most recent financial information for the fiscal year July 2016-June 2017 report that Dementia Australia's revenue was $21 million, with government grants making up $19.4 million (91 per cent) of all income. Expenses totalled approximately $21 million, with the largest expenditure being for donations and grants that fund programming, support, and care for members totalling $14.16 million. Salaries are not publicly available for Dementia Australia in most recent reporting. Figure B.5 and B.6 provide a high level overview of income and expenses for the fiscal year July 2016-2017.[25]

Figure B.5: Income for Dementia Australia



Source: Australian Charities and Not-for profits Commission

Figure B.6: Expenditures for Dementia Australia



Source: Australian Charities and Not-for profits Commission

Appendix C – Case study of The National Creutzfeldt-Jakob Disease Research & Surveillance Unit (NCJDRSU) in the UK

Origins of CJD Surveillance in The United Kingdom

Surveillance for CJD in the UK began as a response to the outbreak of bovine spongiform encephalopathy in cattle and the idea that it could be transmitted to humans.The National Creutzfeldt-Jakob Disease Research and Surveillance Unit was created in 1990 and the first case of vCJD from BSE was diagnosed in 1996.[26] It is funded by the federal government through the Department of Health and the Scottish Government Policy Research Programme. Though it was created in response to BSE, the most prevalent form of CJD seen in the United Kingdom is sCJD.

Conducting surveillance in the United Kingdom

Referrals are made to the NCJDRSU through various sources, and the general pathway is described further in Figure C.1. Once referrals are made testing is carried out through the University of Edinburgh. The University of Edinburgh conducts testing and research for prion diseases for the UK as well as EuroCJD and other countries upon request. The University also works with the Roslin Center which is also at the University of Edinburgh to monitor animal diseases.

The national surveillance system acts as the central reporting and information dissemination vehicle, however there are groups followed by additional clinics that work in conjunction with the NCJDRSU and provide additional services as needed:

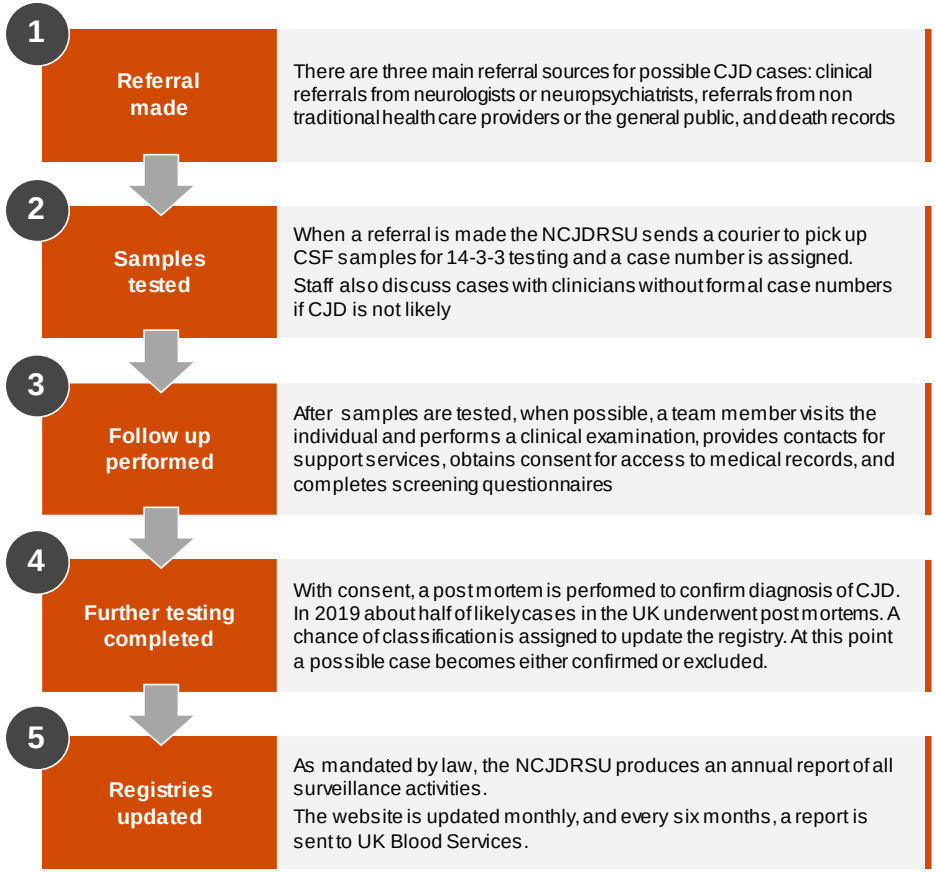
- The **Institute of Child Health** follows individuals at risk for receiving growth hormones as a child
- The **National Prion Clinic** follows cases of genetic CJD

Products of the NCJDRSU

The NCJDRSU provides year round education, consultation, and support services to healthcare professionals and those impacted by CJD. In addition to these services they also produce an annual report that includes cases of all subtypes of CJD, a summary of potential occupational exposures and follow up, laboratory activities.

