

# FINAL REPORT

# Review of the Australian Brain Cancer Mission



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# Glossary

ANZCHOG	Australian and New Zealand Children's Haematology/Oncology Group
ANZCTR	Australian and New Zealand Clinical Trials Registry
BCBA	Brain Cancer Biobanking Australia
BCC	Brain Cancer Centre
CIE	Centre for International Economics
COGNO	Cooperative Trials Group for Neuro-Oncology
CSO	Common Scientific Outline
CRT	Chemoradiotherapy
CTC	Clinical Trials Centre
CTG	Clinical Trial Group
DIPG	Diffuse Intrinsic Pontine Glioma
EAP	Evaluation Advisory Panel
HMRO	Health and Medical Research Office
ICRP	International Cancer Research Partnership
КСР	Kids Cancer Project
LOGGIC	Low Grade Glioma In Children and adolescents
MAGMA	Multi-Arm GlioblastoMa Australasia
MHF	Mark Hughes Foundation
MRFF	Medical Research Future Fund
MSAG	Mission Strategic Advisory Group
NCI	National Cancer Institute
NHMRC	National Health and Medical Research Council
NSW	New South Wales
PdCCRS	Priority-driven Collaborative Cancer Research Scheme
SCCT	Support for Cancer Clinical Trials
TJBCM	Tessa Jowell Brain Cancer Mission

UK	United Kingdom
UNSW	University of New South Wales
US	United States
WEHI	Walter and Eliza Hall Institute
ZERO	Zero Childhood Cancer Program

# Summary

This report examines the Australian Brain Cancer Mission (the Mission), half-way through its ten-year period. It reviews whether investments made through the Medical Research Future Fund (MRFF) align with objectives set out in the Mission Roadmap, and whether investments have made any achievements (or are on track to make any achievements) against the MRFF Measures of Success. The Mission is also comprised of investments made by Mission Funding Partners. These broader investments are examined as a critical part of the brain cancer research landscape, and provide important context for future opportunities for the MRFF to optimise its investments in the Mission.

This review has been undertaken by the Centre for International Economics (CIE). The terms of reference for the review, the approach, and limitations, are summarised in box 1.

# About the Australian Brain Cancer Mission

The Mission was announced in 2017 to provide a dedicated and substantial financial commitment to brain cancer research in Australia to better resource and coordinate effort to address long standing poor survival and survivorship outcomes. The stated high-level objectives of the Mission are to:<sup>1</sup>

- double the survival rate of Australians living with brain cancer over 10 years
- improve quality of life for people with brain cancer
- give all adult and child patients with brain cancer a chance to join a clinical trial, and
- boost Australian research and build research capacity.

In the long-term, the Mission aims to defeat brain cancer.

The Mission Roadmap outlined four key investment strategies aligned to these goals, each with corresponding objectives and activities, and early implementation priorities<sup>2</sup>.

Unlike other MRFF initiatives, the Mission is co-funded by the Australian Government through the MRFF and twelve Funding Partners that include some State Governments and a range of philanthropic organisations.

<sup>&</sup>lt;sup>1</sup> Australian Government Department of Health and Aged Care 2023, Australian Brain Cancer Mission, https://www.health.gov.au/our-work/australian-brain-cancermission?language=und, accessed 1 December 2022.

<sup>&</sup>lt;sup>2</sup> The four investment pillars included increased patient survival, quality of life and care experiences, increased and equitable access and participation in clinical trials, expanded research platforms and technologies, and increased researcher capacity and excellence.

#### **1** Overview of the review

The purpose of this review in line with the Terms of Reference is to:

- assess all existing investments under the Mission through the MRFF and partner funding<sup>3</sup> from October 2017 to April 2022
- assess all other existing investments in brain cancer research made through the MRFF from October 2017 to April 2022
- consider approaches and the current landscape for health and medical research and treatments for brain cancer internationally and in Australia, and
- suggest opportunities (if any) for improving alignment between the intended goals and implementation of the Mission.

It has involved:

- the development of an evaluation and stakeholder management plan
- desktop scan of the national and international brain cancer research landscape
- interviews with approximately 40 stakeholders including Funding Partners, research bodies and brain cancer researchers, consumer groups, former members of the Mission Strategic Advisory Group (MSAG), industry representatives, and international brain cancer organisations, and
- a survey of recipients of brain cancer related MRFF funding.

This review has been overseen by an Evaluation Advisory Panel. The findings in this report are subject to the following qualifications and limitations:

- the desktop scan primarily reports analysis of data available from databases and clinical trial registries, and less on the whole of the brain cancer research literature, commensurate to the scope of the review and available time and resources. It was also limited to published material, which may have biased the results
- consultations were not held with all interested parties, and it is possible that the views presented to this review are not representative
- consultation with brain cancer patients and carers was limited to three patients, and five consumer representative organisations, which also included carers
- some issues raised by stakeholders were out of scope for this review, including matters relating to how the Mission is administered, and
- findings are limited to the extent they consider only the views put forward by those that were consulted. For instance, it is possible that researchers made positive comments about the Mission because of concerns that future funding might otherwise not be available.

<sup>&</sup>lt;sup>3</sup> The Australian Brain Cancer Mission is the only MRFF initiative that includes co-funding from Funding Partners, which are comprised of government and non-government organisations.

Together, the Mission funders have committed \$136.66 million to invest in Australian brain cancer research, \$60.26 million of which is via the MRFF.

The co-funding model has resulted in the Australian Government and Funding Partners investing more in Australian brain cancer research than otherwise, and promoted synergistic investment across the research continuum.

The Mission is delivered in partnership by the Australian Government Department of Health and Aged Care and Cancer Australia. Cancer Australia leads engagement and collaboration with the Mission Strategic Advisory Group (MSAG) and Funding Partners, and the Department leads the delivery of investments made through the MRFF. The MSAG provides strategic advice and guidance on achieving the Mission Roadmap objectives, including setting priorities for investment.

# **Overview of the Australian brain cancer research landscape**

Brain cancer research in Australia is widely dispersed across research teams in universities, medical research institutes, and in Australian and international research collaborations, and is funded by a variety of government and non-government sources.

In response to relatively poor improvements in survival over many decades, the Mission was launched in 2017 to offer a major fillip to brain cancer research funding from the MRFF and a range of Mission Funding Partners.

The combined efforts of the MRFF and the Mission Funding Partners represent the largest pooled allocation of funding to brain cancer research in Australian history, which since 2017-18 has committed \$136.66 million over 10 years, including:

- \$50 million from the Australian Government to be distributed via the Mission
- \$10.26 million from the Australian Government via other MRFF initiatives, and
- \$76.4 million through Funding Partners.

This provided a major lift to what was, by historical standards, a low level of investment. Based on the 2023 Cancer Australia audit of cancer research in Australia, in 2003-2005, \$1.5 million was allocated to 10 brain cancer specific projects. With some increases in subsequent years, the 2018-2020 period witnessed a large increase in brain cancer research with \$54.1 million allocated to over 161 projects (chart 2). Brain cancer also received the largest increase in single tumour type research funding, which increased in each triennium from 1 per cent in 2003-2005 to 10 per cent in 2018-2020<sup>4</sup>.

While much of this increase represents Mission-related funding from the MRFF and Funding Partners, it also includes an increase in National Health and Medical Research Council (NHMRC) funded brain cancer projects and possibly others, demonstrating increased funding outside of the Mission.

<sup>&</sup>lt;sup>4</sup> Cancer Australia 2023, Cancer Research in Australia: An overview of funding for cancer research projects and programs in Australia, 2012 to 2020, Cancer Australia, NSW.



#### 2 Brain cancer specific projects and programs 2003-2005 to 2018-2020

Note: The shaded area denotes the duration of the Mission, although projects counted are not limited to those funded by the Mission. Data source: Cancer Australia (2023) – Cancer Research in Australia.

Australian brain cancer clinical trials are strongly focused on the early phase of research, and are primarily interventional drug studies to assess the effect(s) of one or more chemical or biological agents including vaccines.

Based on the Australia New Zealand Clinical Trials Registry, there were 84 brain cancer trials registered from 2005 to 2022 (chart 3)<sup>5</sup>.

- 40 per cent of trials were non-drug trials. The majority of total trials (50.1 per cent) were Phase 1 or 2, with Phases 3 and 4 comprising only 9.9 per cent of trials.
- Individual sponsors are primarily focused on non-drug trials. Half of the university sponsored trials are non-drug focused, while 30 per cent focused on Phase 2 drug development. Commercial/industry trials are more focused on the early stages of trials, with Phase 1 and 2 trials comprising 89 per cent of trials.



#### 3 Characteristics of Australian brain cancer clinical trials

Data source: CIE analysis of ANZCTR database for brain cancer trials 2005 to 2022.

<sup>5</sup> Recruitment was from both Australia and internationally. Data accessed 7 November 2022.

## MRFF and the Mission

MRFF is the single largest funder of brain cancer research in Australia, providing funding for research primarily through the Mission as well as other MRFF initiatives.

In total, the MRFF has allocated \$60.26 million to brain cancer research.

- \$50 million will be allocated through Mission grants. From 2017 up until April 2022<sup>6</sup>,
   8 grants were allocated through the Mission totalling \$21.8 million (44 per cent of the total to be allocated through the Mission). This included:
  - 3 directed grants with a total value of \$10.5 million, and
  - 5 competitive grants allocated through 3 competitive grant opportunities with a total value of \$11.3 million.
- \$10.26 million will be allocated through other MRFF initiatives. From 2017 to April 2022, 11 grants with a total value of \$8.77 million had been awarded.

A key theme of Mission grants has been improving health-related quality of life for brain cancer survivors, reflecting the focus on survivorship. Survivorship grant opportunities comprise 44 per cent of Mission funding<sup>7</sup> (not including brain cancer research funding from other MRFF initiatives).

# **Mission Funding Partners**

The Funding Partners of the Mission include a range of non-government and charitable organisations, as well as some State and Territory Governments. Some are single tumour type funders (brain cancer only) and some are not, and some only fund brain cancer research through their contributions to the Mission, and some fund broader research activities.

To date, \$73.97 million has been committed to projects under the Mission<sup>8</sup>.

It is noted that some Funding Partners invest in brain cancer research outside of their commitments made to the Mission, including internationally.

## Funding models for Australian brain cancer research

Various approaches to funding are used to invest in Australian brain cancer research. The Mission has used a combination of (initially) targeted grants, and (more recently) competitive grants. Charitable funds tend to support research teams with baseline funding, without directing research purpose or outcomes.

<sup>&</sup>lt;sup>6</sup> Since April 2022, 4 grants have been awarded worth \$11.45m, which includes two additional lead organisations (the Walter and Eliza Hall Institute of Medical Research and the Council of the Queensland Institute of Medical Research).

<sup>&</sup>lt;sup>7</sup> As of April 2022.

<sup>&</sup>lt;sup>8</sup> This amount does not include funding from the Cure Brain Cancer Foundation, details of which were not available at the time of publication. It is also noted that several Funding Partners have spent more than their initial commitment.

A common approach is to use an Expert Panel or Scientific Advisory Committee to decide on funded projects, used by the Mission and several other brain cancer funders.

## Comparisons with international brain cancer research

According to the International Cancer Research Partnership (ICRP)<sup>9</sup>, there were 13 699 brain tumour related projects as defined by ICD-10 C71 funded internationally between 2017 and 2022.

This points to a vast collection of international brain cancer research.

An analysis of ICRP projects by CSO reveals that most studies internationally focus on treatment, followed by biology, early detection and diagnosis and prognosis, then aetiology and survivorship (chart 7). The outcomes of the ICRP data compared with the Cancer Australia audit of Australian brain cancer research funding reveal that **Australia has**:

- a larger focus on treatment (51 per cent of total projects), compared to 34 per cent internationally
- a larger focus on early detection, diagnosis and prognosis (26 per cent), compared to 18 per cent internationally
- a larger focus on survivorship (13 per cent), compared to 8 per cent internationally
- a substantially smaller focus on biology (9 per cent of projects), compared to 24 per cent internationally<sup>10</sup>, and
- no focus on aetiology and prevention, which internationally comprises 16 per cent of total projects.

<sup>&</sup>lt;sup>9</sup> ICRP maintains the only public source, worldwide, of current and past grants, totalling over \$80 billion in cancer research since 2000 from 32 ICRP Partners and 156 international funding organisations (all cancers). See https://www.icrpartnership.org/, Accessed 9 August 2022.

<sup>&</sup>lt;sup>10</sup> It is noted that this data does not include the most recent Mission projects that have either a particular focus on biology (three under the 2021 Brain Cancer Research grant opportunity) or provide infrastructure support that will help enable biology research (one under the 2022 Australian Brain Cancer Research Infrastructure grant opportunity).



4 ICRP brain cancer projects by CSO and Cancer Australia Audit of Australian brain cancer funding, 2018-2020

Data source: International Cancer Research Partnership, CIE.

# International brain cancer clinical trials

The key clinical trial registry for international cancer clinical trials is ClinicalTrials.gov<sup>11</sup>, which holds registrations from over 425 000 trials from over 200 countries.

Running a query for brain cancer within the trials database yielded 2 539 clinical trials<sup>12</sup>, which includes over 685 800 participants. Chart 5 shows summaries of the funding, age groups, phases, and gender composition of the trials. Other government sources, philanthropy, consumers, and foundations were funders in over 50 per cent of brain cancer trials. Over 63 per cent of trials were in either Phase 1 or 2.

<sup>11</sup> https://clinicaltrials.gov/about-site/about-ctg

<sup>12</sup> Date accessed 18 August 2022



#### 5 Clinical trials database summary

Note: Funding Other\* includes other government sources, philanthropy, consumers and foundations. Data source: Clinicaltrials.gov, CIE.

# Mission progress and key achievements to date

Findings regarding the progress of the Mission to date are based on analysis of feedback from stakeholder consultations and the survey of MRFF brain cancer research grantees.

Some comments are specific to MRFF funded projects within the Mission, and some are broader observations.

## Increased funding for brain cancer research in Australia

Overall, the Mission has successfully increased the amount of funding for Australian brain cancer research.

When the Mission was established, the Australian Government pledged to match commitments by Funding Partners to the Mission up to \$50 million, which was a major impetus for several Funding Partners joining the Mission, and in many cases resulted in these funders spending more on brain cancer research themselves than they otherwise would have.

Based on stakeholder interviews, increased funding for brain cancer research has led to a higher number of brain cancer researchers, mainly due to researchers transitioning from other cancer fields, such as liver and lung cancer. This reflects the increased financial

certainty that the Mission has provided to support future brain cancer research in Australia.

It has also supported research along the discovery continuum, from basic through to translational research, albeit to varying degrees. The MRFF has had a much stronger focus on clinical trials, and Funding Partners have done more to support basic research, the latter of which is particularly important to attracting industry, and seeding new treatments.

## More Australians are able to access clinical trials

The security of funding provided by the Mission to clinical trials has already started to allow researchers to seek out international trials more efficiently. As funding is secured, researchers can focus on applying to the trial immediately, as opposed to discovering the trial, then raising funds, then applying. Particularly for paediatrics, where often the best treatments can only be accessed via clinical trials, this certainty of funding has been critical.

Based on the survey of MRFF brain cancer research funding:

- 17 (out of 19) MRFF brain cancer grants gave Australian patients access to clinical trials that they otherwise would not have had access to, and
- MRFF grant recipients indicated that approximately 1 350 additional patients were given access to a clinical trial that they otherwise would not have had access to<sup>13</sup>.

In addition, the MRFF brain cancer research grants helped to build clinical trial capacity that is expected to lead to additional clinical trial sites in Australia, and more Australians having access to clinical trials in the future.

MRFF brain cancer research grant recipients considered it 'likely' or 'very likely' that the capacity built through 12 of the MRFF brain cancer grants will lead to more clinical trial sites in Australia, and it was considered 'likely' or 'very likely' that the capacity built through 17 of the MRFF brain cancer grants will improve access to clinical trials for Australian patients in future.

Over the next five years, MRFF grant recipients estimated that the capacity built through MRFF brain cancer grants will:

- lead to around **70** additional clinical trial sites in Australia, and
- give an additional 1600-1700 Australian patients the opportunity to participate in a clinical trial that they would not otherwise have had access to.

## More capacity for translational research

The Mission has already had a positive impact on building capacity for translational research in terms of attracting researchers into the brain cancer field, and funding shared infrastructure. Most MRFF brain cancer research grant recipients also believe their grant

<sup>&</sup>lt;sup>13</sup> It is not possible to know, based on the data available, how this compares to the number of patients that would have had access to a clinical trial without Mission funding.

has contributed to building translational research capacity, which was a key focus for 17 out of 19 grants.

However, the Mission is yet to have a direct impact on fostering larger scale collaborations (although the ANZCHOG and COGNO grants have helped those collaborations build international networks) or links with industry, which are important enablers of translational research.

The Mission is also not yet believed to have had an impact on commercialisation, with minimal impact on building links between researchers and industry, or otherwise contributing to other aspects of the commercialisation environment.

### Investment in survivorship

MRFF funded Mission grants have filled a gap in survivorship research to improve patient quality of life, with three of the eight MRFF Mission grants up until April 2022 focused on survivorship<sup>14</sup>, accounting for 44 per cent of Mission grants to date.

This has filled a gap in an area of research that matters to patients, who are seeking to be better cared for.

### Outstanding unmet needs

The most outstanding areas of unmet need raised during stakeholder consultations included:

- funding for innovations that do more than make incremental improvements to existing survival prospects. To date there has been relatively less investment in basic research than is needed to create a pipeline to feed future clinical trials. Some stakeholders felt this should have been an early focus of the Mission given the long timeframes before any impacts are felt
- less funding for adult brain cancer than paediatric cancer, particularly relative to the number of patients affected
- less support than is needed for larger scale multi-team/disciplinary collaborations that focus on improved survival and linkages with clinicians and industry, and
- underfunding /lack of funding for basic high risk/high reward research that might discover new treatments. While this is partly a function of the competitive grants process, which is believed to foster conservatism from grant assessment or peer review panels, it remains a widely held view. The same sentiment can also arguably be said for the way that grants are scientifically assessed across the broader research sector.

<sup>&</sup>lt;sup>14</sup> It is noted that the most recent survivorship projected awarded from the MRFF to the WEHI (see https://www.wehi.edu.au/news/collaborative-brain-cancer-research-awarded-46m-grant) is out of scope for this review due it being announced after the commencement of this review.

#### Other potential impacts are too soon to observe

It is too early to be definitive about what impact MRFF brain cancer research grants have, or will, achieve regarding new health technologies and new health interventions, although the prospects for both are positive.

There were **10** MRFF brain cancer grant recipients that indicated that developing, identifying or validating a new health technology (or technologies) was an objective of the research. Of these 10 projects:

- 3 indicated they were 'certain' a new health technology would be delivered (or already had been delivered)
- 6 indicated they considered it 'likely' or 'very likely' that the research would deliver a new health technology, and
- only 1 project considered it unlikely that the MRFF grant would deliver a new health technology directly; however, it was considered 'likely' that future planned research leveraged from the MRFF grant would deliver a new health technology.

In terms of the potential impacts that new technologies will deliver, it is the researchers' assessment that:

- 7 projects are expected (certain, very likely or likely) to deliver a new technology that will improve the chance of survival (although the extent of the improvement is not known)
- 7 projects are expected to deliver a new technology that will lead to 'other improvements' (i.e. excluding reduced impact on cognitive function, reduced pain and reduced fatigue) in health-related quality of life for patients, and
- 6 projects are expected to deliver a new technology that will reduce the burden on the health system.

### Alignment to the Roadmap

The Mission Roadmap was intended to provide a high level implementation plan for MRFF and Funding Partner investment, with the MRFF funding research that met the objectives and requirements of the MRFF, and Partner Funding extending investment into complementary areas.

In general, MRFF-funded grants aligned well with the Mission Roadmap (based on researcher assessments, as reflected in the survey responses). This included both Mission grants (which were explicitly intended to align with the Roadmap), and grants under other MRFF initiatives (which were not explicitly intended to align with the Roadmap). However, some areas of the Roadmap had no MRFF grants in close alignment, with Funding Partners dominating investment in those areas (chart 6).

MRFF-funded grants aligned most closely (from the perspective of both the number of projects and the dollars invested in those projects) with the *Increased and equitable access and participation in clinical trials* pillar. 17 (out of 19) MRFF brain cancer grants gave Australian patients access to clinical trials.

MRFF-funded grants aligned less well with the *Increased researcher capacity and excellence* pillar. Some items under this pillar had no MRFF grants in close alignment (although some partner funding aligned with those areas of the Roadmap).



#### 6 MRFF and Funding Partner investments across the Mission Roadmap

Note: MRFF and Funding Partner Investment information as of July 2023. All Funding Partner projects have been mapped to roadmap pillars by each respective Funding Partner. While some MRFF grants may align with more than one roadmap pillars, allocation has been to the pillar determined to be the best fit.

Data source: Cancer Australia 2023.

# Key opportunities

Looking forward, there are several opportunities for the Mission to further strengthen its impact and capacity to make a difference to brain cancer survival. Many of these involve addressing barriers to better progress to date, and aligning future MRFF funding to areas where the MRFF is strategically well placed to make a difference.

## **Opportunity #1 Defining the role and purpose of the Mission**

It is recommended that the Australian Government, with advice from an advisory panel for the Mission, Cancer Australia, and the Department of Health and Aged Care form a view about the charter of the Mission, and communicate this to stakeholders who can then align their expectations with what the Mission is best placed to do and represent.

The Australian Government should be clear about its role and contribution to the Mission, and how this complements the role of the Funding Partners. Clarity around Australian Government priorities for MRFF funding will make it clearer to Funding Partners what their role in the Mission is, and how to best leverage their own contributions to brain cancer research.

This includes being clear about whether Cancer Australia and the Department of Health and Aged Care should use the Mission to coordinate, and/or rally and coalesce, support around brain cancer research in Australia.

It is acknowledged that the above would need to be considered and answered within existing legislative and policy framework of the Mission and MRFF more broadly.

This role and purpose should also be reflected in the Implementation Plan for the Mission going forward.

## **Opportunity #2: Develop an Implementation Plan**

There is a need for an Implementation Plan for the next phase of investment to provide clarity to the brain cancer research community and focus future effort.

This is expected to include:

- the Mission goal
- priority areas for investment
- delivery horizons, including research to be actioned in the short (1-2 years) and medium term (2-5 years), and potentially longer term expectations beyond the current funded period, and
- activities / amendments required to support research and facilitate aspirational outcomes.

It should clarify findings made in this review with respect to:

- strategic role for the Mission to play to its strengths and best leverage funding from other sources
- effective ways to fund opportunities for early and mid-stage career researchers and clinicians to be involved in research that addresses research barriers
- how consumers will be engaged, and when and how consumers should be involved in projects funded by the Mission, and
- how collaboration across the brain cancer research ecosystem will be nurtured, including how barriers to industry engagement and investment will be addressed.

Opportunity #2.1 to 2.7 should be considered in the Implementation Plan. This should be developed in consultation with Funding Partners to ensure a complementarity of investments between the MRFF and Funding Partners.

#### **Opportunity #2.1: Improved communication and coordination with Mission stakeholders**

Better communication would improve visibility, transparency, as well as strategic coordination between Mission stakeholders. For example, Mission administrators should review how they communicate upcoming grant opportunities to stakeholders. This will allow key stakeholders including Funding Partners and others the opportunity to engage with upcoming grants.

The progress of Mission funded projects, particularly MRFF funded projects over which the Mission administrators have visibility, should be better communicated to provide assurance of progress and celebrate research wins, and allow Funding Partners to better communicate to their inputs to their stakeholders, which in turn will support the Mission's ongoing long-term success.

Information should also be accessible to a non-technical audience. This may mean having a 'what this means for consumers,' section and the use of lay person terminology.

Better coordination could involve providing grant opportunities that invite co-funding from Funding Partners that are only empowered to support types of research (such as adult only, paediatric only, cure-discovery only').

