



# Dementia brain banking in Australia

NNIDR & Dementia Australia

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# 1 Executive Summary

The prevalence of dementia is increasing in Australia. Without a significant medical breakthrough, it is estimated that approximately 6.4 million Australians will be diagnosed with dementia in the next 40 years.<sup>1</sup> Researchers rely on access to well-characterised brain tissue to drive dementia research efforts, with some breakthroughs in types of dementia research only identified through access to brain tissue. Research efforts towards advances in treatment therefore depend on sustained access to brain tissue resources, with over 600 research publications resulting from brain tissue supplied by Australian brain banks between 2004 and 2014.<sup>2</sup> The existence of a sustainable brain banking capability within Australia is an important underpinning of Australia's research reputation and capabilities.

This review provides an analysis of the current state of brain banks contributing to dementia research in Australia and proposes a future state model for sustainable brain banking. It has been developed through extensive stakeholder consultation, documentation review and financial analysis. It explores the operations of the Victorian Brain Bank (VBB), Sydney Brain Bank (SBB), NSW Brain Tissue Resource Centre (NSW BTRC), Queensland Brain Bank (QBB), South Australian Brain Bank (SABB), and the Western Australian Brain Bank (WABB). The VBB, SBB and NSW BTRC provided documentation at different levels of detail (and in confidence) in response to data requests. Consultations yielded further information regarding VBB, SBB, NSW BTRC, QBB and SABB. Interview and data requests could not be secured from WABB due to the busy clinical workload of those involved.

## **Dementia brain banks in Australia face significant operational challenges and a unique funding challenge**

Dementia brain banks in Australia are currently functioning in a fragmented and unsustainable way, posing a risk to dementia research. Brain banks received funding from the NHMRC to operate under the umbrella of the Australian Brain Bank Network (ABBN) from 2005-2014, which resulted in a level of harmonisation. However, since the withdrawal of the NHMRC infrastructure funding, the ABBN has not been funded and the brain banks have operated in a fragmented way, largely independently of each other. Vestiges of harmonisation efforts remain today: brain banks have broadly consistent operational processes, with some exceptions, and share a cost recovery approach based on a pricing model developed under the ABBN. This has created varying levels of productivity across brain banks, with the SABB functioning at very low capacity and the QBB effectively closed. Without sustainable sources of funding, brain banks are restricted in their ability to provide researchers with reliable access to clinically, neuropathologically-documented and well-characterised brain tissue resources for dementia research.

The current state of brain banking presents some significant risks, two of which are critical:

- brain banks face a range of risks if services cannot be continuously provided to prospective donors and their families; these risks include credibility with the community, donors, donor families, government and other funders
- brain banks face a risk of failing to maximise the use of donated tissue if access for researchers is not sufficiently consistent and transparent and lacks high quality characterisation.

The specialised nature of dementia brain banking creates a unique challenge in securing sources of funding. Since tissue collection occurs after death, brain banking largely sits outside the state/territory funded standard healthcare collection protocols and funding structures. Moreover, the dominant funders of dementia research activity do not provide funding for research *infrastructure* such as brain banks. This leads to an ad-hoc approach to funding by individual institutions that is not sustainable. The resulting financial state of brain banking is variable across the individual banks and is unsustainable even for those banks receiving direct funding support. Information provided for this review indicates substantial reliance on in-kind support from research institutions. In some cases international funding for related research activities plays a role in subsidising the costs of operating a brain bank. Despite these challenges, staff

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<sup>1</sup> Alzheimer's Australia, Economic cost of dementia in Australia 2016-2056, Canberra, 2017.

<sup>2</sup> Catriona McLean, Jillian Kril and Claire Shepherd, NNIDR and Brain Banking, 2017.

expertise and commitment remain at a high level, with donor families and researchers generally reporting high quality service from the banks that are functioning at reasonable capacity.

### **International brain banks point to current good practice for brain banks and networks**

This review examines international brain banks such as the UK Brain Bank Network, Netherlands Brain Bank, BrainNet Europe consortium and the network of Alzheimer's Disease Research Centers in the United States. International models provide an indication of current good practice of individual brain banks and brain bank networks. These practices include funding incentivisation for achieving consistency and high quality across a network of banks, accessible inventories and associated information for researchers to make informed decisions about study design, and reliable access to neuropathological expertise to characterise tissue. Most notably, each of the international comparison banks and bank networks received substantial and long-term funding commitments from public sources.

### **A single entity is the most effective means to achieve sustainable dementia brain banking**

In examining options for a sustainable future state for dementia brain banking, this review identifies six critical features of successful brain banking:

1. Sustainability through secure sources of funding
2. Effective donor engagement that values donor contributions and provides a consistent donor experience
3. Ongoing access to neuropathology expertise for high quality characterisation of tissue
4. Ready accessibility for researchers accessing tissue samples
5. Harmonisation of standards to current good practice to ensure the consistency and quality of banked tissue
6. Effective data management strategies for handling and sharing data over the large timespan associated with donation and banking.

A single entity, operating as a hub and node model, would be the most effective means to deliver the six critical features of successful brain banking outlined above. A single entity would enable Australian brain banks to operate as a harmonised body, with consistent standards across tissue collection, processing, characterisation and storage. It would support a consistent experience for donors, who should remain at the centre of the brain banking process. By organising dementia brain banks in Australia as one body, access to tissue samples for researchers would be streamlined, supporting research outputs.

Operationally, a hub and node model for brain banking represents the most efficient allocation of resources for a single entity, while providing the geographic and population reach necessary to meet the needs of donors and their families. It would also provide researchers with a single consistent entry point for access to samples. The collection and processing of brain tissue would occur across different locations in Australia, with multiple nodes undertaking collection activities while the hub performs detailed sample preparation and neuropathological characterisation.

To examine the financial implications of operating as a single entity, this review developed a financial model. The model was constructed using a bottom up approach due to the limited financial information available from the brain banks, and the complex in-kind support arrangements for each. The model was compared to a similar single entity for which financial information was available – in this case the Netherlands Brain Bank.

Operating a single entity under a hub and node model will cost an estimated \$2.6 million per year based on current state activity. The model estimated costs for a single brain banking entity with one hub and six nodes. The current state estimate is drawn from the collective activity reported in the final ABBN report of 2014.

The estimated operating costs of the single entity compare favourably to the operating costs of the Netherlands Brain Bank, and staff estimates are comparable to the NSWBB. Future demand and supply are modelled, indicating a 17% increase in operating cost over 10 years. Cost recovery based on the current

2019 ABBN fees schedule is estimated to generate \$410,255 in revenue, or 16% of total operational expense with an average projected growth of 2% per year to \$499,304 in 10 years. The cost recovery model should be revisited once the new operating model is in place. Consideration will need to be given to what the research market can bear, in the context of what funding is available to support the brain bank operations.

### **Implementation of the single entity model will require an investment of time and money**

Bringing Australian dementia brain banks under a single entity will require an interim consolidation period. This period will include three phases:

1. Establishing the infrastructure for the single entity
2. Selecting the tissue to be included
3. Physically consolidating samples at the hub location(s).

A preliminary assessment of these phases indicates an additional investment of at least \$380,000 is required to conduct the initial consolidation of dementia brain banks in Australia.

### **Sources of funding for research infrastructure are currently limited in Australia**

This review has examined the current state of brain banking for dementia research in Australia and developed an optimal model for the future, together with the likely cost of that model and its implementation. It has also explored the sources of funding for a sustainable future for brain banking, through examination of available funding sources for research infrastructure and engagement with the key organisations in this space in Australia. At the conclusion of the review, there is no single source of funding that provides a way forward for brain banking in Australia. While support from research institutes is integral to brain bank operations, it is currently not sufficient to ensure a sustainable future. Support for research infrastructure remains a key gap in the future of dementia research in Australia.



## 2 Methodology

This review draws primarily on insights from stakeholder consultations, documentation provided by brain banks including financial data, and publicly available information. The review was developed using the following approach:

- analysis of the current state of dementia brain banks, considered through the lens of operators, users and potential donors
- examination of international good practice in brain banking
- development of a future state model including operational, governance and financial arrangements.

As part of this review, we consulted with a wide range of stakeholders including brain banks, federal and state governments, researchers, families of donors, Dementia Australia and those managing donor cohorts for research purposes (also known as cohort custodians). A total of 44 consultations were completed in the course of this review (Table 1). The review also benefited from engagement with a Reference Panel set up by NNIDR.<sup>3</sup> Significant interest was received from Dementia Australia advocates, of which seven were interviewed during the review. Stakeholders contacted for this review are summarised below and a full list located in Appendix A.

**Table 1 | Summary of stakeholder consultations**

Stakeholder category	Number of consultations
Australian brain banks	7
Donors and representative groups	9
Researchers	13
State and Australian Government representatives	9
International brain banks	3
Infrastructure relating to Australian brain banks*	3

\*including state operated biobanks and the Australian Dementia Network (ADNeT)

Operational dementia brain banks in Australia were consulted, including the VBB, the SBB, the NSW BTRC, the QBB and the SABB. Several attempts were made to interview staff at the WABB, which were declined due to their busy clinical workload. Non-dementia-specific brain banks were also consulted for this review to understand the difference between dementia brain banking and other forms of brain banking. Insights from stakeholder consultations were supplemented by documentation from brain banks, which was provided to the review in confidence.

The review also examined international brain banking models in the United Kingdom, the Netherlands, Europe and the United States. These models provided examples of good practice and were used to identify critical features of successful brain banking.

Options for the future state of dementia brain banking in Australia were considered as part of this review, which identified a single entity operating through a hub and node model as the most effective approach. This led to the development of a financial model to examine the financial implications of operating Australian dementia brain banks as a single entity. The model was constructed using a bottom up approach due to the limited financial information available from the brain banks, and the complex in-kind support arrangements for each. The model was compared to a comparable single entity for which financial information was available – in this case the Netherlands Brain Bank.

<sup>3</sup> A full list of NNIDR Reference Panel members is provided in Appendix A.

### 3 The case for dementia brain banking in Australia

Dementia is the second leading cause of death for Australians.<sup>4</sup> In the absence of a significant medical breakthrough, an estimated 6.4 million Australians will be diagnosed with dementia in the next 40 years.<sup>5</sup> Currently, approximately 244 people are diagnosed with dementia each day in Australia and the increased prevalence of dementia will have a significant impact on Australia's healthcare system and aged care sector.<sup>6</sup>

There is currently no cure for dementia, but the World Dementia Council has set the ambitious goal of identifying a cure or disease-modifying therapy for dementia by 2025.<sup>7</sup> Advances in dementia research have the potential to reduce the cost of dementia in Australia, which is estimated to reach \$36.8 billion in 2056.<sup>8</sup>

#### **Brain banks are an essential component of dementia research and support public health outcomes**

Dementia researchers rely on access to well-characterised brain tissue to drive dementia research efforts. The brain banks supply researchers with control and case tissue for research that may eventually lead to potential treatments for dementia. Some breakthroughs in types of dementia research including frontotemporal dementia have only been identified through access to brain tissue. Over 600 research publications resulting from brain tissue supplied by Australian brain banks between 2004 and 2014.<sup>9</sup>

Accurate dementia diagnoses can only be performed through access to brain tissue. Post-mortem diagnoses increase knowledge about dementia and help clinicians treating people living with dementia to make more accurate diagnoses when a person is first diagnosed.

#### **Brain banks underpin Australia's dementia research capabilities and reputation**

Brain banks hold a unique resource, reflecting the characteristics and disease prevalence of Australia's population. Brain banks stand distinct to other biobanks as samples are collected post-mortem and require significant specialisation to process and characterise samples.

Beyond the unique nature of the collection, brain banks are necessary in Australia to provide a resource to attract high-quality researchers to Australia, to ensure specialist neuropathology capability is retained and to facilitate Australian participation in international research.

#### **Brain banks offer key support for many types of research beyond dementia**

Brain banks contribute to the public health and research aims of many types of research including into neurodegenerative diseases and mental illnesses. While the scope of this report is limited to brain banking for dementia research, most brain banks hold diverse collections that contribute to many research topics and their value is significantly broader than their contribution to dementia research.

#### **Community involvement is key to dementia research; brain banking plays a significant role**

The involvement of people living with dementia, their families and carers is critical to dementia research. They may contribute through multiple channels including participation in longitudinal studies, clinical trials, or by choosing to donate their brain. Brain banking has the ability to heighten the engagement of people with dementia, their families and carers by allowing them to contribute to the future of dementia research. Brain banks need to play a key role in this community engagement and effective brain banks need to have the capacity to continue to involve the community in dementia research and ensure the contribution from potential donors is fully valued.

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<sup>4</sup> Alzheimer's Australia, Economic cost of dementia in Australia 2016-2056, Canberra, 2017.

<sup>5</sup> Ibid.

<sup>6</sup> Ibid.

<sup>7</sup> World Dementia Council, Defeating dementia: the road to 2025, 2018.

<sup>8</sup> Alzheimer's Australia, Economic cost of dementia in Australia 2016-2056, Canberra, 2017.

<sup>9</sup> Catriona McLean, Jillian Kril and Claire Shepherd, NNIDR and Brain Banking, 2017.



## **4 The current state of dementia brain banking in Australia**

### **4.1 Dementia brain banking is fragmented and lacks resources**

Dementia brain banks in Australia currently have no central operating or governance structure and insufficient and insecure ongoing sources of funding, which means that brain banks are operating largely independently of each other. This has created varying levels of productivity across brain banks, with the SABB functioning at very low capacity and the QBB effectively closed.

Resource constraints have impacted the functions of brain banks, particularly over recent years. Without sustainable sources of funding, brain banks are restricted in their ability to provide researchers with reliable access to clinically, neuropathologically-documented and well-characterised brain tissue resources for dementia research. Overall, the environment of substantial uncertainty means that the passion, expertise and hard work of committed staff is the major contributor to the reports from researchers and donor families of high quality service from the banks that are still operating.

#### **4.1.1 Australian brain banking was partially unified under the Australian Brain Banking Network**

Established in 2005 using funding of \$10.5 million over ten years from the National Health and Medical Research Council (NHMRC), the Australian Brain Banking Network (ABBN) aimed to integrate Australian brain banks through provision of dedicated staff and infrastructure. The ABBN led to the partial standardisation of procedures and some common approaches across the banks – such as a single website, a common entry point for researchers, standardised protocols and a cost recovery policy. However, the ABBN did not achieve full unification of the banks.

At the conclusion of NHMRC funding in 2014, the ABBN formally ceased to operate although the website continues to be maintained by the VBB to provide information for donors and researchers and to provide an entry point for researchers looking to access tissue.

### **4.2 Current brain banking arrangements are unable to meet supply and demand requirements**

SABB is operating at low capacity and, as a result, is no longer able to accept donations from all registered donors. The situation is similar in Queensland, with the QBB no longer functioning. The failure to honour donor intentions means that brain banks for dementia research are currently unable to keep up with supply uniformly across Australia. This risk is explored in more detail in Section 4.3.1.

A number of those consulted reported anecdotally that Australian brain banks for dementia research are unable to meet all research requests. This is challenging to quantify, as the presence of an informal application process prior to commencement of formal tissue requests means that the number of applicants turned away at this preliminary stage is not documented. However, multiple brain banks indicated that it is not possible to supply tissue for all requests due to limited tissue from regions of the brain in high demand, or because the requested neuropathology or characteristics requested are not available.

## 4.3 There are risks to the continuation of current state

The current state of brain banking cannot be sustained without risk, of which two predominate:

- brain banks face a range of risks if services cannot be continuously provided to prospective donors and their families, these risks include credibility with the community, donors, donor families, government and other funders.
- brain banks face a risk of failing to maximise the use of donated tissue if access for researchers is not sufficiently consistent and transparent, and lacks high quality characterisation.

These are considered in greater detail below.

### 4.3.1 The failure to honour commitments to donors and donor families presents a significant risk

Brain donation is by nature a highly personal and sensitive issue that involves deep generosity at an emotional time for donors and their families. Brain banks take on an ethical and moral obligation to honour commitments to donation and face a substantial risk in the community if the donor's intention is not honoured. Some families of donors have expressed through consultation that they wish to be kept informed of any findings emerging from the donation, with the knowledge that their family members' tissue is being used actively in research.

In consultation with the SABB it was heard that the inability of the SABB to accept new donations due to lack of resources resulted in dissatisfaction in the community in the form of ministerial letters and complaints. The consequences of a breakdown in community credibility has the potential to jeopardise community participation in dementia research, and medical research more broadly. This has implications for research outputs, as researchers depend on access to a diverse collection of tissue samples, which may be impacted by a lack of community support for brain banking. Researchers who manage longitudinal studies have advised that the closure of the QBB has restricted their ability to access brain tissue from some participants of their longitudinal study, due to the lack of staff to honour the donation request and collect tissue from Queensland-based donors.

### 4.3.2 Realisation of the full value of donations depends on consistent and transparent access for researchers

Researchers interviewed for this review noted variable experiences in accessing tissue and a lack of transparency when determining what tissue is available. This presents a risk to equitable access to tissue for research purposes. If structures are not in place to ensure that all researchers (regardless of their organisational affiliation) have consistent and transparent access, researchers with closer ties to the brain bank may receive preferential access. Review processes associated with formal tissue requests can mitigate this risk.

Researchers initiate the tissue request process by directly contacting individual brain banks or by placing an expression of interest through the ABBN website (which is then forwarded to the relevant brain bank). Brain banks in NSW and Victoria use Scientific Review Committees to determine researcher access to tissue, while in other states similar but less formalised processes are in place. The tissue request process requires multiple points of informal contact between researchers and the brain bank - to provide preliminary information prior to formal tissue request and in negotiations for access to tissue samples with the desired characteristics. Variable processes in each bank and dependence on case-by-case communication is likely to generate inconsistent practices and reduce the equality of access for researchers looking to use Australian brain tissue.

Researchers do not have access to a database detailing the relevant characteristics of inventoried tissue throughout the application process. The lack of a sufficiently detailed database of tissue made available to

researchers means that researchers are reliant on brain bank representatives to communicate what tissue is available that meets their research requirements.

The current bank-centric, personalised approach is time intensive for both brain banks and researchers and presents a risk of inconsistent access to tissue.

## 4.4 The newly established Australian Dementia Network has the potential to increase donor supply and improve data quality

From 2018 – 2023 the National Health and Medical Research Council (NHMRC) has committed \$18 million in funding to establish the Australian Dementia Network (ADNeT). ADNeT aims to link dementia researchers, clinicians and the community through a clinical quality register, a network of memory clinics and better links between clinical trials and potential participants. ADNeT presents potential opportunities to increase the supply of donors and improve the quality of data associated with donors.

### ADNeT could provide a single entry point for donor recruitment

One facet of the ADNeT aims to establish a database of people living with dementia willing to participate in clinical trials which contains a standard data set to aid the rapid selection of cohorts for clinical trials. Brain banking could potentially be integrated by including an option to consent to brain donation during the process of gaining consent for participation in clinical trials. If successful, this could provide a single entry point for potential brain donors and potentially facilitate a rapid increase in the number of registered donors.

ADNeT also aims to work with a number of memory clinics, in which processes and protocols are standardised. This could potentially improve the quality and consistency of clinical data associated with donations.

### ADNeT faces similar sustainability risks to dementia brain banks

Funding for the ADNeT commenced in July 2018 and will continue for five years. ADNeT is currently in developmental stages and is seeking to establish sustainability by the conclusion of the NHMRC grant in 2023. This presents sustainability risks similar to those experienced by Australian brain banks. ADNeT potentially represents an interface between people with dementia and cohort studies that brain banking could effectively partner with during donor recruitment and data collation. Any consideration of partnership with the ADNeT should be cognisant of these sustainability risks.

## 4.5 The current financial state of brain banking is unsustainable

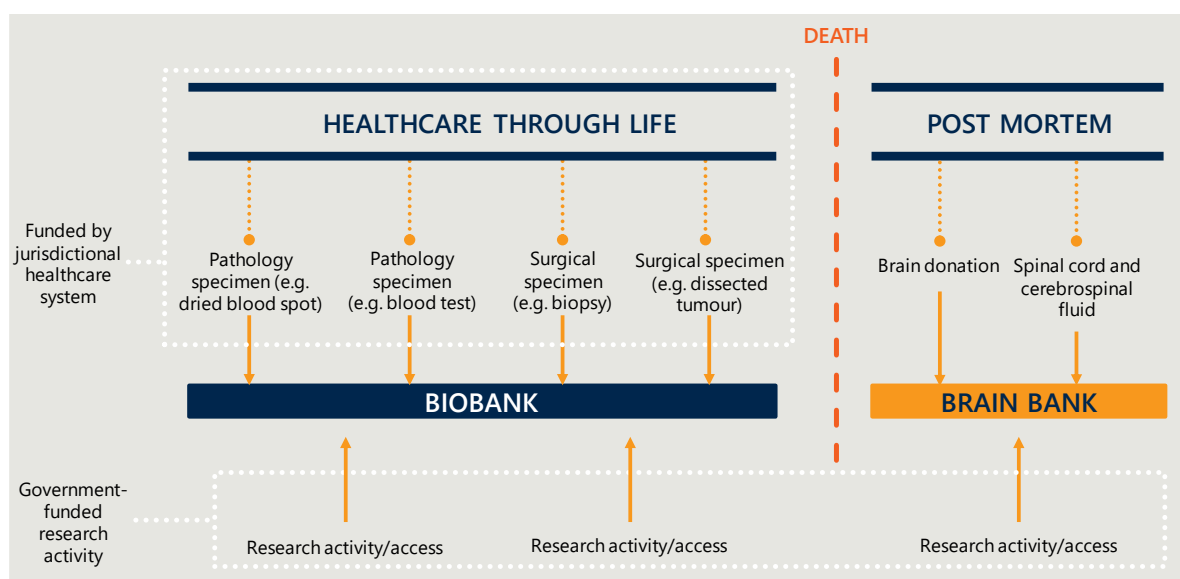
Brain banks are currently predominantly operating in an ad-hoc fashion, sourcing funding on a year-to-year basis to sustain operations. This is due to a unique funding challenge faced by brain banks and a limited availability of funding for research infrastructure, and manifests in brain banks operating under distinct funding arrangements and reliant upon in-kind support.