The official testing that confirms CJD is either a post mortem examination or 14-3-3 protein testing. However, due to increasing evidence on the efficacy of RT-QuIC testing, since 2014 all samples sent to the NCJDRSU are tested via RT-QuIC if there is enough fluid available.

Figure C.1: Function of the NCJDRSU



Source: National CJD Research and Surveillance Unit surveillance protocol, 2017

Case study comparison of The NCJDRSU and the ANCJDR

How variant CJD impacts surveillance

Because of the UK's history with vCJD as a result of a BSE outbreak, multiple steps are taken to contain and prevent a future outbreak and deal with the long term implications of the public health crisis.

- Creation of the National Care Team which is funded by the federal government to provide support services to those diagnosed with CJD*
- Monitoring of blood products to track individuals who donated and went on to develop vCJD and the recipients of the blood products
- Tailored questionnaires to determine past exposure or clusters are designed so that in the event of a case of variant CJD the source can be identified.

Management or services for those at increased risk of CJD

Prospective

Those who are at an increased risk for iatrogenic and genetic CJD are covered by the infection control guidelines. There is no additional funding or support for those who received human growth hormones for short stature.

Retrospective

When a case is identified by the NCJDRSU, researchers retrospectively examine medical records and identify what surgeries the individual had before death. The public health department is then notified so any additional tracing can take place.

Ongoing "issues" for the NCJDRSU

The NCJDRSU began as a surveillance system to monitor BSE. Once vCJD was identified in the population, additional measures were included to support those infected. Since its inception, the NCJDRSU has expanded to include the additional surveillance and support measures required in the UK for all forms of CJD.

A significant number of referrals are met in person to perform examinations and provide support, however, the onset of the COVID-19 Pandemic required the transition to telehealth services, which a recent study showed was an effective way to carry out surveillance in the UK.[18]

Table C.1 presents a comparison of the Australian and UK surveillance systems.

*In addition to the National Care Team which is a part of the NCJDRSU, there is also a charity called the CJD Support Network which participates in support services and fundraising

Table C.1: Comparison of the Australian and United Kingdom's surveillance systems

Surveillance began	1990	1993
Cause for creation	BSE outbreak	AHPHP
Annual referrals (2019)*	146	513
Total cases (2019)	135	51
Animal TSEs of interest	BSE	Scrapie, BSE
Monitoring of blood supply	yes	no
Funding	UK Government	Australian Government, NHMRC & donations
Primary location	University of Edinburgh MRC Prion Unit and Institute of Prion Diseases UCL	Florey Institute/University of Melbourne

Source: The National CJD Research & Surveillance Unit and The Australian National CJD Registry
Abbreviations: BSE, bovine spongiform encephalopathy; MRC, Medical Research Council; NHMRC, National Health and Medical Research Council; TSE, Transmissible spongiform encephalopathies; UCL, University College London

*Referrals are as classified in the most recent reporting from each country. Countries do not offer a case definition for a referral and criteria for inclusion may vary. This is the likely explanation for the significant variation in referral rates between the UK and Australia in Table C.1.

Key findings

- The United Kingdom maintains a robust surveillance system through the NCJDRSU at the University of Edinburgh and the Medical Research Council Prion Unit and Institute of Prion Diseases at the University College London
- This is due to the significant BSE outbreak that caused vCJD in the 1990s
- Surveillance is aided by high levels of community awareness of CJD
- There is a dedicated government funded health care team that helps patients navigate the health care landscape
- The population density of the United Kingdom allows for many in person follow up visits

Case study of the Creutzfeldt-Jakob Disease Surveillance System (CJDSS) in Canada

Origins of CJD surveillance in Canada

Canada began surveillance for CJD in 1998 due to the growing threat of vCJD that had been reported in the UK.[27] Canada's first case of BSE was in a cow that was imported from the UK in 1993. In 1996, when the UK announced the first case of vCJD and it was identified and linked to BSE, Canada acted to monitor their population.

The Creutzfeldt-Jakob Disease Surveillance System (CJDSS) is operated by the Public Health Agency of Canada and funded through the Canadian government with one central database.[27] The system relies on data sharing from the different provinces which can create challenges in reporting and follow up of suspected cases.