#### **Opportunity #2.2: Increased funding for biology and basic research**

Increased funding for biology and basic research would better create a pipeline to feed into the enhanced translational capacity invested in by the Mission. This would build on the most recent competitive grant rounds that have included a focus on basic research.

While Funding Partners have invested in researcher capacity through Centres of Excellence and fellowships, much of their allocation to the Mission has been invested, and the MRFF has not substantially supported this kind of research.

Subject to Key Finding #1, an advisory panel for the Mission could consider whether the Mission's role may include funding larger scale basic research collaborations within Australia and internationally, leveraging laboratory-based research of Funding Partners, scaling up promising basic research, and offering a grant opportunity for innovative approaches to brain cancer biology research.

# *Opportunity* #2.3: *Innovative funding to retain early and mid-stage researchers and clinician researchers*

An advisory panel for the Mission should consider how to support early and mid-stage career and clinical researchers as part of developing the Implementation Plan.

This will need to acknowledge that the competitive grants model makes it hard for early and mid-career researchers to get research funding, which can be a disincentive for talented researchers to pursue a career in brain cancer research, and there are limited mechanisms for clinicians to be allocated research time. It should be noted that this is a systemic problem for the medical research sector, which may not be addressed by the Mission alone.

One option is for the Mission to include a separate program to provide block funding for these opportunities to be allocated on a merit, or percent of researcher headcount, basis (capitation).

If competitive grants are retained as a form of funding, then potential grantees could be required to nominate/include an allocation for clinical involvement and/or training and development, which could be considered by assessors.

#### **Opportunity #2.4:** Alternative innovating funding models

The standard competitive funding model alone is unlikely to be able to achieve some of the strategic priorities of the Mission.

Alternative funding models could be explored, and where appropriate made available, for projects that can increase total funding for brain cancer research, and direct research into areas of unmet need. Those with promise are expected to include:

- matched funding from the MRFF for projects of national significance that involve partners outside of the existing Funding Partner model
- the coordination of forums around key unmet needs that can bring funding partners together and create coordination of effort and resources, and
- cradle-to-grave or breakthrough grants for high-risk research opportunities.

The Mission Funding Partners could also be involved to ensure investments made inside and outside the MRFF's competitive grants model are well leveraged.

#### **Opportunity #2.5: Encouraging greater industry involvement**

Stronger links with industry should help break down barriers to industry investment in clinical trials and brain cancer research in Australia, which is challenged by Australia's small population. A precursor to better industry investment is greater industry involvement and visibility of Australia's brain cancer research expertise.

An opportunity for greater industry links should form part of Key Findings #1 and #2 and may involve:

- industry involvement in the development of the Implementation Plan, and
- greater industry representation within any future advisory panel for the Mission.

#### Opportunity #2.6: Aligning future funding with the best role for the Mission

Once the role and purpose of the Mission is clear and following the development of the Implementation Plan, remaining disbursements from the Mission can be allocated in a way that reflects the strategic positioning and strength of the Mission.

Based on stakeholder consultations, this review has formed the view that investments in national infrastructure to support Australians accessing clinical trials, such as ANZCHOG and COGNO, appear to be well aligned with a role for the Australian Government. Larger scale projects that scale up promising discovery research, as well as larger projects that facilitate national/international research collaborations, would also appear to be well aligned.

Future funding should also consider how all Australian brain cancer patients get access to standard treatment for brain cancer.

While access to standard treatment is a service delivery issue, guidance is sought on how equity of access can be supported by the Mission going forward, in particular how research can help discover barriers, or find pathways to better adoption.

#### **Opportunity #2.7: Consumer engagement framework**

The Implementation Plan should set out how consumers will be engaged, and set an agenda for when and how consumers should be involved in projects funded by the Mission.

## **Opportunity #3: Improvements to the competitive grants model**

While administrative issues are outside the scope of this review, the following findings were captured from stakeholders and summarised here as they support the broader objectives of the Mission.

Consider ways to increase representation of brain cancer experts (researchers or otherwise) on review panels to provide greater opportunity for a scientific/clinical consensus based selection of projects.

Explore ways to better communicate upcoming grant opportunities with sufficient lead time for the research sector to develop high value proposals. This should include being transparent about funding priorities in the Implementation Plan.

Provide feedback on unsuccessful grant applications.

It should be noted that many of these have been or are being addressed by the Department via other consultation and continuous improvement processes. For example, the Department now publishes a calendar of forecast MRFF grant opportunities,<sup>15</sup> and outcomes, news and celebrating research wins are provided on the Department's website<sup>16</sup> and the MRFF newsletter.

# **Research qualifications and limitations**

The findings in this report are subject to the following qualifications:

- the desktop environmental scan of Australian and international research did not examine all brain cancer research, and was limited by the time and resources available for this review
- the desktop environmental scan was limited to published material, which may have biased scientific/laboratory-based testing and discovery rather than research with a more translational and commercialisation focus
- consultations were not held with all interested parties, and it is possible that the views presented to this review are not representative. Stakeholders were approached as agreed with the Health and Medical Research Office of the Department of Health and Aged Care and Cancer Australia. It is noted that:

<sup>&</sup>lt;sup>15</sup> See Department of Health and Aged Care website: https://www.health.gov.au/ourwork/medical-research-future-fund/mrff-grant-opportunities-calendar.

<sup>16</sup> See Department of Health and Aged Care website: https://www.health.gov.au/resources/publications/medical-research-future-fund-mrff-grant-recipients?language=und

- there was no call for public input to the review, and
- private hospitals were not consulted
- consultations were primarily held with representative organisations, which are not necessarily able to provide the viewpoint of all constituents
- some stakeholders were unable to participate in this review due to other commitments and the timing of the review
- consultation with brain cancer patients and carers was limited to three patients, and five consumer representative organisations, which also included carers
- some issues raised by stakeholders were out of scope for this review, including matters relating to how the Mission is administered, and
- this consultation report may reflect response bias, as findings are limited to only the views put forward by those that were consulted. For instance, it is possible that researchers made positive comments about the Mission because of concerns that future funding might otherwise not be available.

# 1 Introduction

This report is an interim review of the Australian Brain Cancer Mission (the Mission), half-way through its ten year commitment period. The objectives of the Mission are to double the survival rate of Australians living with brain cancer over 10 years, improve quality of life for people with brain cancer, give all adult and child patients with brain cancer a chance to join a clinical trial, and boost Australian research and build research capacity<sup>17</sup>. In the long-term, the Mission aims to defeat brain cancer. Its specific objectives are set out in the Mission Roadmap<sup>18</sup>. The Australian Government funds its contribution to the Mission through the Medical Research Future Fund (MRFF), which supports Australian health and medical research<sup>19</sup>.

This review assesses whether MRFF-funded projects are on track to meet the objectives set out for it in the Mission Roadmap, and how it aligns to the MRFF Measures of Success. These projects are only part of the broader Mission, which also includes substantial commitments from Mission Funding Partners to brain cancer research in Australia. These commitments are examined in this review as part of the brain cancer landscape.

# Unmet need in brain cancer research

In 2022, brain cancer accounted for 1.2 per cent of new cancer diagnoses, but almost triple that in terms of deaths from cancer (3.1 per cent), and it is the ninth most common cause of cancer death in Australia<sup>20</sup>.

In 2014-2018, the chance of surviving brain cancer at five years was 23 per cent, with only minimal improvement since 1989-1993 when five-year survival was 20 per cent. This compares to a considerable improvement in five year survival for all cancers, which

<sup>&</sup>lt;sup>17</sup> Australian Government Department of Health and Aged Care 2023, Australian Brain Cancer Mission, https://www.health.gov.au/our-work/australian-brain-cancermission?language=und, accessed 1 December 2022.

<sup>&</sup>lt;sup>18</sup> Australian Government Department of Health and Aged Care 2022, Medical Research Future Fund Australian Brain Cancer Mission, https://www.health.gov.au/sites/default/files/doc uments/2022/07/australian-brain-cancer-research-roadmap.pdf, accessed 1 December 2022.

<sup>19</sup> Australian Government Department of Health and Aged Care 2016, 'Australian Medical Research and Innovation Strategy 2016-2021', see https://www.health.gov.au/resources/ publications/australian-medical-research-and-innovation-strategy-2016-2021.

<sup>&</sup>lt;sup>20</sup> Cancer Australia 2022, Brain Cancer in Australia Statistics, see https://www.canceraustralia.gov.au/cancer-types/brain-cancer/statistics

was 70.1 per cent in 2014-2018, compared to 52.3 per cent in 1989-1993<sup>21</sup>. Survival is particularly poor for certain brain cancer types, with the five year survival rate for glioblastoma being 4.6 per cent.<sup>22</sup>

The relatively minimal progress in survival reflects the absence of substantive change in the treatment regime for brain cancer in the last 30 years, and treatments that do exist, result often result in a range of physical and mental health problems.

# The Australian Brain Cancer Mission

The Mission was announced in 2017 to provide a dedicated and substantial financial commitment to brain cancer research in Australia to better resource and coordinate effort to address these long standing poor survival and survivorship outcomes. The stated high-level objectives of the Mission are to:<sup>23</sup>

- double the survival rate of Australians living with brain cancer over 10 years
- improve quality of life for people with brain cancer
- sive all adult and child patients with brain cancer a chance to join a clinical trial, and
- boost Australian research and build research capacity.

In the long-term, the Mission aims to defeat brain cancer.

Based on advice from a Brain Cancer Research Roundtable of experts and patients, the Australian Brain Cancer Research Roadmap, or Mission Roadmap, was developed to outline the investment strategy, rationale and implementation of the Mission. It outlines four key investment strategies in line with the goals above<sup>24</sup>, each with corresponding objectives and activities, and identified early implementation priorities.

# **Mission Governance**

The Mission is delivered in partnership by the Australian Government Department of Health and Aged Care and Cancer Australia. Cancer Australia leads engagement and collaboration with the MSAG and Funding Partners. The Department leads the delivery of investments made through the MRFF, and this review.

The MSAG meets twice annually and provides strategic advice and guidance on achieving the Mission Roadmap objectives, including setting priorities for investment.

<sup>22</sup> AIHW 2017, Brain and other Central Nervous System Cancers, Cat. No. CAN 106, Canberra.

<sup>&</sup>lt;sup>21</sup> Australian Institute of Health and Welfare (AIHW) 2022, Cancer data in Australia, Cat No. CAN 122, Canberra and early data from the AIHW.

<sup>&</sup>lt;sup>23</sup> Australian Government Department of Health and Aged Care 2023, Australian Brain Cancer Mission, https://www.health.gov.au/our-work/australian-brain-cancermission?language=und, accessed 1 December 2022.

<sup>&</sup>lt;sup>24</sup> The four pillars of the Mission investment strategy include (i) Increased patient survival, quality of life and care experiences, (ii) Increased and equitable access and participation in clinical trials, (iii) Expanded research platforms and technologies, and (iv) Increased researcher capacity and excellence.

Since 2018, the group has met 12 times, and is led by an independent Chair and membership includes people affected by brain cancer (consumers), clinicians, researchers, Funding Partners, industry representatives, and a member of the MRFF Australian Medical Research Advisory Board.<sup>25</sup> Cancer Australia convenes these meetings.

Funding Partners play a critical role in delivering on the objectives and priorities outlined in the Mission Roadmap. Each Funding Partner's collaboration in the Mission is formalised through either a Memorandum of Understanding or Letter of Intent with Cancer Australia, which describes Funding Partner roles and responsibilities, priorities and planned investments.

Cancer Australia convenes an annual meeting for Funding Partners to discuss collaboration and coordination opportunities under the Mission, share progress and learnings, and discuss emerging opportunities. Since 2019, four Funding Partner meetings have been held and included the sharing of each Funding Partner's investments under the Mission, a summary of recent and upcoming MRFF grant opportunities, an overview of the Mission budget, and an update from each Funding Partner on their key achievements and upcoming activities.

## Funding

The Mission is a \$136.66 million investment co-funded by the Australian Government through the Medical Research Future Fund and 12 Funding Partners that include some state governments and philanthropic organisations (table 1.1). In total, the MRFF has allocated \$60.26 million to the Mission.

- An initial \$50 million will be allocated through Mission grants. From 2017 up until July 2023, 12 grants were allocated through the Mission totalling \$33.24 million (67 per cent of the total to be allocated through the Mission). This included:
  - 3 directed grants with a total value of \$10.5 million
  - 9 competitive grants with a total value of \$22.8 million, and
- A further \$10.26 million will be allocated through other MRFF initiatives. From 2017 to July 2023, 11 grants with a total value of \$8.77 million had been awarded.

Initial Mission Funding Partners were the Cure Brain Cancer Foundation (CBCF) and Minderoo Foundation's Eliminate Cancer Initiative (now Collaborative against Cancer), collectively allocating 30 million. Since that time, Cancer Australia has expanded the funding partnership, bringing in another 10 Funding Partners and more than \$45 million in additional partner funding to take the Mission's total Funding Partner allocation to \$76.4 million.

A summary of MRFF investments to date is provided in appendix A. A list of Funding Partner investments to date is provided in appendix  $B^{26}$ .

<sup>&</sup>lt;sup>25</sup> Cancer Australia, Australian Brain Cancer Mission Strategic Advisory Group, https://www.canceraustralia.gov.au/key-initiatives/australian-brain-cancer-mission/strategicadvisory-group, accessed 2 July 2022.

<sup>26</sup> Excludes substantial funding from the Cure Brain Cancer Foundation. Details on their investments through the Mission were not available at the time of publication. It is also noted

Funder	Allocation to the Mission	Commitment to projects to date
	\$ million	\$ million
MRFF		
Initial funding	50.00	33.24
Additional funding	10.26	8.77
MRFF total	60.26	42.01
Funding partners		
Cure Brain Cancer Foundation	20.00	NFP
Minderoo Foundation (Eliminate Cancer Initiative)	10.00	10.79
Carries Beanies 4 Brain Cancer	5.40	5.40
Mark Hughes Foundation	3.00	1.17
Children's Hospital Foundation Queensland	10.00	6.09
State of Victoria	2.00	24.00
The Kids Cancer Project	5.30	6.07
State of NSW	7.50	9.50
Financial Markets Foundation for Children	5.00	5.00
Robert Connor Dawes Foundation	1.25	1.25
ACT Health and Canberra Health Services	3.95	1.82
NeuroSurgical Research Foundation	3.00	2.88
Funding partners total	76.40	73.97
Total	136.66	115.98

#### **1.1** Funding allocated to the Mission and commitments to date

Note: Excludes substantial funding from Cure Brain Cancer Foundation, details of which were not available at the time of publication. As shown, some Funding Partners have invested more in the Mission than they had originally committed to. Source: Cancer Australia.

The MRFF has committed more than half its total allocation (as at July 2023), while funding partners have committed over 90 per cent of their total Mission allocation. Funding Partners have committed \$73.97 million to Mission projects to date<sup>27</sup>.

## Mission Roadmap and the MRFF Measures of Success

The specific objectives as set out in the Mission Roadmap are set out in box 1.228.

that some Funding Partners have invested more in the Mission than they had originally committed to.

<sup>27</sup> Excludes substantial funding from the Cure Brain Cancer Foundation. Details on their investments through the Mission were not available at the time of publication.

<sup>&</sup>lt;sup>28</sup> Australian Government Department of Health and Aged Care 2022, Medical Research Future Fund Australian Brain Cancer Mission, https://www.health.gov.au/sites/default/files/doc uments/2022/07/australian-brain-cancer-research-roadmap.pdf, accessed 1 December 2022.

### 1.2 Mission Roadmap

#### Increased patient survival, quality of life and care experiences

- Promote the benefits of surgery or treatment at centres of clinical excellence, and the merits of immediate referral.
- Audit and build national care standards, support decision-making, and articulate clinical pathways for patients.
- Define patient navigator roles and work with governments to improve transport and other support schemes.
- Invest in survivorship research to better understand lifelong impact of brain cancer.

#### Increased and equitable access and participation in clinical trials

- Define and overcome barriers to participation to ensure every patient has access to a clinical trial.
- Enhance capacity of ANZCHOG sponsored trials and adequately support top trial centres.
- Expand the capacity of the COGNO trials for adults.
- Invest in and expand the capacity of known innovative clinical trials of great potential – with an immediate focus on GBM AGILE and ZERO
- Ensure research (domestic and international) is integrated with existing platforms and data collections.
- Open a grant program for innovative clinical trials capable of supporting international collaborations.

#### Expanded research platforms and technologies:

- Build a national bio-banking, laboratory, registry data management capacity for the entire patient cohort.
- Upscale existing pre-clinical technologies and platforms, including animal and invitro modelling capacity, immunotherapy, proteomics and genomics.
- Explore opportunities to encourage the biopharmaceutical industry to collaborate on drug discovery and trial new drugs in children.
- Identify drugs of potential, and ensure access to new drugs by adults and children.

#### Increased research capacity and excellence

- Establish a new centre for basic and clinical research excellence in paediatric and adult brain cancer.
- Support protected research time for clinicians through targeted PhD scholarships, postdoctoral and senior researcher and practitioner fellowships.
- Build domestic research talent through a contestable grant program for innovative research capable of supporting international research collaborations.

Support and expand the Brain Cancer Discovery Collaborative to include all centres of brain tumour research excellence and entice new talent.

The program logic model is a key component of the evaluation framework to help identify Mission achievements to date. While brain cancer research does not fit a linear program logic model (with connectivity across multiple projects, and iterative features), it is still useful to step through a structured articulation of:

- Objectives What is the purpose of the Mission, what changes does it seek to generate, what difference is it expected to make?
- Inputs What competitive and targeted grants have been made, highlighting differences in funding models between the MRFF and funding partners.
- Outputs What has, or will be delivered? For example: cross-organisational collaborations and networks, consumer engagement, new knowledge, health datasets created, monitoring and reporting of brain cancer data, new/expanded research platforms and technologies, centres of excellence
- Outcomes What has changed or could change from the application or adoption of outputs: improved survivorship, quality of life and care experiences, improved access to innovative clinical trials and treatment, improved skills and capacity of health providers etc, and
- Impacts What is the value of improved survivorship or probability thereof, improved research efficiency, and improved allocation of health system resources.

To ensure the program logic is fit-for-purpose, it incorporates:

- the 8 MRFF Measures of Success (aligned to the program logic framework):
  - increased focus of research on areas of unmet need
  - more Australians access clinical trials
  - new health technologies are embedded in health practice
  - new health interventions are embedded in health practice
  - research community has greater capacity and capability to undertake translational research (capacity built is an output)
  - health professionals adopt best practices faster
  - the community engages with and adopts new technologies and treatments
  - increased commercialisation of health research outcomes, and
- the 5 MRFF Impact Measures (which align with impacts under the program logic framework):
  - better health outcomes
  - economic growth
  - beneficial change to health practice
  - increased health efficiency, and
  - increased job and export potential.

# About this review

The Centre for International Economics (CIE) was commissioned to undertake a review of the Mission funded through the MRFF. The purpose of the review in line with the Terms of Reference is to:

- assess all existing investments under the Mission through the MRFF and partner funding<sup>29</sup> from October 2017 to April 2022
- assess all other existing investments in brain cancer research made through the MRFF from October 2017 to April 2022
- consider approaches and the current landscape for health and medical research and treatments for brain cancer internationally and in Australia, and
- suggest opportunities (if any) for improving alignment between the intended goals and implementation of the Mission (see box 1.3).

It is recognised that the Mission includes significant Funding Partner investments outside of the MRFF. Where information is available, these are examined in this review as a critical part of the brain cancer research landscape, and provide context in formulating the future opportunities for the MRFF to optimise its investments in the Mission.

### **1.3** Aims of this review

The Terms of Reference states that the evaluation aims to assess:

- progress made through the MRFF in supporting brain cancer research in Australia
- the alignment of the Mission with long-term objectives set out in the MRFF 10 year investment plan and the MRFF Monitoring, Evaluation and Learning Strategy.

The key evaluation questions include:

- how the MRFF has contributed to brain cancer research in Australia
- how MRFF funded brain cancer research compares with other national and international funded brain cancer research, and
- identifying opportunities (if any) to enhance MRFF funding and granting arrangements to enhance the efficiency and effectiveness of MRFF funded brain cancer research.

The scope is to focus on MRFF brain cancer research related investments and progress made in achieving the objectives of the MRFF. The evaluation also needs to consider the uniqueness of this particular MRFF Mission, including the additional funding through the Mission Funding Partners. It is acknowledged that this evaluation focuses primarily on MRFF related aspects of the Mission. Where information is available, Funding Partner investments outside of the MRFF are examined as part of the brain cancer research landscape, however this review does not provide analysis of those investments, which are primarily aligned to the priorities of the Funding Partners. The review scope excludes the Department's administrative processes of the MRFF.

<sup>&</sup>lt;sup>29</sup> The Australian Brain Cancer Mission is the only MRFF initiative that includes co-funding from Funding Partners, which are comprised of government and non-government organisations.

# Methodology

The key steps in the methodology for this review have included the following.

# Development of an evaluation and stakeholder management plan

An evaluation and stakeholder management plan were developed for this review which:

- set out a fit-for-purpose program logic (see chart 1.4) that aligns with the MRFF Monitoring, Evaluation and Learning Strategy 2021-22 to 2023-24 (Evaluation Strategy) to review progress towards MRFF outcome and impact measures, and alignment with the goals and priorities of the Mission
- provided a search strategy for the literature review to support an environmental scan of the brain cancer research landscape
- identified how literature would be collated and assessed to draw insight for the purpose of the Mission evaluation, and
- set out a proposed consultation strategy, including the type of information to be collected from surveys, and from semi-structured interviews.

The plan was reviewed by the Health and Medical Research Office (HMRO) of the Department of Health and Aged Care, and the Evaluation Advisory Panel (EAP) that was established for this review. Feedback on the plan was incorporated to confirm the final methodology.

# Desktop scan of the brain cancer research landscape

An environmental scan was undertaken to canvas approaches and the current landscape for health and medical research and treatments for brain cancer internationally and nationally in Australia.

# Stakeholder consultation

The stakeholder engagement process included:

- individual and group semi-structured interviews with key stakeholders, and
- a survey of recipients of brain cancer related grant funding from the Mission and other MRFF initiatives up until April 2022. The survey was sent to all lead chief investigators ('Chief Investigator A') covering 19 brain cancer related grants distributed by the Mission and other MRFF initiatives. Responses were received for all projects. A list of all relevant grants is provided in appendix A.

Interviews were held from December 2022 to March 2023 guided by consultation questions developed for each stakeholder group, approved by the HMRO, and provided to stakeholders in advance. Approximately 40 stakeholders were consulted including:

- Funding Partners of the Mission
- research bodies and brain cancer researchers in Australia
- consumer groups in Australia and internationally

- former members of the (Australian Brain Cancer) Mission Strategic Advisory Group
- industry representatives including Medicines Australia, and
- international brain cancer organisations.

The focus of the desktop scan and stakeholder engagement is summarised in appendix B.

## **Oversight by an Evaluation Advisory Panel**

This review has been overseen by an EAP (initially an Interim EAP, and then a final EAP). The EAP has provided comment on the evaluation and stakeholder management plan, the desktop environmental scan, the consultation report, and an interim report with the findings and opportunities identified during this review.

# **Research qualifications and limitations**

The findings in this report are subject to the following qualifications:

- the desktop scan of Australian and international research did not examine all brain cancer research, and was limited by the time and resources available for this review
- the desktop environmental scan was limited to published material, which may have biased scientific/laboratory-based testing and discovery rather than research with a more translational and commercialisation focus
- the desktop scan primarily reports analysis of data available from databases and clinical trial registries, and less on the whole of the brain cancer research literature, commensurate to the scope of the review and available time and resources. Its reliance on published material may have biased the results
- consultations were not held with all interested parties, and it is possible that the views presented to this review are not representative. Stakeholders were approached as agreed with the Health and Medical Research Office of the Department of Health and Aged Care and Cancer Australia. It is noted that:
  - there was no call for public input to the review, and
  - private hospitals were not consulted
- consultations were primarily held with representative organisations, which are not necessarily able to provide the viewpoint of all constituents
- some stakeholders were unable to participate in this review due to other commitments and the timing of the review
- consultation with brain cancer patients and carers was limited to three patients, and five consumer representative organisations, which also included carers
- some issues raised by stakeholders were out of scope for this review, including matters relating to how the Mission is administered, and
- this consultation report may reflect response bias, as findings are limited to only the views put forward by those that were consulted. For instance, it is possible that researchers made positive comments about the Mission because of concerns that future funding might otherwise not be available.