### 4.5.1 Dementia brain banking faces a unique funding challenge

Biobanks, regardless of tissue type collected, face funding challenges and tend to source funding from a number of direct and in-kind sources to remain operational. Biobanks collecting brain tissues face these funding challenges with added complexity, as tissue collection occurs after death and therefore sits outside of state/territory standard healthcare collection protocols and funding structures. The complexity of sample collection and preparation, and the logistics of sample storage further differentiate brain banking from other biobanks. From a research perspective, the dominant funder of dementia research activity is the NHMRC and potentially the Medical Research Future Fund (MRFF), which do not provide

funding for research infrastructure such as brain banks. This culminates in a funding gap, as shown in Figure 1.

Figure 1 | Unique funding gap experienced by brain banks



This gap is largely observable as a shortage of neuropathological and technical specialist time and expertise for the collection, processing and characterisation of brain tissue.

Funding for brain banks is generally received indirectly, with some exceptions. Indirect funding for brain banks includes the provision of space and equipment, largely supported by institutions exercising discretion in the use of infrastructure funds from government (both State and Federal), such as the Research Block Grant (RBG). Indirect support also includes staff time, such as coroners, health services and neuropathologists during sample collection and characterisation. This is explored more fully later in this section.

#### 4.5.2 Research infrastructure funding is limited

Research infrastructure funding is available in several forms in Australia, each form having discrete criteria and timeframes that would need to be considered in the development of a national-scale response to the challenge of dementia brain banking. The total quantum of research infrastructure funding is currently limited, introducing a further challenge.

Brain banking activity that establishes a resource accessible to the broader research community is a form of research infrastructure. The 2016 National Research Infrastructure Roadmap<sup>10</sup> defines research infrastructure as:

*...the nationally significant assets, facilities and services to support leading-edge research and innovation. It is accessible to publicly and privately funded users across Australia, and internationally.*

Research infrastructure funding is distinct from research project and program funding in Australia. At a Commonwealth level, infrastructure funding is provided through the National Collaborative Research Infrastructure Scheme (NCRIS), the Research Block Grant (RBG) component of the dual funding system,

<sup>10</sup> 2016 National Research Infrastructure Roadmap, Department of Education and Training.

and potentially through the MRFF. However, funding from these sources are insufficient, unavailable, or uncertain.

The NHMRC enabling scheme that provided infrastructure funding to the ABBN until 2014, was the last iteration of infrastructure funding from the NHMRC. This type of funding is no longer available from the NHMRC.

NCRIS is the Commonwealth's primary direct investment in infrastructure. However, it is unlikely the NCRIS funding will be available for any bio banking activity until 2023 at the earliest. The timelines for NCRIS are explored in more detail in Section 5.3.

The RBG scheme of funding to universities is provided to support the indirect costs of research, including infrastructure. However, this funding is generally considered insufficient, as confirmed by a recent House of Representatives Committee investigation into research funding in Australia.<sup>11</sup> In addition, this form of research infrastructure funding is deployed at the discretion of the recipient university to meet the needs of its researchers, and is therefore not suitable for strategic investments of national scale.

The MRFF does not currently provide funding for research infrastructure, however the 2019-20 Federal budget included a 10-year investment plan for MRFF that includes references to research and data infrastructure (see Section 5.3). Finalisation of the investment plan in 2019 will determine the applicability and availability of this funding for infrastructure activities.

#### 4.5.3 Dementia brain banks operate under distinct funding arrangements and rely on in-kind and institutional support

The dementia brain banks have funding arrangements that are often complex with varying levels of costs recognised by the banks' budget line, and other costs covered by host institutions. Broadly, the funding can be categorised into:

- **direct funds** which refers to funds received through grants, cost recovery measures and any internal revenue raising measures
- **in-kind funding for operational purposes** which refers to the provision of goods or services that would be accounted for as an operational expense
- **capital investment** which refers to the provision of long-term assets including research infrastructure equipment and commercial space.

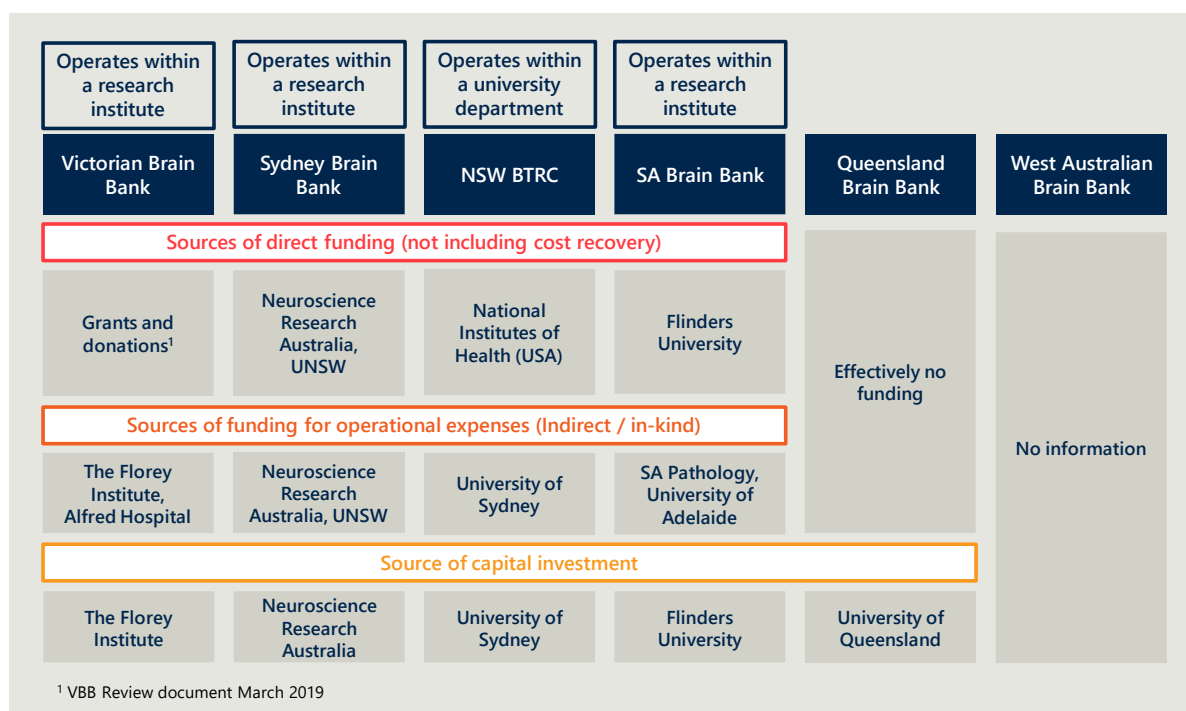
Each dementia brain bank receives funds in different proportions among the three categories and each from different sources. Figure 2 illustrates the breakdown of funding sources for each dementia brain bank. Qualitative data indicates that it is often the host institutions that provide a large proportion of the capital investment required.

For example, the Florey Institute of Neuroscience and Mental Health provides both the accommodation and infrastructure equipment for the VBB. Significant operating expenses are also often provided in-kind, including neuropathologist time for both the VBB and the SBB. In the VBB, the neuropathologist at the VBB only has an FTE of 0.1, with the remainder provided by Alfred Hospital. In the SBB, neuropathologists are not funded at all by the SBB. This diversity of funding and the gaps in financial data due to in-kind contributions means an accurate picture of the financial aspect of brain banking cannot be ascertained.

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<sup>11</sup> Standing Committee on Employment, Education and Training. Inquiry into funding Australia's research, 2018.

Figure 2 | A breakdown of funding sources for the Dementia brain banks



## 4.6 Each brain bank has similar structures, but unique features

There are currently six brain banks in Australia that collect tissue used for dementia research, as summarised in Table 2 below.

Table 2 | Summary of Australian brain banks for dementia research

Brain bank	Location	Operational status
NSW Brain Tissue Resource Centre (NSW BTRC)	Sydney	Operational
Queensland Brain Bank (QBB)	Brisbane	Effectively closed
South Australian Brain Bank (SABB)	Adelaide	Low functioning
Sydney Brain Bank (SBB)	Sydney	Operational
Victorian Brain Bank (VBB)	Melbourne	Operational
Western Australian Brain Bank (WABB)	Perth	No information provided

During this review, qualitative information was received through consultation with representatives from the NSW BTRC, the QBB, the SABB, the SBB and the VBB. Some quantitative information was provided by the NSW BTRC, the SBB and the VBB. No information was received regarding the WABB.<sup>12</sup>

Each brain bank has collections with differing focuses and scope; such as frontotemporal dementias and Parkinson’s disease in the SBB, Alzheimer’s Disease and psychosis at the VBB, and alcohol-related

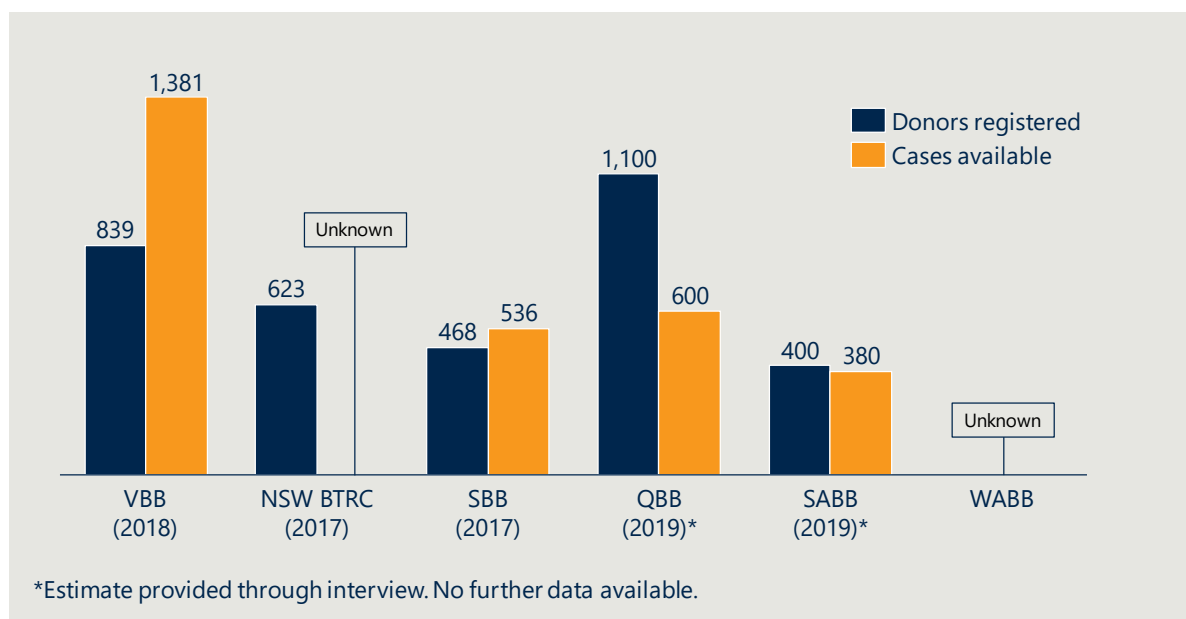
<sup>12</sup> Several attempts to elicit information through interview and data requests were unsuccessful due to the busy clinical workload of those involved.



disorders in the NSW BTRC and the QBB. The information below provides an overview of the entire collections held by brain banks that contribute to dementia research, not solely cases with some type of dementia diagnosis.

Brain banks in NSW and Victoria dominate in terms of both supply and demand, with each of the three brain banks in Victoria and NSW distributing over 3,000 tissue samples per year from approximately 60 tissue requests. The collection size and number of registered donors varies by bank and is not proportional to current activity. The number of registered donors and cases (that is donated brains, noting that one case will yield a large number of tissue samples) available for each Australian brain bank (where data is available) is summarised in Figure 3 below.

**Figure 3 | Summary of Australian brain bank activity**

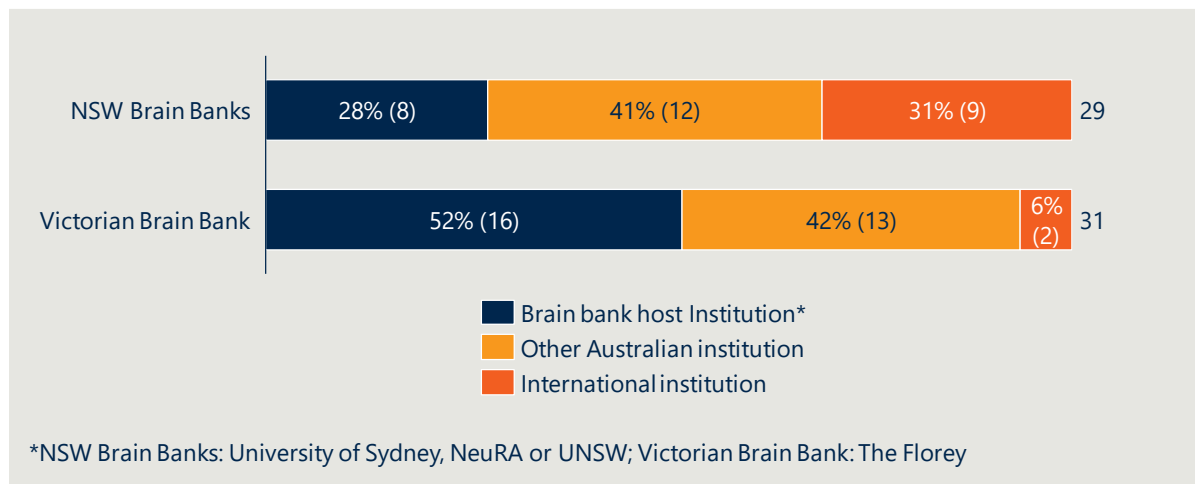


**Victorian and NSW brain banks field approximately 30 formal tissue requests per year**

The two states with fully operational brain banks field a similar number of formal tissue requests, as shown in Figure 4. International institutions comprise 31 per cent of NSW Brain Banks tissue requests, reflective of the international source of funding for the NSW BTRC from the NIH. Over half of tissue requests for Victorian Brain Bank come from its host institution, the Florey Institute of Neuroscience and Mental Health.

The results in Figure 4 are not a true representation of demand. The first instance of tissue request is an informal request that determines the availability of desired tissue, and this informal phase hides the number of unserviceable requests.

Figure 4 | Number of formal tissue requests by institution requesting tissue, 2017

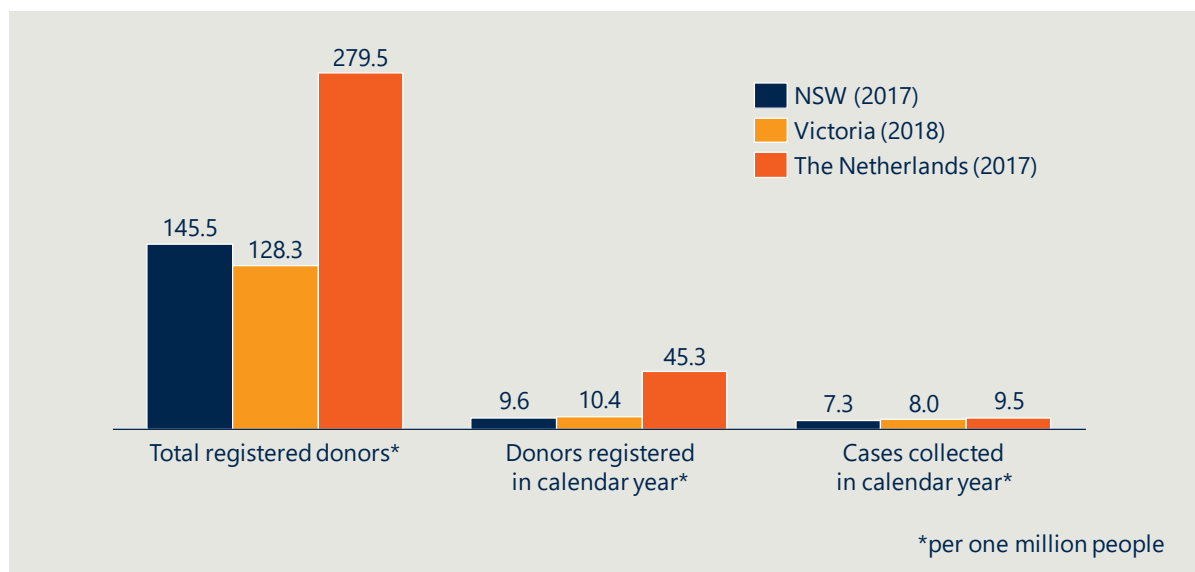


**NSW and Victorian case collection activity is comparable with the Netherlands Brain Bank, but donor recruitment lags**

Brain banks in NSW and Victoria bank approximately 100 cases per year, from a combined NSW and Victorian population of 14 million people. The Netherlands Brain Bank is a key example of international good practice and banks approximately 160 cases per year from a population of 17 million people. Considering the vast geographic distribution of the Australian population compared to the Netherlands, this level of activity is comparable.

The number of donors registered in the Netherlands far exceeds the number registered in NSW and Victoria, both in terms of total recruited donors and on the number recruited annually. Netherlands Brain Bank has a total of 4,752 registered donors, compared to a combined NSW and Victorian total of 1,930 registered donors. Per capita, fully operational Australian brain banks have half as many registered donors and are recruiting at a quarter of the rate (Figure 5).

Figure 5 | Comparison of operational Australian dementia brain bank and Netherlands Brain Bank activity, per one million people



## Australian brain banks contributing to dementia research participate in a number of networks

Australian brain banks have formed or participated in numerous networks to facilitate collaboration and coordinate processes:

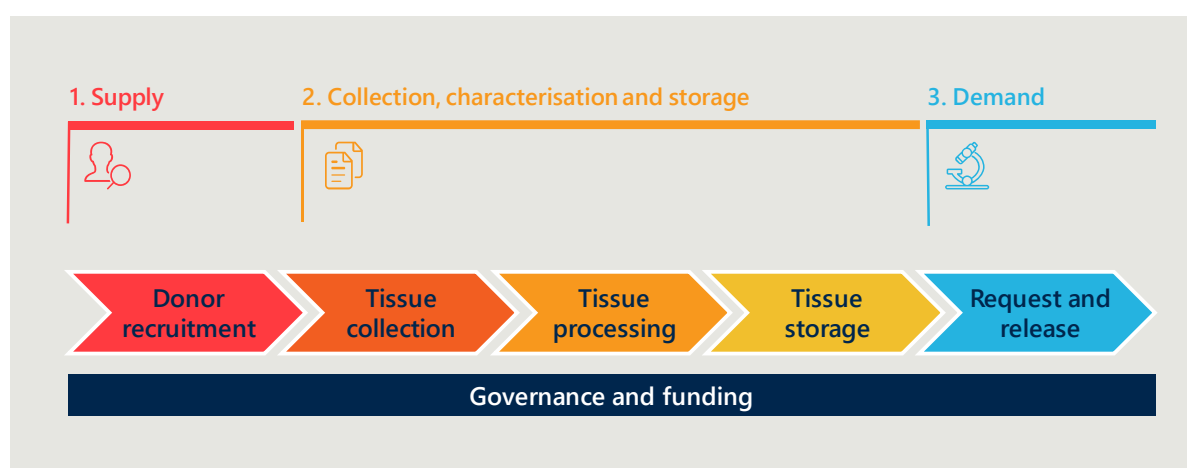
- **Australian Brain Bank Network (ABBN):** established in 2005 using funding of a total of \$10.5 million over ten years from the National Health and Medical Research Council (NHMRC), the ABBN aimed to integrate Australian brain banks through provision of dedicated staff and infrastructure. At the conclusion of the NHMRC funding in 2014, brain banks reverted to stand-alone operations, although the ABBN website continues to be maintained to provide information for donors and researchers.
- **NSW Brain Banks:** a formal arrangement between the SBB and the NSW BTRC, aiming to ensure that the operations of the two NSW brain banks are harmonised, effective and efficient. NSW Brain Banks coordinates the donor recruitment and researcher access processed for the SBB and the NSW BTRC.
- **Victorian Brain Bank Network (VBBN):** a network of brain banks in Victoria, including the Victorian Brain Bank, MS Research Australia Brain Bank and Victorian Neurotrauma Brain Bank. The Victorian Brain Bank is the sole contributor to dementia research in this network.