Conducting surveillance in Canada

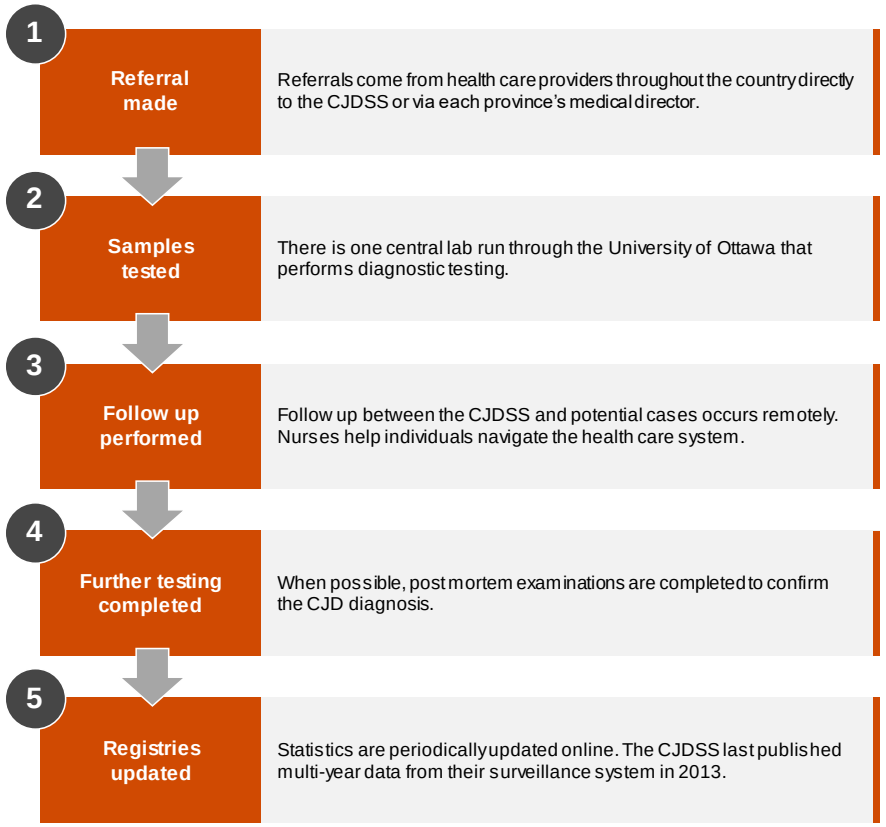
Reporting and data sharing occurs between provinces and the central surveillance team. Cases can be reported directly to the CJDSS from medical providers who will provide guidance on follow up and testing to further rule CJD in or out. If a referral comes directly to the CJDSS, the team will tell the provider to contact the provinces medical director. The CJDSS will also update each province's medical director each month with a report of cases in their province.

In addition to referrals made directly to the CJDSS, the chief medical officers holding meetings where cases are discussed and monthly reports from the federal CJDSS that identify cases within the different provinces. The general function of the CJDSS is described in Figure C.2.

Products of the CJDSS

The CJDSS provides education and consultation for health services throughout the country. In addition to the monthly reports to provinces, they provide a newsletter to health care providers and update their website with case statistics. The CJDSS also publishes data from their surveillance.

Figure C.2: Function of the CJDSS



Source: Public Health Agency of Canada and stakeholder consultation

Case study comparison of The CJDSS and the Australian National Creutzfeldt-Jakob Disease Registry

How animal prion diseases impact surveillance

The origin of surveillance in Canada was due to the outbreak of BSE in the UK and the associated risk of vCJD. BSE was the first known animal TSE that was able to transfer to humans, however, since the 1990's BSE epidemic, another animal prion disease, Chronic Wasting Disease (CWD) has been shown to be transmittable into mammals. CWD is an animal TSE that is prevalent in North American deer and elk.

While Canada, or any other country, has not had a case of a new variant CJD related to CWD, the known mammal transmission and the long latency periods for prion diseases creates an ongoing need for enhanced surveillance. To accomplish this, the Alberta Prion Research Institute (among other research organisations), which is funded by the Alberta government to study prion diseases was created. The institute partners with the Public Health Agency of Canada and the University of Ottawa where the CJDSS is housed.

Management or services for those at increased risk of CJD

Canada does not have a large population that is at risk for CJD through iatrogenic exposure, therefore there are no additional services to prospectively manage this group.

When Canada updated their infection control guidelines in 2007, it was stated that those who are at an increased risk for CJD, including those who have known genetic or iatrogenic risk factors, do not need any additional infection control measures for the surgical theatre or instruments used. However, is important to note that, Canada did not have a hormone program for either short stature or infertility.

Assistance for those with CJD in Canada

Canada is a geographically large country with a low population density and assistance is often provided remotely via the CJDSS. They offer support from nurses to assist a family in navigating the health care system once a referral is made and when CJD is a likely diagnosis.

Ongoing "issues" with CJD surveillance in Canada

The CJDSS is impacted by the presence of many remote locations throughout the country. This lead to areas where providers are not as familiar with protocols for diagnostics or infection control.

Table C.2 presents a comparison of the Australian and Canadian surveillance systems

Table C.2: Comparison of the Australian and Canadian surveillance systems

		
Surveillance began	1998	1993
Cause for creation	BSE outbreak	AHPHP
Annual referrals (2019)*	140	513
Total cases (2019)	78	51
Animal TSEs of interest	CWD, BSE	Scrapie, BSE
Monitoring of blood supply	No	No
Funding	Government	Australian Government, NHMRC & CJDSGN
Primary location	University of Ottawa	Florey Institute/University of Melbourne

Source: The CJD Surveillance System, the Australian National CJD Registry, and Stakeholder consultation

*Referrals are as classified in the most recent reporting from each country. Countries do not offer a case definition for a referral and criteria for inclusion may vary.