# **1.4** Mission evaluations – program logic

Inputs	Activities	Outputs	Outcomes	Impacts
Australian Government	Contestable or targeted	New knowledge     Publications and citations	Increased focus of research on areas of unmet need, including	Better health outcomes, including improved survivorship
	that directs	Research collaborations     Creation of datasets/monitoring and reporting of brain	survivorship	Economic growth
Funding partners	research	cancer data	More Australians access clinical trials	Beneficial change to health practic
Other MRFF grant opportunities	New treatment options     New/expanded health technologies and research     platforms     New health interventions	New health technologies are embedded in health practice	Increased health efficiency	
	contributing to brain cancer	Capacity building	New health interventions are embedded in health practice	Increased job and export potentia
	Other Mission projects funded by	<ul> <li>New researchers enticed/attracted</li> <li>New national and international research collaborations between centres of brain cancer research</li> <li>Targeted PhD scholarships, postdoctoral and senior researcher and practitioner fellowships</li> </ul>	Research community has greater capacity and capability to undertake translational research (capacity built is an output)	
	Funding Partner investments	<ul> <li>New centre for basic and clinical research excellence in paediatric and adult brain cancer</li> <li>Increased cross-organisational networking efforts</li> </ul>	Health professionals adopt best practices faster	
(examined as part of the brain cancer research	Survivorship  Increased research into trends in patient survivorship	The community engages with and adopts new technologies and treatments		
	Iandscape)         Increased research into patient experience and QoL           Increased clinical trials on improving survivorship         Increased commercialisation on health research outcomes	Increased commercialisation of health research outcomes		
		Consumer involvement     Engagement with consumers in prioritysetting     Focus on patient-based outcomes in trial design     Engagement with patient groupsfor research     outcomes, dissemination, and translation		

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# 2 Local and international approaches to research

Brain cancer research in Australia is widely dispersed across research teams in universities, medical research institutes, and in Australian and international research collaborations, and is funded by a variety of government and non-government sources. Funding strategies vary from targeted and competitive grants, expert panel selection, and untied funding for designated research groups or research centres.

In the last triennia (2018-2020), 51 per cent of Australian funded brain cancer research projects were directed towards the Common Scientific Outline (CSO) category of Treatment. Twenty six per cent of Australian research was directed towards Early Detection, and the remainder towards Survivorship (13 per cent), and Biology (9 per cent of projects). No Australian funding was directed towards the CSO categories of Aetiology or Prevention.

Internationally, funding is more evenly distributed across all CSO categories (34 per cent on Treatment, 24 per cent on Biology, 18 per cent on Early Detection, Diagnosis and Prognosis, 16 per cent on Actiology and Prevention, and 8 per cent on Survivorship).

# Overview of Australian brain cancer research

Brain cancer research in Australia has received a fillip since the Mission was established, lifting what has been by historical standards a low level of investment. Based on the 2023 Cancer Australia audit of cancer research in Australia, in 2003-2005, \$1.5 million was allocated to 10 brain cancer specific projects. With some steady increases in subsequent years, the 2018-2020 period witnessed a substantial increase in brain cancer research with \$54.1 million allocated to over 161 projects (chart 2.1). Brain cancer has also received the largest increase in single tumour type research funding, which increased in each triennium from 1 per cent in 2003-2005 to 10 per cent in 2018-2020<sup>30</sup>.

<sup>&</sup>lt;sup>30</sup> Cancer Australia 2023, Cancer Research in Australia: An overview of funding for cancer research projects and programs in Australia, 2012 to 2020, Cancer Australia, Surry Hills, NSW.


#### 2.1 Brain cancer specific projects and programs 2003-2005 to 2018-2020

Note: The shaded area denotes the duration of the Mission, although projects counted are not limited to those funded by the Mission. Data source: Cancer Australia (2023) – Cancer Research in Australia.

Over time, there has also been a shift in the focus of brain cancer research. For instance:

- Treatment related projects now account for the highest proportion of direct funding, ranging from 48 to 59 per cent over the last three triennia (and 51 per cent in the most recent triennia)<sup>31</sup>, compared to 3 per cent in 2003-2005
- Early Detection, Diagnosis and Prognosis projects have accounted for between 17 to 26 per cent of direct funding since 2003, except for a decrease to 7 per cent in 2006-2008
- Biology has accounted for 13 to 26 per cent of direct funding since 2003-2005, but has reduced to 9 per cent in 2018-2020 taking a smaller share of the much greater pool of funding that has become available since the Mission
- Aetiology accounted for 7 per cent or less of direct funding in most triennia, with a high of 24 per cent in 2006-2008 and none in the most recent triennia, and
- Cancer control, Survivorship and Outcomes Research accounted for 48 per cent of all direct funding in 2003-2005 but then fell dramatically, ranging from 2 per cent to 8 per cent in subsequent triennia, until an uptick to 13 per cent in the Mission period (chart 2.2).

**Prevention** has received no research funding in any triennium.

An overview of brain cancer treatments is provided in appendix C.

<sup>31</sup> 

<sup>31 2012-2014, 2015-2017</sup> and 2018-2020.



#### 2.2 Australian brain cancer research projects by CSO category over time

Note: Prevention CSO received no funding over all time periods. It is noted that percentages within triennia do not round to 100 per cent. Data is displayed here as it is provided in the Cancer Australia report.

Data source: Cancer Australia (2023), Cancer Research in Australia: An overview of funding for cancer research projects and programs in Australia, 2012 to 2020, Cancer Australia, Surry Hills, NSW, p. 78.

#### Australian clinical trials for brain cancer

Based on the ANZCTR<sup>32</sup>, there were 84 brain cancer trials registered from 2005 to 2022, with all but two targeting males and females. Most (71) had a minimum age of 18 years, with the remainder spread between the ages of 5, 6, 16 and 50. Most (65) had a sample size below 100 participants, with 15 trials between 100 and 500 participants and the remainder up to a maximum of 10 000<sup>33</sup>.

The trials were primarily interventional (74), which prospectively assigns human participants to one or more health-related interventions to evaluate the effect on outcomes. The remainder were observational, where no experimental intervention or protocol driven treatment is applied.

The primary purpose was Treatment (58), followed by Diagnosis (9), Prevention  $(3)^{34}$  and Education (4). The endpoint of studies was oriented towards Safety and Efficacy (30), Efficacy (19) and Safety (7).

<sup>33</sup> Recruitment was from both Australia and internationally. Data accessed 7 November 2022.

<sup>&</sup>lt;sup>32</sup> The ANZCTR is an online public registry of clinical trials, held at the NHMRC Clinical Trials Centre, University of Sydney. It accepts interventional and observational studies for registration from all countries and from the full spectrum of therapeutic areas including trials of pharmaceuticals, surgical procedures, preventive measures, lifestyle, devices, treatment and rehabilitation strategies and complementary therapies. See https://anzctr.org.au/Faq.aspx#g1. This is not the only source of Australian trial information, which can also be found at Clinicaltrials.gov.

<sup>&</sup>lt;sup>34</sup> The prevention category for the purpose of an ANZCTR trial means a study designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition. This differs from the CSO category prevention, which is research that looks at

Most trials were interventional drug studies to assess the effect(s) of one or more chemical or biological agents including vaccines. This was followed by Other Treatment, which includes trials focused on radiotherapy and chemotherapy, as well as survivorship and supportive care (rehabilitation, mental health, and diet among others)<sup>35</sup>.



2.3 Characteristics of Australian brain cancer clinical trials

Data source: CIE analysis of ANZCTR database for brain cancer trials 2005 to 2022.

Most Australian trials are funded by charities/societies/foundations, the commercial sector/industry, and government bodies.

Australian clinical trials are strongly focused on the early phases of research.

- Approximately 40 per cent of trials were non-drug trials. Of the remaining trials, the majority (50.1 per cent) were Phase 1 or 2, with Phases 3 and 4 comprising only 9.9 per cent of trials (chart 2.4).
- Individual sponsors are primarily focused on non-drug trials. Half of the university sponsored trials are non-drug focused, while 30 per cent focused on Phase 2 drug development. Commercial/industry trials are more focused on the early stages of trials, with Phase 1 and 2 trials comprising 89 per cent of trials (chart 2.5).
- Trials funded by the commercial sector/industry are primarily focused on Phase 1 and 2 (three-quarters of their trials). Charities have a relatively equal split between Phase 1, Phase 2 and non-drug (not applicable) trials. Over half of government funded trials are non-drug, with the remainder equally split between trials in Phases 1-4 (chart 2.6).

identifying individual and population-based primary prevention interventions, which reduce cancer risk by reducing exposure to cancer risks and increasing protective factors. Hence trials identified here cannot be compared to research funded by CSO mentioned previously.

<sup>&</sup>lt;sup>35</sup> For example see ANZCTR trials #382953 - Group cognitive rehabilitation via telehealth for brain cancer, #376213 - Evaluation of a telehealth intervention for delivering psychological support to people with brain tumour and their families, #367120 - Pilot study of a ketogenic (low-carbohydrate) diet in patients receiving chemotherapy and radiation for glioblastoma multiforme (aggressive brain tumour)

#### 2.4 Australian clinical trial phases



Data source: CIE analysis of ANZCTR database for brain cancer trials 2005 to 2022.



#### 2.5 Key sponsor types by phase of trial

Note: The sponsor refers to the individual, organisation, group or other legal person taking on responsibility for securing the arrangements to initiate and/or manage a study, including arrangements to ensure that the design of the study meets appropriate ethical and regulatory standards and to ensure appropriate conduct and reporting. Individual sponsors in all cases are part of a university, hospital or medical research institute.

Data source: CIE analysis of ANZCTR database for brain cancer trials 2005 to 2022.



#### 2.6 Key funding sources by phase of trial

Data source: CIE analysis of ANZCTR database for brain cancer trials 2005 to 2022.

## Funders of Australian brain cancer research

Brain cancer research in Australia is funded by various government, charitable and philanthropic organisations, and pharmaceutical and biotechnology companies.

#### MRFF and the Mission

MRFF is the single largest funder of brain cancer research in Australia, providing funding for research primarily through the Mission as well as other MRFF initiatives.

The Mission is unique in that it is the only MRFF initiative that includes financial commitments from Funding Partners, which in some cases is dispersed through the MRFF grant process, and in some cases is not.

The combined efforts of the MRFF and the Mission Funding Partners represent the largest pooled investment of brain cancer research in Australian history, which since 2017-18 has committed \$136.66 million, including:

- \$50 million from the Australian Government to be distributed via the Mission<sup>36</sup>
- \$76.4 million through Funding Partners, and
- \$10.26 million from the Australian Government distributed via other MRFF initiatives<sup>37</sup>.

The co-funding model has resulted in the Australian Government and Funding Partners investing more in Australian brain cancer research than they otherwise would have, and promoted synergistic investment from funders across the research continuum.

An example of the cross-collaboration of the MRFF and the Funding Partners is provided in box 2.7.

<sup>&</sup>lt;sup>36</sup> Includes \$25 million allocated in the updated 10-year investment plan from 2022-23 to 2026-27.
<sup>37</sup> MRFF 2<sup>nd</sup> 10-year investment plan from 2022-23 to 2031-32.

#### 2.7 Case Study: Australian & New Zealand Childrens Haematology/Oncology Group (ANZCHOG)

Originally established in 1986, the ANZCHOG is the national sponsor for children's cancer clinical trials, providing consistency and regulatory oversight, managing clinical trials to the standard required for international collaborations, and working with international partners to ensure that Australian children have access to the best possible treatment options through clinical trials.

In 2018, funding to expand the capacity of the ANZCHOG was announced as part of the Mission, with an early \$2.5 million disbursement from the MRFF that:

- enabled Australian paediatric neuro-oncologists to strengthen connections with international trials groups, bringing new trial opportunities to Australia
- supported centralised trials infrastructure within ANZCHOG to streamline and coordinate the start-up and conduct of the trials nationally, and
- provided assistance to hospitals to offset the cost of participating in paediatric brain cancer trials.

Guaranteed funding for five years provided ANZCHOG with an opportunity to implement a national strategy for paediatric brain cancer trials. ANZCHOG's ability to participate in global, collaborative clinical trials was further strengthened in 2019, through an investment of \$5 million from Mission Funding Partner Financial Markets Foundation for Children, under which ANZCHOG committed to develop a dedicated Childhood Brain Cancer Clinical Trials Program. This program allowed all children's cancer centres around Australia to enhance clinical trial capacity and embed clinical trial research into clinical care.

This investment was leveraged by ANZCHOG to achieve additional contributions of over \$2 million from the Australian Government and Mission Funding Partners, Robert Connor Dawes Foundation and Carrie's Beanies for Brain Cancer, to achieve a total investment of almost \$10 million under the Mission.

The funding provided to ANZCHOG under the Mission has enabled it to exceed its original target of opening five new paediatric brain cancer trials in Australia, opening 11 trials developed by leading international trial consortia to date. Equally important, ANZCHOG has been able to capitalise on opportunities for trial involvement as they emerge, rapidly activating trials to maximise the time they are available for Australian children. The collaboration between the Australian Government and Mission Funding Partners has been described as a 'game-changer' for children with brain cancer, transforming ANZCHOG's capacity and capability to fund novel and innovative quality research and translate this research into better outcomes for children through access to clinical trials.

#### National Health and Medical Research Council

The National Health and Medical Research Council (NHMRC) is a significant funder of brain cancer research in Australia. The majority of NHMRC funding is investigator-lead, meaning that researchers have been successful in having their chosen research topic approved through a competitive, peer reviewed, scheme.

In general, in addition to administering MRFF grant opportunities on behalf of the Department of Health and Aged Care, NHMRC also allocates grants through programs such as Ideas, Investigator, Clinical Trial and Cohort Studies, and Synergy Grants. Of note for brain cancer research, the NHMRC Clinical Trials Centre (CTC), a centre of excellence funded by the NHMRC based at the University of Sydney, coordinates trial activity within Cooperative Trials Group for Neuro-Oncology (COGNO).

Based on a search of SCOPUS<sup>38</sup> relating to Australian brain cancer research over the period 2014 to 2023, the NHMRC was the most active funding group, funding (in part) 201 projects, almost double the second most active funder<sup>39</sup> (chart 2.8).



#### 2.8 SCOPUS Research by funding sponsor

Data source: Based on 1279 articles and reviews extracted from SCOPUS on output from peer-reviewed literature for Australian researchers over the period 2014-2023 relating to brain cancer.

The CIE's analysis of NHMRC grants on a year-on-year basis suggested that brain cancer research funding has been particularly strong over the last two years, suggesting that the Mission may have positively impacted on investigator interest in brain cancer research (chart 2.9). Sixty-four per cent of these projects are for basic science, with 31 per cent

<sup>&</sup>lt;sup>38</sup> Scopus is an abstract and citation database of peer-reviewed literature including scientific journals, books, and conference proceedings. Scopus provides a comprehensive overview of worldwide research output in the fields of science, technology, medicine, social sciences, and arts and humanities. See https://www.scopus.com/home.uri

<sup>&</sup>lt;sup>39</sup> The search identified 1 279 articles and reviews with involvement from Australian researchers. The research was primarily articles (76 per cent), with the remainder being reviews.

classified as clinical medicine and science, and 3.3 per cent classified as health services research.<sup>40, 41</sup>.



2.9 NHMRC funding to projects related to brain cancer

Note: NHMRC funding grants from 2013 to 2022 were analysed to determine the number of brain cancer specific projects funded. Projects were filtered and coded as brain cancer-specific if they included brain cancer related terms in the project key words and description fields.

Data source: CIE, based on the NHMRC Outcomes of funding rounds. https://www.nhmrc.gov.au/funding/data-research/outcomes. Accessed 27 January 2023.

The type of research funded by the NHMRC can be extracted from analysis of the International Cancer Research Partnership (ICRP)<sup>42</sup>, which over the 2017-2022 period recorded 14 000 brain tumour related projects funded internationally, including 862 clinical trials relating to brain cancer<sup>43</sup>.

NHMRC funded Australian brain cancer research is relatively diverse. Based on a review of 74 NHMRC-funded brain cancer research projects captured in the ICRP over the 2017-2022 period of the Mission, 46 per cent of NHMRC funded research focused on 'Treatment', 19 per cent on 'Biology', 18 per cent on 'Early Detection, Diagnosis and Prognosis', 10 per cent on Cancer Control, Survivorship and Outcomes Research, and 7 per cent on 'Etiology'.

- <sup>42</sup> The International Cancer Research Partnership (ICRP) is an alliance of cancer research organisations from Australia, Canada, France, Japan, the Netherlands, United Kingdom, and the United States. https://www.icrpartnership.org/
- 43 Refers to trials from all funding sources in the ICRP, not just the NHMRC. The ICRP codes brain cancer using ICD-10 C71.

<sup>40</sup> NHMRC 2022, Grant Outcomes 2013-2022, see https://www.nhmrc.gov.au/funding/dataresearch/outcomes, accessed 6/02/2023

<sup>&</sup>lt;sup>41</sup> The ICRP codes projects using the Common Scientific Outline (CSO), which is a classification system organised into six broad areas of scientific interest in cancer research. CSOs are standardised internationally which make it possible to compare and contrast the research portfolios of public, non-profit, and governmental research agencies. See https://icrpartnership.org/cso for more details.

#### **Cancer** Australia

In addition to its role as co-administrator of the Mission, Cancer Australia is also a major contributor to brain cancer research in Australia. Cancer Australia administers two national research grant programs:

- 1 Priority-driven Collaborative Cancer Research Scheme (PdCCRS). It was established in 2007 to bring together government and other funders to collaboratively fund cancer research and since inception has awarded \$11.83m to 34 grants in brain cancer research, with \$6.29m from Cancer Australia and \$5.54m from funding partners.
- 2 Support for Cancer Clinical Trials (SCCT). It was established in 2006 and aims to build Australia's capacity to undertake industry-independent cancer clinical trials by supporting Australia's 14 Multi-site Collaborative Cancer Clinical Trials Groups (CTGs) to develop industry-independent cancer clinical trial protocols, including \$2.5m over 2.5 years (2022 to mid-2024) to ANZCHOG and COGNO.

The PdCCRS grants represent a substantial contribution to brain cancer research funding in Australia. Table 2.10 shows the grant funding by tumour type. The most funding was awarded to medulloblastoma and DIPG. Grants that were awarded for clinical trials were primarily focused on gliomas from low to high grade, apart from one trial on medulloblastoma.

Tumour type	Grants	Of which were trials	Funding
-	No.	No.	\$
Diffuse Intrinsic Pontine Gliomas	5	-	2 048 592
Glioblastoma	6	-	1 964 486
Glioma	2	1	583 719
Glioma (GII anaplastic all types in GBM)	2	2	586 388
Glioma (Grade III/IV)	1	1	503 586
Glioma (High Grade, III/IV)	4	2	1 747 654
Glioma (malignant)	2	-	175 188
Medulloblastoma	6	1	2 443 899
Neuroblastoma	6	-	1 776 863
Total	34	7	11 830 375

#### 2.10 Cancer Australia PdCCRS grants by tumour type

Source: ICRP, CIE.

The majority (68 per cent) of Cancer Australia's brain cancer related collaboration on ICRP research projects involves the CSO classification 'Treatment', primarily focused systemic therapies – discovery and development.

#### **Mission Funding Partners**

The Funding Partners of the Mission include a range of non-government and charitable organisations, as well as and State and Territory Governments. Some are single tumour type funders (brain cancer only) and some are not, and some only fund brain cancer research through their contributions to the Mission, and some do not.

In alphabetical order, the Funding Partners include:

- ACT Health and Canberra Health Services, which has funded Brain Cancer Specialist Nurses, capital costs for stereotactic treatment, Canberra Health Service research and clinical trials, and provided research grants to the ACT Health Directorate
- Carrie's Beanies 4 Brain Cancer, which is a founder of the Brain Cancer Centre (BCC), which was established in partnership with the Walter and Eliza Hall Institute (WEHI), with support from the Victorian Government. It has also contributed cofunding to various clinical trials (including MAGMA, SJ-Eliot, COZMOS, ANZCHOG)
- Children's Hospital Foundation Queensland, which funds research at the Children's Brain Cancer Centre, and supports the Queensland Children's Tumour Bank, which is an openly accessible paediatric tumour tissue bank assessing the development of new treatments for neuroblastoma, brain tumours, and other cancers.<sup>44</sup> It also provides multiple research and equipment grants to Queensland universities, and offers fellowship positions in universities for brain cancer research. It committed \$5.6 million to the Mission which is used to fund the Children's Brain Cancer Centre over 5 years.
- Cure Brain Cancer Foundation, which contributes funds towards the Zero Childhood Cancer Program (ZERO), the Cure Brain Cancer Neuro-Oncology Group at the University of New South Wales (UNSW), GBM AGILE and other clinical trials, such as:
  - INTELLANCE 2 for patients with glioblastoma<sup>45</sup>
  - the KB004 clinical trial to prove the drug crosses the blood-brain barrier<sup>46</sup>
  - a pilot clinical trial for Australian children with hypermutant brain cancer
  - a clinical trial that tests veliparib for adults with glioblastoma<sup>47</sup>
- Financial Markets Foundation for Children, which is a trustee of a charitable trust whose purpose is the promotion of the health and welfare of children of Australia, principally funding research at Australian universities. Its only funding for brain cancer (\$5 million) is through the Mission, through which it has contributed funding to ANZCHOG to enhance clinical trial capacity.
- Mark Hughes Foundation (MHF), which has invested in substantial research capacity in Northern NSW through funding a dedicated brain cancer team at the University of Newcastle to build on the work of others, including MHF partners at the Hunter Medical Research Institute (HMRI) and the Brain Cancer Group. It also contributes to the AIM BRAIN Project and funds the Mark Hughes Foundation Brain

<sup>&</sup>lt;sup>44</sup> See Queensland Children's Tumour Bank website, Research - Children's Hospital Foundation (childrens.org.au), Accessed 11 August 2022.

<sup>45</sup> See INTELLANCE 2 - Victorian Cancer Trials Link (cancervic.org.au), Accessed 19 August 2022.

<sup>46</sup> See A Trial of KB004 in Patients With Glioblastoma - Full Text View - ClinicalTrials.gov, Accessed 19 August.

<sup>&</sup>lt;sup>47</sup> See https://curebraincancer.org.au/research/rResearch-we-fund, Accessed 18 August 2022.

Biobank, one of the first post-mortem adult brain banks in Australia to operate with protocols specifically developed for brain cancer. It also invests in clinical trials (co-funding MAGMA, funding independently the IWOT study at the University of Sydney, and a glioblastoma study at Flinders University)<sup>48</sup>. It has committed \$3 million to the Mission, and invested \$7.5 million over five years to the University of Newcastle.