There are several other brain banks in Australia that interact with the brain banks included in this review, including the Australian Sports Brain Bank, the MS Research Australia Brain Bank and the Australian National CJD Registry. The MS Research Australia Brain Bank is newly established and has collected five cases to date across Australia, utilising the brain banks included in this review to collect and store tissue.

### 4.6.2 There are six key elements of brain banking

This review breaks down the process of brain banking into six steps, outlined in Figure 6. Broadly speaking, brain banking considerations are separated into supply (donor recruitment); the collection and characterisation of donated tissue (tissue collection, processing and storage); and demand (request and release). The entire process is underpinned by governance and funding arrangements. Brain banking is complicated by the long timespan and numerous players associated with banking a single brain. Effective data management is critical throughout all stages of the brain banking process to ensure that the many different types of data associated with a sample are linked to a sample, allowing researchers to perform high quality research with well-described samples.

Figure 6 | An overview of the brain banking process



Procedures in Australia for the collection, processing, characterisation, storage and distribution of brain tissue were partially standardised under the ABBN from 2004–2014, supported by the NHMRC enabling grant. Complete alignment of bank processes under the ABBN was not possible due to limited availability of resources and the diversity in size of individual brain banks in the network.

#### 4.6.2.1 Donor recruitment

Brains may be collected by recruiting donors ante or post-mortem. Ante-mortem recruitment allows for the collection of significant amounts of clinical and lifestyle data. Australian brain banks rely on a combination of ante-and post-mortem donor recruitment. Different banks use different approaches dependent on the networks, staff and institutional links available. The avenues for donor recruitment available to brain banks are:

- community engagement
- clinician referrals
- donor recruitment programs
- cohort studies (also referred to as longitudinal studies)
- post-mortem recruitment.

Donor recruitment programs refer to formal programs designed to recruit specific cohorts for brain donation. Cohort studies refer to longitudinal studies that collate data throughout the participant's life and may also link to brain donation.

Donor recruitment practices have a significant influence on the nature of the brain bank's collection. Donors are recruited from diverse channels, including community engagement or clinician referrals, which results in a wider range of disease cases collected, compared to donor recruitment programs and cohort studies that focus on the collection of cases for specific research aims.

Donor recruitment is a critical point of contact for the donor and donor families. It is crucial that the contribution from donors and their families is appropriately respected, and that potential donors are valued at this interface.

Engagement with donor families continues following the brain donation. Some families of donors have expressed a desire to be kept informed of any findings emerging from the donation, confirming that their family members' tissue is being used actively in research. Most research and ethics protocols requiring anonymisation of tissue samples prior to analysis. However, regular reporting back to donor families of the aggregate activities and outcomes of the brain bank's tissue collection should be a routine feature of brain banking.

#### 4.6.2.2 Tissue collection, characterisation and storage

Collection must occur as soon as possible after the donor's death to minimise post-mortem delay (the period of time between death and brain tissue collection) and ensure that the quality of the donated tissue is preserved. Brain banks achieve this through liaison with next of kin, hospitals, care facilities and funeral directors.

For a pre-consented donor, collection of samples begins when the brain bank receives notification of death from the next of kin, GP or nursing facility. A representative of the brain bank will liaise with the funeral director selected by the donor's family to arrange transport of the body to a mortuary for collection and back to the funeral home. A Designated Officer at the mortuary where collection is performed verifies consent for donation prior to removal of the brain. Brain banks can mitigate the cost of transport for collection through arrangements with funeral directors. Post-mortem tissue collection is governed at the state level and is therefore the details of tissue collection are specific to each jurisdiction.

After collection and transfer to brain bank facilities, the brain is processed, characterised and stored for future use. Generally speaking, the brain is separated into hemispheres and blocks are taken from each region of interest in the brain, half of which are frozen, and half fixed in formalin. The exact process differs by bank and by brain; brains with different clinical indications may be processed differently.

Once processed, fixed tissue is stored at room temperature, while frozen tissue is stored in -80°C freezers.

### 4.6.2.3 Release for use by researchers

Researchers seeking access to tissue follow the general process outlined below:

1. An informal enquiry is made by the researcher seeking access to tissue
2. Human research ethics approval is obtained from the host institution
3. A formal tissue request made through the brain bank or associated network
4. Application is reviewed by the brain bank
5. Researcher signs a Tissue/Material Transfer Agreement
6. Tissue is dispatched.

A number of characteristics can influence the selection of a tissue sample for research. Information required for a researcher designing experiments involving brain tissue may include diagnostic information, the brain tissue regions available, the post-mortem delay, and the type of processing performed on the tissue.

### 4.6.2.4 Governance and funding

Governance and funding impact every stage of brain banking operations. Brain banks may be governed through their host institution or through the primary providers of funding. For example, the SBB is joint funded by the University of New South Wales (UNSW) and Neuroscience Research Australia (NeuRA), and hosted by NeuRA. Funding may come from a range of sources, including:

- in-kind funding for service provision or access to infrastructure
- university/research institutions
- philanthropic grants
- public and memorial donations
- cost recovery.

Cost recovery efforts must comply with ethical guidelines that prohibit trade in human tissue.

## 4.6.3 Operational processes are broadly consistent, with exceptions

All brain banks for dementia research follow the broad structures laid out in Section 4.6.2. Brain banks in NSW and Victoria, being larger in size and operating at a higher level, tend to have more rigorously defined procedures.

There are two elements where marked differences between brain banks is apparent. Donor recruitment is possible through a wide range of channels and influences the composition of the brain bank inventory. Similarly, tissue characterisation varies by bank and influences the way in which brain tissue is used, both in isolation and with other tissue as part of cohort studies. Both are discussed in further detail below.

### **Donor recruitment channels influence inventory diversity**

Donors may be recruited through a range of structured and unstructured channels. Donors recruited through community engagement, clinician referrals and post-mortem are more likely to have a diverse range of pathologies than those recruited through donor programs and cohort studies that target particular diseases. Australian brain banks that contribute to dementia research recruit donors across the full spectrum of recruitment practices and therefore the collections held by each bank vary widely.

### **Tissue processing and characterisation methodologies affect the way brain tissue is used**

After autopsy, donated brains are sectioned into blocks of significant regions of the brain, each block is fixed or frozen, and neuropathological characterisation is completed. The results of characterisation carried out by a clinical neuropathologist may be used for both research purposes and passed on to the

clinician treating the donor prior to their death and their families. In brain banks where characterisation is carried out by a research neuropathologist, results are restricted to use for research purposes. Both models are currently employed by brain banks in Australia.

The extent of characterisation and the criteria applied for diagnosis of pathology is also variable across brain banks. Researchers accessing brain banks noted variation between banks in the degree of characterisation performed and the criteria used.

During its existence, the ABBN worked to standardise processing and characterisation methodologies across the brain banks. In practice, this was not possible to achieve completely due to variable bank size and resource constraints at individual brain banks.

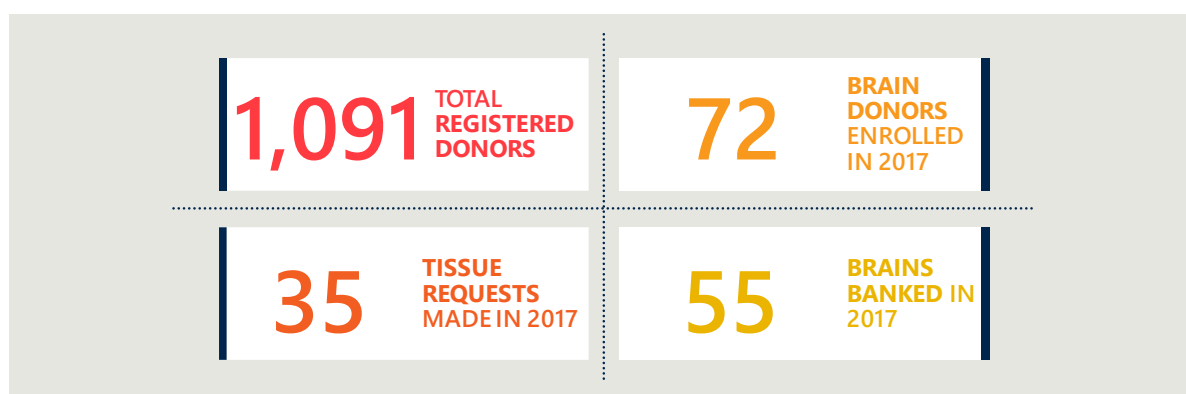
#### 4.6.4 Each Australian brain bank for dementia research has unique features

The unique features of each brain bank contributing to dementia research in Australia is considered in greater detail below.

##### 4.6.4.1 NSW Brain Banks

The SBB and the NSW BTRC are formally affiliated through NSW Brain Banks and have aligned a number of their processes. The joint NSW Brain Banks' activity in 2017 is summarised in Figure 7 below.

Figure 7 | NSW Brain Banks activity summary, 2017



The processes shared by the SBB and the NSW BTRC under NSW Brain Banks are summarised below, and the features unique to each bank in the arrangement highlighted.

#### NSW Brain Banks harmonises donor recruitment, governance and tissue access practices for the SBB and the NSW BTRC

##### Donor recruitment

NSW Brain Banks recruits all donors through brain donor programs which facilitate the collection of longitudinal clinical assessment data. NSW Brain Banks has 11 donor programs with a total of 1,091 enrolled donors as of end 2017. The Brain Donor Programs Committee reviews standardisation and good practice for recruitment strategies, longitudinal data collection and data storage to maximise the research outcomes on tissue collected by the NSWBB. Donors cannot be directly enrolled by the brain bank but must be a participant in a brain donor program.

Recruitment of donors through donor recruitment programs allows banks to target diseases of interest. It also facilitates the collection of large amounts of data in standardised forms. NSW Brain Banks' donor recruitment programs are reliant on competitive research grants. This presents a risk if the timeline of the grant is shorter than that of the recruitment process for a donor.



Access to post-mortem donors through the coronial system is currently not pursued in NSW. In general, access through the coronial system is dependent on the interpretation of the state-specific Coroner's Act.

#### *Governance*

Under the auspices of the NSW Brain Banks, the SBB and the NSW BTRC have a harmonised governance arrangement. The NSW Brain Banks Board acts as the overarching governing body, which ensures that the SBB and the NSW BTRC operations are harmonised. The NSW Brain Banks Board reports on operations and external funding to the Deputy Vice Chancellors (Research) and CEOs of the University of Sydney, UNSW and NeuRA. Budget and operational matters are overseen at the individual brain bank level. In the case of the SBB, this is performed by SBB Management Committee.

#### *Researcher access to tissue*

Researchers apply to access tissue through the NSW Brain Banks' website (and researchers placing an expression of interest through the ABBN website will be redirected to the NSW Brain Banks website). An overview of tissue available for access is provided on the website; further detail is provided after an enquiry has been submitted. Ethical approval is required at the time of tissue request. Tissue requests are evaluated by the Tissue Manager, then, if appropriate, passed on to the NSW Brain Banks Scientific Review Committee for scientific review. All tissue requests are reviewed in a standardised, confidential process; approval is based on the merit of the research project and the researcher's expertise.

When approval is granted, the relevant brain bank manager arranges a Tissue Transfer Agreement and the tissue is dispatched to the researcher. Cost recovery is performed in accordance with the ABBN schedule of fees updated annually and used by other brain banks.

NSW Brain Banks is not able to supply tissue for all requests due to limited tissue from regions of the brain in high demand, or because the requested neuropathology or characteristics requested are not available. NSW Brain Banks will work with the researcher to find a suitable compromise where possible.

#### **NSW Brain Banks operate largely outside of the state health system**

The SBB and the NSW BTRC are funded solely through research channels and do not rely on the hospital system for staff funding or tissue processing. An exception to this is during tissue collection, when the SBB links with hospital mortuary services for support relating to the autopsy process. Tissue collection is performed by SBB staff but is overseen by mortuary pathologists.

In NSW, diagnostic reports are required for all post-mortems. The brain tissue and associated research reports are provided to the overseeing hospital pathologists for diagnostic reporting purposes.

#### **Sydney Brain Bank is supported by two research institutions**

The SBB is operated under a cooperative agreement between the UNSW and NeuRA, with NeuRA responsible for managing the SBB operations. NeuRA has committed funding for 5 years<sup>13</sup> while the UNSW funding for the SBB will expire at the end of 2020. SBB currently receives \$625,000 per annum which covers staff salaries and running costs including laboratory consumables, body transport and minor equipment.

SBB focuses on research into neurodegenerative diseases and collects approximately 40-50 cases per year. It has a small collection of control cases and is predominantly reliant on other banks to provide control tissue.

The personnel supporting the SBB operations are described in Table 3.

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<sup>13</sup> NSW Health provides funding to NeuRA; an example of the way in which state governments contribute to brain banks through the host institution.

**Table 3 | SBB personnel**

Position	FTE	Responsibilities
Director	0.8	Oversight of resourcing, management and quality assurance, chair of Management Committee, perform case characterisation
Manager	1.0	Day-to-day operations, management of tissue request processes
Research Officer	1.0	Collection of neural tissue at post-mortem, dissection and sampling of tissue for characterisation, manage the NeuRA Volunteers Brain Donors program, secretarial duties associated with NSW Brain Banks Scientific Review Committee
Research Assistant	1.0	Processing of tissue, assisting the SBB Manager with tissue requests, back up for tissue collection, supervision and support of students and staff using the laboratory
Laboratory Assistant	0.4	General laboratory and equipment maintenance, assisting with routine tissue preparation
Liaison Officer	0.6	Oversight of the SBB donor registration procedures, liaison with brain donor coordinators, brain donors and relatives, and other health care providers as required
Research neuropathologists	Not funded by the SBB	Case characterisation

The Director of the SBB reports to the Management Committee regarding management and performance, and to the CEO of NeuRA for operational matters.

#### **NSW Brain Tissue Resource Centre provides control tissue for dementia research**

NSW BTRC is hosted by the University of Sydney Discipline of Pathology. The primary focus of the NSW BTRC is to support research into brain changes relating to alcohol use and mental health disorders and the collection of healthy control tissue. NSW BTRC has been almost entirely funded through a National Institutes of Health (NIH) R24 competitive grant for research into alcohol and alcoholism of approximately \$500,000 AUD per annum since 2000.

NSW BTRC supports dementia research through the provision of control tissue via its affiliation with NSW Brain Banks.

#### **4.6.4.2 Queensland Brain Bank**

No financial information or operational documentation was provided for analysis in this review. The content below relies solely on consultations with former staff and others with links to Queensland Brain Bank.

#### **QBB has been closed, but limited activity continues**

QBB is housed in the University of Queensland, but the university has formally 'closed' the brain bank and requires the stored tissue to be moved. Alternative facilities are currently being sought for the stored tissue. Queensland Health has reportedly indicated that it will support the transfer of the brain bank to another institute. In the meantime, the frozen samples remain essentially in limbo.

Despite the closure of the QBB, some activity is continuing. The bank continues to receive donations and perform a limited number of autopsies. Consultations indicated that the operational status of the bank is

not clear to researchers or donors. Cohort custodians who manage longitudinal studies have advised that the closure of the QBB has restricted their ability to access brain tissue from some participants in their longitudinal study, due to the lack of staff to honour the donation request and collect tissue from Queensland-based donors.

When the brain bank was operational, donors were recruited through community engagement and word of mouth. The bank maintained a database of over 1,100 registered donors, and 10 to 20 tissue requests were approved per year.

#### **QBB has no funding**

There are currently no funding sources for the brain bank. QBB had previously received funding from the NIH for research relating to alcohol abuse and from the ABBN arrangement.

Cost recovery was put in place when the QBB was a part of the ABBN, but the current director of QBB reported challenges with researchers unwilling to pay cost recovery fees.

#### **4.6.4.3 South Australian Brain Bank**

SABB was established in 1986 and joined the ABBN upon its formation. Originally established as a brain bank to support research into Parkinson's disease, the SABB expanded its collections to include other disease categories using funding received under the ABBN. The collection is currently broadly focused, with approximately 200 cases with some form of dementia and 10 control cases.

SABB offices and laboratories are located within the Flinders Medical Centre, and the brain bank is administered through Flinders University.

No financial information or operational documentation was provided for analysis in this review. The content below relies solely on consultations with staff and others with links to the SABB.

#### **SABB is effectively closed**

SABB has historically been staffed by a coordinator, a manager and a research assistant. The manager role has been unfilled since 2016 and cannot currently be filled due to funding constraints. In addition, access to neuropathology services for tissue characterisation has become limited. As a result, the SABB is low functioning. SABB is no longer recruiting new donors and is currently accepting brain donations from previously registered donors on a discretionary basis only.

#### **Lack of access to neuropathological expertise is a significant barrier to effective operations**

Previously, the SABB relied on the provision of in-kind support from SA Pathology for neuropathological characterisation. This support has been scaled back in recent years, as the work sits outside the core duties of SA Pathology staff. Some neuropathological characterisation services continue to be provided by an original founder of the SABB who now has an honorary appointment at the University of Adelaide. The reliance on a single semi-retired neuropathologist for characterisation work has resulted in a two-year backlog of tissue pending characterisation.

#### **Donations from existing registered donors are being accepted on a discretionary basis**

In recent years, resource limitations have forced the SABB to become discretionary about receiving brain donations from existing registered donors. SABB continues to try to honour the intent of donation where possible. In situations where it is not possible to honour a donation, community concern has been demonstrated through complaints and ministerial letters submitted after donations could not be honoured. This illustrates the significant credibility risk inherent in the current state of brain banking in Australia.

When the bank was fully operational, donor recruitment was performed through community engagement activities organised by the SABB manager. Those interested in recruitment were provided with an information pack including consent and donor information forms which were completed and returned to the SABB coordinator. At present, recruitment of new donors has ceased entirely.

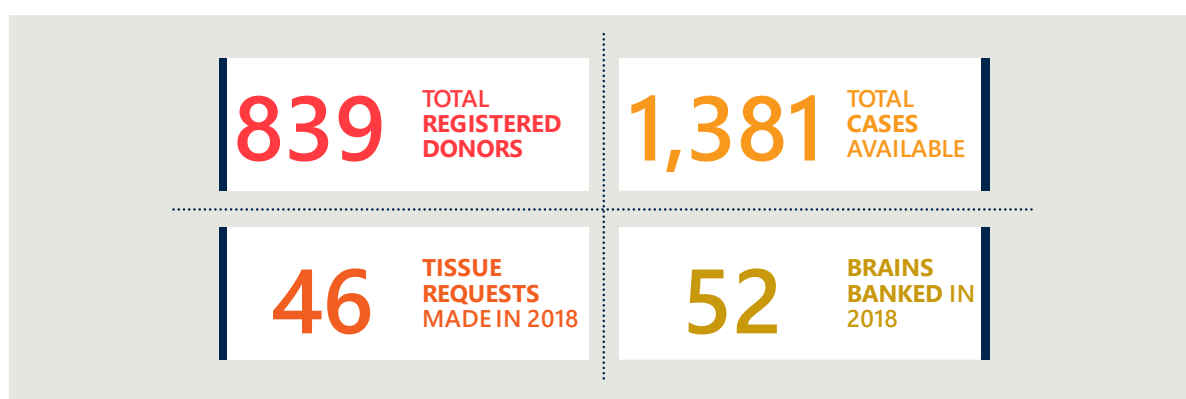
### Current funding is provided on a year-to-year basis

Limited funding provided by Flinders University on a year-to-year basis, combined with public donations, allows the bank to continue to operate at a low level. Underlying infrastructure support is provided by Flinders University and limited additional in-kind support is provided by staff from SA Pathology, who support tissue collection efforts on an as-needed basis. SABB uses the ABBN recommended schedule for cost recovery for tissue provided to researchers, noting that a fee discount is applied to smaller local research groups.

#### 4.6.4.4 Victorian Brain Bank

Victorian Brain Bank was originally established to support research groups with interests in schizophrenia and depression. It holds a diverse collection and acted as the recipient of the ABBN enabling grant funding. The VBB provided significant operational and financial information to this review, and as such is assessed in greater detail than other brain banks. VBB's activity in 2018 is summarised in Figure 8 below.

Figure 8 | VBB activity summary, 2018



#### VBB relies on its connections with research and clinical specialists for donor recruitment

VBB receives donor tissue through three primary processes: referral of potential donors by clinicians; collaboration with observational and longitudinal research studies; and through collaboration with the Donor Tissue Bank of Victoria (DTBV) for coronial cases. The VBB also fields direct enquiries from potential donors and their families.

For referral of potential donors, the VBB relies on neurologists, psychiatrists, geriatricians, specialist consultants and disease-specific associations. Potential donors are directed to contact the VBB and assessed against set criteria to determine their suitability before registration. A donor questionnaire is sent at this stage which collects details such as lifestyle factors, family history, current diagnoses, GPs and specialists, and other information about the donor.