Key findings

- Canada does not have a strong history of iatrogenic CJD linked to a human pituitary hormone program
- CWD has been recorded in deer and elk in the country and the CJDSS and animal research institutes study animal prion diseases
- Remote locations lead to diagnostic challenges
- There are ongoing data-sharing issues between the CJDSS and provinces.

Appendix D – AHPHP participant survey and interview data analysis

AHPHP participant survey and interviews

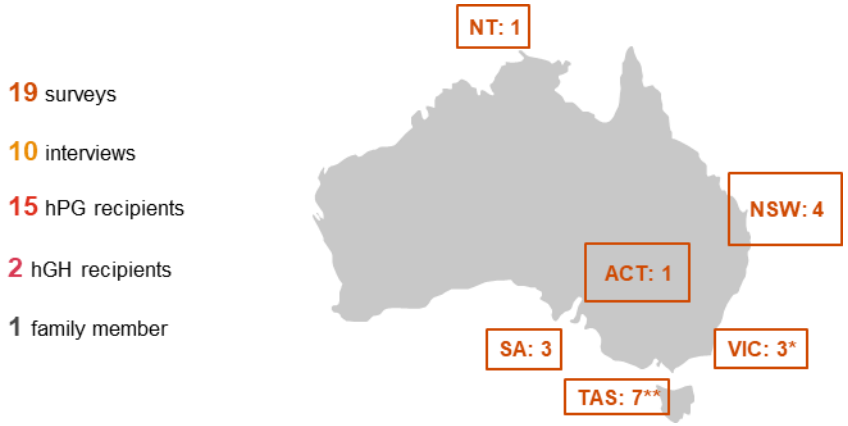
Due to the sensitive nature of this review, a Human Research Ethics (HREC) review of the methodology was undertaken and approved by Bellberry Limited (reference number 2021-02-150). Considerations were taken to minimise distress to AHPHP participants by offering an 'opt-in' method of participating in a survey or interview. Third-party counselling options were provided for any distress experienced during the review.

The data collection process for AHPHP participants included a paper-based mail survey and optional follow up interview either via teleconference or video conference (where consent was provided). The purpose of this data collection was to understand:

- the current and future needs for the cohort
- their experiences with the CJDSGN.

Details of this data collection methodology can be found in Appendix E. As of 8 June 2021, 19 participants responded to the survey (see Figure D.1). A key limitation is that the sample is not representative of the ~2,100 person AHPHP participant group and the sample under-represents those who have not used the CJDSGN for support.

Figure D.1: Overview of AHPHP participants who responded to the data collection



*1 no response to hormone type

**family member received growth hormone

Participant concerns about the risk of CJD

> *"It's a significant grief over what has happened and the anticipated grief about the unknown."* – AHPHP participant

Surveyed participants indicate they have varying levels of concerns around developing CJD. This concern increases when they interact with the medical community or when they experience forgetfulness.

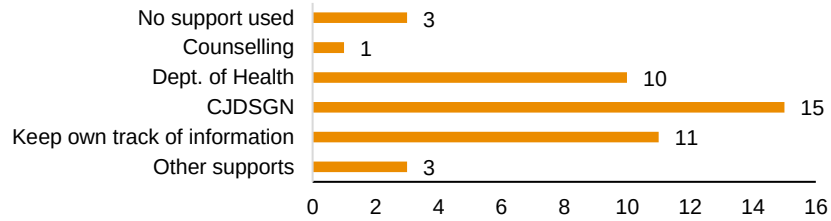
The average response of how often participants think about their risk of developing CJD (responses ranged from 1-10)

5.21 the average response of how worried participants are about developing CJD 1 = not worried at all, 10 = extremely worried (responses ranged from 1-10)

Current needs of AHPHP Participants

When asked about what services they use to assist with concerns about CJD, most AHPHP participants surveyed cited using some form of support. The most commonly used support is that provided by the CJDSGN. *Other commonly used means of support include seeking information from the Department regarding initiatives related to AHPHP participants; or individually keeping track of information about new treatments or diagnosis. Figure E.2 outlines the support services AHPHP participants report they are currently using.

Figure E.2: Current supports or services to help with concerns about CJD



Source: PwC analysis of AHPHP survey data

Note: Respondents may select multiple responses, resulting in a total greater than the number of completed surveys.

*Due to the nature of participant recruitment, survey participants who utilise CJDSGN services are overrepresented.