- Minderoo Foundation's Collaborate Against Cancer, which focuses on seed funding catalytic research initiatives, fast tracking collaborative, precision medicine programs in paediatric cancer, and facilitating the linking and sharing of data to support research collaboration globally, such as seeding the Mission, the Tessa Jowell Brain Cancer Mission, and the US Brain Cancer Mission to support next-generation sequencing to expand the understanding of brain cancer, and fund transformational brain cancer research<sup>49</sup>. It also provides research grants to Cure Brain Cancer Foundation and the Charlie Teo Foundation, and contributes to funding for clinical trials (ZERO, MoST Clinical Trial, and Snow Ball Donation). It committed \$17.2 million to the Mission to dedicate to ZERO, with most of its brain cancer funding allocated overseas.
- NeuroSurgical Research Foundation, which funds brain cancer research projects at various South Australian universities, as well as research infrastructure, such as laboratory equipment for processing brain tumour tissue, and a comprehensive database management system for the South Australian Neurological Tumour Bank. It also funds Research Chair positions and Fellowships at South Australian universities. It committed \$2.5 million to the Mission, which is used to fund \$500 000 of research each year through its own grant processes.
- New South Wales Government, which contributes to multiple clinical trials, provides multiple equipment and research grants, translational research grants, and Fellowships via universities in NSW, and funds technology research (Cancer Proteogenomics Collaboration and ZERO), and
- Robert Connor Dawes Foundation, which established the AIM BRAIN Project initiative, an Australian first, in collaboration with ANZCHOG (Australian and New Zealand Children's Haematology/ Oncology Group) and Cancer Australia, bringing molecular diagnostic testing to every child diagnosed in Australia. It also funds the immunotherapy program at WEHI, a world-first innovative CRISPR project at Hudson Institute, ongoing investment in personalised treatment through ZERO, and contributes funds to ANZCHOG to help accelerate and participate in global trials<sup>50</sup>
- **The Kids' Cancer Project**, which is an independent national charity supporting childhood cancer research. It funds scientific studies to help children with many types of cancer, including brain cancer, with studies selected by an expert Research

<sup>&</sup>lt;sup>48</sup> https://markhughesfoundation.com.au/, and Mission Evaluation Funding Partners Meeting, August 2022, unpublished.

<sup>49</sup> See Global Brain Cancer Mission | Collaborate Against Cancer | The Minderoo Foundation, Accessed 17 August 2022.

<sup>&</sup>lt;sup>50</sup> See Robert Connor Dawes Foundation website, Infosheet 2020 (rcdfoundation.org), Accessed 10 August 2022.

Advisory Committee. It also undertakes fundraising activities to support an awareness campaign for childhood cancer in general. It commits around \$700 000 annually to brain cancer projects, and

Victorian Government, which funds the Centre for Research Excellent in adult brain cancer at the Olivia Newton-John Cancer Research Institute. This includes \$4 million over eight years to the Olivia Newton-John Cancer Research Institute, \$16m to Walter and Eliza Hall Institute for the Brain Cancer Centre, and \$4 million into Gamma Knife Facility.

To date, five Funding Partners have contributed funding to MRFF brain cancer projects, but most Funding Partner funds have been committed to projects outside of the MRFF. Some Funding Partner allocations to the Mission are not yet committed to specific projects.

It is noted that some Funding Partners invest in brain cancer research outside of their commitments made to the Mission, including internationally.

Mission Funding Partner	MRFF projects	Other Mission projects	Total
-	\$m	\$m	\$m
ACT Health and Canberra Health Services	0.00	1.82	1.82
Carrie's Beanies 4 Brain Cancer	1.40	4.00	5.40
Children's Hospital Foundation Queensland	0.0	6.09	6.09
Cure Brain Cancer Foundation	NFP	NFP	NFP
Financial Markets Foundation for Children	5.00	0.00	5.00
The Kids' Cancer Project	0.00	6.07	6.07
Mark Hughes Foundation	0.5	0.67	1.17
Minderoo Foundation	0.00	10.79	10.79
Neuro Surgical Research Foundation	0.00	2.88	2.88
NSW Government	0.00	9.50	9.50
Robert Connor Dawes Foundation	1.25	0.00	1.25
Victorian Government	0.00	24.00	24.00
Total	8.15	65.82	73.97

#### 2.11 Funding Partner commitments to MRFF and other Mission projects to date

Note: MRFF projects refers to projects funded through the MRFF up until July 2023 Other Mission projects refers to investments funded outside of the MRFF but in line with Funding Partner commitments to the Mission.

NFP = Not for publication. Details on investments by the Cure Brain Cancer Foundation were not available at the time of publication. Source: CIE, based on information from Cancer Australia.

Funds already committed by funding partners by funding category are summarised in table 2.12. Most of the Funding Partner commitments have been to: research grants, Centres of Excellence, and clinical trials.

•	Amount committed	Share of total
-	\$ million	Per cent
Centres of Excellence	26.03	35
Clinical trials	13.01	18
Clinical trial capacity	6.65	9
Equipment grant	5.06	7
Fellowships	3.07	4
Research chairs	1.00	1
Research grants	16.12	22
Staff	0.36	0
Technology research	2.02	3
Other	0.65	1
Total	73.97	100

#### 2.12 Funds committed by funding categories – Funding Partners

Note: The relevant information is not available for all Funding Partners .

Source: Cancer Australia.

#### Other non-government and community-based funders

Brain cancer research in Australia attracts a large and growing proportion of single tumour type research from non-government and community-based organisations, including some representatives of the Mission Funding Partners as well as others.

According to the 2023 Cancer Australia cancer research audit, there are 38 nongovernment and community-based organisations that mostly funded research in a single tumour type, accounting for 15 per cent of direct cancer research funding in 2012-2020. Over this period, brain cancer research received 19 per cent of its direct funding from non-government and community-based sources<sup>51</sup>.

Non-government and community-based funders of Australian brain cancer research outside of the Mission Funding Partners include (in alphabetical order):

- Australian Cancer Research Foundation, which funds physical buildings for brain cancer research, as well as technology, equipment, and physical and virtual infrastructure.
- Benny Wills Brain Tumour Research Program, which was established by the family after the loss a child to DPIG. It is run by Dr David Zeigler, Staff Specialist Oncologist at Sydney Children's Hospital to focus on finding a cure for DPIG, and is funded through the Benny Wills Gala Dinner.
- Brain Foundation, which is the largest non-government funder of neurological and neuroscientific research in Australia, supporting quality research into a wide range of brain disorders, including brain cancer.

<sup>51</sup> Cancer Australia 2023, Cancer Research in Australia: An overview of funding for cancer research projects and programs in Australia, 2012 to 2020, Cancer Australia, Surry Hills, NSW, p. 63.

- **Cancer Councils,** works across research, prevention and support for all cancers in all states and territories. They are the largest non-government funder of cancer research in Australia.
- Cancer Institute NSW, which funds The Kids Cancer Alliance Translational Cancer Research Centre, and has funded clinical trial grants through the COGNO, translational research grants and career support grants relating to brain cancer.
- **Charlie Teo Foundation**, the foundation was formed by Dr Charlie Teo AM and focuses solely on research of brain cancer under the key themes of more data, better tools and out of the box thinking.
- Children's Cancer Foundation, the Foundation supports game-changing cancer research projects that aim to eliminate children's cancer while ensuring children have access to the best possible and latest proven treatments. It funds clinical research and trials, clinical care and provide family support.
- Dainere's Rainbow Brain Tumour Research Fund, also established by a family after the loss of a child to brain cancer, with funds used to support Dr David Zeigler's research at Sydney Children's Hospital to develop and test new treatments for children with incurable cancers.
- Isaac McInnes Fund, also established by a family after the loss of a child to anaplastic astrocytoma grade III, with funds used to support Dr David Zeigler's research at Sydney Children's Hospital to support new treatment strategies for malignant childhood brain cancers.
- Levi's Project, which funds the Brain Cancer Research Group at Children's Cancer Institute for DIPG using a Total Therapy approach.
- My Room Children's Cancer Charity, is a volunteer led organisation, working together to support patients and families affected by cancer. They rely on donors to fund support for families, medical equipment, clinical care, research and trials.
- Perth Children's Hospital Foundation, the projects and initiatives they fund include ground-breaking research to world-class expertise, innovative equipment and technology to positive patient and family experiences. They fund Dr Nick Gottardo at the Telethon Kids Institute in Perth, who is working towards finding a cure for Medulloblastoma.
- Pirate Ship Foundation, charity which funds vital research into childhood brain cancer through a range of initiatives, adventures, events and partnerships. Funds are invested directly into childhood brain cancer research programs, including to the Brain Tumour Research Program co-led by Dr Nick Gottardo and Dr Raelene Endersby at the Telethon Kids Institute in Perth.
- Run DIPG, charity dedicated to improving outcomes for patients and families who experience DIPG by raising awareness, empowering advocates and fundraising to support DIPG research.
- **The Cure Starts Now**, which funds elimination-focused research primarily for DIPG, providing research grants to institutions and medical professionals whose research focuses on cancers that present the greatest opportunities for a cancer cure, and
- **Tour de Cure**, fundraising charity focused on cancer research, support and prevention since 2017.

Together, these entities fund research at the Brain Cancer Centre, COGNO, Kids Cancer Alliance, Children with Brain Cancer Centre, Children's Cancer Institute, Bill Walsh Lab Translational Cancer Research Centre, Telethon Kids Institute, Mark Hughes Foundation Centre for Brain Cancer Research, and brain cancer research undertaken at universities principally in New South Wales, Victoria, Queensland, South Australia, Western Australia, and Tasmania.

## Australian research affiliations

Based on a search of SCOPUS<sup>52</sup> relating to peer-reviewed Australian brain cancer research over the period 2014 to 2023, the University of Melbourne had the most number of publications by affiliation (chart 2.13). Affiliations were concentrated among Melbourne and Sydney between universities and hospitals, with only the University of Queensland and the University of Western Australia appearing outside these regions in the top 10 affiliates<sup>53</sup>.

This is similar to the affiliations for Mission and other MRFF brain cancer research grant recipients, whereas at April 2022, all MRFF grants relating to brain cancer research were awarded to five universities (table 2.14).



#### 2.13 SCOPUS Research by affirmation: the top 10

Data source: Based on 1279 articles and reviews extracted from SCOPUS on output from peer-reviewed literature for Australian researchers over the period 2014-2023 relating to brain cancer.

<sup>&</sup>lt;sup>52</sup> The search identified 1 279 articles and reviews with involvement from Australian researchers. The research was primarily articles (76 per cent), with the remainder being reviews.

<sup>&</sup>lt;sup>53</sup> It is noted that the number of publications is not directly associated with the amount of research, nor is it a measure of quality or impact of research.

	Mission	Other MRFF initiatives	Grand Total
-	(# grants) \$	\$	\$
University of Sydney	(3) 7 975 584	4 647 786	12 623 370
University of New South Wales	(2) 6 943 599	1 128 498	8 072 097
University of Melbourne	(1) 2 615 278	958 215	3 573 493
Monash University	(1) 3 010 000	2 035 455	5 045 455
La Trobe University	(1) 1 246 612	0	1 246 612
Total	21 791 073	8 769 953	30 561 027

#### 2.14 MRFF brain cancer grant funding by institution

Source: Mission, CIE.

The geographic distribution of Australian brain cancer research broadly reflects in the recruitment jurisdiction for clinical trials, with NSW, Victoria, and Queensland researchers involved in most trials. However, when controlling for population size, NSW and Victoria are underrepresented, and South Australia and Tasmania overrepresented.

#### 2.15 Australian brain cancer clinical trials by recruitment state



*Data source:* CIE, based on analysis of the ANZCTR database of the 84 registered brain cancer clinical trials from 2005 to 2022, ABS 2022 National, state and territory population.

Australian brain cancer research teams are spread across Australian universities, medical research institutes, and hospital-based research centres. In some cases, research teams are brain cancer-specific, and in some cases not. Research teams (in alphabetical order) include:

- Australia and New Zealand Children's Haematology/Oncology Group (ANZCHOG), the peak professional body for paediatric oncologists and health professionals who care for children with cancer. ANZCHOG is also the national cooperative clinical trials group for childhood cancer.
- Bill Walsh Lab Translational Cancer Research Centre located at Royal North Shore Hospital NSW, which collaborates with medical oncologists, radiation oncologists, neuro-pathologists, and neuro-surgeons in undertaking brain cancer research.
- Brain Cancer Centre, which was established by Carrie's Beanies 4 Brain Cancer is managed by the WEHI and headed by Professor Douglas Hilton, Director of WEHI, involving collaborators from The Royal Melbourne Hospital, The University of

Queensland, Murdoch Children's Research Institute, VCCC Alliance, Peter MacCallum Cancer Centre, the WEHI, The Royal Children's Hospital Melbourne.

- Centre for Research Excellence in Brain Cancer, established within the School of Cancer Medicine at La Trobe University through the Victorian Cancer Agency,
- Children's Cancer Institute, which is an independent medical research institute wholly dedicated to curing childhood cancer (brain and other cancer types).
- Children with Brain Cancer Centre, which focuses solely on paediatric brain cancer, treatment, and survivorship and involves collaborators at QIMR Berghofer Medical Research Institute, Queensland University of Technology Institute of Health and Biomedical Innovation, The University of Queensland's Institute of Molecular Bioscience, The Diamantina Institute and Queensland Brain Institute, and the clinical infrastructure and specialists of Children's Health Queensland Hospital and Health Service.
- **COGNO**, located at the NHMRC CTC, at the University of Sydney.
- Kids Cancer Alliance, which is a Translational Cancer Research Centre for childhood cancer researchers in NSW Australia, where successful research experiments can be rapidly translated to clinical trial through the KCA trials centre.
- Lee Wong Lab (Monash University), the lab's research focus is to identify new chromatin factors that control chromosome stability and genetic transmission. It investigates genome-wide epigenetic defects associated with H3.3 and ATRX mutations in cancers, particularly brain and bone cancers.
- Mark Hughes Foundation Centre for Brain Cancer Research, which integrates multidisciplinary research and clinical experts and consumers/patient groups, building on the existing capacity of the University of Newcastle.
- Sid Faithfull Brain Cancer laboratory (QIMR Berghofer), the lab focuses on glioblastoma, medulloblastoma and DIPG, designing therapies that specifically treat the tumour while keeping the healthy developing brain intact.<sup>54</sup>
- **Telethon Kids Institute**, with strong ties to Perth Children's Hospital, with an established Brain Tumour Research Laboratory.
- The Brain Cancer Invasion Group at the University of Melbourne.
- **The Brain Cancer Microenvironment and Biology Laboratory** at the University Melbourne investigates the brain tumour microenvironment as part of its goal to understand the molecular and cellular biology of brain cancer.
- The Cure Brain Cancer Neuro-Oncology Groups within the UNSW Lowy Cancer Research Centre (a collaboration between the University of New South Wales and the Children's Cancer Institute) focusing on learning how childhood and adult cancers start, and developing personalised medicine for patients diagnosed with brain cancer.
- The Hudson Institute of Medical Research does some research on childhood brain cancer as part of its broader research interest in childhood cancers. The Hudson Institute of Medical Research was formed in 2014 through a merger of the Monash Institute of Medical Research and Prince Henry's Institute of Medical Research.

<sup>54</sup> See https://www.qimrberghofer.edu.au/our-research/cancer-research/sid-faithfull-braincancer-laboratory/, accessed 10 February 2023

- **The Monif Group** within the Department of Neuroscience at Monash University studies brain cancer as part of a broader research program that studies neuroinflammation in several neurological conditions (also including Multiple Sclerosis, Autoimmune Encephalitis as well as brain cancer).
- Westmead Cancer Centre, the centre is multi-disciplinary and undertakes research, clinical trials as well as treatment and support for brain cancer patients.<sup>55</sup>
- **ZERO,** led by the Children's Cancer Institute and Kids Cancer Centre at Sydney Children's Hospital.

## Funding models for Australian brain cancer research

Various approaches to funding are used to invest in Australian brain cancer research. An overview of key funders and their funding strategies is summarised in table 2.17.

The Mission has used a combination of (initially) targeted grants, and (more recently) competitive grants.

Charitable funds tend to support research teams with baseline funding, without directing research purpose or outcomes. For instance, the Benny Wills Brain Tumour Research Program, Dainere's Rainbow Brain Tumour Research Fund, and Isaac McInnes Fund provide research funds to support Dr David Zeigler's research at Sydney Children's Hospital. The Levi's Project is more directive, providing funds for three research positions, preclinical research costs, and costs for three clinical trials at the Brain Cancer Research Group at Children's Cancer Institute for DIPG.

A common approach is to use an Expert Panel or Scientific Advisory Committee to decide on funded projects, used by the Mission and several of the brain cancer funders. For matters apart from grant funding decisions, the Mission is supported by a Mission Strategic Advisory Group (MSAG).

<sup>&</sup>lt;sup>55</sup> See http://www.sydneywestcancer.org/research/clinical-trials/, accessed 10 February 2023

## **2.16** Overview of brain cancer research in Australia and funding strategies

	Type of research funded					Approaches to fu	nding	
•	Basic theoretical research	Pre-trial translational research	Trial focus (clinical/ observational)	Translation from research to practice	Capacity building incl. infrastructure	Block funding	Competitive grants	Multi-site or speciality collaboration
MRFF (Mission and other)		✓	✓	✓		✓	✓	$\checkmark$
NHMRC	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$	$\checkmark$
Cancer Australia		$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$		$\checkmark$
Mission Funding Partners								
ACT Health and Canberra Health Services						✓		$\checkmark$
Carrie's Beanies 4 Brain Cancer	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$		$\checkmark$
Children's Hospital Found. Queensland	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$	$\checkmark$	
Cure Brain Cancer Foundation	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$			$\checkmark$	$\checkmark$
Financial Markets Foundation for Children	$\checkmark$	$\checkmark$				$\checkmark$		
The Kids Cancer Project							$\checkmark$	
Mark Hughes Foundation	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$		
Minderoo Foundation		$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$
NeuroSurgical Research Foundation	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	
Robert Connor Dawes Foundation	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$
NSW Government	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Victorian Government	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$		
Other funders								
Australian Cancer Research Foundation					✓		$\checkmark$	
Benny Wills Brain Tumour Research Prog.						$\checkmark$		
Brain Foundation	$\checkmark$	$\checkmark$					$\checkmark$	
Cancer Councils	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Cancer Institute NSW	$\checkmark$	$\checkmark$	~	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Charlie Teo Foundation	$\checkmark$	~	✓	✓			✓	

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-	Type of research funded					Approaches to fu	nding	
-	Basic theoretical research	Pre-trial translational research	Trial focus (clinical/ observational)	Translation from research to practice	Capacity building incl. infrastructure	Block funding	Competitive grants	Multi-site or speciality collaboration
Children's Cancer Foundation			✓	✓		$\checkmark$		
Dainere's Rainbow Brain Tumour Research Fund						$\checkmark$		
Isaac McInnes Fund						$\checkmark$		
Levi's Project		$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$		
My Room Children's Cancer Charity	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$		
Perth Children's Hospital Foundation	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	
Pirate Ship Foundation		$\checkmark$				$\checkmark$	$\checkmark$	
Run DIPG	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	✓	$\checkmark$	$\checkmark$	
The Cure Starts Now		$\checkmark$	$\checkmark$	$\checkmark$			$\checkmark$	
Tour de Cure	$\checkmark$	$\checkmark$		$\checkmark$			$\checkmark$	

Note: Based on publicly available information only. Funding entities may be involved in additional areas that are not indicated here. Table refers to Mission projects up until April 2022. Since, then there have been projects funded for basic research and research infrastructure.

Source: CIE.

## Comparisons with international brain cancer research

According to the ICRP<sup>56</sup>, there were 13 699 brain tumour related projects as defined by ICD-10 C71 funded internationally between 2017 and 2022. Additionally, there are 2 539 clinical trials relating to brain cancer, with over 685 849 participants<sup>57</sup>.

This points to a vast collection of international brain cancer research.

An analysis of ICRP projects by CSO reveals that most studies internationally focus on treatment, followed by biology, early detection and diagnosis and prognosis, then aetiology and survivorship (chart 2.17). The outcomes of the ICRP data compared with the Cancer Australia audit of Australian brain cancer research funding reveal that Australia has:

- a larger focus on treatment (51 per cent of total projects), compared to 34 per cent internationally
- a larger focus on early detection, diagnosis and prognosis (26 per cent), compared to 18 per cent internationally
- a larger focus on survivorship (13 per cent), compared to 8 per cent internationally
- a substantially smaller focus on biology (9 per cent of projects), compared to 24 per cent internationally<sup>58</sup>, and
- no focus on aetiology and prevention, which internationally comprises 16 per cent of total projects.

# 2.17 ICRP brain cancer projects by CSO and Cancer Australia Audit of Australia brain cancer funding, 2018-2020



Data source: International Cancer Research Partnership, CIE.

- 57 See Clinicaltrials.gov, Accessed 9 August 2022.
- <sup>58</sup> It is noted that this data does not include the most recent Mission projects that have either a particular focus on biology (three under the 2021 Brain Cancer Research grant opportunity) or provide infrastructure support that will help enable biology research (one under the 2022 Australian Brain Cancer Research Infrastructure grant opportunity).

 <sup>&</sup>lt;sup>56</sup> ICRP maintains the only public source, worldwide, of current and past grants, totalling over
 \$80 billion in cancer research since 2000 from 32 ICRP Partners and 156 international funding organisations (all cancers). See https://www.icrpartnership.org/, Accessed 9 August 2022.

#### International brain cancer clinical trials

The key clinical trial registry for international cancer clinical trials is ClinicalTrials.gov<sup>59</sup>, which is run by the United States National Library of Medicine at the National Institutes of Health, and is the largest clinical trials database. It holds registrations from over 425 000 trials from over 200 countries.

Running a query for brain cancer within the trials database yielded 2 539 clinical trials<sup>60</sup>, which includes over 685 800 participants. Chart 2.18 shows summaries of the funding, age groups, phases, and gender composition of the trials.

Other government sources, philanthropy, consumers, and foundations were funders in over 50 per cent of brain cancer trials. Approximately 75 per cent of trials were targeted at adults and older adults, while only 15 per cent of trials were targeted and children and adults. Over 63 per cent of trials were in either Phase 1 or 2. Almost all trials were gender non-specific (97.2 per cent), with the remainder predominately female focused (2.6 per cent).



#### 2.18 Clinical trials database summary

Note: Funding Other\* includes other government sources, philanthropy, consumers and foundations. Data source: Clinicaltrials.gov, CIE.

<sup>59</sup> https://clinicaltrials.gov/

<sup>&</sup>lt;sup>60</sup> Date accessed 18 August 2022

## 3 Mission and other MRFF brain cancer research

MRFF funded brain cancer research occurs primarily through the Mission, but has also been directed through other MRFF initiatives.

Up until April 2022, which defines the scope of the current review, the MRFF awarded 19 grants for brain cancer research, valued at \$31 million. Eight of these were provided through the Mission and account for 71 per cent of MRFF funding. Since then, up until June 2023, the MRFF awarded 12 grants for brain cancer research valued at \$42 million, with 12 provided through the Mission. Most recent Mission grants have been awarded through grant opportunities for brain cancer research and brain cancer research infrastructure.

Most Mission grants are directed towards translational research, and other MRFF brain cancer grants are predominately to support clinical trials.

## MRFF-funded brain cancer research

In total, the MRFF has allocated \$60.26 million to the Mission.

- An initial \$50 million will be allocated through Mission grants. From 2017 up until July 2023, 12 grants were allocated through the Mission totalling \$33.2 million (67 per cent of the total to be allocated through the Mission). This included:
  - 3 directed grants with a total value of \$10.5 million
  - 9 competitive grants with a total value of \$22.8 million, and
- A further \$10.26 million will be allocated through other MRFF initiatives. From 2017 to July 2023, 11 grants with a total value of \$8.77 million had been awarded.

#### 3.1 Overview of MRFF funding

-	MRFF funding	Share of allocated MRFF funding	Share of total MRFF funding
-	\$ million	Per cent	Per cent
Mission grants	21.79	71.3	36.2
Grants through other MRFF initiatives	8.77	28.7	14.6
Total allocated	30.56	100.0	50.7
Not yet allocated	29.70		49.3
Total MRFF funding	60.26		100.0

Source: CIE based on information provided by HMRO.

#### Mission research grants

#### Funded projects

The first year of Mission grant opportunities resulted in targeted grants to existing research networks to build capacity and set a research agenda. From then until April 2022, Mission grants have prioritised survivorship, and been awarded on a competitive basis. Most recent Mission grants have been awarded through grant opportunities for brain cancer research and brain cancer research infrastructure.