VBB also works with a number of Australian and international observational and longitudinal research projects, linking information gained during these studies with the results of research conducted on donated brain tissue.

VBB works with the DTBV located at the Victorian Institute of Forensic Evidence for post-mortem donor recruitment. DTBV screens coroner's cases to identify potential cases for the VBB collection, obtains authorisation from the Coroner and Forensic Pathologist, then contacts the next of kin to obtain consent. DTBV performs the collection of the brain and cerebrospinal fluid in the presence of VBB staff before transfer to the VBB for sample processing and analysis.

VBB's broad range of donor recruitment strategies means that the brain bank collection is diverse in nature.

When a donor is recruited they are provided with information about the donation process through interviews with brain bank staff or through information packs before signing donor consent forms. The

consent forms are then filed (a copy retained by the donor) and must be sighted prior to collection of tissue. For post-mortem recruitment, consent is sought from next of kin with permission from the coroner. The donation is acknowledged four weeks after donation through a letter sent to the donor family from the VBB director.

### **VBB's approach to donor recruitment encourages clinician use of neuropathology diagnostic services**

After collection, characterisation and clinical diagnosis of collected brain tissue is performed by a clinical neuropathologist. Information is supplied to researchers accessing samples and a clinical diagnostic report is provided to the treating clinician to use or pass on to surviving family members.

### **Processing and data storage procedures are standardised at the VBB**

All processes associated with brain collection, tissue processing and characterisation are standardised to ensure consistency in the inventory where possible. Autopsy is performed at the Alfred Hospital, and macroscopic processing is performed at the Florey Institute of Neuroscience and Mental Health. A collection of 12 blocks are taken from regions of interest, alongside an additional four taken if the spinal cord is collected.

Data held by the VBB exists in the form of paper files, electronic records and photographs. Paper files such as consent forms, clinical data and neuropathology reports are stored in duplicate in secure areas with restricted access. Electronic data includes donor details and is stored using a dedicated database.

### **Researchers apply for access to tissue directly through the ABBN or the VBB websites**

The ABBN website continues to be maintained, despite the dissolution of the ABBN when funding ceased in 2014. Requests for access to brain tissue can be made through the ABBN website, or directly to the VBB. The VBB acts in line with the National Access Policy developed by the ABBN. The researcher is required to submit a formal tissue application along with proof of ethics approval for the research project. The application is vetted by the VBB Coordinator, then scientific review is completed by the Scientific Review Committee and evaluated for scientific merit, feasibility and availability of requested tissue. Upon approval, the researcher signs a Material Transfer Agreement and tissue is dispatched. Cost recovery for tissue is charged as per the ABBN schedule, which continues to be updated annually.

The VBB requires that it is acknowledged in all written and oral presentations and publications arising from the use of the VBB tissue. As part of the scientific review process, the requirement for the VBB to be listed as an author on research outputs is assessed.

### **VBB is governed by the Florey Institute of Neuroscience and Mental Health**

The VBB is a platform within the Florey Institute of Neuroscience and Mental Health. It is also affiliated with the Alfred Hospital, the Victorian Institute of Forensic Medicine and the University of Melbourne. The VBB Management and Operations Committee is responsible for overall operations and reports to the Head of Scientific Operations at the Florey Institute of Neuroscience and Mental Health.

The VBB covers operating costs through a number of avenues, including:

- the Florey Institute of Neuroscience and Mental Health covers infrastructure costs including laboratory and storage space, utilities and freezer alarm systems
- funeral directors provide in-kind support for transport to and from mortuary
- philanthropic grants
- research grants that incorporate the direct research cost for accessing brain tissue
- public and memorial donations
- cost recovery, as according to the ABBN schedule which continues to be updated annually.

VBB staff are predominantly funded by the Florey Institute of Neuroscience and Mental Health, with 1.6 FTE distributed across three staff members as described in Table 4.

**Table 4 | Distribution of the VBB operational responsibilities**

Position	FTE	Responsibilities
Director/Neuropathologist	0.1	Oversight, neuropathology services
Coordinator	0.5	Operational processes including donor recruitment, tissue collection and data collection
Research Assistant	1.0	Sample processing and storage

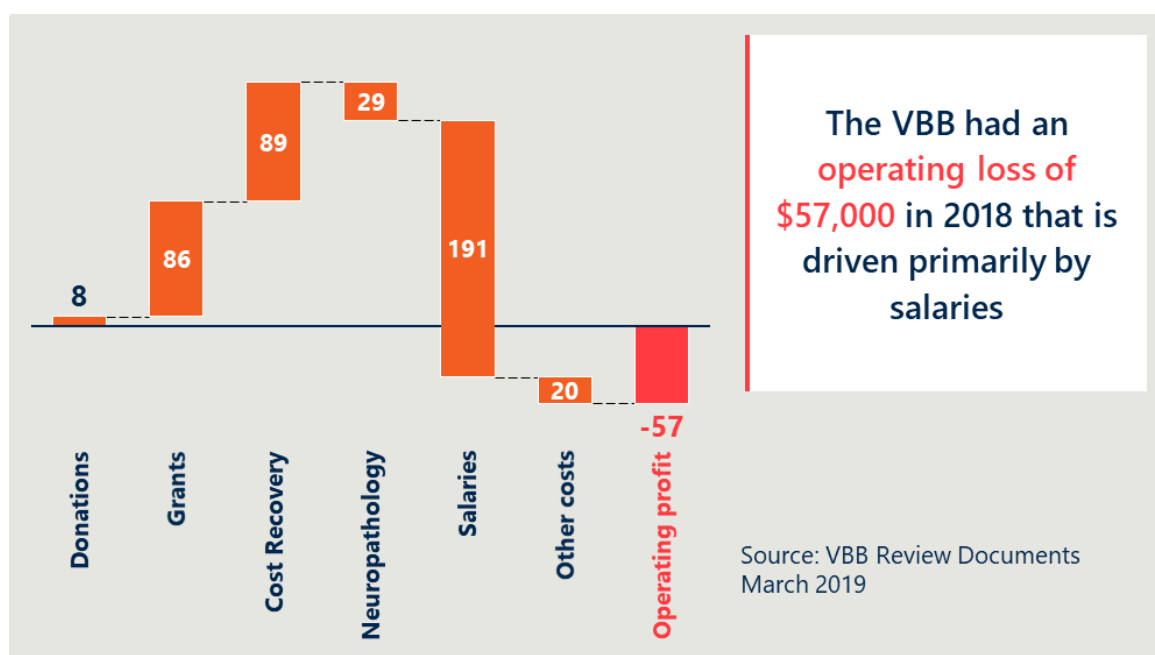
A significant amount of work completed by the VBB Director/Neuropathologist is not covered by the above allocation.

**The VBB operated at a loss in 2018 and relies extensively on in-kind funding**

The 2018 cash flow statement of the VBB indicates that the VBB had an operating loss of \$57,000, or an operating profit margin of **-32%**. Salaries account for 80% of operating expenses and is greater than the cash raised in 2018. See Figure 9 for a summary of the VBB’s income and operating expenses.

Given that the VBB receives extensive in-kind support from the Florey Institute of Neuroscience and Mental Health and coupled with its negative cash position, the financial position of the VBB is currently non-viable.

**Figure 9 | VBB income and expenditure 2018 (\$ '000)**



**The NHMRC Enabling Grant formed a significant portion of the VBB’s annual funding from 2003-2014**

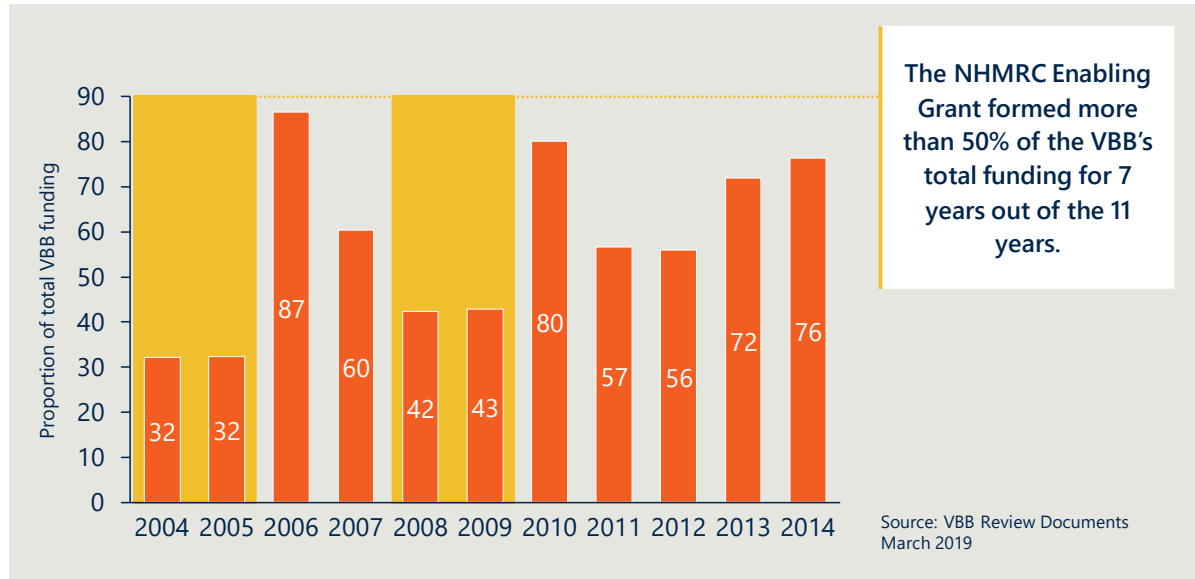
Examining the funding of the VBB from 2003 to 2014, the VBB was a recipient of the NHMRC’s Enabling Grants from 2004 to 2014 where they received:

- \$97,500 annually from 2004 to 2009
- \$189,000 from 2010 to 2014.



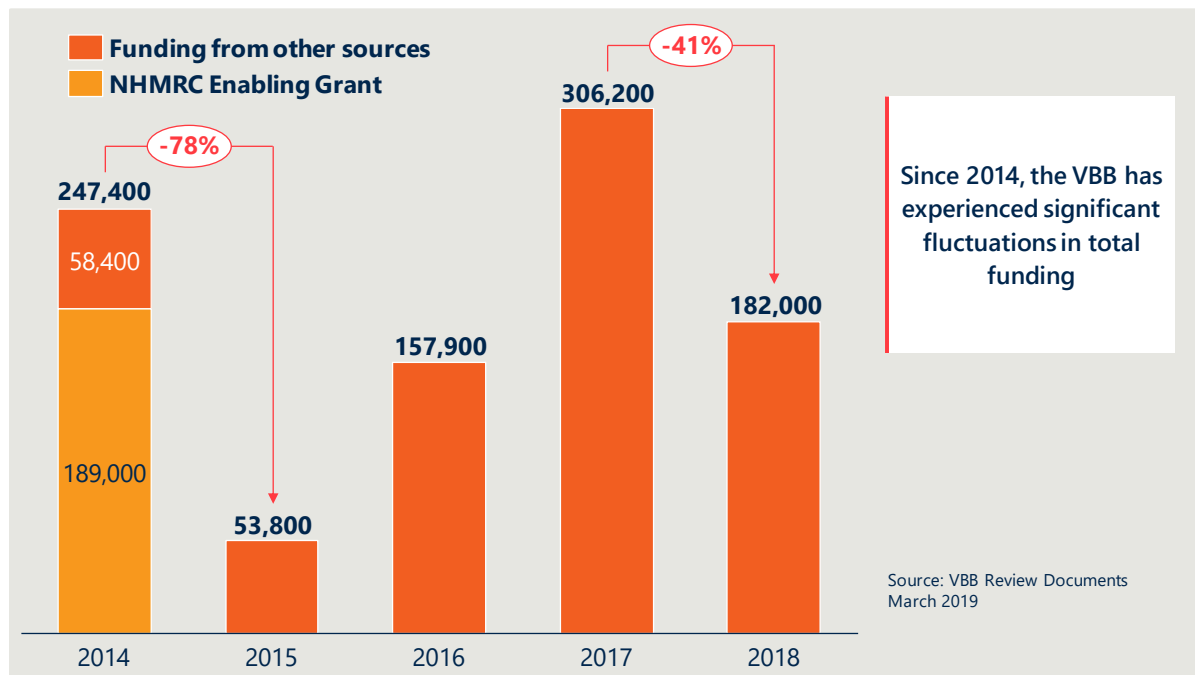
The Enabling Grant formed an average of 58% of the VBB's annual funding. In the 11 years that the VBB received this grant, it formed more than 50% of the VBB's total funding for 7 of those years. See Figure 10 for a breakdown of the proportion of the Enabling Grant of the total funding.

Figure 10 | Proportion of NHMRC Enabling Grants to VBB's total funding from 2003 to 2014



Examining at the total funding that the VBB received from 2015-2018, there are large fluctuations in total funding year-on-year and this indicates that the VBB has not secured consistent funding in the absence of the grant (Figure 11).

Figure 11 | Analysis of the VBB's total funding from 2014 to 2018



#### 4.6.4.5 Western Australia Brain Bank

No information was available regarding the WABB for this review.<sup>14</sup>

## 4.7 International good practice points to key success factors for brain banks

Examination of the UK Brain Bank Network, Netherlands Brain Bank, BrainNet Europe consortium and the network of Alzheimer's Disease Research Centers in the United States provide an indication of current good practice of individual brain banks and brain bank networks. An overview of each is highlighted below.

### 4.7.1 UK Brain Bank Network

The UK Brain Bank Network is a network of ten nationally coordinated brain banks supported by the UK Medical Research Council (MRC). Brain banks participating in the network harmonise protocols for consent, tissue handling and storage, quality indicators and the access to tissue samples. Partial performance-based funding incentivises harmonisation of protocols.

Banks in the UK Brain Bank Network operate on a mixed funding model. Running costs are subsidised by host institutions (approximately 30 – 40% of total costs), while remaining costs are covered by a number of sponsors including the MRC, NHS Trusts, philanthropic donations and cost recovery.

#### **Performance based funding incentivises process standardisation**

The UK Brain Bank Network distributes a proportion of funding under a performance-based model. This is designed to incentivise brain banks to collect cases and release tissue to researchers, as well as incentivising the standardisation of processes. Process standardisation increases the consistency of tissue and data in the UK Brain Bank Network Inventory, making tissue from various banks more readily integrated into single research studies and maximising the value of donated tissue.

### 4.7.2 Netherlands Brain Bank

The Netherlands Brain Bank (NBB) is the sole brain bank in the Netherlands. Aided by the country's small size (and single jurisdiction), all autopsies are performed in Amsterdam. Five staff members at a time work on a 24/7 roster. The bank operates independently and works to ensure consistent experiences for donors and researchers. The NBB communicates with registered donors and the wider community through a publicly available annual report and a newsletter sent to registered donors that shares major findings of studies that depend upon brain donations.

#### **Cost recovery forms the majority of the NBB funding**

The NBB receives a total of approximately €1,000,000 p.a., of which 20 per cent is comprised of government-provided structural funding provided through the Royal Netherlands Academy of Arts and Sciences (KNAW). An additional 20 per cent of funding is provided through patient organisations, foundations and private donations. The remaining 60 per cent of costs are covered primarily through cost recovery.

Different fee schedules are offered for research and commercial users; commercial users are charged significantly more for access to brain tissue. The NBB is able to charge a high fee for tissue due to the consistency and quality of brain tissue (particularly, low post-mortem delays due in part to legality of

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<sup>14</sup> Several attempts to elicit information through interview and data requests met with no response due to the busy clinical workload of those involved.

euthanasia in the Netherlands) in its inventory. A similar fee schedule would be very difficult to replicate in Australia due to the different legislative environment, a relatively limited commercial user base, and in the context of a network operation across multiple, geographically dispersed brain banks, which is proposed in Section 5.2.

### 4.7.3 BrainNet Europe Consortium

The BrainNet Europe consortium is a network of 19 European brain banks, coordinated by the Centre for Neuropathology and Prion Research, Ludwig Maximilians University Munich, Germany. Established in 2001, BrainNet Europe was funded by the European Commission for 5.5 years. During this time, it established 25 work packages to investigate good practice in various components of brain banking including data protection, tissue sampling, donor programs, and brain bank organisation. Among other achievements, BrainNet Europe has harmonised neuropathological diagnostic criteria including tissue sampling and published standards for quality, safety and ethics for obtaining and handling human tissue. The NBB has played a key role in the BrainNet Europe consortium, setting a quality benchmark for global brain banking.

### 4.7.4 United States' Alzheimer's Disease Research Centers

Alzheimer's Disease Research Centers (ADRC) are a network of research centres funded by the National Institute on Aging, a division of the United States' National Institutes of Health. There are over thirty Alzheimer's Disease Research Centers located at medical institutions across the United States, with the National Institute on Aging committing \$16 million USD to fund an additional five to seven centers.<sup>15</sup> Individual ADRCs have their own particular area of focus, for instance the Stanford ADRC focuses on both Alzheimer's disease and Parkinson's disease.<sup>16</sup> ADRCs collect and store data from clinical trials, studies and patient registries. The National Alzheimer's Coordinating Center (NACC) is exploring the creation of a national database of standardised clinical and neuropathological research data collected from the ADRCs across the United States. At this time, the NACC collects and collates data from the individual centre websites to provide a single access point for researchers. A comprehensive, open-access national database would rely on an effective data management strategy, which in turn would depend on appropriate funding and collaboration between brain banks. Effective data management is one of the critical features of successful brain banking discussed below.

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<sup>15</sup> National Institute on Aging, New Opportunities announced for next-gen Alzheimer's Disease Research Centers grants, 2018, available at: <https://www.nia.nih.gov/research/blog/2018/02/new-opportunities-announced-next-gen-alzheimers-disease-research-centers>

<sup>16</sup> Stanford Alzheimer's Disease Research Center, About the Standford ADRC, 2019, available at: <http://med.stanford.edu/adrc.html>

# 5 Options for the future state of dementia brain banking in Australia

## 5.1 There are six critical features of successful brain banking

Analysis of brain banking operations in Australia and internationally gives rise to six elements that are critical to effective brain banking:

### 1. Sustainability through secure sources of funding

Access to secure and sustainable funding is integral to maintaining stability; a particularly critical feature due to the long-term nature of brain donation. Sustainable funding mitigates the reputation risk and ensures that a donor's intention to donate can be honoured. Fragmentation of the current state of brain banking for dementia research is due in a large part to funding constraints.

### 2. Respectful and timely communication with donors and their families

Donors and their families must be at the centre of the brain banking process. Without appropriate support and engagement that respects and values their contribution, brain banking and dementia research will flounder. Donors and their families must be provided with appropriate information and support throughout the brain banking process. This will require dedicated resources to ensure specific communication and support roles to engage with donors and their families.

### 3. Ongoing access to neuropathology expertise for high quality characterisation of tissue

Neuropathology expertise is required for the characterisation of donated tissue and is critical to maximise the usefulness of donated tissue. There is a shortage risk of neuropathology expertise both nationally and internationally due to limited career progression and training opportunities. This risk must be managed through succession planning and other means to ensure ongoing Australian capability and maximise the value of donated tissue through high quality characterisation.

### 4. Ready accessibility for researchers accessing tissue samples

Readily accessible information about existing inventory allows researchers to design experiments appropriately, apply for funding and engage ethics committees; and reduces time spent by brain bank staff in fielding enquiries. Ready accessibility also implies transparency; allowing for an unbiased platform for researchers to access tissue.

### 5. Harmonisation of standards to current good practice to ensure the consistency and quality of banked tissue

Consistency between banks is desirable to maximise the value for researchers accessing tissue from multiple banks. Harmonisation of standards allows researchers to access tissue from multiple banks while minimising confounding factors that arise from differences in processing and have the potential to affect research quality. Harmonisation also allows the collective banks to fill sample requests more efficiently – making better and more complete use of inventory.

Harmonisation of standards encompasses consistency in processing, clinical diagnoses and characterisation criteria, the type of data collected (such as case characterisation information and photographs) and how it is made searchable for future use. This process should remain sufficiently flexible to change in line with evolving good practice.

### 6. Effective data management strategies for handling and sharing data over the large timespan associated with donation and banking

Brain banks collect data from numerous sources. Prospective donors are asked to complete a questionnaire during registration, treating clinicians provide ongoing medical information, cohort studies may contribute information, and significant information is collected during processing and characterisation of donated brain tissue. This data collation process may span many years. Data

management strategies must account for the large timespan, range of data sources, and privacy requirements for medical data. Data management strategies must be flexible to account for future changes and be prepared for data stored to outlive data management infrastructure.

An effective data management strategy features the following:

- data from every stage of the brain banking process is linked for a given sample, and the management system is capable of processing data from many sources
- data is consistent across samples to allow researchers to make use of the information
- data management remains flexible to adapt to changing good practice in processing and characterisation
- data is handled in a secure and ethical fashion suited to its degree of sensitivity.

Consideration should also be made as to whether data generated through research use of donated tissue may be linked back to banked samples for future use.