Usefulness of support services

When asked about which service they found most useful, 37 per cent of respondents reported the advocacy services for medical procedures were the most useful. Other

Appendix D– AHPHP participant survey and interview data analysis

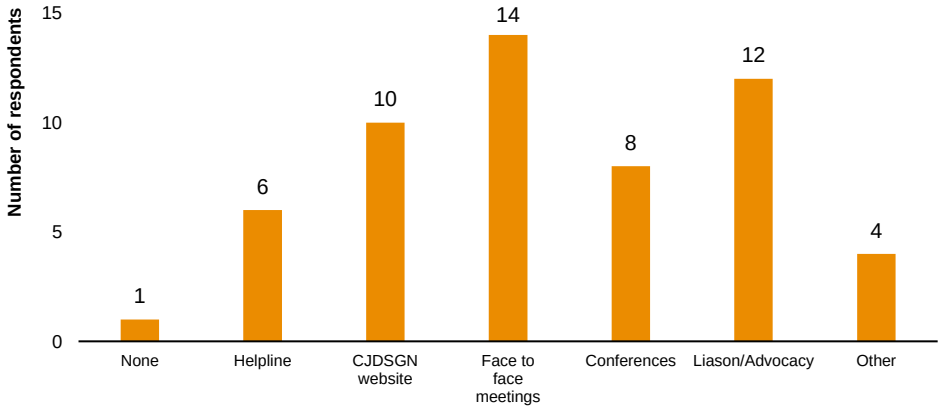
responses include finding out about developments in treatment, diagnosis, and new cases and communication with other participants (16 per cent).

Use of CJDSGN support services

AHPHP participants were asked about what services were used when engaging with CJDSGN. See Figure D.3 for more detail. Of those services, there is an almost equal amount of respondents who reported using the CJDSGN for:

- face to face support meetings with members of the CJDSGN (74 per cent)
- liaison or advocacy services to medical, surgical, or mental health services (63 per cent).

Figure D.3: CJDSGN supports used by AHPHP participants



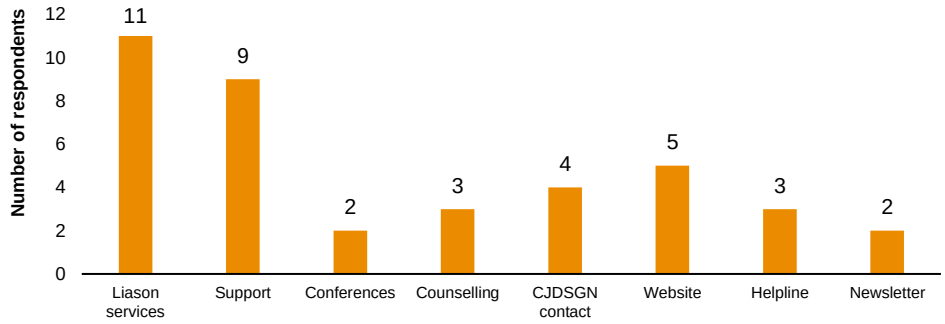
Source: PwC analysis of AHPHP survey data

Note: Respondents may select multiple responses, resulting in a total greater than the number of completed surveys

Most useful CJDSGN supports

Respondents were asked which supports offered by the CJDSGN, were the most helpful to them. There was variation in these responses and they are further described in Figure D.4. The two most frequently reported services are liaison services for medical procedures and support meetings, 58 per cent and 47 per cent, respectively.

Figure D.4: Reported 'most useful' services offered by the CJDSGN



Source: PwC analysis of AHPHP survey data

Note: Respondents may select multiple-responses, resulting in a total greater than the number of completed surveys

Future needs of AHPHP Participants

Participants reported being overall well supported by the CJDSGN with an average score of 9.1 out of 10 for how well their needs are met. Of the 19 respondents, 74 per cent report that if they do not develop CJD they will still need supports. An additional 21 per cent are not sure if they will need the supports, and only one respondent noted that they will not need supports if they do not develop CJD.

The majority (95 per cent) of participants surveyed reported they believed the government should still provide the supports that were available previously to AHPHP participants (e.g. counselling. medical and other care for those who develop CJD). Outside of the supports already described, participants requested that the government provide funding to support research and public awareness of CJD and for the government to formally address what some people believed was a lack of transparency in the past regarding the AHPHP.

Appendix D– AHPHP participant survey and interview data analysis

Future needs of AHPHP participants

Aside from the continuation of support from the government, participants were asked what the CJDSGN could do to improve their services. This question was met with significant variability in responses, however, 10 per cent of respondents requested more face to face meetings. The second suggestion is to continue funding the CJDSGN for their current support and to fund education for medical professionals (10 per cent).

Figure D.5: Areas of improvement for the CJDSGN

"As long as they continue to be funded, they can go on to help all recipients and families in the way they have done to date" – AHPHP Participant

"It is important to know that CJDSGN 'has my back' with support an advice when and if i need it." – AHPHP Participant

Follow up participants interviews

Ten follow up interviews were conducted with participants. During these interviews, participants were given the opportunity to elaborate on their experiences. Figure D.6 outlines the key themes arising from the interview.