Grants funded under the Mission are predominately for translational research, including establishing best practice care for survivors and translating that into clinical practice. Grants funded via other MRFF grant opportunities focus on clinical trials.

-	Grants	Amount
-	No.	\$
Grant opportunity		
2018 Enhanced Capacity of the Australian and New Zealand Children's Haematology Oncology Group (ANZCHOG) Program	1	3 010 000
2018 Enhanced Capacity of the Cooperative Trials Group for Neuro-Oncology (COGNO) Program	1	2 500 000
2018 ZERO Childhood Brain Cancer	1	5 002 023
2019 Brain Cancer Survivorship	2	6 914 602
2019 Innovative Clinical Trials	2	1 749 170
2020 Brain Cancer Survivorship	1	2 615 278
Total - Mission	8	21 791 073

#### 3.2 MRFF grant opportunities – summary

Source: HMRO, CIE. Includes grants issued up to April 2022.

A key theme of Mission grants has been improving health-related quality of life for brain cancer survivors, reflecting the focus on survivorship. A key outcome that Mission grants are seeking to achieve is improvements in survivorship. Survivorship grant opportunities comprise 44 per cent of Mission funding (not including brain cancer research funding from other MRFF initiatives.

#### Mission funding by institution

All Mission grants up until April 2022 have been awarded to five universities (table 3.3):

	No. of grants	Value of grants	% of total
-	#	\$	%
University of Sydney	3	7 975 584	36.6
University of New South Wales	2	6 943 599	31.9
University of Melbourne	1	2 615 278	13.8
Monash University	1	3 010 000	12.0

#### 3.3 Mission grant funding by institution

•	No. of grants	Value of grants	% of total
-	#	\$	%
La Trobe University	1	1 246 612	5.7
Total	8	21 791 073	100.0

Source: HMRO, CIE. Includes grants issued up to April 2022.

## Other MRFF brain cancer research

#### **Funded** projects

Eight brain cancer grants have been awarded through the MRFF's Clinical Trials Activity, and account for 24 per cent of MRFF funding, and a further three brain cancer grants were awarded through the MRFF's Emerging Priorities and Consumer Driven Research, accounting for 4.7 per cent of MRFF funding for brain cancer.

#### 3.4 Summary of other MRFF grants for brain cancer research

•	Grants	Amount
-	No.	\$
Clinical Trials Activity		
2018 Rare Cancers, Rare Diseases and Unmet Need - General	4	3 016 742
2019 Rare Cancers, Rare Diseases and Unmet Need - Childhood Brain Cancers	3	2 332 299
2021 Rare Cancers, Rare Diseases and Unmet Need	1	1 982 681
Total - Clinical Trials Activity	8	7 331 723
Emerging Priorities and Consumer Driven Research		
2018 Accelerated Research - Priority-driven Collaborative Cancer Research Scheme - All Cancers	2	958 215
2018 Accelerated Research - Priority-driven Collaborative Cancer Research Scheme - Childhood Cancers of Low Survival	1	480 015
Total - Emerging Priorities and Consumer Driven Research	3	1 438 231

Source: HMRO, CIE.

A key theme of grants funded through other MRFF initiatives has been targeted therapies.

#### Grant funding by institution

Other MRFF grants relating to brain cancer research have been awarded to four universities (see table 3.5):

#### 3.5 Other MRFF brain cancer grant funding by institution

	No. of grants	Value of grants	% of total
-	#	\$	%
University of Sydney	3	4 647 786	53.0
Monash University	5	2 035 455	23.2

•	No. of grants	Value of grants	% of total
-	#	\$	%
University of New South Wales	1	1 128 498	12.9
University of Melbourne	2	958 215	10.9
Total	11	8 769 953	100.0

Source: Mission, CIE.

## Focus on collaboration

Based on the grantee survey, collaboration has been a dominant characteristic of grants, with most involving collaboration across sites, research institutions, and/or internationally.

All MRFF brain cancer research grants have involved research collaborations.

- All MRFF brain cancer grants involve collaboration within Australia:
  - all but 2 MRFF brain cancer grants (89 per cent) involved collaboration across multiple research institutions, and
  - all but 2 MRFF brain cancer grants (including all Mission grants) involved collaboration with Australian hospital-based researchers.
- Nearly two-thirds of MRFF brain cancer grants (12 out of 19) also involved international collaboration (chart 3.6):
  - 10 out of 19 MRFF brain cancer grants (53 per cent) involved collaboration with international university or research institute-based researchers, and
  - 10 out 19 MRFF brain cancer grants involved collaboration with hospital-based researchers.



#### 3.6 Share of MRFF brain cancer grants involving collaboration

Data source: CIE Survey.

## Consumer engagement in research

Based on the grantee survey, MRFF brain cancer grants exhibit high levels of engagement with consumer groups.

Researchers have engaged with consumer groups during the design of the research for all MRFF brain cancer grants.

There were also high-levels of subsequent engagement with consumer groups for MRFF brain cancer grants, particularly for Mission grants for which consumer engagement after the research is a specific focus of the Mission:

- all Mission grants involved subsequent engagement with consumer groups, and
  - 7 out of 11 grants (63 per cent) of grants through other MRFF brain cancer initiatives involved subsequent engagement with consumer groups.



#### 3.7 Engagement of consumer groups

Data source: CIE Survey.

## Alignment with Roadmap

The Mission Roadmap was intended to provide a high level implementation plan for MRFF and Funding Partner investment, with the MRFF funding research that met the objectives and requirements of the MRFF, and Partner Funding extending investment into complementary areas.

Based on researcher assessments, as reflected in the survey responses, the projects funded through the MRFF has generally been well aligned to the Mission Roadmap. This includes both Mission grants (which were explicitly intended to align with the Roadmap), and grants under other MRFF initiatives (which were not explicitly intended to align with the Roadmap). However, some areas of the Roadmap had no MRFF grants in close alignment, with Funding Partners dominating investment in those areas.

The survey of grant recipients asked Mission and other brain cancer-related MRFF brain cancer grant recipients to indicate how closely the objectives of their project aligns with the various elements of the Mission Roadmap.

Chart 3.8 shows the average number of projects aligning with each element under each of the four pillars of the Roadmap.

- MRFF-funded grants aligned most closely (from the perspective of both the number of projects and the dollars invested in those projects) with the *Increased and equitable access and participation in clinical trials* pillar.
- MRFF-funded grants aligned less well with the *Increased researcher capacity and excellence* pillar. Some items under this pillar had no MRFF grants in close alignment (although some partner funding aligned with those areas of the Roadmap).



#### **3.8** Average alignment with the Mission Roadmap

Note: Chart shows the average number of projects across the various elements of each pillar. Only includes MRFF grants up to April 2022. Since then, there have been four grant opportunities relating to brain cancer research or brain cancer research infrastructure. *Data source:* CIE Survey.

#### Increased patient survival, quality of life and care experiences

While a sizeable proportion of Mission funding has been allocated to survivorship projects, the survey of grantees identifies fewer projects aligning with survivorship than those focusing on treatment. That said, there have been some MRFF brain cancer grants that closely align with each component of this pillar and several others that have some relevance (chart 3.9).



#### 3.9 Alignment of projects with Roadmap – Increased patient survival, quality of life and care experiences

Data source: CIE Survey.

#### Increased and equitable access and participation in clinical trials

Clinical trials have been a clear focus of MRFF brain cancer grants, with grants aligning most closely with this pillar of the Roadmap. At least 6 projects align closely with each of the elements under this theme and other projects that have some relevance (chart 3.10).

#### 3.10 Alignment of projects with Roadmap – Increased and equitable access and participation in clinical trials



Data source: CIE Survey.

#### Expanded research platforms and technologies

Although variable across each element, there were some MRFF brain cancer grants that closely aligned with each element under this pillar (chart 3.11):

- more than half of MRFF brain cancer grants were considered to closely align with 'Identify drugs of potential and ensure access to new drugs by adults and children' (reflecting the focus on clinical trials), and
- there was generally less alignment across the projects with the other elements of this pillar, but still several projects that were considered to closely align with each.

#### 3.11 Alignment with Roadmap – Expanded research platforms/technologies



Data source: CIE Survey.

#### Increased research capacity and excellence

Based on survey responses, '*Increased research capacity and excellence*' has been less of a focus of MRFF brain cancer funded research projects, compared with some of the other pillars of the Roadmap (chart 3.12).

- There was reasonable alignment with one of the elements under this pillar ('Build domestic research talent through a contestable grant program for innovative research capable of supporting international research collaboration'):
  - 4 Mission grants and 4 grants under other MRFF initiatives that have funded brain cancer research were considered to align closely with this element, and
  - a further 5 grants under other MRFF initiatives that have funded brain cancer research were also considered to have some relevance.
- However, there was limited alignment across the remaining 3 elements under this broader theme:
  - No Mission grants aligned closely with any of the other elements, although there
    were some that had some relevance.
  - Only 1 grant under other MRFF initiatives that have funded brain cancer research aligned closely with one of the other elements, although there were some grants

under other MRFF initiatives that have funded brain cancer research that had some relevance.

- No MRFF brain cancer grants aligned closely with 2 elements under this theme:
  - ···· 'Support protected research time for clinicians through targeted PhD scholarships, post-doctoral and senior researcher and practitioner fellowships'
  - ··· 'Establish a new centre for basic and clinical research excellence in paediatric and adult brain cancer.'

#### 3.12 Alignment with Roadmap – Increased research capacity and excellence



Data source: CIE Survey.

Nevertheless, responses to other survey questions indicated that the MRFF brain cancer grants have been successful in building Australian research capacity, but seemingly not in the specific ways envisaged by the Mission Roadmap.

# Comparisons between MRFF funding and Mission funding partners

Although there is limited information on the research activities funded by Funding Partners under the auspices of the Mission, there are some broad comparisons that can be drawn between research activities funded through the MRFF and Funding Partners.

One comparison that can be made is in the types of funding provided. In general, Funding Partners have allocated funding to some areas that have been under-represented in MRFF grants to date (as at April 2022), particularly in relation to building research capacity and excellence (one of the four pillars under the Roadmap).

 Collectively, Funding Partners have provided \$12.5 million to Centres of Excellence under the Mission banner. By contrast, no MRFF grants were considered to align with the relevant element of the Roadmap (i.e. *Establish a new centre for basic and clinical research excellence in paediatric and adult brain cancer*).

 Similarly, while no MRFF grants align with Support protected research time for clinicians through targeted PhD scholarships, postdoctoral and senior researcher and practitioner fellowships (an objective under the Roadmap), Funding Partners have allocated \$5.4 million to fellowships and research chairs.

Another comparison relates to the size of research grants. In general, apart from the larger philanthropic organisations, research grants (including grants identified as clinical trials or other research grants, but excluding funding for Centres of Excellence) tended to be significantly smaller than those provided by the MRFF.

- The average grant provided through the MRFF is \$1.6 million included:
  - an average of \$2.7 million for those provided through the Mission
  - an average of around \$800 000 for those provided through other MRFF initiatives.
- By contrast, based on the information available, the average grant funded by Funding Partners was around \$390 000.
  - Some Funding Partners tended to provide a large number of smaller grants; over one-third of the grants were less than \$50 000 (table 3.13).
  - Less than 10 per cent of grants provided by Funding Partners were more than \$1 million.



#### 3.13 Funding partner research grant value - frequency distribution

Data source: Cancer Australia, CIE.

The above comparisons suggest a degree of complementarity between MRFF-funded research and the activities of Funding Partners.

- Funding Partners have provided some funding in areas of the Roadmap that have been under-funded by the MRFF to date.
- Funding Partners have provided funding for basic research through funding for Centres of Excellence and small research grants — an area that many stakeholders argued had been under-funded by the MRFF.

However, it is not clear that this complementarity was by design, as many Funding Partners commented that their funding choices had not been influenced by the Roadmap or the Mission more generally.

## Comparisons between MRFF and other brain cancer research

Brain cancer research funded by the MRFF through the Mission appears to have a greater focus on survivorship than other brain cancer research, including that conducted internationally.

Identifying ongoing care needs for brain cancer survivors and ensuring that this is reflected in clinical practice has been a particular focus of Mission grants to date. Survivorship has been the theme of two out of the three competitive Mission grant opportunities and projects focused on survivorship have received more than 60 per cent of grant funding through the Mission as at April 2022.

Although consumer groups welcomed the investment in survivorship research, there was generally less interest in this type of research from some researchers and funding partners during consultations. One interpretation of this observation is that Mission grants through the MRFF are filling a gap in existing research funding arrangements (i.e. survivorship research is not being funded through other funding arrangements) and is therefore meeting an unmet need.

Other MRFF initiatives that have funded brain cancer research have tended to focus more on testing the efficacy and safety of new targeted therapies for specific patient sub-groups.

More generally, other Australian and international research tends to focus on efficacy of treatment and translation, as well as basic applied research to answer scientific questions to improve future research and treatment options.

Internationally, there is also arguably a greater focus (compared with research funded through the Mission) on basic applied research as well as clinical and epidemiological trials, where patient numbers support the scale requirements of research. However, it is noted that the desktop analysis of international research is limited to published material, which may account for the observed increase in the focus on scientific/laboratory-based testing and discovery.

# 4 Progress to date against MRFF Measures of Success

Findings regarding the progress of the Mission to date are based on analysis of feedback from stakeholder consultations and the survey of MRFF brain cancer research grantees.

- The Mission's key areas of impact in addressing unmet need include increasing the amount of funding for Australian brain cancer research, and investing in survivorship to improve patient quality of life. The most outstanding area of unmet need still to be addressed is funding for innovations that do more than make incremental improvements to existing survival prospects.
- The Mission has provided more Australians with access to clinical trials and has built additional capacity that will lead to more clinical trials in the future.
  - Researchers indicated that approximately 1350 additional patients were given access to a clinical trial that they otherwise would not have had access to.
  - Furthermore, researchers expect that the clinical trial capacity enhanced through MRFF-funded research grants will lead to around 70 additional clinical trial sites in Australia over the next five years, giving an additional 1600-1700 Australian patients the opportunity to participate in a clinical trial that they would not otherwise have had access to.
- It is too early to be definitive about what impact MRFF brain cancer research grants have, or will, achieve regarding new health technologies and new health interventions, although the prospects for both are positive.
- The Mission has already had a positive impact on building capacity for translational research in terms of attracting researchers into the brain cancer field, and funding shared infrastructure.
- MRFF brain cancer research grantees expect that interventions developed through research grants will contribute to health professionals adopting best practices faster than they otherwise would, although there are outstanding concerns regarding the standardisation of care, particularly for adult patients.
- The Mission has made some progress in community engagement by facilitating a move towards more consumer involvement in brain cancer research.
- The Mission is not yet believed to have had an impact on commercialisation, with minimal impact on encouraging industry to collaborate, engage, and support the Australian brain cancer research sector, or otherwise contribute to other aspects of the commercialisation environment.

### Focus on unmet need

The genesis of the Mission was a Ministerial approach by a parent unable to get a dying child into a clinical trial. It revealed how under-resourced brain cancer research was in Australia, and the importance of a holistic approach to funding the brain cancer research landscape: from discovery through to clinical trials, and the clinical adoption of care pathways that improved patient quality of life.

Virtually all stakeholders consulted in this review believed that a transformative impact of the Mission to date has been the profile and attention brought to the unmet need of brain cancer patients, and the urgency to address the long-standing poor survival outcomes relative to other cancers.

The Mission represents the most substantial financial commitment Australia has yet made to brain cancer research, assisted by the bringing together of a variety of Mission Funding Partners alongside the Australian Government.

The Mission's key areas of impact in addressing unmet need include:

- increasing the amount of funding for Australian brain cancer research, and
- investing in survivorship to improve patient quality of life.

The most outstanding area of unmet need still to be addressed is funding for innovations that do more than make incremental improvements to existing survival prospects. There is also a need to improve equity of patient access to best practice care.

#### Uplift to brain cancer research funding

The Mission has clearly sign-posted that funds from the MRFF will be directed towards brain cancer research for an extended period.

The establishment of the Mission has led to an increase in the amount of brain cancer research funding (including through the Australian Government and the Funding Partners), over and above what would have been allocated in its absence.

Having a dedicated funding allocation for brain cancer is heralded as being particularly important given the low incidence and lack of data and evidence on improved survival, which makes it more difficult to access other funding sources (such as NHMRC funding) where researchers compete with high incidence cancers better able to demonstrate links between research and improved survival. Based on the survey of recipients of MRFF brain cancer research grants, all stated that the MRFF grant allowed recipient institutions to undertake more brain cancer research. In most cases, alternative funding sources were unavailable, with 13 out of 19 projects believed to be 'unlikely to have proceeded in the foreseeable future' without the MRFF grant.

When the Mission was established, the Australian Government pledged to match commitments by Funding Partners to the Mission up to \$50 million, which was a major impetus for several Funding Partners joining the Mission, and in some cases resulted in these funders spending more on brain cancer themselves than they otherwise would have. The Mission Funding Partners have also seed-funded research projects that have gone on to access funding from other grant opportunities (such as the NHMRC), bringing more of that funding pool to brain cancer.

With respect to Funding Partner contributions to brain cancer research, not all Mission funding is 'new' or additional funding.

Examples of additional funds for brain cancer research include the \$5 million allocated by the Financial Markets Foundation for Children, and the increase in brain cancer research funding by the Kids' Cancer Project (KCP), which now allocates \$700 000 a year to brain cancer projects, up from \$175 000 when KCP first committed to the Mission. It is also likely that the Victorian Government made a larger commitment in its state cancer plan to brain cancer research because of their participation in the Mission<sup>61</sup>.

Other philanthropic and charitable Funding Partners generally indicated that their funding for brain cancer in Australia would have occurred without the Mission, but the Mission provided a vehicle that helped ensure their investment would raise the profile of the brain cancer research and would add to the momentum of the Mission.

Not all Mission funding has yet been allocated, including for the MRFF as well as partner funding. One of the pitfalls of MRFF brain cancer research grant opportunities for the disbursement of partner funding has been some lack of alignment between grant opportunities and the Board requirements for charitable funders. For instance nongeneralist Funding Partners (such as 'adult only', 'paediatric only', or 'cure-seeking only') have found that they are unable to contribute to MRFF brain cancer project funding, despite allocating (and tying up) funds in the Mission, leaving Funding Partners frustrated that they can have 'nothing to fund'.

#### Addressing unmet need incrementally

At this stage, the Mission has predominantly allocated funding to projects with the potential to make incremental gains.

When the Mission was formed, there was anticipation among stakeholders that it would speak to the 'big picture', focus on the 'big needs', and offer grants with a national focus that 'fund the boat that lifts everyone'.

There are mixed views as to whether this has been the experience to date, and perhaps not surprisingly, some disappointment with things that were funded, and not funded.

The major criticisms include:

Concern that the allocation of funding to date has not been spread across the research continuum, with relatively less investment in basic research than is needed to create a

<sup>61</sup> For instance, the Victorian Governments most recent Cancer Plan includes contributions to the Olivia Newton John Cancer Research Institute and the Gamma Knife facility at the Peter MacCallum Cancer Centre to combine radiotherapy and surgical interventions. Outside of the Mission, the Victorian Government has also invested \$16 million in the BCC, along with \$3.8 million from Carrie's Beanies for Brain Cancer for the Brain-POP clinical trial platform that draws on researchers and clinicians across Melbourne's biomedical precinct.
pipeline to feed into future clinical trials. Some stakeholders felt this should have been an early focus of the Mission given the long timeframes before any impacts are felt

- less funding for adult brain cancer than paediatric cancer, particularly relative to the number of patients affected
- less support than is needed for larger scale multi-team/disciplinary collaborations that focus on improved survival and linkages with clinicians and industry, and
- underfunding /lack of funding for basic high risk/high reward research that might discover new treatments. While this is partly a function of the competitive grants process, which is believed to foster conservatism from grant assessment or peer review panels, it remains a widely held view. The same sentiment can also arguably be said for the way that grants are scientifically assessed across the broader research sector.

### Contributions to survivorship

Survivorship is an important element of brain cancer research, because of the long-standing reliance on highly toxic treatments that leave survivors with often severe disability. Internationally, survivorship research has historically lagged other CSO categories, and represented a gap in research investment and focus.

The Mission has had an impact on elevating research on survivorship, and is recognised for its contribution to funding survivorship-related projects, with three of the eight MRFF Mission grants up until April 2022 focused on survivorship<sup>62</sup>, accounting for 44 per cent of Mission funding (excluding funding for brain cancer via other MRFF initiatives)

Consumer perceptions are positive, with even a limited focus on survivorship being well regarded by consumer groups. This is particularly the case for consumer groups, who believe it demonstrates how consumer issues have been integrated into Mission funding decisions. Consumer groups have welcomed the emphasis given to carers as well as patients, and the effort being taken to improve the way that information is made accessible to consumers.

Consumer groups also note that there is still a long way to go in addressing survivorship. Examples provided by consumers include:

- feelings that patients are left on their own to manage their condition after treatment or a clinical trial has completed
- difficulty in connecting with other survivors
- families are generally not well supported when caring for a patient with brain cancer
- lack of support provided to assist with accessing the National Disability Insurance Scheme (NDIS) and managing finances, and
- lack of support to deal with vision loss following treatment to help them read and keep up with research.

<sup>62</sup> It is noted that the most recent survivorship projected awarded from the MRFF to the WEHI (see https://www.wehi.edu.au/news/collaborative-brain-cancer-research-awarded-46m-grant) is out of scope for this review due it being announced after the commencement of this review.

Ultimately, significant improvements in the health-related quality of life of survivors will come from improved treatments that displace standard treatment rather than survivorship research.

### Access for Australians to clinical trials

### More Australians access clinical trials

The security of funding provided by the Mission to clinical trials has already started to allow researchers to seek out international trials more efficiently. As funding is secured, researchers can focus on applying to the trial immediately, as opposed to discovering the trial, then raising funds, then applying. Particularly for paediatrics, where often the best treatments can only be accessed via clinical trials, this certainty of funding has been critical.

Several stakeholders also highlighted how Mission clinical trial funding has facilitated international interest in bringing clinical trials to Australia. For instance, clinical researchers involved in paediatric cancer have experienced considerably higher interest from pharmaceutical companies offering hospitals to run a trial site with funding attached. In some cases, Australian children have been offered to participate as the first child in the world to receive a treatment under clinical trial conditions.

Providing more Australians with access to clinical trials was a key success of the MRFF brain cancer grants:

- 17 (out of 19) MRFF brain cancer grants gave Australian patients access to clinical trials that they otherwise would not have had access to, and
- researchers indicated that approximately 1350 additional patients were given access to a clinical trial that they otherwise would not have had access to<sup>63</sup>.

In addition, the MRFF brain cancer grants helped to build clinical trial capacity that is expected to lead to additional clinical trial sites in Australia and more Australians having access to clinical trials in the future (chart 4.1):

- researchers considered it 'likely' or 'very likely' that the capacity built through 12 of the MRFF brain cancer grants will lead to more clinical trial sites in Australia
- researchers considered it 'likely' or 'very likely' that the capacity built through 17 of the MRFF brain cancer grants will improve access to clinical trials for Australian patients in future.

Over the next five years, researchers estimated that the capacity built through MRFF brain cancer grants will:

- lead to around **70** additional clinical trial sites in Australia, and
- give an additional 1600-1700 Australian patients the opportunity to participate in a clinical trial that they would not otherwise have had access to.

<sup>63</sup> It is not possible to know, based on the data available, how this compares to the number of patients that would have had access to a clinical trial without Mission funding.



#### 4.1 Capacity built through MRFF grants and future clinical trial activity

Data source: CIE survey.

While researchers that are accessing Mission funding to support clinical trial activity can identify opportunities for trial access, consumer groups and representatives did not share this same experience. This may reflect a lack of information being provided to consumers, and the experience for many consumers that they are the ones left to investigate trial opportunities.