## 5.2 A single operational entity is the most efficient and effective model for Australia

The review of dementia brain banks in Australia has indicated that a single operational entity using a hub and node model would be the most effective means to deliver the six critical features of successful brain banking outlined above. A unified approach would enable Australian brain banks to operate as a harmonised body, with consistent standards across tissue collection, processing, characterisation and storage. A single entity provides a consistent experience for donors, who should be the core focus of the brain banking process. By organising dementia brain banks in Australia as one body, access to tissue samples for researchers would be streamlined which supports research outputs.

An alternative operating model was considered through this review, in which the individual dementia brain banks are funded in order to provide full functionality to donors and researchers at every location. In this model the banks would continue to operate independently, with harmonisation of processes, and collaborating to fulfil sample requests. This model was not pursued as it re-enforces the current challenges of accessing technical and neuropathological expertise, providing a common experience for donors and their families, and is more costly than the consolidated model due to the additional staffing costs and general operational duplication.

While the proposed single entity model requires a number of stages to implement (outlined below in Section 7.3), it presents several significant advantages over re-funding the existing banks as stand-alone operations. A consolidated model realises efficiencies through a critical mass of technical expertise in the hub, and provides redundancy and back-up for staff. A hub and node model shifts away from the previous ABBN structure in order to address the critical issue of access to neuropathological expertise, which is a technical skillset unique to brain banking. Consultation has indicated that access to neuropathological expertise is a core challenge in brain banking. A single entity operating as a hub and node model ensures this access is maintained by leveraging the existing location of neuropathological expertise in Sydney and Melbourne. The model is referred to as the "Australian Brain Bank" and is outlined below.

### 5.2.1 A hub and node model is the most efficient deployment of resources

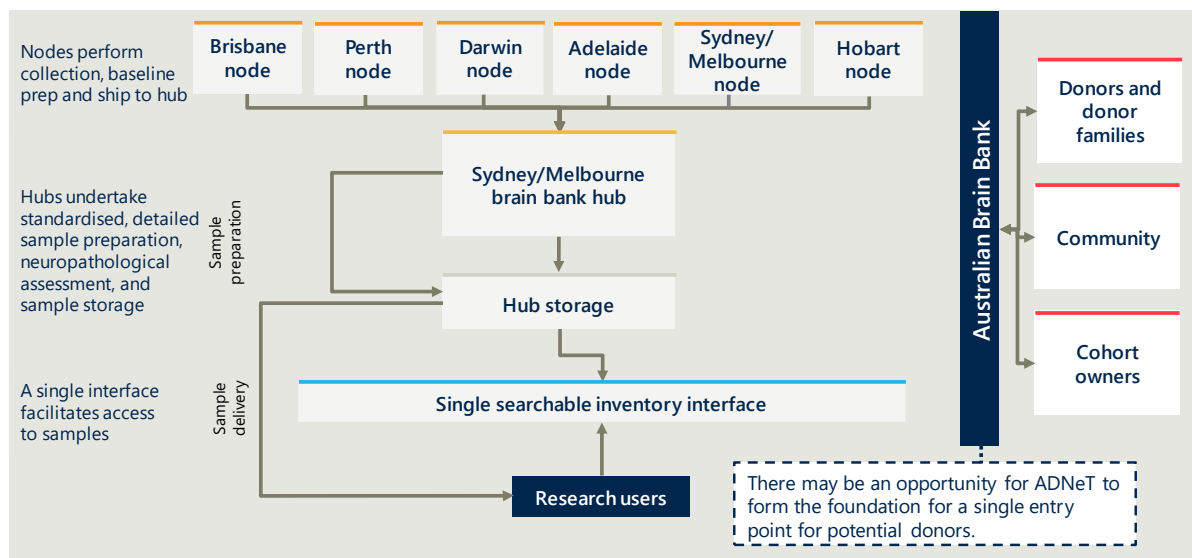
A hub and node model for brain banking in Australia would provide donors, researchers, cohort custodians and the community with a single interface for all brain banking engagement, while the collection and processing of brain tissue occurs across different locations in Australia. The model represents the most efficient allocation of resources, as multiple nodes undertake collection activities while the hub performs detailed sample preparation and neuropathological characterisation, which is significantly more costly.

A hub and node model is designed to accommodate Australia's geographic size and multiple jurisdictions, with nodes located in capital cities across the states and territories, depending on demand and coverage requirements, and the hub located in Sydney or Melbourne. Each node will manage tissue collection independently to account for state-specific legislation governing tissue collection.

The designation of either Sydney or Melbourne as the site for the hub is based on the location of both neuropathological expertise and appropriate facilities, as well as population density. While a single hub is the most cost-effective option in terms of infrastructure, it will incur some additional costs of shipping tissue to a single location. The hub and node model would also lend itself to the possibility of two hubs – i.e. a hub located in both Melbourne and Sydney. A two hub model has the advantage of utilising the existing neuropathological expertise in both Melbourne and Sydney.

By dividing activities associated with brain banking, such as tissue collection, characterisation and storage across banks in Australia, a hub and node model takes advantage of existing facilities and staffing resources. The model is depicted below in Figure 12.

**Figure 12 | A hub and node model for brain banking in Australia**

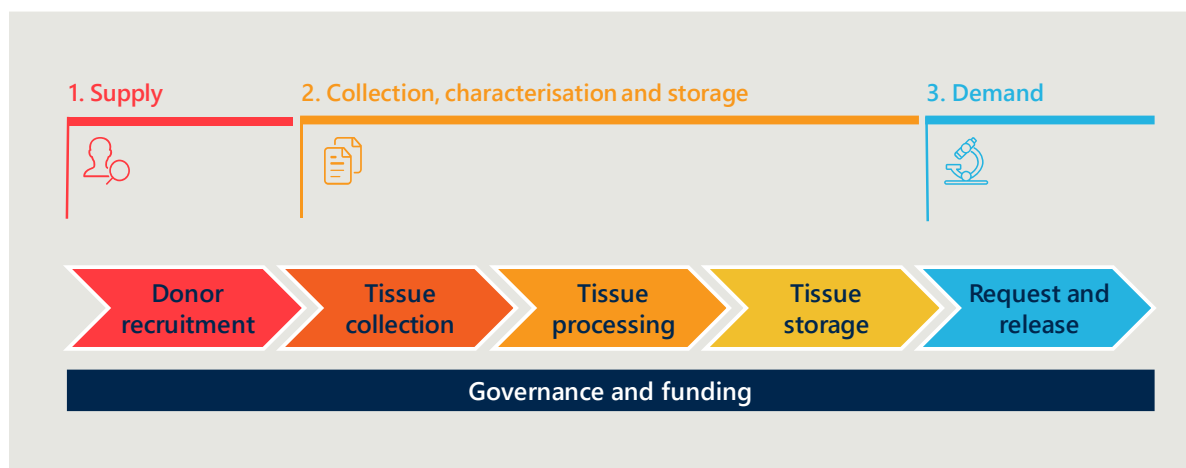




## 5.2.2 Each step in the banking process can be managed efficiently

The hub and node model will allow each stage of the process to be well managed. Each stage in the model is described below. Figure 13 reproduces an overview of the stages in brain banking.

Figure 13 | An overview of the brain banking process



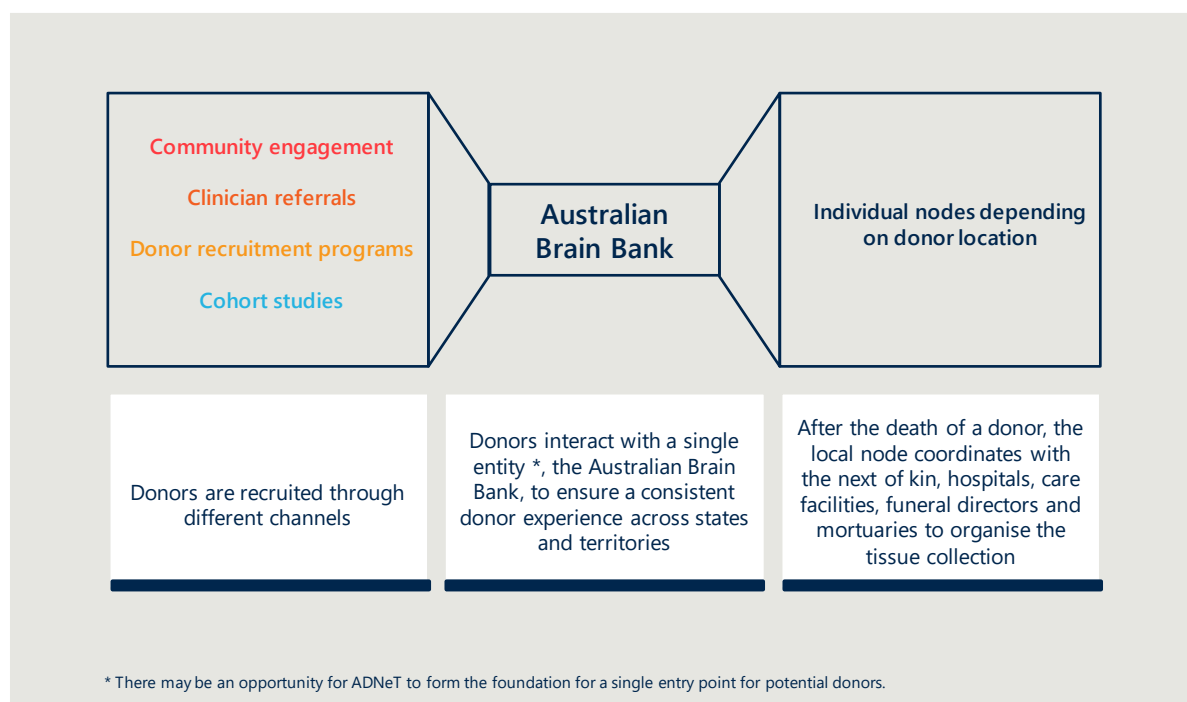
### 5.2.2.1 Donor recruitment

Donor recruitment is the first stage of the brain banking process. In a hub and node model, donor recruitment activities are managed through the hub. Potential donors communicate with a single entity, the Australian Brain Bank, to ensure a consistent donor experience across states and territories.

There may be an opportunity for the ADNeT to act as this entry point for potential donors, since the ADNeT is pursuing the creation of a registry of people living with dementia for researchers to recruit into longitudinal studies. Ideally, the ADNeT registry would be incorporated into the brain bank network, providing researchers with access to both potential research participants and tissue samples. A comprehensive registry would strengthen the link between clinical data and tissue samples, as the latter is enriched by access to the former. With the creation of a single interface, issues of patient confidentiality and consent would need to be appropriately managed by the parties involved, including the ADNeT. Moreover, since funding for the ADNeT is limited to five years, the issue of sustainable funding still needs to be addressed.

After the death of a donor, the local node (depending on the donor's location) coordinates activities with relevant bodies including hospitals, care facilities, funeral directors and mortuaries, as well as families of donors to organise tissue collection. Figure 14 presents the relationship of donors with the Australian Brain Bank.

Figure 14 | The relationship of donors with the Australian Brain Bank



It should be noted due to differing legislative requirements in states and territories, post-mortem recruitment would remain with the individual nodes, drawing on existing links with the coronial system.

### 5.2.2.2 Tissue collection

Nodes and hubs collect brain tissue samples and in some cases spinal cord and cerebrospinal fluid from donors and provide baseline preparation for the processing of tissue that is performed the hub. The brain is divided into two hemispheres, which are fixed in formalin and frozen. The samples are then shipped to the hub in Sydney or Melbourne.

### 5.2.2.3 Tissue processing and characterisation

The tissue is sectioned into blocks that capture significant regions of the brain. Neuropathological characterisation is performed by a clinical pathologist, which ensures that the results may be used for both research purposes and clinical diagnoses.

### 5.2.2.4 Tissue storage

Once processed, the tissue is stored at the hub. This review has investigated the possibility of using the NSW Health Statewide Biobank as a cost-effective storage option if the hub is located in Sydney. It has been determined that this is not feasible for two reasons. First, the NSW Biobank lacks appropriate storage options to house brain tissue collections. Secondly, the specialised nature of brain tissue processing would require brain bank staff and their existing operations to relocate to the Biobank, which is not practical. Consultation has indicated that Biobanking Victoria, located at Monash Health Translation Precinct, could potentially be used to store brain tissue collections if the hub is to be located in Victoria but this option needs to be investigated further with the relevant parties including Monash Health. Regardless of the hub's location, the tissue remains at the hub until requested for release by researchers.

### 5.2.2.5 Request and release

Researchers access a single searchable interface that provides an inventory of tissue samples available from the hub. The interface presents a single entry point to brain banking for donors, researchers, cohort custodians and the community. The hub is responsible for assessing tissue applications, communicating

with researchers and distributing tissue for use. Ethical and operational guidelines must be followed by the hub to maintain equal access, responsible reporting and communications. The hub is also responsible for implementing guidelines to provide oversight over nodes. The guidelines should ensure that the hub(s) and nodes comply with legislative requirements and create a mechanism for reporting complaints.

### 5.2.3 The required number of hubs and nodes depends on donor supply and sample demand

A hub and node approach to brain banking is flexible as the structure of the model depends on the supply and demand of tissue. In Figure 12, a node is located in each capital city to ensure coverage across Australia but the exact number of nodes is determined by donor supply, which varies between states and territories due to differing levels of donor recruitment activity, and the need for geographic spread. Similarly, a hub and node model may feature more than one hub, potentially located in Sydney and Melbourne. A two-hub model helps ease demand for tissue processing services, but incurs greater operating costs, as an additional structure with appropriate staffing resources is required.

## 5.3 Funding remains a challenge for a single entity

A future state in which dementia brain banking is delivered under a single operating entity would continue to be subject to the current challenges of research infrastructure funding in Australia. The operating entity – in whatever form it takes – will likely need to source funds through a mixed funding model that includes government grants (such as Commonwealth or state direct funding), institutional contributions, cost recovery, and philanthropy. The Netherlands, UK and US brain banks each operate under mixed funding models, with significant differences in the contributions of each funding type.

This review explored potential funding sources within the Commonwealth and state/territory governments. Little traction could be identified in the state/territory governments, largely due to the marginal role of brain banking within the health system due to its post-mortem role (as described in section 4 of this report). Both Victoria and NSW contribute non-earmarked funding to research entities (i.e. to the Florey Institute and NeuRA respectively) which in turn provide support to the brain banks. Information provided to the review indicated that there is little or no funding from the state health services used for brain banking. For example, the services of the clinical neuropathologist who operates 0.1 FTE at the VBB is funded by the VBB.

Other options which could be explored in the future include a substantial role for philanthropy, given the increasing prevalence of dementia.

Options for Commonwealth direct funding are described below.

### Commonwealth infrastructure funding is evolving

The Commonwealth's primary research infrastructure investment vehicle is NCRIS. The current NCRIS Investment Plan<sup>17</sup> is effective until the 2021/22 financial year, and invests a total of \$572.2 million in 24 research infrastructure facilities and a series of scoping studies – including a study of biobanking arrangements across agriculture, plant science, environmental science and biomedical science. This scoping study will commence in mid-2020, and is anticipated to take two years to complete. Three sequential hurdles would need to be overcome for NCRIS funding to be a reality for dementia brain banking:

- Dementia brain banking must take a leading role in the national conversation about biobanking
- The national research infrastructure scoping study into biobanking would need to articulate substantial benefits to establishing a national biobanking capability

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<sup>17</sup> Australian Government Research Infrastructure Investment Plan.

- The NCRIS investment strategy would need to make a funding commitment to national biobanking, including dementia brain banking.

Considering the current NCRIS planning cycle that re-evaluates the investment strategy every two years, the earliest time at which this investment might be realised is mid-2023, and more likely 2024 or 2025. An interim solution would be required to establish and provide initial support to a single dementia brain banking entity.

At the time of writing (June 2019), the MRFF 10-year investment plan<sup>18</sup> has been released through the 2019-20 Federal Budget, but has not yet been confirmed. The MRFF investment plan includes funding for *National Critical Infrastructure* of \$605 million over nine years, beginning in 2019-20, and for *Data Infrastructure – Registries, biobanks, linkage platforms* of \$80 million over eight years, beginning in 2020-21. The terms of these funding schemes are still to be finalised, but present a potential source of funds for establishing national-scale dementia brain banking, and the necessary supporting data infrastructure to manage sample inventories and clinical information.

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<sup>18</sup> <https://www.health.gov.au/internet/budget/publishing.nsf/Content/budget2019-factsheet51.htm>

## 6 A financial model of a single brain banking entity

Operating a hub and node model of brain banking will cost an estimated \$2.6 million per year based on current state activity. A bottom-up financial model was created to estimate costs for a single brain banking entity with one hub and six nodes. The final composition of the organisation will be determined through the implementation phase, including the number and locations of hubs and nodes. The current state estimate is drawn from the collective activity reported in the final ABBN report of 2014. The model quantifies in-kind contributions normally absent from brain bank financial statements.

The estimated operating costs of the single entity compare favourably to the operating costs of the Netherlands Brain Bank, and staff estimates are comparable to the NSWBB. Future demand and supply are modelled, indicating a 17% increase in operating cost over 10 years. Cost recovery based on the current 2019 ABBN fees schedule is estimated to generate \$410,255 in revenue, or 16% of total operational expense with an average projected growth of 2% per year to \$499,304 in 10 years.

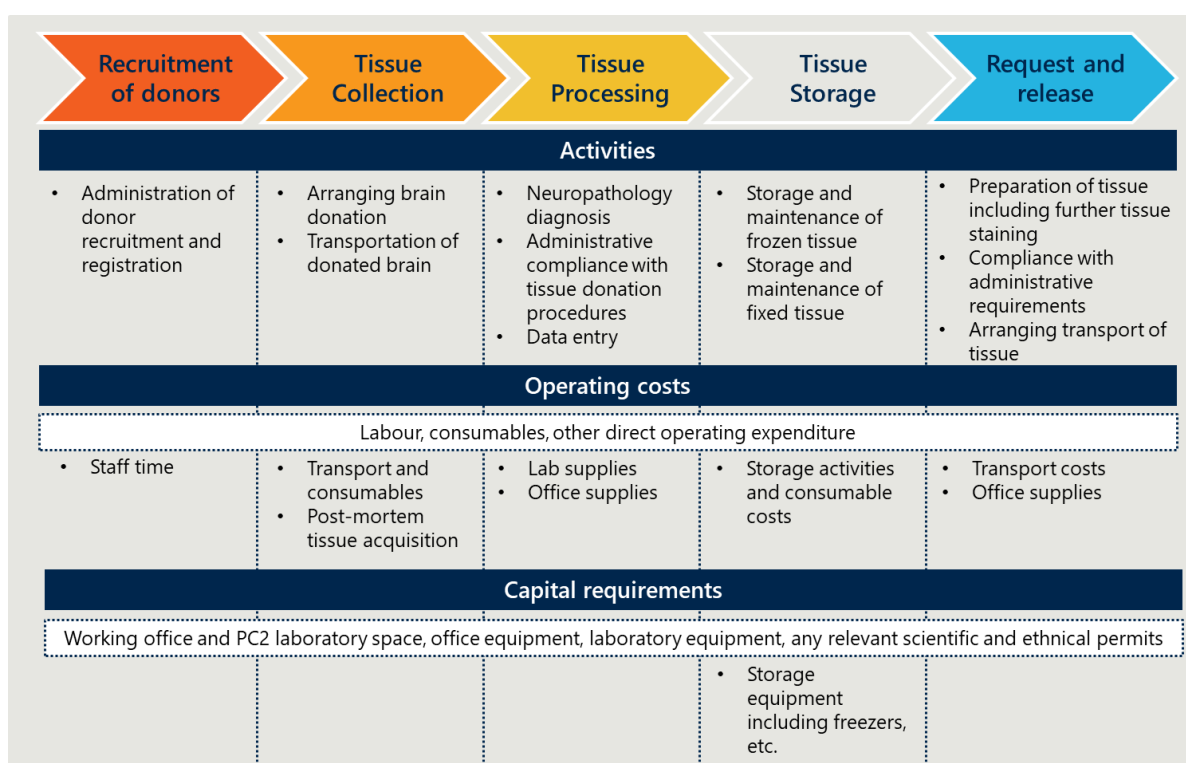
### 6.1 A bottom-up approach was used in the financial model

A bottom-up approach was used to construct a financial model of brain banking to address two key challenges:

- Each of the brain banks has **complex funding arrangements**. The banks rely extensively on in-kind contributions and these contributions are not consistent among the banks.
- **Incomplete financial information** has meant that the thinking is mainly guided by qualitative data, expert experience and desktop research.

Due to these constraints, scaling up from current budgets is not feasible. A bottom-up approach is used instead to create the financial model of a single brain banking entity. A bottom-up approach refers to analysing the operational processes of the brain banks to understand and reconstruct the cost drivers of a bank. The six elements of brain banking described earlier were used to guide the financial reconstruction. Figure 15 presents the breakdown of operational costs and capital requirements identified through this process.

Figure 15 | The five-stage process with operational costs and capital requirements



The bottom-up approach has two main advantages:

- **All costs are quantified, including any in-kind funding or contribution.** This creates a **complete and transparent understanding** of the financial drivers and goes beyond an analysis of the current financial information and arrangements of the banks.
- **Scale and projected demand and supply can be easily factored** in the model. This creates additional utility in the model by forecasting future costs.