Figure D.6: Themes from interviews with AHPHP participants

Source: Analysis of interviews conducted by PwC with AHPHP participants

Appendix E – Detailed methodology

In this section, we specifically outline the methodology for:

- The evidence review
- Stakeholder consultations
- AHPHP participant survey and consultations
- sCJD future projections.

Evidence review

A review of the evidence was undertaken to examine the currently available literature regarding the risk landscape of CJD and prion diseases. Specifically, this included:

- A consideration of the current international guidelines on best practice in communicating with and supporting those impacted by or at increased risk of prion diseases
- The transmission risk status of cadaveric human pituitary hormone recipients
- An assessment of the 2013 CJD Infection Control Guidelines and its underpinning evidence as developed by the Communicable Diseases Network Australia (CDNA) in comparison to international approaches.

The sources used to inform the review included peer-reviewed journal articles as well as grey literature materials (including legislation and government reports). To ensure relevancy and recency, the evidence that was reviewed was only from 2010 onwards, related to the above lines of enquiry and published in English. Given the rarity of this disease, we did not undertake any formal process to assess evidence quality. Instead, we prioritised evidence in peer-reviewed medical journals and from CJD specific organisations in our review of evidence.

Consultation with stakeholders

We undertook consultations with several stakeholders including the two organisations who are subject to this review (ANCJDR and CJDSGN), Australian and international stakeholders.

Page 48 outlines the stakeholders that we met with and the purpose for consultations. Consultations were held between 6 April and 6 May 2021.

In addition to consultation interviews, we also reviewed documents provided by stakeholders including written responses to review questions as well as documents shared and provided by stakeholders.

Appendix E– Detailed methodology

Stakeholder	Consultation group	Consultation purpose
International stakeholders	• surveillance units • CJD support networks • CJD researchers.	The purposes for consultation were to understand: • the current evidence base and guidelines for CJD in your country • the surveillance system structure and scope • existing consumer support services in your country • non-published evidence or emerging research
CDNA representatives (Australia)	CDNA representatives from: • Tasmania • Western Australia • New South Wales • South Australia	The purposes for consultation were to understand: • understand the current process of data sharing between states and territories and the ANCJDR • obtain an overview of the support services provided by states and territories for people with or at risk of CJD and other prion diseases • collect any non-published evidence, emerging research and evidence-based guidelines or policies on the diagnosis, management and monitoring of CJD and other prion diseases
Clinical peak bodies (Australia)	• Rare Voices Australia • Australian Association of Psychologists • Australian Dental Association • Neurosurgical Society of Australasia • Royal Australasian College of Dental Surgeons • The Royal Australian and New Zealand College of Psychiatrists • Royal College of Pathologists of Australasia • Royal Prince Alfred Hospital • Victorian Clinical Genetics Services • La Trobe University	The purposes for consultation were to understand: • the current evidence-based policies and guidelines for the diagnosis, management and surveillance of CJD and other prion diseases • different surveillance systems and how the functions of the ANCJDR can be improved • existing consumer support services and how the services provided by the CJDSGN can be improved • collect any non-published evidence, emerging research on the diagnosis, management and monitoring of CJD and other prion diseases • the future needs of Australian Human Pituitary Hormone Program Participants and people with or at risk of, developing CJD and other prion diseases.
Consumer peak bodies (Australia)	• Pindara Private Hospital • NSW Health • Department of Diagnostic Genomics	The purposes for consultation were to understand: • how the CJDSGN meets the current needs of people with or at risk of developing CJD and other prion diseases • existing consumer support services and how the services provided by the CJDSGN can be improved • how the ANCJDR meets the current needs of people with or at risk of developing CJD and other prion diseases • how the ANCJDR can be improved to meet the future needs of people with or at risk of developing CJD and other prion diseases • the future needs of AHPHP Participants and people with or at risk of, developing CJD and other prion diseases.

AHPHP participant survey and consultations

We undertook a specific data collection process for AHPHP participants. This included a paper-based mail survey and an interview (where consent was provided). The key purpose for this data collection was to understand:

- the current and future needs for the cohort
- their experiences with the CJDSGN.

Given that the cohort comprises ~2,100 people and due to the sensitivity of the subject matter, we adopted a voluntary approach to participation. AHPHP cohort was recruited to this evaluation via the Department that sent out an expression of interest request to them. The CJDSGN also promoted the review through their network. Those interested in participating in the review contacted the Department and provided their updated contact details. The Department disseminated 26 surveys to AHPHP participants. Complete surveys and consent forms were sent via reply mail to the PwC review team. A total of 19 participants completed the survey and 10 participants were interviewed as of
27 May 2021.

This voluntary approach, however, limits the generalisability of our findings given:

- The small and non-random sample size
- The method of recruitment meant that we engaged with those who sought out the CJDSGN's services. There may be others who do not actively seek out support and we have a very limited understanding of this specific group of AHPHP participants.