Stakeholder views on the discrepancy in access to clinical trials indicates that:

- access to clinical trials depends on geographic setting patients in rural and remote locations are not receiving equity of access, partly because of the (unaffordable) higher costs patients incur when accessing a clinical trial out of their geographic area, and
- there is variability in clinical management patients unable to access brain cancer specialists and/or centres of excellence are not experiencing the same clinical pathway.

These challenges were echoed by consumer groups in New Zealand, who note that low socioeconomic, Māori, and rural populations are less likely to be offered treatment, and patients sometimes choose not to access treatments due to the difficulties in reaching research centres.

It was also noted that in the United States and Europe there are still more opportunities to access a clinical trial for brain cancer than in Australia, albeit can be dependent on insurance status<sup>64</sup>.

<sup>64</sup> Compared to the United States, Australians are more constrained accessing clinical trials due greater population remoteness and fewer cancer facilities. Regarding trial activity, an analysis of the clinical trial locations listed in the clinicaltrials.gov database shows the United States has 3.4 times the number of clinical trial locations per person than Australia when adjusted for population. We note that clinical trial locations do not necessarily include recruitment, nor is recruitment contained only to clinical trial locations. We also note that not all Australian clinical trials are captured by this database. Hence this estimate should be treated with caution.

### New health technologies embedded in health practice

In general, the progression from a research grant through to a new technology becoming embedded in health practices can be long. As this review commenced five years after the Mission was formed and four years after the first grants were made, it is too early to make a definitive assessment of what MRFF brain cancer grants have achieved.

Nevertheless, based on responses to the survey, the prospects of new health technologies developed through the MRFF brain cancer grants to eventually become embedded into health practices appear positive.

Embedding new technologies in health practices depends on new technologies being developed through research. There were **10** MRFF brain cancer grant recipients that indicated that developing, identifying or validating a new health technology (or technologies) was an objective of their research. Of these 10 projects (chart 4.2):

- 3 indicated they were 'certain' a new health technology would be delivered (or already had been delivered)
- 6 indicated they considered it 'likely' or 'very likely' that the research would deliver a new health technology, and
- only 1 project considered it unlikely that the MRFF grant would deliver a new health technology directly; however, it was considered 'likely' that future planned research leveraged from the MRFF grant would deliver a new health technology.



#### 4.2 Likelihood of delivering a new health technology

Data source: CIE Survey.

The types of new health technologies that were expected to be delivered through MRFF brain cancer grants (and subsequent research where relevant) is shown in chart 4.3.



#### 4.3 Types of new health technologies developed through MRFF brain cancer grants

Data source: CIE survey.

The prospects of the new technologies developed through MRFF brain cancer grants (and in some cases subsequent research) becoming embedded in health practices appear positive (chart 4.4):

- researchers reported one new technology already having become embedded in health practices, and
- for a further 7 projects, researchers considered it either likely or very likely that the new technologies developed would become embedded in health practices.



#### 4.4 Likelihood of new technologies becoming embedded in health practices

Data source: CIE survey.

Chart 4.5 shows the potential impacts that researchers expect these new technologies will deliver (as well as the researchers' assessment of the level of certainty with which a new technology will be delivered).

- 7 projects are expected (certain, very likely or likely) to deliver a new technology that will improve the chance of survival (although the extent of the improvement is not known)
- 7 projects are expected to deliver a new technology that will lead to 'other improvements' (i.e. excluding reduced impact on cognitive function, reduced pain and reduced fatigue) in health-related quality of life for patients
- 6 projects are expected to deliver a new technology that will reduce the burden on the health system.



#### 4.5 Potential impact of new technologies

Data source: CIE Survey.

### New health interventions embedded in health practice

As with new health technologies, the timeframes from a research grant through to a new health intervention becoming embedded in health practices can be long. As such, it is too early to make a definitive assessment.

Nevertheless, as with new health technologies, the prospects of some new health interventions developed through the MRFF brain cancer grants eventually becoming embedded into health practices appear encouraging (based on researcher's assessments) (chart 4.6):

- 2 survey respondents indicated that it was 'certain' that the MRFF brain cancer grants would lead to new health interventions (or had already done so)
- researchers considered 'likely' or 'very likely' that a further 10 MRFF brain cancer grants will directly lead to a new health intervention, and
- researchers considered it 'unlikely' or 'very unlikely' that 3 of the MRFF brain cancer grants would directly lead to a new health intervention. However, in some cases, it was considered 'likely' or 'very likely' that further research would lead to a new health intervention.



### 4.6 Likelihood of MRFF grants leading to new health interventions

Data source: CIE Survey.

The types of new health interventions expected to be delivered through MRFF brain cancer grants are shown in chart 4.7.



#### 4.7 Types of new health interventions

Data source: CIE Survey.

There also appears to be good prospects of the new health interventions developed through MRFF brain cancer grants (and in some cases subsequent research) becoming embedded in health practices, although there was also significant uncertainty (chart 4.8):

- one project appears to have already delivered a new health intervention that has become embedded in health practices
- it was considered 'likely' or 'very likely' that the health intervention developed by a further 8 projects would eventually become embedded in health practice, and
- a further 6 respondents considered it 'too early to know'.





Data source: CIE Survey.

### Capacity for translational research

The Mission has already had a positive impact on building capacity for translational research in terms of attracting researchers into the brain cancer field, and funding shared infrastructure.

The survey of MRFF brain cancer grant recipients indicated that all MRFF projects have contributed to building research capacity within Australia, most commonly by establishing and/or expanding collaborative research networks, including among Australian (all MRFF brain cancer grants) and international researchers (12 out of 19 projects) (chart 4.9).

Most grant recipients also believe their grant has contributed to building translational research capacity (17 out of 19).

However, the Mission is yet to have a direct impact on fostering larger scale collaborations or links with industry, which are important enablers of translational research.



#### 4.9 Ways MRFF-funded research projects have built Australian research capacity

Data source: CIE survey.

### Building critical mass and attracting talent

Despite having pockets of excellence, Australia is not considered a world leader in brain cancer research, unlike some other cancers, such as melanoma and breast cancer. However, it is internationally competitive, particularly given Australia's relatively small population size and community of brain cancer patients.

One of the more important aspects of capacity building is achieving a critical mass of researchers, which the Mission has facilitated by providing the surety of funding to attract researchers, including from other cancer fields.

For instance, the Mission has:

- positively contributed to the career prospects and attractiveness of brain cancer research as a field of endeavour by providing security of funding for an extended period
- redirected researchers from established centres and laboratories who are now working in brain cancer, translating their skills in other types of cancers into the brain cancer domain

- attracted world class researchers in brain cancer research
- funded the infrastructure needed to provide data and networks that improve researcher productivity
- facilitated some collaborations that bring together otherwise disparate teams, and
- (directly or indirectly) led to the funding of new research entities, such as the Brain Cancer Centre (BCC).

The result has been more research staff and students engaged in Australian brain cancer research, and more research collaborations, than was the case before the Mission.

However, by and large the journey to achieving critical mass has not yet been reached.

The Australian brain cancer research landscape remains relatively fragmented, particularly with respect to adult brain cancer research, with limited coordination of resources or strategy.

#### Impact on collaborations

One of the key areas of anticipated impact of the Mission was promoting research collaborations and overcoming the fragmentation in brain cancer research which has existed for some time, particularly about adult brain cancer research.

All MRFF-funded brain cancer grants involved collaboration within Australia and almost two-thirds involved international collaboration. Nevertheless, some researchers noted a broader trend toward greater collaboration and questioned whether the Mission had been a significant influence on this broader trend. For instance, notable collaborations that have occurred in recent years are not supported by the Mission, such as:

- the Australian Brain Cancer Research Alliance (ABCARA)<sup>65</sup>, which is a relatively new organisation that focuses on pre-clinical modelling and translational work, and is still in its infancy in terms of developing partnerships and governance structures to support and attract large scale investments
- the Brain Cancer Centre's Brain-POP clinical trial platform that draws on researchers and clinicians across Melbourne's biomedical precinct. The platform is led by The Brain Cancer Centre and research partners including the WEHI, The Royal Melbourne Hospital, Peter MacCallum Cancer Centre, The Royal Children's Hospital and the University of Melbourne
- the Victorian Cooperative Cancer Centre Alliance. While not exclusively focused on brain cancer, it represents a partnership of ten leading research, academic and clinical institutions, working together to fundamentally reshape the way cancer is tackled, and
- OMICO, a nationwide network of research and treatment centres that facilitates, supports and promotes clinical trials in genomic cancer medicine. Whilst not specific

<sup>&</sup>lt;sup>65</sup> ABCARA was established in 2021 by Prof Hui Gan of the Olivia Newton-John Cancer Research Institute, Prof Bryan Day of QIMR Berghofer MRI and Prof Terrance Johns of the Telethon Kids Institute, launched in partnership with the Cooperative Trials Group for Neuro-Oncology (COGNO).

to brain cancer (and significantly dominated by other cancer types), its two programs (Molecular Screening and Therapeutics (MoST) and Genetic Cancer Risk in the Young (RisC) studies are applying the power of genomic technology to characterise molecular changes in a patient's cancer to help identify a targeted therapy, and understand genetic variants that contribute to inherited cancers<sup>66</sup>.

### Contributions to clinical trial research and infrastructure

Bringing clinical trials to Australia is critical to changing the status quo for Australian brain cancer patients, and the contribution of the Mission to clinical trial capacity is the most significant impact of the Mission to date.

Investments in clinical trial capacity include the following:

- ANZCHOG, which has been widely applauded by stakeholders, with major funders describing it as 'extraordinary what they have achieved'. Key areas of contribution include providing clinical trial support, digital data sharing, advocacy, supporting digital platforms, and filling research gaps. Several stakeholders, spanning researchers, funders, and former MSAG members, highlighted the collaborative nature of paediatric brain cancer research in Australia, which put ANZCHOG in particularly good stead to leverage off previously established collaborations. Several stakeholders noted that 'all it needed was the money', and when it was provided through the Mission, ANZCHOG was able to enhance Australian capacity in relation to paediatric clinical trial activity. Several stakeholders from across the sector also remarked on the importance of maintaining funding for ANZCHOG to continue this work.
- COGNO, which is generally well regarded and considered a positive hallmark of the Mission, although was described as being at a different stage of evolution to its paediatric counterpart in relation to building collaborations. Some stakeholders voiced stronger concerns about progress to date, but generally stakeholders see COGNO as being at the start of the journey to build collaborations in adult brain cancer research, which have traditionally worked under a more independent and competitive model. COGNO generally seen as on track to becoming a reputable international clinical trials group, which puts Australia in good stead to offer clinical trials to adult patients over time.
- ZERO, the national clinical trial for Australian children with high-risk or relapsed cancer. The Australian Government provided \$60 million to ZERO, \$5 million of which was through the Mission (with a further \$55 million through the Emerging Priorities and Consumer Driven Research initiative for high-risk cancers not limited to brain cancer). The Minderoo Foundation was also a substantial funder, providing \$17.2 million through the Mission.

Other clinical trial activity includes AIM BRAIN, which was co-funded by the Australian Government, through Cancer Australia, the Robert Connor Dawes Foundation, and Carrie's Beanies 4 Brain Cancer (Mission Funding Partners), and has recently achieved NATA accreditation to offer clinically validated methylation profiling. Outside of the

<sup>66</sup> See https://www.omico.com.au/, Accessed 31 January 2023.

Mission, the Robert Connor Dawes Foundation has also funded inter-connect overseas to leverage clinical trials, including Collaborative Ependymoma Research Network (CERN), Pacific Pediatric Neuro-Oncology Consortium (PNOC-022), and DIPG/DMG Collaborative.

### Contributions to research infrastructure and capacity

The Mission has resulted in an investment in platforms that immediately and over time will build the capacity of researchers to undertake innovative discovery.

This includes three projects designed to build a national bio-banking, laboratory, registry data management capacity for the entire brain cancer patient cohort:

- Prospective, multicentre trial evaluating Fluoroethyl-L-tyrosine positron emission tomography (FET-PET) in radiotherapy (RT) planning, evaluation of post-treatment changes versus disease progression and prognostication in high grade glioma (FIG Study). It will provide data on the role of FET-PET in GBM management, and the robust nuclear medicine (NM) and radio oncologist (RO) credentialing program will build capacity and expertise in FET-PET production, acquisition, and image interpretation
- LOGGIC: A phase III, randomised international multi-centre trial for Low Grade Glioma In Children and adolescents. The registry LOGGIC Core BioClinical Data Bank aims to enhance the understanding of tumour biology in paediatric low-grade glioma (pLGG) and provide clinical and molecular data, and
- MAGMA: Multi-Arm GlioblastoMa Australasia Trial, which is a platform trial that aims to assess several options in standard of care for the management of glioblastoma. Initial questions of interest are whether to give daily temozolomide as soon as possible after surgery prior to chemoradiotherapy (CRT), and whether to give 6 cycles of temozolomide after CRT, or continue monthly treatment until disease progression.

Stakeholders also referred to MRFF funding being provided to Brain Cancer Biobanking Australia (BCBA), which provides access to tissue samples and data by networking and harmonising the disparate brank cancer biobanking operation across Australia. The BCBA consortium was established under the umbrella of COGNO<sup>67</sup>.

However, the investment in capacity has not been matched by an investment in discovery research, which many stakeholders believed should have predated, or at least aligned with, spending on infrastructure.

### Faster adoption by health professionals

Grantees expect that interventions developed through MRFF research grants will contribute to health professionals adopting best practices faster than they otherwise would. Researchers considered it 'likely' or 'very likely' that 8 of the grants would lead to health professionals adopting best practices faster (chart 4.10).

<sup>67</sup> See http://www.bcba.org.au/about-us.



4.10 Likelihood an intervention will lead to faster adoption of best practice

Data source: CIE survey.

Nevertheless, several stakeholders felt that raising the standard of care (including through improved standardisation of care across brain cancer centres and other hospitals) was a missed opportunity for the Mission, particularly for adult brain cancer patients.

- In general, stakeholders reported that care of paediatric brain cancer patients was well standardised.
- However, there were concerns among some stakeholders about the quality and consistency of care of for adult brain cancer patients, with not all practitioners adopting best practice. Some specific scenarios identified during consultations included the following.
  - There can be differences between the standard of care given in the major cities, compared with regional centres.
    - Specialist brain cancer centres are located in the major cities and given Australia's relatively small population (compared with the US or Europe) and the concentration of the population in the major cities, this is unlikely to change in the foreseeable future.
    - ... The model for treating patients outside of the major cities is described as a 'hub and spoke' model involving: a non-specialist oncologist close to home and a brain cancer specialist located in a specialist brain cancer centre. This model works well for many patients, but not always.
  - One stakeholder referred to instances of non-specialist oncologists in the private system taking on brain cancer patients. This can lead to care that falls short of best practice because cases do not get discussed in multi-disciplinary teams as is the case in specialist brain cancer centres.

Improving the standard of care was a major early focus of the Tessa Jowell Brain Cancer Mission (TJBCM) in the UK, with several stakeholders commenting that this program had been very successful in lifting the standard of care within the NHS. There has also been some interest in bringing the model developed by the TJBCM to Australia.

That said, it is not clear that this type of program is within the purview of the MRFF as it is not research.

### Community engagement with new technologies / treatments

The Mission has made some progress in community engagement by facilitating a move towards more consumer involvement in brain cancer research.

### Consumer involvement in brain cancer research

Consumer involvement in research is an emerging feature of the research landscape. This includes involving consumers early in the research process in designing a research question to focus on issues that matter to patients, through to thinking about how consumers can be informed about research outcomes.

Key reasons why consumer involvement is important identified in this review include:

- putting a human face to a research question, particularly for 'benchtop research' when researchers can forget that the output is going to have to be valued/adopted by patients
- identifying issues that researchers might not have thought of, which can be included in research early and produce better outcomes
- allowing consumers to be active participants in research, rather than only being 'told what is being done to them'
- improving the accountability of researchers to the patient community
- improving research methods to ensure that adverse impacts on patients are minimised, and
- directing research into areas that will improve the life and wellbeing of survivors.

The Mission has supported the increased involvement of consumers in Australian brain cancer research, which is important for research prioritisation, and clinical and patient adoption of research findings. In particular, the Mission has:

- helped educate consumers on how to be involved in research by including consumer representatives on grant opportunity panels, and
- educated researchers on how to improve research design, method, and outcomes to better meet the needs of the patient and carer community, by requiring consumer involvement as part of the selection criteria.

This is also supported by the researcher perspective, with the survey of MRFF brain cancer research recipients finding that:

many of the health interventions developed through MRFF brain cancer grants focus on helping clinicians and other health professionals identify the best treatment options, as well as improving access for patients, including:

- tools/approaches to aid earlier/better diagnosis (3 projects)
- identification of (and improved access to) best practice treatment (11 projects)
- improved access to nursing and allied health services that matter to patients (3 projects)
- identification of best practice post-treatment care to improve health-related quality of life for survivors (6 projects)
- improving access to post-treatment interventions to improve health-related quality of life for survivors (5 projects), and
- new tools/systems to facilitate easier care management for clinicians (4 projects).
- several projects developed health interventions that helped to promote patient and carer engagement with these treatments, including:
  - development of evidence-based materials for patients (4 projects)
  - development of tools/approaches to identify patient needs (4 projects), and
  - the development of tools/approaches to identifying the needs of carers (2 projects).

It is also noted that all MRFF brain cancer projects to date have involved collaboration with consumer groups in developing the research design, and 15 (out of 19) involved subsequent engagement with consumer groups.

Areas where consumers feel their needs are less well recognised includes:

- finding a cure for brain cancer, in particular finding a different agent
- surviving it well, addressing and lessening the side effects of treatment, and
- being reassured that progress is being made, with insufficient information being communicated to patients about Mission projects and findings.

### Commercialisation of research outcomes

The Mission is not yet believed to have had an impact on commercialisation, with minimal impact on encouraging industry to collaborate, engage, and support the Australian brain cancer research sector, or otherwise contribute to other aspects of the commercialisation environment.

Matters raised during stakeholder consultations include:

- lack of industry involvement in developing the Mission Roadmap and strategy
- inadequate use made of industry advisors to the Mission, and no scope for industry representatives on the MSAG to direct research projects
- a restrictive approach to managing conflicts of interest of MSAG members, with members excluded from meetings where there is a potential conflict present resulting in a loss of commercial expertise in decision making
- lack of focus on translational research, which often requires collaboration with industry, and
- aversion to investigating research opportunities originating from industry.

This is also reflected in the survey of grant recipients, with only 2 survey respondents indicated that commercialisation of a new technology was 'likely' or 'very likely'. On the other hand, 3 respondents thought commercialisation was unlikely, while 4 respondents indicated they 'don't know' (chart 4.11).





Data source: CIE Survey.

## 5 *Opportunities for the future*

Looking forward, there are several opportunities for the Mission to further strengthen its impact and capacity to make a difference to brain cancer survival.

### **Opportunities overview**

Key opportunities to emerge from this review with respect to improving the Mission itself include the following:

- **Opportunity #1: Defining the role and purpose of the Mission** the Mission needs to have a more clearly defined leadership role. This requires being clearer about what the Mission is and does, and its role in the broader Australian brain cancer research landscape, clarifying its role across the research continuum from discovery to translational research, and by implication, the role of other research funders.
- Opportunity #2: Develop an Implementation Plan there is a need for an Implementation Plan for the next phase of investment, which reflects a strategic role for the Mission to play to its strengths and best leverage funding from other sources.
- The following opportunities should also be considered in the development of the Implementation Plan.
  - Opportunity #2.1: Improved communication and coordination with Mission stakeholder.
  - Opportunity #2.2: Increased funding for biology and basic research.
  - Opportunity #2.3: Innovative funding to retain early and mid-stage researchers and clinician researchers.
  - Opportunity #2.4: Alternative innovating funding models
  - Opportunity #2.5: Encouraging greater industry involvement
  - Opportunity #2.6: Aligning future funding with the best role for the Mission
  - Opportunity #2.7: Consumer engagement framework
  - Opportunity #3: Improvements to the competitive grants model

There are also **key roles for other stakeholders to play** to help achieve Mission objectives. These include:

- increasing funding for brain cancer biology. More funding is needed for discovery research but it remains to be determined who best should fund this, and at what point the Mission can be most impactful
- engaging in innovative ways to fund research in areas of unmet need outside the competitive grants model
- better communicating research wins to the brain cancer community, and providing information to consumers that is relevant and accessible to them, and

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 coordinating with Funding Partners to promote an integrated approach to Mission investments.

Other **administrative improvements**, which are out of scope for this review but were raised by stakeholders to support Mission objectives, include:

- considering ways to increase representation of brain cancer experts on review panels to support a more scientific/clinical consensus based approach to the selection of projects
- exploring ways to better communicate upcoming grant opportunities with sufficient lead time for the research sector to develop high value proposals
- providing feedback on unsuccessful grants to support continuous improvement.

### Leadership in brain cancer research

The Mission has done an excellent job of profiling the importance of brain cancer research and providing a forum for brain cancer research funders to undertake horizon scanning and information exchange.

It has also provided a national strategic framework that has been particularly beneficial to smaller charities and not-for-profit organisations to provide expertise on funding brain cancer research for impact. For instance, several of the smaller charity based Funding Partners have valued the strategic frameworks of the Mission Roadmap as a guide to what good quality research looks like.

However, notwithstanding the good will surrounding the Mission, consultations revealed considerable negative feedback from stakeholders who were disappointed, underwhelmed, or unsure about what the Mission actually is or does. For instance:

- the Mission is not yet believed to have helped define what the optimal clinical pathway is, with several stakeholders stating that who your oncologist is continues to make a difference to how patients are treated
- the Roadmap was often criticised as being too high level to provide meaningful direction
- some felt that the Mission should have been able to better avoid duplication of funding where Funding Partner research was not channelled through the MRFF
- several Funding Partners felt they were not informed about what each of the Funding Partners was doing, and they were unsure about whether Cancer Australia or the Department of Health and Aged Care was coordinating funding across the Funding Partners
- some had hoped that the Mission would have encouraged greater collaboration between Funding Partners, and
- some believed the Mission could do more to provide focus to the Australian brain cancer sector, making clear how stakeholders can work together, and fund together, to achieve a coordinated objective.

Looking forward, the question for the Mission is what should it represent and do, and what type of leadership role should it perform? This refocusing of the role of the Mission could then be reflected in the Mission Implementation Plan going forward. For instance:

- Should Cancer Australia or the Department of Health and Aged Care be coordinating funding outside of the MRFF but under the Mission umbrella to minimise duplication, cover research gaps, and best leverage resources? Although Funding Partners are unlikely to cede control over their investment decisions, there may be a role for the Mission to achieve better co-ordination across funders.
- Should Mission funding be scaling up validated new ideas with no role in basic research?
- Should the Mission have a Board with strategic responsibilities, rather than a body with advisory capacity only?
- Should the Mission be a vehicle for funding larger projects only?
- Should Cancer Australia or the Department of Health and Aged Care as coadministrators of the Mission have a strategic priority to champion Australia as a destination for clinical trials where it can be more competitive (such as in Phase 0 and Phase 1 adult clinical trials) and/or find innovative ways for Australian patients to access international Phase 2 and Phase 3 trials?

Stakeholders feel that the role of the Mission needs to be clarified, which will help manage expectations, and ensure that MRFF brain cancer research funding is channelled into areas that represent a 'sweet spot' for nationally, primarily government funded brain cancer research. Such questions would need to be considered and answered within the existing legislative and policy framework of the Mission and the MRFF more broadly

#### 5.1 Opportunity #1: Defining the role and purpose of the Mission

It is recommended that the Australian Government, with advice from an advisory panel for the Mission, Cancer Australia, and the Department of Health and Aged Care form a view about the charter of the Mission, and communicate this to stakeholders who can then align their expectations with what the Mission is best placed to do and represent.

The Australian Government should be clear about its role and contribution to the Mission, and how this complements the role of the Funding Partners. Clarity around Australian Government priorities for MRFF funding will make it clearer to Funding Partners what their role in the Mission is, and how to best leverage their own contributions to brain cancer research. This includes being clear about whether Cancer Australia and the Department of Health and Aged Care should use the Mission to coordinate, and/or rally and coalesce support around brain cancer research in Australia.