The financial model breaks down costs into fixed costs and variable costs (Figure 16):

- **Fixed costs** refer to costs that are independent of volume or quantity of services delivered
- **Variable costs** refer to costs that vary in proportion to the volume and quantity of services delivered.

The fixed costs and variable costs are identified through the bottom-up approach, analysis of financial information from the VBB and qualitative data.

It is important to note that neuropathology services are modelled as a variable cost and not as FTE. This is due to the variable way in which these services are accessed across the existing brain banks, and the anticipation this variability will continue in the future. Neuropathology services may ultimately be accessed through joint appointments, services fees to health services, or in-kind contributions by jurisdictions. The inclusion of neuropathology as a service makes financial modelling of the full costs of dementia brain banking possible, including all relevant inputs.

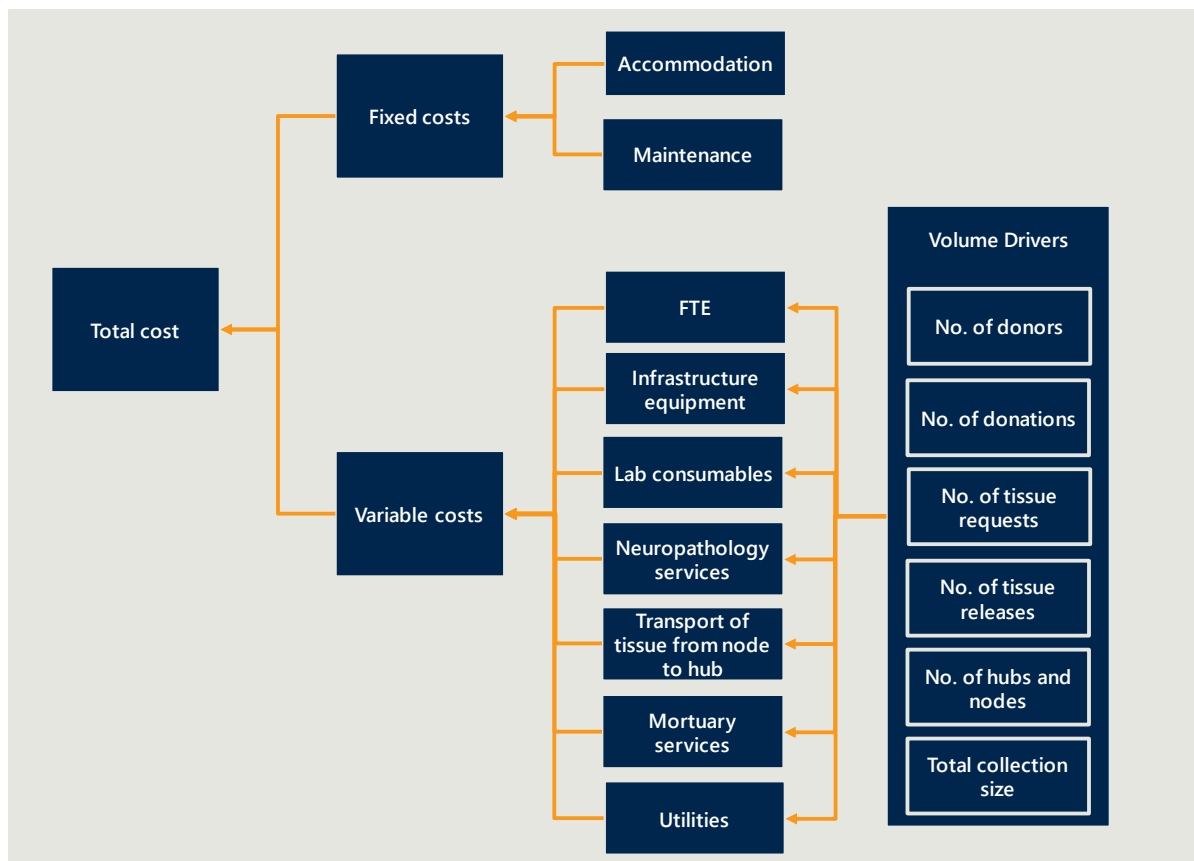
The fixed costs are:

- **Accommodation** refers to the space needed to house all FTEs across the entire network and the entire collection of the brain bank
- **Maintenance** refers to the maintenance costs required to ensure the smooth function of all freezers and relevant equipment to brain banking.

The variable costs are:

- **FTE** refers to the necessary FTE across the entire network to ensure smooth functioning of brain banking
- **Infrastructure equipment** refers to the equipment necessary for the activities of brain banking -these include lab equipment and tissue storage equipment
- **Lab consumables** refers to items and reagents required for the activities of brain banking
- **Neuropathology services** refers to pathology services required to characterise all brains
- **Transport of tissue from node to hub** refers to the transport of the fixed and frozen tissue from the nodes to the hubs for further processing
- **Mortuary services** refers to the brain removal from donors performed at an external facility
- **Utilities** refers to all utility costs required for brain banking.

Figure 16 | The breakdown of the financial model by fixed costs and variable costs



The quantities that drive the variable costs are referred to as volume drivers. The volume drivers are then driven by the associated unit cost of the variable cost of each volume driver. Note that this means that two variable costs may share the same volume driver, but different unit costs associated to that volume driver. The variable costs are then determined by multiplying the respective volume drivers with the associated unit costs and summing them. These volume drivers are identified through the bottom-up approach and qualitative data. Refer to Figure 17 for a complete breakdown of variable costs by their respective volume drivers and associated activity unit costs.



Figure 17 | The breakdown of variable costs by their respective volume drivers and associated activity unit cost

Variable cost	Volume driver and associated activity unit cost		
FTE	No. of donors	X	Staff time per donor
	No. of donations	X	Staff time per donation
	No. of tissue requests	X	Staff time per request
	No. of tissue releases	X	Staff time per release
Infrastructure Equipment	No. of hubs and nodes	X	Cost of infrastructure equipment required for a node; and hub
	Total collection size	X	Cost of infrastructure required to house collection
Lab consumables	No. of donations	X	Average cost of consumable per donation
	No. of tissue releases	X	Average cost of consumable per release
Neuropathology	No. of donations	X	Average cost of neuropathology per donation
Mortuary Services	No. of donations	X	Average cost of mortuary services per donation, excl. transport costs
Transport	No. of donations	X	Average cost of transport of brain tissue from node to hub
			Average cost of transport of body from funeral home to mortuary and back

Capital expenditure is not separately identified in the model of operating costs. Initial capital investment for equipment is included in the implementation phase of the project, as outlined in Section 7.3.1.

## 6.2 A hub and node model is a cost effective option

ABBN reported activity from 2014 is used to estimate current state funding requirements. This estimate indicates the total funding required for a national network based on numbers that reflect Australian demand and supply. Under these modelling inputs, the central hub function of the proposed brain banking entity is broadly in line with the Netherland Brain Bank operating costs, and model estimates of total FTE are comparable to that of the collective NSWBB.

Taking these two comparisons together, the model demonstrates accuracy in quantifying the costs of brain banking and the efficiencies sought in a node-and-hub model. The detailed workings of the financial model are set out in Appendix B.

## 6.2.1 The financial model estimates a total operational cost of \$2.6 million based on 2014 ABBN figures

The model of current state is based on ABBN activity for 2014. The 2014 statistics are the most recent data available for all brain banks in an operational state. Subsequent reporting by the VBB and NSWBB indicates activity levels in these States are largely unchanged, suggesting 2014 ABBN figures are a reliable source of national activity levels for the model. The key 2014 ABBN figures are:

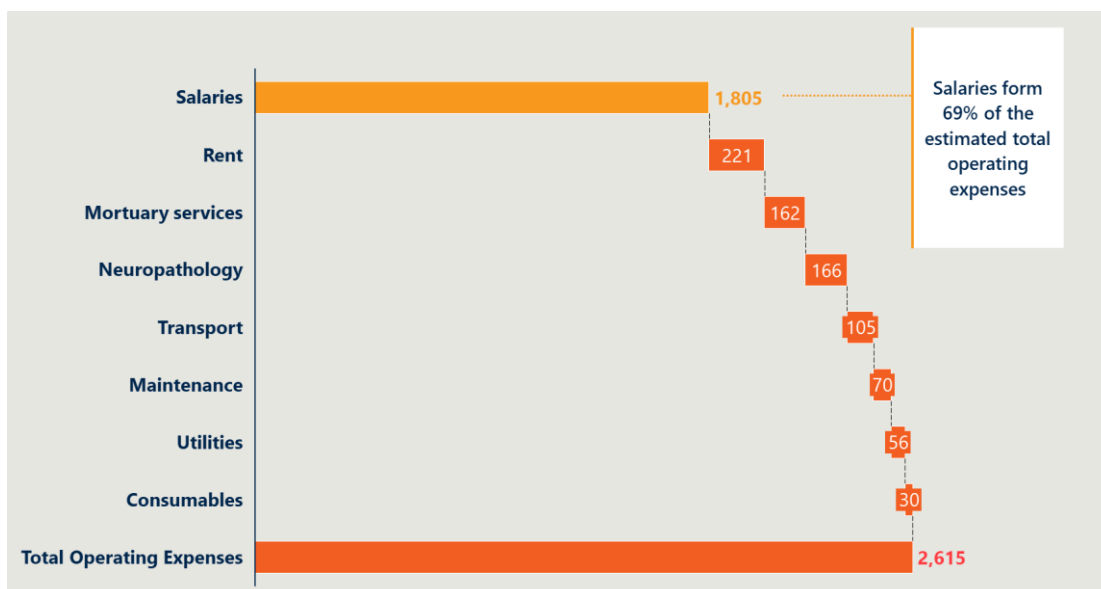
- 230 new registered donors
- 180 new donations
- 3,000 cases in the collection
- 120 requests
- 110 releases.

The model estimates FTE required per year and is referenced to July 2019 salary levels from the University of Sydney 2018-2021 Enterprise Agreement. Whilst salary levels will vary throughout the country, it is assumed the University of Sydney rates represent a conservative baseline from which modelling can be conducted:

- 4 FTE administrative staff (HEO5.1) with an annual salary of \$74,898
- 11 FTE scientific staff (HEO7.1) with an annual salary of \$93,986
- 1 FTE for management positions (HEO8.3) with an annual salary of \$111,921.

On-costs for salaries are estimated at 30%, and will include superannuation, payroll taxes, leave allowances and workers compensation premiums. On-costs are in addition to the salaries listed above.

Figure 18 | Estimated operational costs using baseline figures (\$ '000)



The financial model estimates an annual total operating expense of \$2.6 million (Figure 18). As expected, salaries form a significant portion of the operational expenses, accounting for 69%. Rent is the next biggest portion, accounting for 8% of expenses. Mortuary services and neuropathology account for 6% each. Collectively, these four categories account for a cumulative 89% of total operational expenses.

To gauge the performance of the model as an accurate representation of the costs of brain banking, the total operational cost estimated by the model is compared with the Netherlands Brain Bank and FTE figures compared to the NSWBB.

## 6.2.2 Modelled operating costs are broadly in line with Netherlands Brain Bank

The total operational cost estimated by the financial model is compared to the Netherlands Brain Bank by using quantities from the Netherlands Brain Bank. The comparison is informative in that the central facility is broadly comparable with the Netherlands Brain Bank with additional costs attributable to running a node network to cover the expanse of Australia.

In 2017, the Netherlands Brain Bank had 162 donations, 770 new donors and 235 requests from researchers with a total collection size of 4,000 cases.<sup>19</sup> The bank received annual funding of approximately €1,000,000<sup>20</sup> or \$1.6 million.<sup>21</sup>

Using the Netherlands Brain Bank activity as an input scenario, the financial model estimates a total operational expense of \$3.15 million. Note that rent is not included in this figure as the Netherlands Brain Bank is housed within a host institution. The higher figure from the model compared to the reported costs of running the Netherlands Brain Bank reflects the additional costs imposed by the nodes compared to just a central hub model. Without the node costs, the central hub has an estimated operational expense of \$2.4 million. Considering volatility in exchange rates, differences between costs of living in Australia and the Netherlands, significant differences in geographic scale, and limited contextual information on the operations of the Netherlands Brain Bank, the core of the hub and node model is considered broadly comparable to the Netherlands Brain Bank.

## 6.2.3 FTE assumptions are comparable to NSWBB

Due to the complex funding arrangements of the brain banks, funding figures from the brain banks cannot be scaled up to compare to the funding figures from the financial model. However, a top down view of FTE to the number of donors, donations, and requests from each of the banks can be performed to better understand how the FTE assumptions in the model compare to FTEs in the brain banks.

The FTE outputs of the financial model were validated against a NSWBB activity scenario. The number of new donors, donations and requests reported by the NSWBB in 2017 were matched to reported staffing numbers. We estimate total NSWBB staffing levels at 7.8 FTE across the two banks, based on the most recent information provided. This estimate assumes the five staff at the NSW BTRC have an average FTE load of 0.7.

The financial model estimates total FTE of 7.8 based on the NSWBB volume drivers shown in Table 5 below. The financial model assumes a minimum of 0.3 FTE is present at every node.

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<sup>19</sup> The Netherlands Brain Bank 2017 Progress Report, 2019, available at <https://www.brainbank.nl/about-us/nbb-progress/>

<sup>20</sup> Interview with Inga Huitinga 10th April 2019.

<sup>21</sup> Average December 2017 EUR to AUD exchange rate used.

Table 5 | Total FTE, number of staff, donors, donations and requests at the SBB and the NSW BTRC

	Total FTE	No. of new donors	No. of donations	No. of requests
SBB FTE	4.8			
NSW BTRC FTE (estimate)	3.5	72	55	35
Total FTE (estimate)	8.3			

## 6.3 Financial model projections

Operational costs and total cost recovery revenue of the entity for 10 years are projected using population growth estimates. For ease of interpretation, the dollar figures are all presented in 2019 dollars.

The financial model uses the 2014 ABBN figures as a baseline and projected forward using probabilistically-determined growth rates on the volume drivers. A Monte Carlo simulation is run to account for the inherent uncertainty in future projections. For full details, refer to Appendix B. The data is presented as a fan chart with the following key statistics:

- the annual average operating cost of the model
- a coloured region containing the range of values centred around the average containing 75% of the simulated data (or the region containing the 25<sup>th</sup> -75<sup>th</sup> percentile of the data)
- a second coloured region, which taken together with the above point contains the range of values centred around the average containing 90% of the simulated data (or the region containing the 10<sup>th</sup> - 90<sup>th</sup> percentile of the data).

The model estimates that:

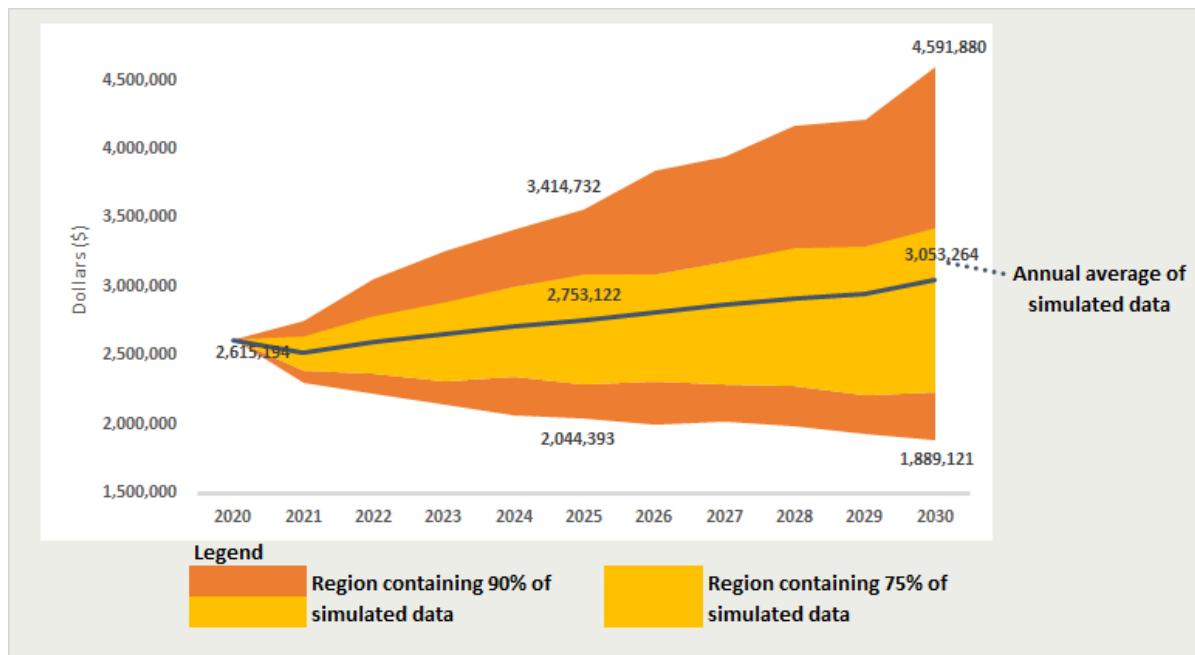
- an annual operational cost of \$ 3.1 million at the end of 10 years, or a 17% increase of operational costs
- cost recovery revenue based on the current ABBN fees schedule forms an average of 16% of annual operational cost year-on-year.

### 6.3.1 Operating Costs projections

Total operational costs are projected forward 10 years using probabilistically-determined growth rates based either on population projections from the ABS or a positive percentage rate based on past quantitative data from the brain banks. See Appendix B.2 for full details.

The model estimates a growth of 29% in donor registration, 28% in donations and 22% in tissue requests over 10 years and an overall increase in 17% growth in total operational expenses over 10 years. The model projects an average operational cost of \$3.1 million at the end of 10 years, with an annual growth rate of 2%. Based on the simulated data from the model, any value between \$1.9 million to \$4.6 million can occur with at least 90% probability. Figure 19 demonstrates the results of the Monte Carlo analysis.

Figure 19 | Simulated growth in operational costs (\$) over 10 years



### 6.3.2 Cost Recovery projections

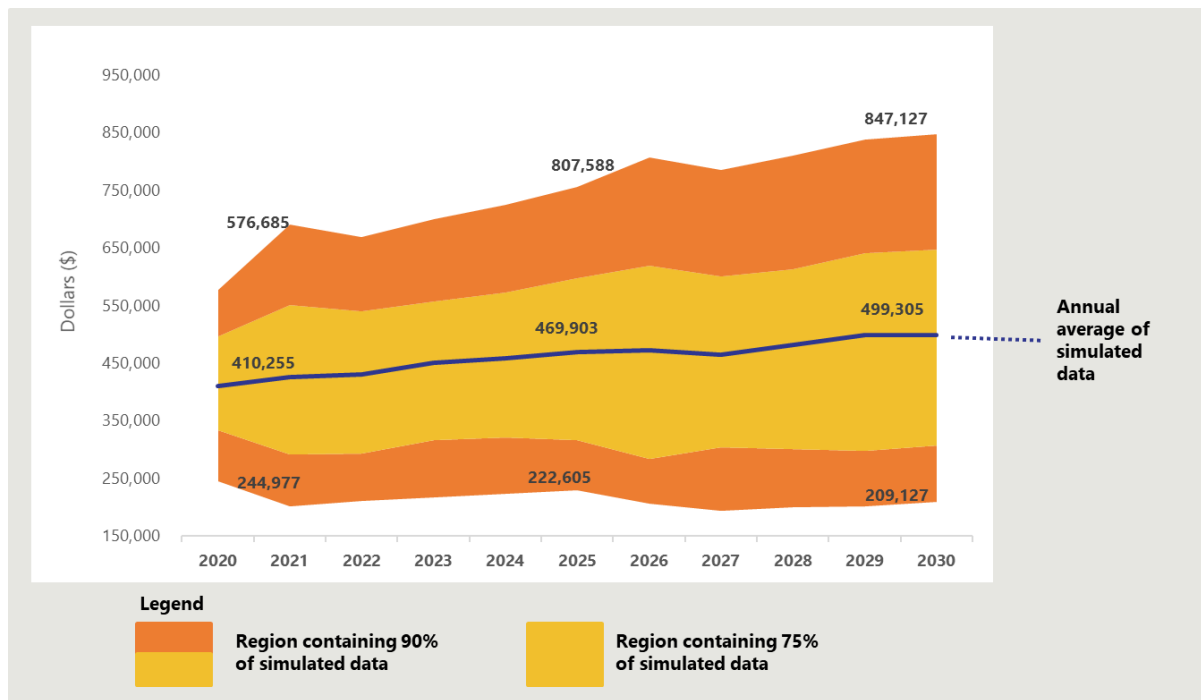
The 2019 the ABBN cost recovery schedule indicates that researchers from parent institutes of the banks enjoy a weighted average discount of 34% compared to their counterparts from other institutions. The Netherlands Brain Bank has a different model for cost recovery that considers instead if researchers are from non-for-profit organisations or for-profit organisations. As data indicates that the VBB and the NSWBB have not had a record of a tissue request from a for-profit organisation, the model does not consider this third model for cost recovery due to a lack of information. As such, the two models for cost recovery are:

- the current ABBN fees schedule with the discounts for researchers from host institutions
- the external rates in the ABBN fees schedule applied to all researchers.