AHPHP participants are also considered to be 'vulnerable' under the National Statement on Ethical Conduct in Human Research (section 4.3), therefore, necessitating a human research ethics clearance process prior to any data collection from them.

As part of this, an ethics review application was submitted to Bellberry Limited – reference number 2021-02-150. The process entailed a review of all data collection tools as well as plans to provide support in the case of distress or adverse events. Approval and confirmation were provided on 28 April 2021.

sCJD future projections

A projection of future sCJD cases was undertaken to determine the potential number of future cases that will be observed. The data used to inform the number of future projections included:

- The 2020 number of sCJD cases in Australia (provided by the ANCJDR)
- Future population projections provided by the ABS[1].

Note that for future population projections, we have assumed the medium levels of:

- Fertility
- Life expectancy
- Net overseas migration.

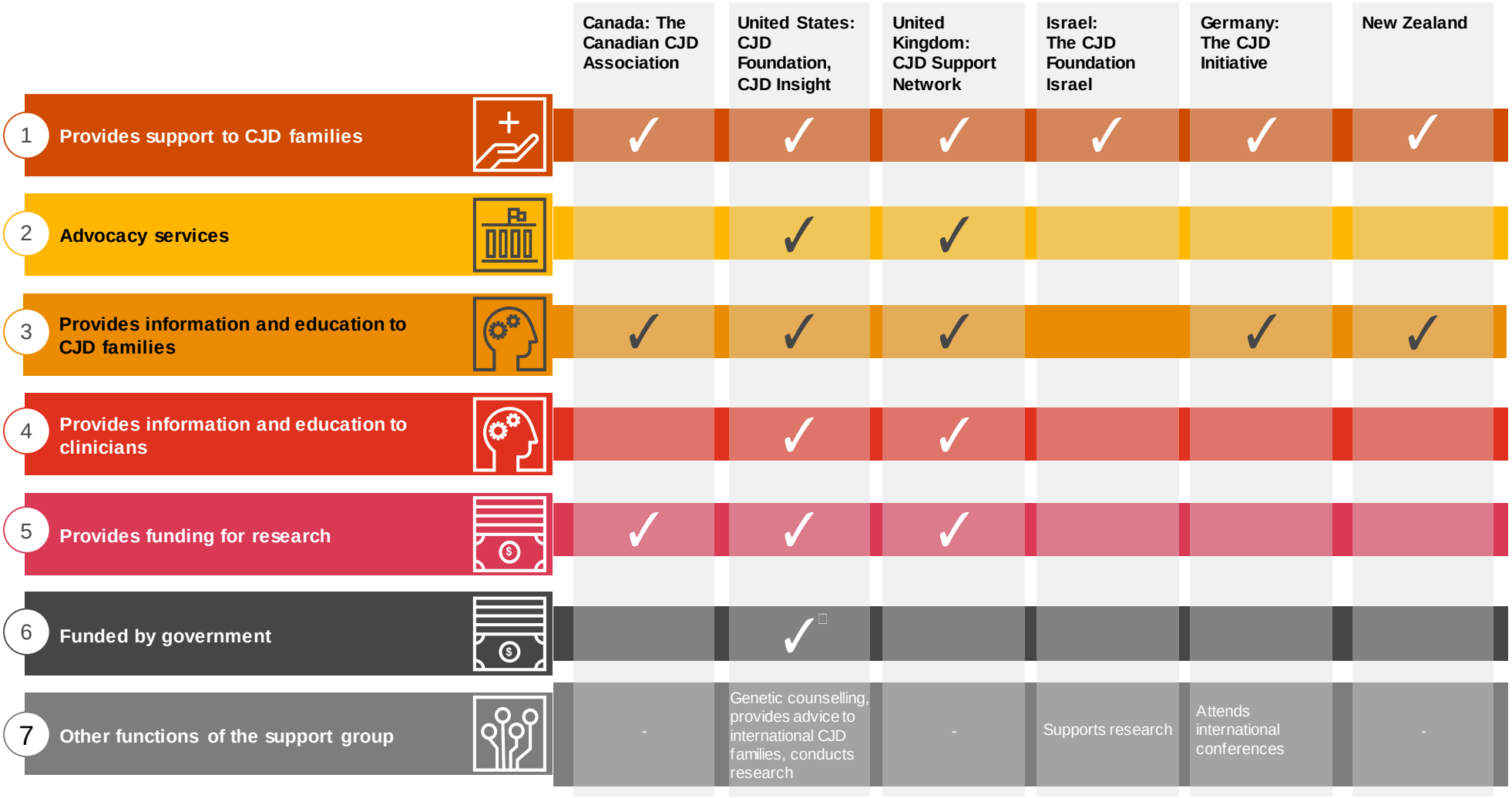
Projections were made by first calculating the crude mortality rate in 2020. This was undertaken as follows:

$$\frac{\text{Number of deaths in 2020 by age group}}{\text{Number of people in 2020 by age group}} \times 1{,}000{,}000$$

The number of future cases was then calculated by multiplying the 2020 crude mortality rate (of a specific age group) to the population size of that same age group over subsequent years.