It is acknowledged that the above would need to be considered and answered within existing legislative and policy framework of the Mission and MRFF more broadly. This role and purpose should also be reflected in the Implementation Plan for the Mission going forward.

### Implementation Plan for the Mission

Unlike other MRFF Mission initiatives, the Mission does not have a detailed Implementation Plan beyond the guidance provided in the Mission Roadmap. This is likely to have contributed to the confusion among some stakeholders about what the Mission is, or is not, achieving. A more detailed Implementation Plan for the next phase of investment is an appropriate and useful complement to the recommended articulation of the Mission's charter highlighted above. The Implementation Plan should include a research strategy that considers allocation of funding across e.g.:

- various elements of the Mission Roadmap
- paediatric (only) and adult (only) brain cancer research, and/or
- Iower risk (incremental) research and higher risk ('shift the dial') research, depending on advice as to the strategic role of the Mission.

In particular, key findings #2.1 to #2.7 should be considered in the development of the Implementation Plan. This should be developed in consultation with Funding Partners to ensure a complementarity of investments between the MRFF and Funding Partners.

#### 5.2 Opportunity #2: Developing and Implementation Plan

An Implementation Plan for the next phase of investment should be developed for the Mission to provide clarity to the brain cancer research community and focus future effort. This is expected to include:

- the Mission goal
- priority areas for investment
- delivery horizons, including research to be actioned in the short (1-2 years) and medium term (2-5 years), and potentially longer term expectations beyond the current funded period, and
- activities / amendments required to support research and facilitate aspirational outcomes.

It should clarify findings made in this review with respect to:

- strategic role for the Mission to play to its strengths and best leverage funding from other sources
- effective ways to fund opportunities for early and mid-stage career researchers and clinicians to be involved in research that addresses current barriers
- how consumers will be engaged, and when and how consumers should be involved in projects funded by the Mission, and

how collaboration across the brain cancer research ecosystem will be nurtured, including how barriers to industry engagement and investment will be addressed.

### Improved communication and coordination

While there is an acceptance that research, and research outcomes, take time, there is concern about the amount of information that is available and communicated about what the Mission is doing, and what the outcomes are to date.

There have also been recent changes to Mission processes that stakeholders feel they are not adequately informed about.

For instance:

- researchers and Funding Partners feel they are not forewarned about the timing or topic of competitive grant grounds, making them ill-prepared to respond
- limited information is provided to stakeholders when grants are announced about why
  projects have been funded and their expected value
- researchers are not provided with feedback about unsuccessful grant opportunities, and therefore do not know how to reorientate their research programs to align with the strategic intent of the Mission, and
- information about Mission successes and project updates are not shared with stakeholders. For instance, charity-based Funding Partners are not given information that can be communicated to a donor audience about the value of their investment in the Mission, and consumers are not provided information that is accessible to them on what is being done to make a difference to the care they can expect to receive. Funding Partners also want greater transparency about the progress of funded research, including summaries for non-technical stakeholders.

There is an overwhelming appetite for more information about what the Mission is doing, and to what end, and an expectation that the Mission will/should communicate information about:

- what the Mission is doing across multiple channels, including social media avenues
- how research is progressing, and
- clinical trials and other cure/treatment-based research that patients may be able to access, without the need for consumers to undertake their own research and navigate trial databases that are challenging to interpret.

To the greatest extent possible, information should be communicated in a way that consumers in particular can understand, having suffered the poor cognitive effects of treatment.

While some of these concerns have been and/or are currently being addressed by administrators of the Mission, some remain outstanding, and those that have been addressed are not necessarily well communicated to the brain cancer research sector. It task is not limited to the purview of the Mission, with researchers, research organisations, peak bodies, and Funding Partners all being able to contribute to the communication opportunities identified above.

## 5.3 Opportunity **#2.1**: Improved communication and coordination with Mission stakeholders

Better communication would improve visibility, transparency, as well as strategic coordination between Mission stakeholders. For example, Mission administrators should review how they communicate upcoming grant opportunities to stakeholders. This will allow key stakeholders including Funding Partners and others the opportunity to engage with upcoming grants.

The progress of Mission funded projects, particularly MRFF funded projects over which the Mission administrators have visibility, should be better communicated to provide assurance of progress and celebrate research wins, and allow Funding Partners to better communicate to their inputs to their stakeholders, which in turn will support the Mission's ongoing long-term success. Information should also be accessible to a non-technical audience. This may mean having a 'what this means for consumers,' section and the use of lay person terminology.

Better coordination could involve providing grant opportunities that invite co-funding from Funding Partners that are only empowered to support types of research (such as adult only, paediatric only, cure-discovery only').

### Gaps for future Mission focus

There are several elements of the Mission Roadmap that have not yet been addressed, and other aspects of research that stakeholders feel are underserved.

### Contributions to laboratory-based research

Compared to clinical trial and survivorship-based research, there has been substantially less focus on fundamental basic research funded through the Mission.

For instance, although '*Establish a new centre for basic and clinical research excellence in paediatric and adult brain cancer*' was identified as a priority in the Mission Roadmap, no MRFF grants (Mission grants or other MRFF brain cancer research grants) were considered to align closely with this objective in the survey of grant recipients. Some grants were considered to have some relevance.

It appears that some laboratory based seed projects are being funded by the Funding Partners, along with untied grants to brain cancer research teams. Examples include:

- \$8 million in innovation grants for basic research into adult brain cancer funded by the Mark Hughes Foundation
- \$7.5 million in funding for the Mark Hughes Foundation Centre for Brain Cancer Research at the University of Newcastle
- a series of typically small (\$50 000-\$100 000) grants offered by various Funding Partners intended to seed fund ideas that can be positioned to later access funding from the NHMRC or the Australian Research Council (ARC), and

• funded fellowships to stimulate laboratory based research.

There has also been more recent funding of basic research by the Mission (post April 2022 which is the scope for this review). This includes:

- three brain cancer research grants to the WEHI ((\$4.6 million), University of New South Wales (\$0.6 million), and the Council of the Queensland Institute of Medical Research (\$0.3 million), and
- a \$6 million brain cancer research infrastructure grant to the University of Sydney that will contribute towards enabling biology research.

While the amount of funding for laboratory research remains somewhat opaque, stakeholders interviewed as part of this review believe it is insufficient to meet the survival aspirations of the Mission.

Many of the stakeholders undertaking brain cancer research that were interviewed for this review expressed a feeling of disappointment in the lack of focus of Mission funding on biology and basic research. When laboratory-based research is funded, it is believed to be incremental in nature and not aligned to achieving substantive changes in survival or a move away from high dose radiation.

However, this sentiment should be considered in the context of Australian Government funding, with the MRFF typically focussing more on translational research, compared to the NHMRC, which generally funds more basic science.

#### 5.4 Opportunity #2.2: Increased funding for biology and basic research

Increased funding for biology and basic research would better create a pipeline to feed into the enhanced translational capacity invested in by the Mission. This would build on the most recent competitive grant rounds that have included a focus on basic research.

While Funding Partners have invested in researcher capacity through Centres of Excellence and fellowships, much of their allocation to the Mission has been invested, and the MRFF has not substantially supported this kind of research.

Subject to Key Finding #1, an advisory panel for the Mission could consider whether the Mission's role may include funding larger scale basic research collaborations within Australia and internationally, leveraging laboratory-based research of Funding Partners, scaling up promising basic research, and offering a grant opportunity for innovative approaches to brain cancer biology research.

### Early and mid-stage and clinician career opportunities

One of the barriers to achieving critical mass of brain cancer researchers is the leakage of researchers to other cancers and/or clinical practice due to lack of early and mid-stage career opportunities for research.

This was recognised in the Mission Roadmap which identified the need for 'Support protected research time for clinicians through targeted PhD scholarships, postdoctoral and senior researcher and practitioner fellowships'.

Whilst some Mission projects may indirectly support PhD candidates and postdoctoral researchers, no Mission funding has (as at April 2022) been allocated to targeted PhD scholarships or postdoctoral fellowships that would improve earlier stage career opportunities. This was confirmed by the survey of grant recipients which found that no MRFF brain cancer grants (Mission or other MRFF brain cancer grants) were considered to align closely with this objective (although some were considered to have some relevance).

There are also aspects of existing arrangements within employing organisations that were considered unconducive to career progression, such as:

- commonality of short term (one year) contracts, and
- absence of funding or protected time for clinicians to do research, which is undertaken in 'spare time', and only financially sustainable for clinicians that are otherwise renumerated by seeing patients.

# 5.5 Opportunity #2.3: Innovated funding to retain early and mid-stage researchers and clinician researchers

An advisory panel for the Mission should consider how to support early and midstage career and clinical researchers as part of developing the Implementation Plan. This could be akin to the competitive grants for Early and Mid-stage Career Researchers that are earmarked in the Million Minds Implementation Plan.

This will need to acknowledge that the competitive grants model makes it hard for early and mid-career researchers to get research funding, which can be a disincentive for talented researchers to pursue a career in brain cancer research, and there are limited mechanisms for clinicians to be allocated research time.

It should be noted that this is a systemic problem for the medical research sector, which may not be addressed by the Mission alone.

One option is for the Mission to include a separate program to provide block funding for these opportunities to be allocated on a merit, or percent of researcher headcount, basis (capitation).

If competitive grants are retained as a form of funding, then potential grantees could be required to nominate/include an allocation for clinical involvement and/or training and development, which could be considered by assessors.

### Future funding models to consider

This review has explored various funding models through a desktop scan of the literature and discussions with a wide range of stakeholders.

The following comments are put forward for consideration in developing the Implementation Plan for the Mission:

- that the competitive grants model be retained for MRFF funded brain cancer research grants, subject to improvements (see below)
- other innovative approaches (see below) be explored to leverage Mission funding to achieve specific outcomes that are too immature or risky to be successful in a typical competitive grant environment, and
- links with industry be improved to increase industry funding for brain cancer research in Australia.

### Other innovative approaches to funding key priorities

This review has identified several models that could be used to increase research funding further by leverage future contributions from the Mission. While these are likely to complement, rather than replace, the competitive grants model, they may provide a suitable model for achieving specific objectives.

The key models identified include the following:

- Matched funding. There are already examples where this has been used, such as the Gamma Knife facility which received matched funding from the Victorian Government and the Peter McCallum Cancer Centre. This model is only likely to be appropriate for specific projects because it tends to preference large, over small, institutes, and may become a barrier to research when matched funds cannot be found.
- Multi-funder collaborations to address a specific need. Several stakeholders identified AIM-BRAIN: Access to Innovative Molecular Diagnostic Profiling for Paediatric Brain Tumours as being one of the most successful achievements in Australian brain cancer research, and indicated that its funding model could offer lessons for the Mission. In the case of AIM-BRAIN, a specific research need was identified by the research community, and funders interested in supporting this area of need were brought together to support it.
- Approaches to funding high risk research. Stakeholders noted the tendency for the Mission's current model (and research funding models in Australia more generally) to favour lower risk research that is likely to lead to modest incremental improvements, rather than the research capable of 'shifting the dial' that is needed to improve outcomes for brain cancer patients. To achieve a better balance, higher risk projects with greater potential for a breakthrough should be represented in the pool of funded projects. Examples include:
  - Breakthrough grants, which have been used by the Canadian Institute of Health Research to fund more high risk/reward grants. In the Canadian case (and consistent with how most MRFF grant opportunities are allocated), breakthrough grants need to be team-based, rather than chief investigator-based, apply to larger funding opportunities, require partnerships with international researchers or charities, multi-disciplinary teams/collaborations (combining researchers focused)

on basic research, translational research, and quality of life), and be inclusive of a clinical trials component, and

 Cradle-to-grave funding for innovative projects, which is being used by the United States Department of Defence, which awards grants from a concept stage through to translation. It is currently requesting applications for lung cancer, and has been used for other cancers. A summary of this approach is set out in appendix D.

#### 5.6 **Opportunity #2.4: Alternative innovating funding models**

The standard competitive funding model alone is unlikely to be able to achieve some of the strategic priorities of the Mission.

Alternative funding models could be explored, and where appropriate made available, for projects that can increase total funding for brain cancer research, and direct research into areas of unmet need. Those with promise are expected to include:

- matched funding from the MRFF for projects of national significance that involve partners outside of the existing Funding Partner model
- the coordination of forums around key unmet needs that can bring funding partners together and create coordination of effort and resources, and
- cradle-to-grave or breakthrough grants for high risk research opportunities.

The Mission Funding Partners could also be involved to ensure investments made inside and outside the MRFF's competitive grants model are well leveraged.

### Tapping into industry funding

This review has highlighted the lack of success to date in harnessing links between the Mission and industry.

It is also noted that compared to other cancer types, there is a lower representation of private industry funding for brain cancer research in Australia more generally, and a higher representation of charitable funding. The former likely reflects relatively low patient numbers and treatment options, and the latter likely reflects the typical co-funding of research with wider patient support services and awareness raising activities that shine a light on the communities' responsibility to support patients, families, and researchers.

In this environment, tapping into industry funding for Australian brain cancer research is unlikely to increase organically, and is likely to require proactive measures on the part of the Mission.

#### 5.7 Opportunity #2.5: Encouraging greater Industry involvement

Stronger links with industry should help break down barriers to industry investment in clinical trials and brain cancer research in Australia, which is challenged by Australia's small population. A precursor to better industry investment is greater industry involvement and visibility of Australia's brain cancer research expertise.

An opportunity for greater industry links should form part of Key Findings #1 and #2 and may involve:

- industry involvement in the development of the Implementation Plan, and
- greater industry representation within a future advisory panel for the Mission.

### Future funding focus

This review has identified several issues for the consideration of an advisory panel for the Mission, which is encouraged to provide guidance on how to address these matters for the Mission Implementation Plan and future grant opportunities.

For instance:

- Critical mass and capacity to explore wicked problems like brain cancer benefit from research collaborations given the unique challenges posed by the rare cancer types, and the slow historical pace of efficacious and curative treatments. This includes collaborations that are multi-site, between multiple Australian and/or international research teams, and across disciplines (researchers, neurosurgeons, patient advocates etcetera). How can future grant opportunities achieve more significant research collaboration?
- Consumer involvement in research throughout the research continuum will help identify approaches to research that best align to patient consent and address aspects of research that matter to patients. This includes consumer involvement in the formative stages of research, approaches to patient participation in research, and consumer and clinical adoption of research findings. What more can or needs to be done to ensure that consumer involvement achieves better research outcomes?
- Maintaining a national focus and equity of access is important. The Mission is an Australia wide initiative, and while some Funding Partners have a jurisdictional remit, the Mission should prioritise equity of access to best practice research for all Australian brain cancer patients. This may require standard care to be at specialist brain cancer centres, particularly for those in regional, rural, and remote locations where brain cancer expertise is often inaccessible, in which case gaps in access to travel expense programs need to be addressed. How can the Mission better support equity of access to best practice research, particularly when patient access is impeded by shortcomings in state based patient assisted transport schemes?
- **Opportunities for leveraging investment should be maximised.** There are several funders of brain cancer research, who working together, or recognising each others comparative advantage, can minimise duplication, and maximise the value of output.

What advice can an advisory panel for the Mission provide to ensure that MRFF funding for brain cancer research reflects the best role for MRFF funding via-a-vis funding from other sources?

#### 5.8 Opportunity #2.6: Aligning future funding with best role for the Mission

Once the role and purpose of the Mission is clear and following the development of the Implementation Plan, remaining disbursements from the Mission can be allocated in a way that reflects the strategic positioning and strength of the Mission. Based on stakeholder consultations, this review has formed the view that investments in national infrastructure to support Australians accessing clinical trials, such as ANZCHOG and COGNO, appear to be well aligned with a role for the Australian Government. Larger scale projects that scale up promising discovery research, as well as larger projects that facilitate national/international research collaborations, would also appear to be well aligned.

Future funding should also consider how all Australian brain cancer patients get access to standard treatment for brain cancer. While access to standard treatment is a service delivery issue, guidance is sought on how equity of access can be supported by the Mission going forward, in particular how research can help discover barriers, or find pathways to better adoption.

### **Consumer engagement framework**

Several consumers highlighted the need for a consumer engagement framework that can be accessed by funders and researchers to efficiency and effectively engage with consumers. Based on broader stakeholder feedback, this would usefully include:

- participation in review panels for research proposals
- identifying consumers that are keen to participate in research
- inclusion of consumers on the investigator list for grant applications, and
- inclusion of consumers on committees that oversee brain cancer research centres.

These elements are consistent with the Principles for Consumer Involvement in Research Funded by the Medical Research Future Fund<sup>68</sup>.

It is also noted that these elements are included in the MRFF Principles, and the task is to consider how they should be reflected in the Implementation Plan.

<sup>&</sup>lt;sup>68</sup> Australian Government 2023, Principles for Consumer Involvement in Research Funded by the Medical Research Futures Fund, Advice from the Medical Research Future Fund Consumer Reference Panel – March 2023, see principles-for-consumer-involvement-in-research-fundedby-the-medical-research-future-fund.docx (live.com)

### 5.9 Opportunity #2.7: Consumer engagement framework

The Implementation Plan should set out how consumers will be engaged, and set an agenda for when and how consumers should be involved in projects funded by the Mission.

### Scope for administrative improvements

While administrative issues are outside the scope of this review, the following findings were captured from stakeholders and summarised here as they support the broader objectives of the Mission.

#### Opportunities to improve the current competitive grants model

The competitive grants model is expected to best suit the distribution of the majority of remaining MRFF funds under the Mission, however, this reinforces the importance of selecting the right projects.

Scope for improvement in this regard includes the following:

- providing greater transparency over funding decisions: while grant assessment committees score projects based on guidelines, it is not evident to applicants why some applications have been successful and others not
- foreshadowing up-coming grant opportunities (including topics, themes and timing) to overcome a barrier to the formation of competitive collaborations and evidence collections within the timeframe of the grant process, and
- strengthening of grant assessment processes, such as ensuring that the panel has sufficient expertise in brain cancer research. Notwithstanding the challenges in drawing from a relatively small pool of experts compared to other cancer fields, stakeholder feedback indicates that the number and breadth of brain cancer experts deciding on grant opportunities is insufficient. It places too much pressure on individual(s) and misses the opportunity to form a scientific consensus
- providing feedback on unsuccessful grant applications to provide reasons why a grant application was not successful, and improve the quality of future applications (particularly where an unsuccessful application is refined and then re-submitted for a future grant opportunity).

It should be noted that many of these have been or are being addressed by the Department via other consultation and continuous improvement processes. For example, the Department now publishes a calendar of forecast MRFF grant opportunities<sup>69</sup>, and

<sup>&</sup>lt;sup>69</sup> See https://www.health.gov.au/our-work/medical-research-future-fund/mrff-news.

outcomes<sup>70</sup>, news and celebrating research wins are provided on the Department's website and the MRFF newsletter<sup>71</sup>.

### 5.10 Opportunity #3: Improvements to the competitive grants model

Consider ways to increase representation of brain cancer experts (brain cancer researchers or brain cancer clinicians/clinical researchers) on review panels to provide greater opportunity for a scientific/clinical consensus based selection of projects.

Explore ways to better communicate upcoming grant opportunities with sufficient lead time for the research sector to develop high value proposals. This should include being transparent about funding priorities in the Implementation Plan.

Provide feedback on unsuccessful grant applications.

<sup>&</sup>lt;sup>70</sup> See https://www.health.gov.au/resources/publications/medical-research-future-fund-mrffgrant-recipients?language=und

<sup>&</sup>lt;sup>71</sup> See https://www.health.gov.au/using-our-websites/subscriptions/subscribe-to-mrff-newsletter.

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# Appendices


# A Brain cancer research grants awarded by the MRFF

Until April 2022, the MRFF has awarded 19 grants for brain cancer research, valued at \$31 million. Eight of these were provided through the Mission and account for 71.3 per cent of MRFF funding<sup>72</sup>.

Grants funded under the Mission are predominately for translational research, including establishing best practice care for survivors and translating that into clinical practice.

Grants funded via other MRFF grant opportunities focus on clinical trials. Eight grants have been awarded through the MRFF's Clinical Trials Activity, and account for 24.0 per cent of MRFF funding, and a further three grants were awarded through the MRFF's Emerging Priorities and Consumer Driven Research, accounting for 4.7 per cent of MRFF funding for brain cancer.

	Grants	Amount
-	No.	\$
Australian Brain Cancer Mission		
2018 Enhanced Capacity of the Australian and New Zealand Children's Haematology Oncology Group (ANZCHOG) Program	1	3 010 000
2018 Enhanced Capacity of the Cooperative Trials Group for Neuro-Oncology (COGNO) Program	1	2 500 000
2018 ZERO Childhood Brain Cancer	1	5 002 023
2019 Brain Cancer Survivorship	2	6 914 602
2019 Innovative Clinical Trials	2	1 749 170
2020 Brain Cancer Survivorship	1	2 615 278
Total - Mission	8	\$21 791 073
Clinical Trials Activity		
2018 Rare Cancers, Rare Diseases and Unmet Need - General	4	3 016 742
2019 Rare Cancers, Rare Diseases and Unmet Need - Childhood Brain Cancers	3	2 332 299
2021 Rare Cancers, Rare Diseases and Unmet Need	1	1 982 681
Total - Clinical Trials Activity	8	7 331 723
Emerging Priorities and Consumer Driven Research		
2018 Accelerated Research - Priority-driven Collaborative Cancer Research Scheme - All Cancers	2	958 215

#### A.1 MRFF grants for brain cancer research – summary

<sup>&</sup>lt;sup>72</sup> Since April 2022, 4 grants have been awarded worth \$11.45m, which includes two additional lead organisations (The Walter and Eliza Hall Institute of Medical Research and The Council of the Queensland Institute of Medical Research)

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•	Grants	Amount
-	No.	\$
2018 Accelerated Research - Priority-driven Collaborative Cancer Research Scheme - Childhood Cancers of Low Survival	1	480 015
Total - Emerging Priorities and Consumer Driven Research	3	1 438 231
Total	19	\$30 561 027

Source: Health and Medical Research Office, CIE.

## Grants awarded under the Mission

To date, there have been six Mission grant opportunities<sup>73</sup>.

### Targeted grants

The initial 2018 grant opportunities were directed grants to existing research networks within Australia:

- two focused on developing capacity within Australia to undertake clinical trials and contribute to a coordinated research agenda (including identifying future research trials) through grants to:
  - Coordinated Trials Group for Neuro-Oncology (COGNO), and
  - Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG)
- a third provided funding to consolidate ZERO as a national clinical trial open to all Australian children diagnosed with high-risk brain cancer.<sup>74</sup>

Table A.2 summaries the objectives and expected outcomes for these targeted grants. Subsequent opportunities have been via a competitive process.

Grant opportunity	Objectives	Expected outcomes
2018 Enhanced Capacity of the Australian and New Zealand Children's Haematology Oncology Group (ANZCHOG) Program	<ul> <li>To improve therapy and outcomes for children with brain cancer through Australian-based access to innovative and cutting-edge approaches with the aim of pursuing research breakthroughs.</li> <li>The objectives of the ANZCHOG Grant Opportunity are to:</li> <li>Enhance the capacity of ANZCHOG to take the leadership role in the conduct of clinical trials for children in Australia</li> </ul>	<ul> <li>The expected outcomes of the Program are:</li> <li>Development and implementation of an Australian Research Agenda that identifies current and upcoming leading international trials of high potential relevance/ significance to Australian brain cancer patients</li> <li>Enabled participation and expedited time to start-up in Australia of approved trials by identifying the most appropriate sites for specific trials (hopefully informed by knowledge built in phase above) through support provided and coordinated nationally</li> </ul>

#### A.2 Mission 2018 targeted grants awarded

<sup>73</sup> Up until May 2022.

<sup>&</sup>lt;sup>74</sup> The Zero Childhood Cancer Program is a personalised medicine program for children who have less than a 30 per cent 5-year survival rate, either on first diagnosis or after relapsing.