In both models, the cost recovery projections grow an average of 2% per year, with a cumulative 21% growth in both models at the end of 10 years.

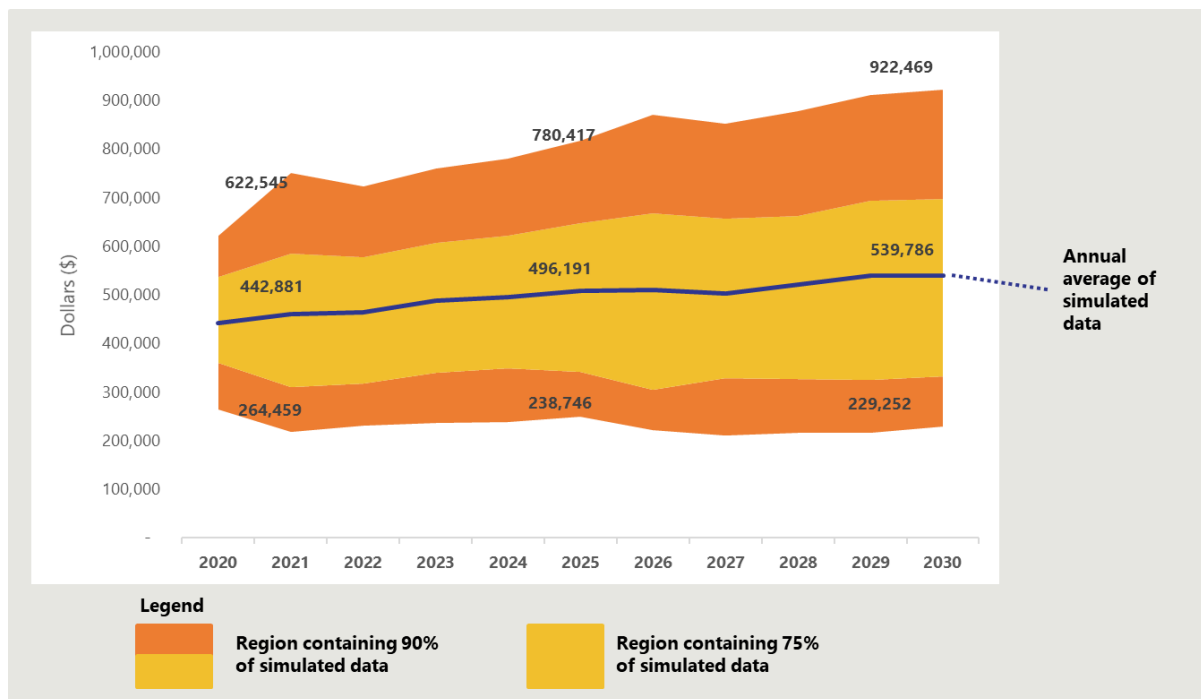
A continuation of current host institution discounts results in an estimated average revenue of \$499,305 at the end of 10 years (Figure 20). This form of cost recovery forms an average of 16% of total operational expense. The average cost per sample across the 10 years is \$3,072.

Figure 20 | Simulated cost recovery rates with continuation of host institution discounts (\$)



A flat rate cost recovery model results in \$539,786 at the end of 10 years (Figure 21). This form of cost recovery forms an average of 18% of total operational expense. The average cost per sample across the 10 years is \$3,717.

Figure 21 | Simulated cost recovery rates with flat rates to all users (\$)



A 50% cost recovery model that recognises all in-kind funding and contributions would lead to an average price of \$12,000 per fulfilled tissue request based on the current state model. This is four times the average cost of the estimates of the cost recovery model based on the 2019 ABBN fees schedule.

The cost recovery model should be revisited once the new operating model is in place. Consideration will need to be given to what the research market can bear, in the context of what funding is available to support the brain bank operations.



## 7 Several governance arrangements are possible for a single brain banking entity

Various governance arrangements are possible for the Australian Brain Bank. Two approaches are explored in this review, along with the individual benefits and risks associated with each arrangement. The first approach draws on the previous Australian Brain Banks Network governance structure and is based on a multi-institutional agreement between the brain banks and their host institutions. The second governance arrangement is adapted from the not-for-profit structure employed by the Australian Red Cross Blood Service. This arrangement could be a function of a new entity or an existing one such as the Organ and Tissue Authority.

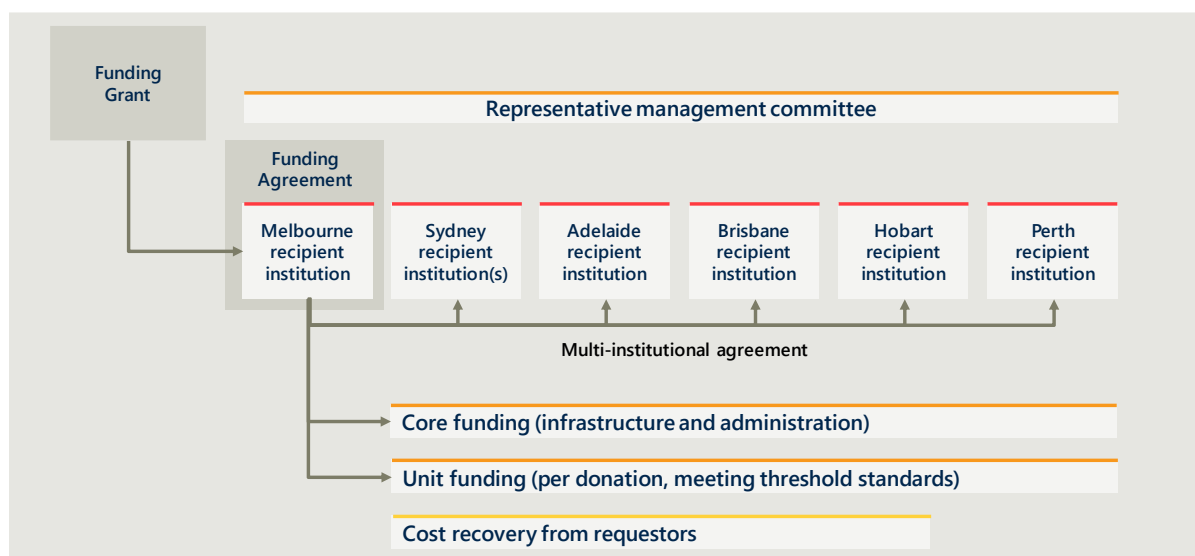
This review explores two distinct options but there are many possible governance arrangements that fall in a spectrum between the options presented here, including the establishment of a corporate Commonwealth entity, which is also discussed below. Regardless of which governance framework is adopted, there is a need to ensure brain banks adhere to consistent ethical and operational standards. Standards may include the management arrangements for running the brain banks, for review of tissue requests and for oversight of the network (including the way in which the interests of donors and their families will be represented). Compliance to standards should be monitored and form a condition of continued funding.

These considerations and others are explored below.

### 7.1.1 Option one: Multi-institutional agreement between research institutions

The first governance arrangement is based on a multi-institutional agreement between the brain banks and the institutions that host them. Under this arrangement, one institution receives funding through a grant. Funding from the grant is then distributed to other brain banks, with the terms and conditions set out in a multi-institutional agreement. This arrangement is overseen by a representative management committee formed by members of the brain banks and host institutions. Figure 22 presents the governance structure of this model.

Figure 22 | A multi-institutional agreement between research institutions (with Melbourne as the recipient for example purposes only)



### A multi-institutional agreement is cost-effective due to in-kind support by host institutions

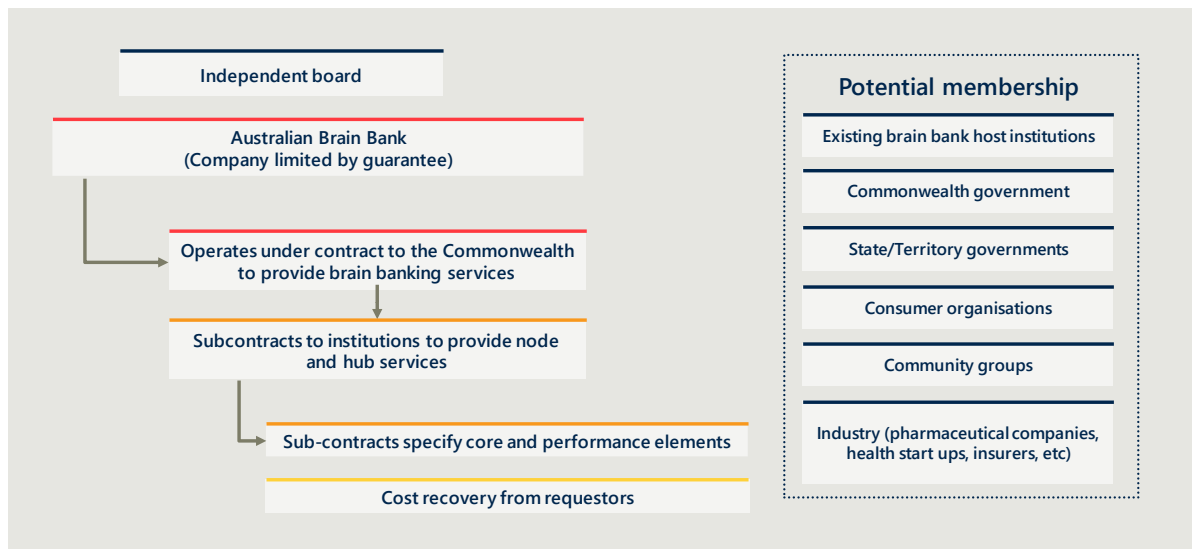
The agreement with the recipient institution sets out the core funding for infrastructure and administration, as well as the unit funding per donation. Funding is tied to the brain bank meeting standardised processing and data requirements per donation. A cost recovery system is in place to recoup some costs associated with brain banking from users. The fee schedule for cost recovery would be negotiated between the institutions to maintain consistency.

A multi-institutional agreement approach is cost-effective as host institutions provide in-kind support for the brain banks. In-kind contributions may include lab and office space, office hardware and IT infrastructure and storage hardware, such as freezers. However, in-kind contributions are dependent on good will between the brain banks and their host institutions. Institutions may not commit to long-term in-kind support, which creates a barrier to sustainable funding for brain banking.

## 7.1.2 Option two: Company limited by guarantee

Another governance arrangement for the Australian Brain Bank is possible through the creation of a company limited by guarantee. This approach draws on the not-for-profit structure employed by the Australian Red Cross Blood Service. This arrangement could be a function of a new entity or an existing one such as the Organ and Tissue Authority. A company limited by guarantee is a public company registered under the *Corporations Act 2001*. Figure 23 presents an example of an Australian Brain Bank as a company limited by guarantee.

Figure 23 | Company limited by guarantee example



### A company limited by guarantee has a clear chain of responsibility and performance measures

As a company limited by guarantee, the Australian Brain Bank is governed by an independent board of directors with expertise on brain banking. Directors of the Australian Brain Bank will have legal duties, responsibilities and liabilities as outlined in the *Corporations Act 2001*. This promotes a clear chain of responsibility for managing risks.

Members of the Australian Brain Bank as a company limited by guarantee may include existing host institutions of brain banks, Commonwealth or State/Territory governments, consumer organisations including Dementia Australia, and industry. These members effectively act as shareholders in the company.

A constitution sets the Australian Brain Bank's powers and objects. The constitution also specifies what will occur in the event the Australian Brain Bank is wound up, so that the rights and interests of donors and

potential donors are protected if the company is shut down. As a company limited by guarantee, the Australian Brain Bank is contracted by the Commonwealth to provide brain banking services in states and territories. The Australian Brain Bank then sub-contracts to institutions to provide services through a hub and node model, as outlined in Section 5.2. The sub-contracts specify core and performance elements of brain banking, which promotes accountability and transparency. By outlining specific performance requirements of banks, the standardisation of tissue collection and processing practices across brain banking in Australia is encouraged. Moreover, funding that is dependent on performance incentivises tissue collection and distribution to users by brain banks.

Since costs are contained with the company structure, there is high visibility of the costs associated with brain banking. However, unlike in the multi-institutional agreement approach, it is more challenging for brain banks to rely on host institutions to provide in-kind support, as the subcontracting arrangements may not be eligible for research block grant funding.

### 7.1.3 There are a multitude of possible governance arrangements

There are many possible governance arrangements for the Australian Brain Bank, in addition to the approaches described above. One option that sits between the two governance arrangements set out above is a corporate Commonwealth entity (CCE). A CCE is a body corporate with a separate legal personality to the Commonwealth and is able to enter into contracts in their own right. They generally have enabling legislation that establishes the scope of their activity and an accountable authority with multiple members such as a board of directors.

As a CCE, the Australian Brain Bank can commit and spend Commonwealth money by contracting entities to provide brain banking services. To ensure that the Australian Brain Bank is accountable for its management of Commonwealth resources, it can be listed as an entity that must comply with the Public Governance, Performance and Accountability Act 2013 (PGPA Act). The PGPA Act sets out the requirements for the governance, reporting and accountability of Commonwealth entities. While it is not required for a CCE to comply with PGPA Act, there are some advantages in having enabling legislation for a CCE. Enabling legislation means that functions, powers and relationship to government can be clearly set out, which promotes a high level of accountability and transparency. Another potential advantage of establishing the Australian Brain Bank as a CCE is that it may be able to leverage Commonwealth resources such as space, which could reduce overheads.

## 7.2 Risks of operating under a single entity are manageable

The current state of Australian brain banking confers credibility and service delivery risks. Those risks and others may be managed effectively under a single entity operational model.

### **A single interface for donor recruitment manages a credibility risk**

Operating as a single entity allows brain banks to establish a single interface for potential donors, regardless of location or route of referral. This allows for greater awareness of and control over the experience of potential and registered donors and mitigates the credibility risk that brain banks currently face due to inconsistent experiences.

### **A coordinated Australian brain bank will mitigate the risk of inconsistent tissue processing**

Standardising tissue collected by Australian brain banks will increase the value of tissue to researchers, more fully honouring the value of donation and mitigating the risk of researchers accessing tissue from international sources.

Under current arrangements, researchers are managing the risk that tissue sourced from different banks are potentially processed differently, resulting in observable effects that reduces confidence in research findings. A coordinated Australian brain bank with standardised processes will mitigate this risk, with newly

collected samples processed consistently, using the same case characterisation criteria and similar available data. Work conducted by UK Brain Banks Network and the BrainNet Europe consortium can inform efforts to standardise processes and criteria.

Previous attempts to standardise Australian brain banking practices were not fully successful. During implementation of a single entity structure, a discrete consolidation phase is required. See Section 7.3.1 for further detail.

### **A single Australian brain bank is more able to obtain sustainable funding**

A single cost-effective entity is more likely to attract and retain sustainable funding sources than multiple smaller entities working in an uncoordinated fashion. A single brain banking entity is also more capable of distributing funds among hubs and nodes to meet the changing needs of each site of operation.

### **Considered governance approaches mitigates the risk of closure**

A considered governance approach with a medium to long-term contract would allow the Australian brain bank to operate under the 'going concern' assumption, providing stability. In addition, governance through a board comprised of members representing all key stakeholders increases the likelihood of a comprehensive and considered approach to brain bank management; ensuring that no single person is responsible for major brain banking decisions.

### **Sustained access to neuropathology expertise remains a risk**

Brain banking is a highly specialised process requiring specialist knowledge at the tissue processing and characterisation stages. Access to the required expertise is a current risk that would require ongoing management under a single brain bank. Consolidating activities might generate enough work in a single location to allow for a dedicated neuropathologist. Jurisdictions may also continue to contribute neuropathological expertise if some processing is performed at the node location.

## **7.3 Implementation has six key stages**

Implementation of a future state of Australian brain banking based upon a single entity structure follows an ordered set of key decision steps. These are outlined below.

### **1. Form an initial agreement**

The first stage of implementation is to form a broad agreement regarding the operating model with all brain banks and key stakeholders related to brain banking. Agree on the details of a single entity approach, probe how state jurisdictions will contribute to node functions and then determine the extent of the role nodes will play in neuropathological characterisation activities.

### **2. Source funding**

Closely linked to and running in parallel with the first stage, the next step is to establish sources of funding, including the approach to cost recovery. Avenues to explore may include the NHMRC, MRFF and NCRIS as well as further state/territory funding and the potential for philanthropic donations. See Section 5.3 for further detail.

### **3. Agree on governance model**

With an operational model and sources of funding established, a governance approach can be finalised. Governance arrangements should consider actions in case of future closure and how state-specific issues should be managed such as Tissue Act and approaches to post-mortem recruitment.

### **4. Investigate opportunities to leverage existing infrastructure**

Investigate how existing or emerging infrastructure can be leveraged to support brain banking. For example, the ADNeT may provide an opportunity for a single interface through which donor registration can occur.

## 5. Establish operating procedures and business plan

Establish unified operating procedures for hubs and nodes. Build on the results of the first four steps to finalise the business plan. Consent arrangements should be carefully considered at this stage.

## 6. Consolidate brain banking activity

Consolidation of brain banking activity involves establishing the infrastructure required and physically consolidating samples at the hub(s). The implementation phase will require upfront investment, with the bulk of the expense incurred during the consolidation phase. This is considered in greater detail in Section 7.3.1 below.

### 7.3.1 Unification of brain banking activities will require an interim consolidation phase

Bringing Australian brain banks under a single entity will require an interim consolidation period. This period is broken down into three components:

- establishing the infrastructure for the single entity
- selecting the tissue to be included
- physically consolidating samples at the hub location(s).

Each component and an overview of the financial implications are considered in greater detail below.

#### Establish physical and IT infrastructure

Effective physical and IT infrastructure is critical to support brain banking. Consolidation of brain banking activities will bring a large amount of tissue into a single location. All information pertaining to those samples and registered donors will be under a single data management system.

Data management infrastructure should be established early in the process, as should decisions regarding the physical infrastructure required to support a brain banking hub or node. Data management infrastructure should incorporate the following:

- flexibility to adapt for future changes to characterisation criteria, testing performed, or data collation methods over time
- structures to incorporate and where possible standardise data from multiple sources
- controls to ensure risks associated with the collection and storage of sensitive data are minimised.

Physical infrastructure includes the laboratory space, freezers and consumables required to collocate brain tissue from multiple brain banks.

#### Decide what tissue should be kept or discarded

With core infrastructure in place, the next phase of consolidation is the assessment of all tissue that could enter the nationalised brain bank. Consultations indicated that the quality of brain tissue available in current brain banks is not consistent. It is likely that there is tissue currently in storage that will not be used for research purposes. The criteria for bankable tissue should be defined and current brain bank inventories assessed to determine if any tissue should not be retained in the consolidated inventory, or if further testing should be performed on any tissue to increase its potential to be used. After the consolidation phase, it may be useful to repeat tissue assessments on a regular basis (for example, every five years) to discard tissue that is no longer able to be used.

#### Ship materials to central location

Once the tissue to be shipped has been finalised, samples can be shipped to the hub location(s) where labelling, categorisation and storage can take place.

The current distribution of brain tissue around Australia is estimated in Table 6 below, noting that not all cases listed below are dementia or control cases.

**Table 6 | Quantity and location of brain tissue**

Location	Number of cases
Victorian Brain Bank	1380
Sydney Brain Bank	540
South Australian Brain Bank	380
Queensland Brain Bank	600
Western Australian Brain bank	Unknown

If the two-hub model is accepted, then all cases from outside of Victoria and NSW will have to be transported to the hubs – approximately 1,000 cases not including the unknown number of cases in Western Australia.

#### **The financial implications of consolidation**

The consolidation phase will require an upfront investment of a greater scale than ongoing operational costs. Using the same assumptions made during financial analyses earlier in the review, the cost of the consolidation phase is estimated in Table 7 below.

**Table 7 | Estimation of costs associated with consolidation of Australian brain banks**

Cost item	Quantity	Cost	Notes
Laboratory space	60 square metres	\$30,000 upfront for first year	Based on capital city commercial rent. Use of existing resources may be possible
-80°C freezers	5	\$150,000	Assuming existing surplus freezers can be transported to the hub location for use
Computers	2	\$4,000	Estimate only. Use of existing resources may be possible
Staff to assess brain tissue	1 FTE for six months	\$62,000	Based on HEO7.1 plus on-costs
Consumables to assess brain tissue	Lump sum	\$5,000	Estimate only
Shipping of tissue to hubs (at -80°C and room temperature)	1,000 cases	\$70,000	Based on an estimated cost of \$550 per shipment for frozen tissue and \$150 per shipment for fixed tissue transfer and assuming 10 cases can be shipped per container
Shipping of freezers to hubs	5	\$10,000	Quantity listed is an estimate only
Staff to label and store tissue at hubs	1 FTE for six months	\$49,000	Based on HEO5.1 plus on-costs
<b>TOTAL</b>		<b>\$380,000</b>	

This provides an indication only of the most significant costs associated with consolidation. It does not include the cost of commissioning a database to manage the collection, the cost of which may be significant.