1 Australian Bureau of Statistics (2020) Population Projections, Australia, 2017-2066 *[http://stat.data.abs.gov.au/Index.aspx?DatasetCode=POP_PROJ_2011],* accessed 5 May 2021.

Appendix F – Comparison of the features of international CJD support networks



* A small proportion is funded by the Centre of Disease Control and Prevention. The majority of funding is obtained via fund raising activities

Source: Stakeholder consultation interviews conducted by PwC

Appendix G – Comparison of the features of international CJD surveillance units

	Personnel	Surveillance process	Data collected	Functions/services of the registry	Government obligations to HPH recipients	Legislation supporting CJD surveillance	Source of funding
Canada	4 nurses 1 data manager 1 admin assistant 1 director 1 neuropathologist/MD	MDs report cases to the registry and provinces' public health unit Consent required to access patient data Monthly report (CJD cases) for provinces	Biographical data Pathology results MRI reports Biopsy reports	Diagnostic testing Helping families navigate the health system Clinician education/support Collaboration among clinicians	No specialised government support for HPH recipients	Yes – physicians are required to report all cases of probable, possible or definite cases of CJD	The Public Health Agency of Canada
UK	2 nurses 3 registrars 1 consultant	Neurologists inform the surveillance unit of CJD cases. The surveillance unit passes this information to the public health department. Gene testing/counselling services managed by MRC Prion Unit at UCL	Age, gender, ethnicity, history of residence and employment, history of medical procedures and blood donation/transfusion	Support CJD families from diagnosis till death; Links CJD families with the support network; Clinician education/support; Funding for additional care services Research; Diagnostic testing; Brain tissue storage; Update guidelines	Compensation (unspecified) is provided to HPH participants if they develop CJD symptoms via a care package	CJD is not a notifiable disease. Surveillance arose from the government's response to vCJD	The Department of Health and NHS
US	-	Coordinates autopsies, performs diagnostic testing Positive cases are reported to the CDC; Registry contains data only from autopsies; CDC maintains a list of HPH participants.	-	Clinician education/support, research, encourage CJD families to attend conferences. In the future registry data will be used as a comparator for clinical trials	No compensation is available for HPH Participants who develop CJD	CJD is notifiable in some states only Hospitals do not screen for CJD patients prior to procedures No existing legislation to support HPH recipients	CDC funds certain states to undertake CJD surveillance and the National Prion Disease Pathology Surveillance Centre
Germany	Neuropathologist Blood pathologist	Discusses test results with clinicians Classification of CJD cases Clinicians notify health authorities of CJD cases	Age, gender, when symptoms started, how it progressed, CSF test results, MRI scans, previous medical procedures, family genetic tests, lifestyle, travel, profession, history of residence	Diagnostic testing, research, clinician education/support, organises logistics for brain autopsies but analysis is performed by other facilities; genetic counselling	No specialised government support as there were no HPH recipients	CJD is a notifiable disease	Funded by the government

	Personnel	Surveillance process	Data collected	Functions/services of the registry	Government obligations to HPH recipients	Legislation supporting CJD surveillance	Source of funding
Israel	Doctors Scientists	Registry refers suspected CJD cases to the national CJD clinic for testing and patient counselling; CJD cases are reported to the Ministry of Health	Genetic test results	The testing clinic stores genetic samples (blood) and CSF for national/international research;; PGD; clinician and patient education/support; organise conferences	No specialised government support for HPH recipients	CJD is a notifiable disease. Doctors do not need to obtain patient consent in order to run genetic tests	Not funded by the government All costs for tests are covered by the public health system
New Zealand	1 part time neurologist1 administration coordinator	Doctors notify the local office of health and the CJD Registry. Surveillance data is reported to WHO. The Registry can access patient clinical data if needed without consent. Post mortem tests are conducted in Australia and UK	History of medical procedures, history of blood donation, history of residence	Offer postmortem testing to CJD families, clinician education/support, counselling for CJD families, share reports to the ESR which manages the food supply	-	CJD is a notifiable disease	New Zealand Ministry of Health

Abbreviations: CDC, Centre for Disease Control and Prevention; CSF, cerebrospinal fluid; ESR, the Institute of Environmental Science and Research; HPH, human pituitary hormones; MD, medical doctor; MRC, Medical Research Council; MRI, magnetic resonance imaging; NHS, National Health Service; PGD, preimplantation genetic diagnosis; UCL, University College London; WHO, World Health Organisation

www.pwc.com.au

© 2021 PricewaterhouseCoopers Consulting (Australia) Pty Limited. All rights reserved.
PwC refers to PricewaterhouseCoopers Consulting (Australia) Pty Limited, and may sometimes refer to the PwC network. Each member firm is a separate legal entity.
Please see www.pwc.com/structure for further details. Liability limited by a scheme approved under Professional Standards Legislation.
WLT127082695