## Appendix A Stakeholder Consultations

The table below lists the NNIDR Reference Panel Members.

**Table 8 | NNIDR Reference Panel**

Panel Member	Affiliation/organisation
Janice Besch	NHMRC National Institute for Dementia Research (NNIDR)
Professor Glenda Halliday	The University of Sydney, The University of New South Wales (UNSW)
Louise Heuzenroeder	Donor family experience
Professor Seth Love	University of Bristol, UK Brain Banks Network
Professor Colin Masters	University of Melbourne, The Florey Institute of Neuroscience and Mental Health
Jo Mond	Department of Health, Dementia and Supported Ageing Branch
Professor Peter R Schofield	Neuroscience Research Australia (NeuRA) and UNSW
Kaele Stokes	Dementia Australia

The following tables (Table 9-Table 11) outline the approach to stakeholder engagement for this review, including the identified stakeholders, purpose for consultation and dates. Consultations were completed by 30 May 2019.

**Table 9 | Consultation phase 1**

Stakeholder group	Organisation	Individual(s)
Brain banks (also received an information request)	Sydney Brain Bank	Claire Shepherd
Brain banks (also received an information request)	NSW Tissue Resource Centre	Jillian Kril
Brain banks (also received an information request)	Victorian Brain Bank	Fairlie Hinton Catriona McLean
International brain banks	UK Brain Bank Network	Seth Love
Commonwealth Government	Department of Health	Jo Mond
Commonwealth Government	Department of Education and Training	Ryan Winn

Stakeholder group	Organisation	Individual(s)
State Government	NSW	Antonio Penna
Dementia Australia	Dementia Australia	Kaele Stokes
Researcher/ family	Flinders University (and member of reference panel)	Louise Heuzenroeder

**Table 10 | Consultation phase 2**

Stakeholder group	Organisation	Individual(s)
Brain banks (also received an information request)	South Australian Brain Bank	Mark Slee
Brain banks (also received an information request)	Queensland Brain Bank	Peter Dodd
Commonwealth Government	National Health and Medical Research Council	Clare McLaughlin
Researchers/clinicians/health workers	Sydney Brain Bank	Glenda Halliday
State Government	Victoria	Michael Furey
Researchers/clinicians/health workers	N/A	Juergen Goetz
Researchers/clinicians/health workers	N/A	Michael Buckland
Researchers/clinicians/health workers	N/A	Alexandra Seewann
Researchers/clinicians/health workers	N/A	Peter Nestor
Dementia network	ADNeT	Cherry Santos
International brain banks	Netherlands Brain Bank	Inge Huitinga
Brain Banking Consultancy Panel Member	The Florey Institute of Neuroscience and Mental Health	Colin Masters
Brain Banking Consultancy Panel Member	NeuRA and UNSW	Peter Schofield

**Table 11 | Consultation phase 3**

Stakeholder group	Organisation	Individual(s)
Donors and representative groups	Dementia Australia advocates	Seven individual interviews (deidentified)
International brain banks	The National Alzheimer's Coordinating Center (US)	Walter A Kukull
Potential brain bank	Tasmania	James Vickers
Cohort custodian	Australian National CJD Registry	Steven Collins
State Government	NSW	Kerry Chant
Commonwealth Government	Office of the Chief Scientist	Sarah Brown
Commonwealth Government	Assistant Secretary, Office of Health and Medical Research	Erica Kneipp
Commonwealth Government	NHMRC	Michael Nutt
Brain donor program	NSW Huntington Disease Service	Clement Loy
Brain donor program	Centre for Health Brain Ageing	Perminder Sachdev Kristan Kang
Brain donor program	University of Newcastle	Andrew Gardner
Researchers	UNSW	Kay Double
Researchers	UNSW	Vladimir Sytnyk
Researchers	Macquarie University	Ian Blair Kelly Williams
State biobank	NSW Statewide Biobank	Tom Karagiannis (with Heather McCann, manager of Sydney Brain Bank)
Biobank	Biobanking Victoria	Melissa Southey

## Appendix B Financial Model Documentation

### B.1 Base assumptions

The operational costs and capital requirements are presented in Table 12 and Table 13. Note that neuropathology is listed as an operational cost as opposed to being considered a component of FTE requirements. This is because it is a specialist service that can be accessed in several different ways.

Table 12 | Operational costs

Cost item	Cost (\$)	Notes
Cost of neuropathology per donation	920	This is based on MBS costs on like medical procedures. This assumes all samples go through staining, 50% further testing and 30% specifically through genetic testing. As noted in the VBB's SOPs, a second opinion is gathered on psychiatric cases--it is assumed 50% of all cases require a second opinion
Cost of autopsy per donor	1,000	This is based on qualitative data <sup>22</sup> which states that the cost of autopsy can 'cost up to \$1000'
Cost of transporting body to mortuary and back	250	This is based on documents provided by the VBB <sup>23</sup>
Cost of transporting tissue from nodes to hubs	650	
Cost of lab consumables per procedure	20	This is estimated using the VBB's financial documents <sup>24</sup>

Table 13 | Capital requirements

Cost item	Cost (\$)	Notes
Estimated cost of upright freezer	30,000	The cost is estimated through desktop research <sup>25</sup>
Estimated cost of chest freezer	18,000	The cost is estimated through desktop research <sup>26</sup>

To estimate the FTEs required for a single brain banking entity, the VBB and the SBB's operating procedures were used extensively to understand work processes and tasks underpinning brain banking. In each stage in the five-stage process, tasks were separated into scientific and administrative.

<sup>22</sup> NNIDR – Brain Banking 1 March 2017 document.

<sup>23</sup> Victorian Brain Bank review document Match 2019.

<sup>24</sup> Ibid.

<sup>25</sup> <https://www.fishersci.pt/shop/products/forma-900-series-86-c-upright-ultra-low-temperature-freezers/10031322>

<sup>26</sup> <https://www.fishersci.pt/shop/products/forma-8600-series-86-c-ultra-low-temperature-chest-freezers/11386371#tab3>

- **Scientific tasks** refer to tasks that involve direct handling of any human tissue and any data entry that involves scientific data (does not include neuropathology).
- **Administrative tasks** refer to tasks relating to donor recruitment and management and any administrative tasks in the tissue request and release processes.

Within both sets, tasks are separated into direct tasks and indirect tasks.

- **Direct tasks** refer to tasks that directly relate and directly contribute to brain banking.
- **Indirect tasks** refer to tasks that support the activity of brain banking. These include maintaining lab supplies, lab inspections, donor database maintenance, etc.

Time taken for each task is allocated either as:

- **time per output** where the total time per year is multiplied by the total quantity of the associated output per year
- **time per occurrence** where the total time is multiplied by the number of occurrences of the task per year.

Table 14 and Table 15 provide a breakdown of scientific direct and indirect tasks.

**Table 14 | Break down of scientific direct tasks**

Task	Place of occurrence	Hours per unit
<b>Tissue collection</b>		
Collection of tissue at post mortem, incl. transport	Node	4
Compliance with administrative procedures	Node	1
<b>Tissue processing</b>		
Routine preparation of fresh and fixed brain and spinal cord tissue	Node	6
Post sample to hub	Node	2
Assist neuropathology/sample key regions for case characterisation	Hub	40
<b>Tissue storage</b>		
Prepare and database documentation and macroscopic reports of tissue	Hub	4
<b>Tissue release</b>		
Collecting tissue regions and distribution to researchers	Hub	20
Perform embedding, microtomy and staining procedures on specimens	Hub	40
Collating results from researchers	Hub	4

**Table 15 | Breakdown of scientific indirect tasks**

Indirect task	Place of occurrence	Frequency	Hours per occurrence
Calibration and compliance with lab SOPs for working with biomaterial	Both	Per donation and release	2.5
Maintenance	Both	Once /week	3
Stock supplies	Both	Once /month	1
Annual lab inspection	Both	Once/ year	24
Miscellaneous tasks	Both	Daily	1

**Table 16 | Breakdown of administrative direct tasks**

Task	Place of occurrence	Hours per unit/ occurrence	Frequency of occurrence
Liaison with relatives of brain donors and other health care providers at time of death	Node	2	-
Initiation of brain-only autopsy process upon death of a donor	Node	2	-
Register donor consent according to procedures	Node	3	-
Facilitating the reconciliation of clinical data with brain bank data on donor death	Hub	2	-
Liaison with brain donor programmes for registration and ensure protocols are adhered for each donor	Hub	2	-
Regular updates and information for all brain donors	Hub	8	Once/month
Publicising brain donation through written reports, seminars and public speaking	Hub	8	Once/month
Generating reports on finances, outcomes and other issues for management	Hub	8	Once/month

Table 17 | Breakdown of administrative indirect tasks

Indirect task	Place of occurrence	Frequency	Hours per occurrence
Donor database maintenance and development	Hub	Once/week	2
Miscellaneous tasks	Hub	Daily	1.5

The quantities that drive the FTE assumptions are task-dependent. For example, most scientific tasks are driven entirely by the number of donations, whereas the admin tasks are driven largely by the number of donors and requests. The total FTE requirements are rounded upwards to the nearest 0.5 to account for the variances in time taken on each of the listed activities. Figure 24 and Figure 25 shows the FTE required at the nodes and with respect to the three quantities: the number of donors, the number of donations, the number of requests and releases. It is assumed that the number of releases is 95% of the number of requests.

Figure 24 | The distribution of FTE/ year required at the nodes collectively with respect to the number of donors and donations

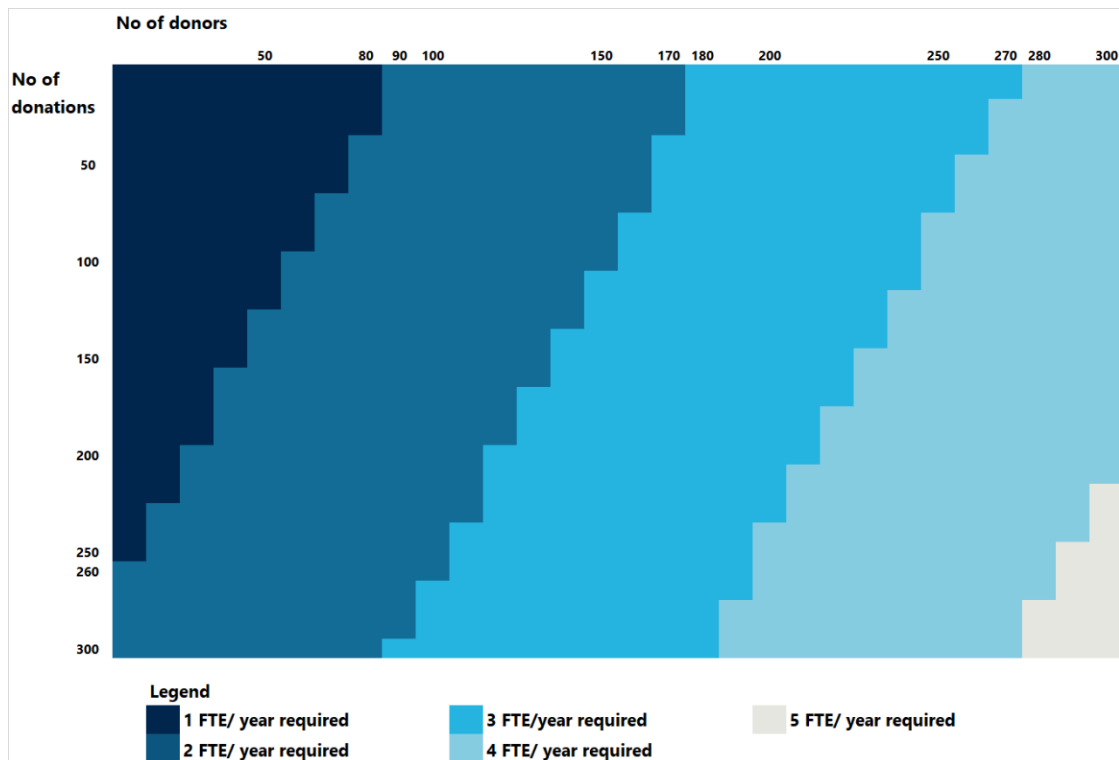


Figure 25 | The distribution of FTE/year required at the hubs with respect to the number of donors, requests and releases

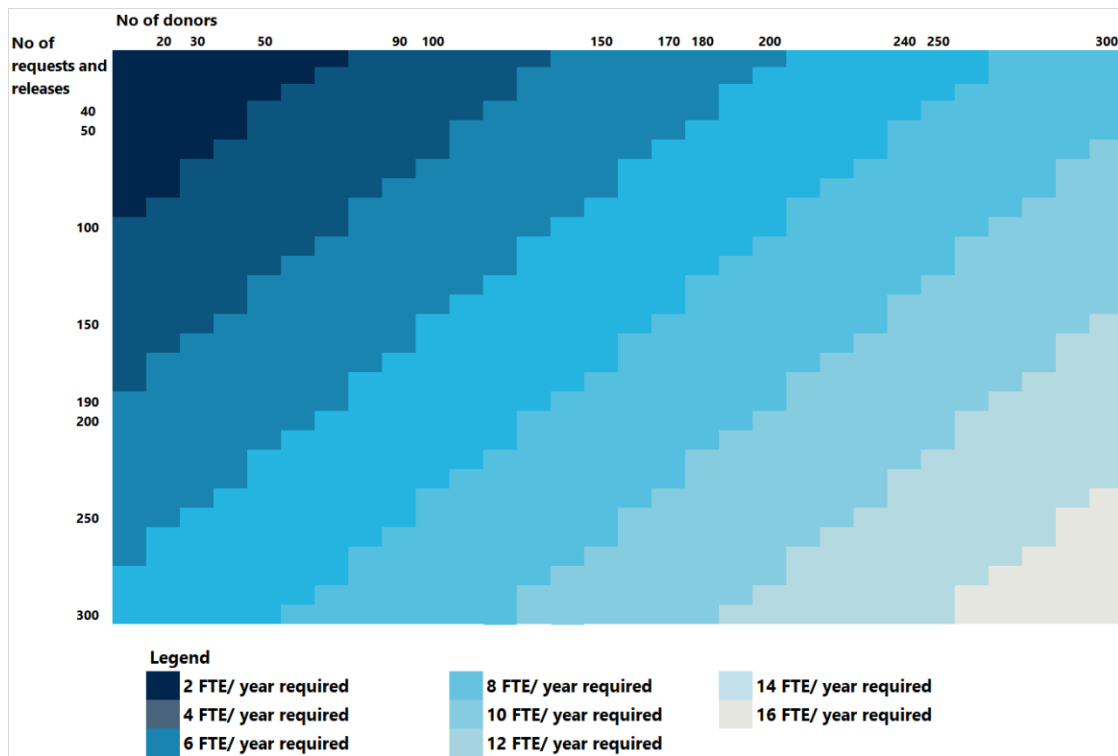


Figure 24 shows a heatmap of the number of FTEs required at the nodes collectively. A minimum of 0.5 FTE/node is implemented to ensure that in the extraordinary event that donors or donations falls too low, the financial model maintains a minimal FTE in the nodes.

## B.2 Financial Model projection assumptions

Future projections are driven entirely by projections on volume drivers used in the model. The assumptions built into the volume drivers are:

- the number of donors is projected forward based on the population growth rate among people aged 60 and greater
- the number of donations is projected forward based on the population death rate among people aged 60 and greater
- the number of requests is projected forward based on an average increase of 2% a year
- the total collection size is projected forward by adding the projected number of donations per year and a decrease proportional to 3% of the number of requests.

A Monte Carlo analysis is used to account for the inherent uncertainty in the future projections. 400 separate 10-year projections were performed and two key statistics are presented: the average value of the projections and values that occur with 90% probability on either side of the average of these 400 projections. The Monte Carlo analysis makes the following assumptions on the following volume drivers:

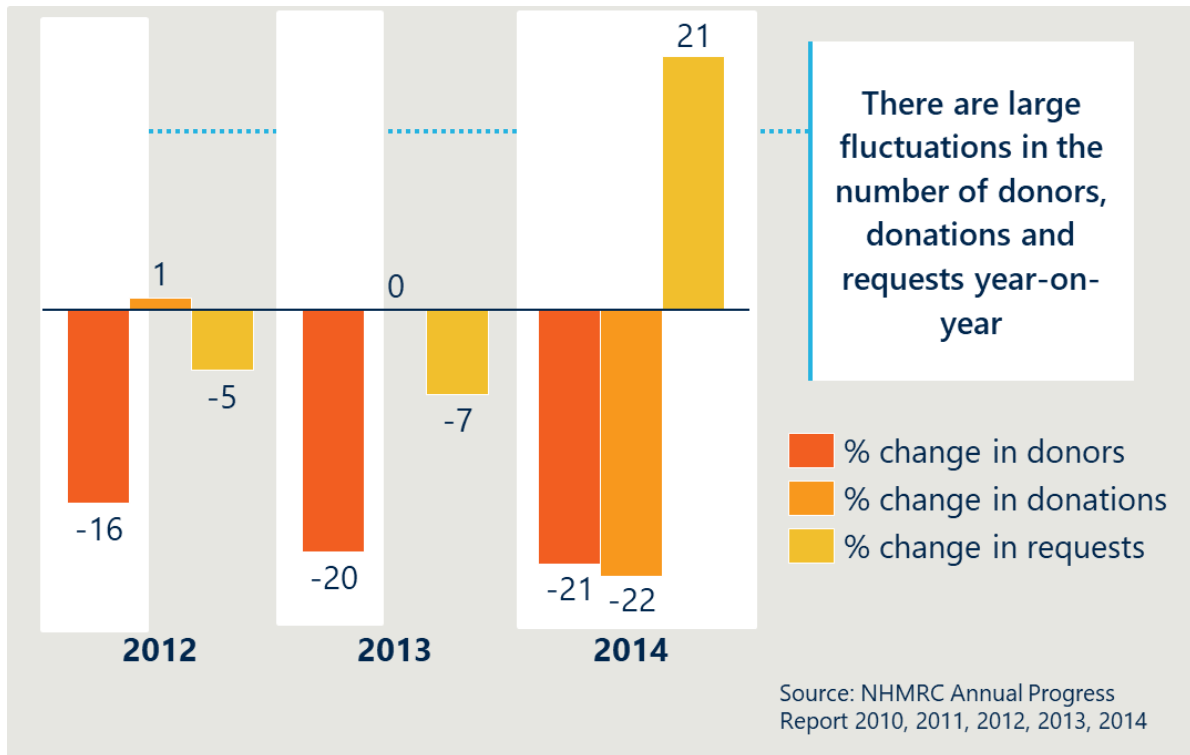
- the number of donors for each year in the model is drawn from a normal distribution with the mean of that year's population growth rate and a standard deviation of 10%
- the number of donations for each year in the model is drawn from a normal distribution with the mean of that year's population death rate and a standard deviation of 10%



- the number of requests is projected forward based on a normal distribution with a mean of 2% and a standard deviation of 10%.

The large standard deviation used in the projections are informed by the large fluctuations seen in the ABBN figures, see Figure 26 below.

Figure 26 | Percentage change in the number of donors, donations and requests from 2011 to 2014



### B.3 Financial Model cost recovery assumptions

The cost recovery model is built using data from the ABBN 2019 Fees schedule and available data from the brain bank. The model estimates the average cost per sample using the VBB tissue release data.

Table 18 | Calculation of tissue request average costs from total cost recovery data provided by the VBB

	2011	2012	2013	2014	2015	2016	2017	2018
Total cost recovery (\$)	91,652	111,172	59,650	44,181	38,843	67,991	168,695	88,750
Calculated cost per sample (\$)	31.32	22.35	18.24	13.81	21.33	14.01	33.53	23.42
Calculated cost per sample in 2019 dollars (\$)	38.52	26.69	21.14	15.54	23.31	14.86	34.54	23.42

The average and standard deviation of the cost per sample in 2019 dollars is \$24.75 and \$8.35 respectively.

The model estimates the average number of samples per request using the ABBN data from 2010 to 2014. The reason why the ABBN data is used as opposed to the VBB data is because the database that researchers would access in a single brain bank entity would more closely resemble that of the ABBN than just the VBB.

**Table 19 | Calculated average samples per tissue request based on the ABBN data**

	2010	2011	2012	2013	2014
<b>ABBN Sample Releases</b>	13,705	14,625	27,005	16,850	11,924
<b>ABBN Tissue requests</b>	105	108	103	96	116
<b>Average no. of sample/request</b>	130.52	135.42	262.18	175.52	102.79

The average and standard deviation of the number of samples per requests is 161 and 62 respectively.

Two cost recovery models are used:

1. The first cost recovery model uses a weighted average discount for 34% (based on the 2019 ABBN fees schedule) for internal requests.
2. The second cost recovery model charges the external rate regardless of whether the request is made internally or externally.

The assumptions in the cost recovery model are:

- The proportion of internal requests to total requests follows a normal distribution with a mean of 30% and a standard deviation of 5% (applicable to the first cost recovery model)
- The average cost per sample follows a normal distribution of \$25 and a standard deviation of \$8.

The number of samples requested per researcher follows a normal distribution with mean 140 and standard deviation 35.

# nous

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## ABOUT NOUS

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