Grant opportunity	Objectives	Expected outcomes			
	<ul> <li>Enable the development and implementation of a research agenda that identifies current and upcoming leading international trials and make a case for bringing those trials to Australia</li> </ul>	<ul> <li>Working with the Mission in its initial analysis of existing brain cancer platforms and technologies (identified as an immediate / early investment priority), and efforts to expand and coordinate these assets based on the outcomes of the analysis</li> <li>Contribute to a collaborative and coordinated</li> </ul>			
	<ul> <li>Enable participation and expediting time to start-up of approved trials in Australia</li> </ul>	approach to investment across government, philanthropy, industry and the private sector to maintain focus on the best ideas and talent and maximise opportunities for impact			
	<ul> <li>Contribute to Cancer Australia's initial analysis of existing brain cancer platforms and technologies and efforts</li> </ul>	<ul> <li>National and international collaboration to consolidate expertise and dedicate effort</li> </ul>			
	to expand and coordinate these assets	<ul> <li>Reinforcement of Australia's position as a preferred destination for clinical trials</li> </ul>			
2018 Enhanced	The objectives of the COGNO Grant Opportunity are to:	In implementing the Program, COGNO will undertake the following activities:			
Capacity of the Cooperative Trials Group for Neuro- Oncology (COGNO) Program	<ul> <li>Expand the capacity of the COGNO to take the leadership role in the conduct of clinical trials for adults in Australia</li> <li>Enable the development and implementation of a research agenda that identifies current and upcoming leading international trials and make a case for bringing those trials to Australia</li> <li>Enable participation and expediting time to start-up of approved trials in Australia</li> <li>Contribute to Cancer Australia's initial analysis of existing brain cancer platforms and ecforts</li> </ul>	<ul> <li>Build on activities already funded by Cancer Australia – to establish/foster existing international specialist networks, to support existing trial sites with expertise in coordination, ethics, auditing and monitoring in addition to developing trial protocols which are being funded by Cancer Australia.</li> </ul>			
		<ul> <li>Identify and prioritise trials in partnership with existing Trial Centres, networks and their respective brain cancer patients / anticipated populations as appropriate and based on highest needs and patential significance.</li> </ul>			
		<ul> <li>Consider Australia's capacity and capability to conduct trials, including existing or potential Australian expertise, value for money, likely start-up time, and potential impact on patient access.</li> </ul>			
	to expand and coordinate these assets	<ul> <li>Give consideration to trials that have been through a peer-review process internationally and are under way (to demonstrate that appropriate protocols have been developed, have sound scientific evidence and appropriate approach).</li> </ul>			
		<ul> <li>Ensure the newly funded activities do not duplicate core Cancer Australia funding which provides support for the development of trial protocols.</li> </ul>			
		<ul> <li>Following consideration of the Agenda, a selection of these trials (probably between 1- 3) would be approved for commencement by Cancer Australia, using funds provided via the Australian Brain Cancer Mission. There would then be no need to go through a lengthy competitive grant funding process within Australia (which may or may not be successful) before trial commencement – so patient access would be expedited.</li> </ul>			

Grant opportunity	Objectives	Expected outcomes
2018 ZERO Childhood Brain Cancer	<ul> <li>To support research activities which enable the provision of a personalised medicine program to improve outcomes for Australian children with high-risk or relapsed brain cancers with the ultimate goal of improving survival outcomes for Australian children with high-risk brain cancers. The objectives are to:</li> <li>Establish the Program as a national clinical trial open to all Australian children with high-risk brain cancers</li> <li>Consolidate the Program and make available the platforms, technologies, infrastructure, systems and research capabilities to assess genetic characteristics and identify the most appropriate therapeutics for Australian children with high-risk brain cancers</li> <li>Establish/ expand/ refine referral structures and processes to maximise access to the Program for Australian children with high-risk brain cancers</li> <li>Engage and collaborate with national groups. including the Australian and New Zealand Children's Haematology Oncology Group (ANZCHOG)to maximise clinician and patient participation in ZERO</li> <li>Engage and collaborate with international groups to share data and information to improve outcomes for Australian children with high-risk brain cancers.</li> </ul>	<ul> <li>The Program is a national clinical trial open to all Australian children with high-risk brain cancers</li> <li>The provision of personalised cancer therapy, tailored to children with high-risk brain cancers</li> <li>An increased number of Australian children participating in the Program</li> <li>Increased patient and clinician participation in the Program and</li> <li>Process agreements in place to share and utilise national and international data.</li> </ul>

Source: Mission Grant Opportunity Guidelines.

## Improving quality of life/Survivorship grant opportunities

Mission grants opportunities in 2019 and 2020 have focused on survivorship, awarding three grants totalling \$9.5 million (62 per cent of grant funding awarded by the Mission to date).

Table A.3 sets out the principles of cancer survivorship as set out by Cancer Australia. Key details of the Mission survivorship grants are summarised in table A.4.

Principle	Outcome	Elements
Principle 1: Consumer involvement in person-centr ed care	<ul> <li>People affected by cancer are enabled to be involved in shared decision- making and supported to self-manage according to their preferences</li> <li>Informed and engaged consumers lead to better health outcomes and improved safety</li> </ul>	<ul> <li>People affected by cancer are provided with timely evidence-based information tailored to their individual circumstances and needs and supported to participate in shared decision-making according to their preferences</li> <li>People affected by cancer are empowered and supported to self-manage according to their preferences, with identified pathways for timely access to specialist providers as required</li> <li>Care is person-centred with consideration and respect diven to consumer preferences</li> </ul>
Principle 2: Support for living well	<ul> <li>The supportive care needs (including physical, psychological, social, cultural, information and spiritual needs) of people affected by cancer are assessed and they receive appropriate referrals to promote optimal health and quality of life outcomes</li> <li>People affected by cancer are supported to make informed lifestyle choices to promote wellness, manage treatment related side effects and comorbidities, and reduce risk of second and recurrent cancers</li> </ul>	<ul> <li>The supportive care needs of people affected by cancer are systematically assessed at key points across the continuum of care with appropriate interventions and referral as required to promote optimal quality of life</li> <li>People affected by cancer receive information on healthy lifestyles and are actively encouraged and supported in making lifestyle choices to promote optimal health and to prevent disease and distress</li> </ul>
Principle 3: Evidence- based care pathways	People affected by cancer receive consistent, safe, high-quality evidence- based cancer care in line with Optimal Cancer Care Pathways, according to their individual circumstances and needs.	<ul> <li>People affected by cancer receive timely evidence- based care in line with Optimal Cancer Care Pathways, including personalised care planning across the continuum of care</li> <li>A multidisciplinary team considers all relevant treatment and supportive care options and develops recommended individual treatment plans which are adjusted over time to address changing patient needs</li> <li>Stratified pathways for follow-up are based on tumour characteristics, treatments applied and individual circumstances, with identified pathways for timely access to specialist providers as required</li> </ul>
Principle 4: Coordinated and integrated care	<ul> <li>People affected by cancer receive holistic patient-centred care which is coordinated and integrated across treatment modalities, providers and health settings, including public and private sectors; and specialist, primary, community based and not-for-profit services</li> <li>Care is delivered in a logical, connected and timely manner for optimal continuity and to meet the individual needs of people affected by cancer</li> </ul>	<ul> <li>Care is integrated and coordinated between health and other service providers to enable seamless holistic patient-centred care for people affected by cancer</li> <li>Clear and timely communication processes are adopted between providers and with consumers</li> </ul>

### A.3 Principals of cancer survivorship

Principle	Outcome	Elements
Principle 5: Data-driven improvemen ts and investment in research	<ul> <li>National collection and reporting of key cancer data, including consumer experience and outcome data, provides an indicator for high-quality care, influences health service improvements and informs investment in research</li> <li>Published research in cancer survivorship enriches the evidence base and informs improvements to enhance the care and outcomes of people affected by cancer</li> </ul>	<ul> <li>Consumer and carer experience, treatment and outcome data are routinely captured and consistently reported for accountability and to improve quality of care.</li> <li>Research in cancer survivorship is translated to inform practice, innovation and improvement in cancer care.</li> </ul>

Source: Cancer Australia 2017, Principles of Cancer Survivorship https://www.canceraustralia.gov.au/sites/default/files/publications/principles-cancer-survivorship/pdf/pocs\_-\_principles\_of\_cancer\_survivorship.pdf, Accessed 18 August 2022.

Grant opportunity	Objectives	Expected outcomes
2019 Brain Cancer Survivorship	To support the development of better approaches to address the medical, functional and psychosocial impacts of brain cancer to improve quality of life and the survivorship experience. Survivorship must be focused on children, adolescents and young adults, or adults with malignant brain cancer, their families or carers.	<ul> <li>The intended outcomes are to develop:</li> <li>a better understanding of the effects and impact of symptoms on quality and quantity of life, independence, function and disability</li> <li>develop new care models that improve the experience of survivors, their families and carers.</li> <li>Areas of focus may include:</li> <li>medical, functional and psychosocial impacts of brain cancer - for example: cognitive, executive and memory impairment; fatigue; behavioural issues; seizures or toxicities of anticonvulsants; and fitness to drive</li> <li>impact on survivors, their families and carers - for example: anxiety and depression; and long-term impacts including economic impact</li> <li>efficacy of new or existing models of care and interventions, including the factors that contribute to success - for example: efficacy of new or existing models of care which involve nurse care coordinators, and components of the care model which contribute to success; and impact of rural and remote patient locality on effectiveness of survivorship clinics.</li> </ul>
2020 Brain Cancer Survivorship	<ul> <li>The objectives of the 2020 Brain Cancer Survivorship Grant Opportunity are to:</li> <li>support the development of new approaches and the use of technologies to improve communications between brain cancer survivors, their families, carers and health care professionals; and</li> </ul>	<ul> <li>Areas of focus may include:</li> <li>research into new educational and communication methods and approaches, including special approaches and considerations for underserved and at-risk populations</li> <li>research on new methods and strategies to disseminate cancer information/innovation to health care providers (for example, web-based information, telemedicine, smartphone apps etc.) and the effectiveness of these approaches</li> <li>research on new communication processes and/or media and information technologies within the health care system and the effectiveness of these approaches.</li> </ul>

Mission grant opportunities for brain survivorship A.4

Grant opportunity	Objectives	Expected outcomes
	<ul> <li>understand how information technologies and platforms can be used to support people with brain cancer, their families and carers, and their impact on the physical, psychosocial and economic sequelae of a brain cancer diagnosis.</li> </ul>	

Source: Mission Grant Opportunity Guidelines.

#### Innovative clinical trial grant opportunities

Up until April 2022, there has been one grant opportunity focused on innovative clinical trials (2019) under the Mission. Two grants were allocated with total funding of \$1.75 million. The stated objectives and expected outcomes from the innovative clinical trial grant opportunity are summarised table A.5.

Grant opportunity	Objectives	Expected outcomes
2019 Innovative Clinical Trials	To support increased and equitable access and participation in clinical trials for people	The expected outcomes of the Grant Opportunity are:
	with brain cancer. Specifically, through this funding, the Australian Brain Cancer Mission is seeking	<ul> <li>new opportunities for clinical trial participation and associated benefits from accessing the latest research</li> </ul>
	to fund new or expanded innovative clinical trials in brain cancer that could involve international collaborations. Trials should:	<ul> <li>deployment of innovative trial designs and recruitment strategies</li> </ul>
	<ul> <li>be for children, adolescents and young adults, or adults with malignant brain cancer, and</li> </ul>	<ul> <li>•purposeful health service engagement to improve the translation of research into practice and improve outcomes for nations, and</li> </ul>
	<ul> <li>support increased and equitable access and participation</li> </ul>	<ul> <li>new health treatments, drugs and devices to improve health and wellbeing</li> </ul>
	The clinical trials may be in areas of:	devices to improve health and wendering.
	Diagnosis	
	Treatment, and	
	<ul> <li>Cancer Control, Survivorship &amp; Outcomes – Patient Care, Survivorship, or End-of-Life Care.</li> </ul>	

#### A.5 Mission grant opportunities – innovative clinical trials

Source: Mission.

# **B** Summary of Funding Partner investments

A detailed summary of Funding Partner investments in the Mission are provided in table B.1.

It is noted that this does not include a detailed breakdown of investments by the Cure Brain Cancer Foundation, which were not available at the time of publication. It is noted, however, that the Cure Brain Cancer Foundation originally allocated \$20 million to Australian brain cancer research through the Mission.

Most Funding Partners have invested in projects outside the MRFF.

In some cases, Funding Partners have invested much more than they had originally allocated to the Mission, reflecting their increased interest in contributing to funding brain cancer research over the course of the Mission.

					Funding	contribution (\$m)		
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*	
ACT Health and	Staff	Provision of a Brain Cancer Specialist Nurse	Canberra Health Service		0.36	1.82	3.95	
Canberra Health Services	Equipment grant	Provision of stereotactic treatment	Canberra Health Service		0.30			
	Other	Brain tumour multi-disciplinary team meeting	Canberra Health Service		0.29			
	Other	Brain tumour multi-disciplinary meeting	Canberra Health Service		0.14			
	Clinical trial	Canberra Health services research and clinical trials	Canberra Health Service		0.14			
	Research grant	Research grant: Research and innovation fund	ACT Health Directorate		0.29			
	Research grant	Research grant: Research and innovation fund	ACT Health Directorate		0.30			
Cure Brain Cancer Foundation						NFP	20.00	
Carrie's	Clinical trial	MAGMA	University of Sydney	0.65		5.40	5.40	5.40
Beanies 4 Brain Cancer	Clinical trial	SJ-ELIOT	Monash University	0.23				
	Clinical trial	COZMOS	Monash University	0.12				
	Clinical trial capacity	Australian and New Zealand Children's Haematology/ Oncology Group (ANZCHOG)	Monash University	0.40				
	Centres of Excellence	The Brain Cancer Centre	WEHI		4.00			
Children's	Research grant	Exploiting CDK 4/6 inhibition to treat medulloblastoma	University of Queensland		0.20	6.09	10.00	
Hospital Foundation Queensland	Research grant	New strategies for targeting immune evasion in children's brain tumours	University of Queensland		0.10			
	Research grant	Integrating innovative models of the brain microenvironment to identify new treatment strategies for medulloblastoma	University of Queensland		0.05			
	Centres of Excellence	Unallocated - research tbc	The University of Queensland; Queensland University of Technology; QIMR Berghofer & CHQ		1.11			

### B.1 Funding partner contributions to the Australian Brain Cancer Mission (July 2023)

					Funding o	contribution (\$m)	
nding tner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
	Research Grants	Assessment of the Novel OLIG2 Inhibitor CT179 as an EffectiveTherapy for Paediatric Medulloblastoma	QIMR Berghofer		0.50		
	Research Grants	EphA3 a Valid Tumour Specific Therapeutic Target for Paediatric Brain Cancer	QIMR Berghofer		0.53		
	Research Grants	Effects of therapeutic exercise in paediatric survivors of childhood posterior fossa brain tumors	Queensland University of Technology		0.32		
	Research Grants	Addressing survivorship and palliative care needs in children and adolescents with brain cancer	Queensland University of Technology		0.32		
	Research Grants	Developing novel therapeutic approaches for treatment of vincristine-induced neuropathy	The University of Queensland		1.01		
	Research Grants	Risk factors for speech and language impairments and long term outcomes in survivors of childhood primary posterior fossa tumours	Queensland University of Technology		0.33		
	Research Grants	Embryonal Tumours with Multilayered Rosettes - basic biology and tools for translation	The University of Queensland		0.20		
	Research Grants	Shared Program Resources for Centre for Child and Adolescent Brain Cancer Research	The University of Queensland; Queensland University of Technology; QIMR Berghofer & CHQ		1.00		
	Equipment Grants	Small-Animal Micro-Irradiation Facility	University of Queensland, Queensland University of Technology, Mater Medical Research Institute and Queensland Health		0.30		
	Fellowships	A new and effective combination therapy for children with brain cancer	University of Queensland		0.11		
	Other	Functional genomics identifies clinically actionable novel therapeutic targets for all non-WNT medulloblastoma (travel grant)	University of Queensland		0.01		

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					Funding o	contribution (\$m)	
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
Financial Markets Foundation for Children	Clinical trial capacity	Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG)	Monash University	5.00		5.00	5.00
The Kids' Cancer Project	Research grant	Development of personalised medicine approaches to treat medulloblastoma, Professor Bryan Day	QIMR		0.47	6.07	5.30
	Research grant	New therapies for incurable paediatric brain tumours, Professor Brandon Wainwright	Institute of Molecular Bioscience		0.48		
	Research grant	Novel therapies for diffuse intrinsic pontine glioma (DIPG), A/Professor David Ziegler	Children's Cancer Institute & Sydney Children's Hospital		0.27		
	Research grant	Using targeted chemotherapies to reduce intensity of radiotherapy in medulloblastoma, Dr Nick Gottardo	Telethon Kids Institute		0.26		
	Research grant	Epigenetic targeted therapy in Diffuse Intrinsic Pontine Glioma (DIPG) A/Professor David Ziegler	Children's Cancer Institute		0.25		
	Research grant	Targeting novel therapeutic opportunities for diffuse intrinsic pontine glioma (DIPG), A/Professor David Ziegler	Children's Cancer Institute		0.28		
	Research grant	Application of gene-silencing nanodrugs to inhibit medulloblastoma growth, A/Professor Joshua McCarroll	Children's Cancer Institute		0.30		
	Research grant	Using modern targeted chemotherapies to reduce the intensity of radiotherapy in medulloblastoma and decrease treatment-related side effects, Dr Nick Gottardo	Telethon Kids Institute		0.13		
	Research grant	3D printers and mini-brains. New approaches for brain cancer research. Geraldine O'Neill	The Children's Hospital at Westmead		0.12		
	Research grant	Pre-clinical anti CD-47 therapy for High Grade Glioma, Dr Nick Gottardo	Telethon Kids Institute		0.10		
	Research grant	Connect 1903 Clinical trial - Dr Nick Gottardo	ANZCHOG		0.05		
	Research grant	Dr Elizabeth Hovey - Personalised targeted therapy for adolescent and young adult medulloblastoma patients	Nelune Comprehensive Cancer Centre		0.17		
	Research grant	Dr Nick Gottardo - Using smarter new drugs to reduce long term debilitating side effects for aggressive childhood brain cancer	Telethon Kids Institute		0.11		

					Funding o	contribution (\$m)	
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
	Research grant	Matt Dun - Pharmaco-phospho-proteo-genomics of paediatric high-grade glioma	University of Newcastle		0.30		
	Research grant	Danielle Upton - Targeting the thioredoxin system as a novel strategy for Diffuse Intrinsic Pontine Glioma	Children's Cancer Institute		0.33		
	Research grant	Nick Gottardo - Enhancing radiation therapy using brain specific immunotherapy to improve survival outcomes for children with aggressive brain cancer.	Telethon Kids Institute		0.11		
	Research grant	Targeting the DC-T cell axis to treat glioblastoma, Dr Tessa Garret	Royal Adelaide Hospital		0.30		
	Research grant	Discovering new ways to treat deadly childhood brain cancers by understanding the immune system, A/Professor Raelene Endesby	Telethon Kids Institute		0.12		
	Research grant	A new and effective combination therapy for children with brain cancer, Professor Brandon Wainwright	Institute of Molecular Bioscience		0.24		
	Fellowships	Polyamine pathway inhibition as a targeted therapy for MYC-amplified medulloblastoma in paediatric patients, Aaminah Khan	Children's Cancer Institute		0.46		
	Fellowships	Developing novel treatments for high-risk childhood brain cancer, Dr Marion Mateos	Kids Cancer Centre Sydney Children's Hospital		0.28		
	Fellowships	Precision neurosurgical image-guidance: improving the outcomes of childhood brain tumour surgery using artificial intelligence-based automated MRI tractography, Joseph Yuan-Mou Yang	Murdoch Children's Research Institute		0.28		
	Research grant	Dissecting drug resistance and guiding targeted therapy in paediatric gliomas -PhD Scholarsip top-up, Philipp Graber	Children's Cancer Institute		0.04		
	Fellowships	Identify a novel low toxicity therapy for high-grade glioma patients to improve the post-treatment quality of lifeKenny Chi Kin Ip	Children's Cancer Institute		0.62		
Mark Hughes	Clinical trial	MAGMA	University of Sydney	0.50		1.17	3.00
Foundation	Clinical trial	The IWOT study: treating lower grade glioma?	University of Sydney		0.10		

					Funding o	contribution (\$m)	
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
	Clinical trial	Glioblastoma: Determining how the molecular microenvironment of the human brain influences cancer progression and treatment efficacy	Flinders University		0.57		
Minderoo Foundation	Clinical trial	Zero Childhood Cancer 1.0	Children's Cancer Institute		5.00	10.79	10.00
	Clinical trial	Zero Childhood Cancer 2.0 (30% of \$12.2M grant relevant to brain tumour patients)	Children's Cancer Institute		3.66		
	Clinical trial	Molecular Screening and Therapeutics (MoST) substudies	OMICO/AGCMC Limited		1.40		
	Clinical trial	Unrestricted research grant (Snow Ball Donation)	Tour de Cure		0.03		
	Research grant	Unrestricted research grant (matched fundraising)	Cure Brain Cancer Foundation		0.20		
	Research grant	Unrestricted research grant (matched fundraising)	Cure Brain Cancer Foundation		0.30		
	Research grant	Unrestricted research grant (Charlie Teo WA Ball Donation)	Charlie Teo Foundation		0.20		
NeuroSurgical Research	Research grant	Immunotherapy Glioblastoma (CAR)-T Dr Lisa Ebert	University of South Australia		0.06	2.88	3.00
Foundation	Research grant	A new approach to deliver drugs to brain tumours Dr Briony Gliddon	University of South Australia		0.06		
	Research grant	Brain organoids for rapid and personalised pre-clinical test of treatments for GBM Dr Guillermo Gomez	University of South Australia		0.06		
	Research grant	Developing a comprehensive glioblastoma brain tumour database Dr Melinda Tea	University of South Australia		0.03		
	Research grant	Developing preclinical models medulloblastoma targeting 14-3-3 Dr Melinda Tea	University of South Australia		0.05		
	Research grant	Chemotherapy effects on cognitive function in child cancer survivors Dr Alexandra Whittaker	University of Adelaide		0.03		
	Research grant	Investigating the role of 14-3-3 in medulloblastoma Dr Quenten Schwarz	University of South Australia		0.02		
	Research grant	Discovering targets for immunotherapy of aggressive childhood cancers Dr Lisa Ebert	University of South Australia		0.03		

				Funding contribution (\$m)			
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
	Research grant	Development of genetically engineered adoptive cell therapies to treat diffuse midline glioma in children Dr Tessa Gargett	University of South Australia		0.05		
	Research grant	Targeting endoplasmic reticulum-specific autophagy to treat glioblastoma Dr Nirmal Robinson	University of South Australia		0.03		
	Research grant	Developing clinically relevant models of recurrent glioblastoma Dr Mel Tea	University of South Australia		0.03		
	Research grant	Genetically engineered invariant NKT cells for dual targeting of DIPG Ms Kristyna Sedivakova	University of Adelaide		0.05		
	Research grant	Pioneering unique models of all glioblastoma subtypes to improve brain cancer treatment Dr Brett Stringer	Flinders University		0.04		
	Research grant	Predicting chemotherapeutic neurotoxicity with electrophysiological and morphological assays of human brain tissue in vitro A/Prof Cedric Bardy	Flinders University		0.04		
	Research grant	Inhibiting ER-stress induced CD47 to treat glioblastoma Dr Nirmal Robinson	University of South Australia		0.04		
	Research grant	Harnessing S1P receptor 1 to enhance CAR-T cell immunotherapy for glioblastoma Dr Briony Gliddon	University of South Australia		0.04		
	Research grant	A novel technique for defining brain tumours on MRI Dr Minh-Son To	University of South Australia		0.04		
	Research grant	Identifying mechanisms that guide T cells into tumours to improve CAR-T cell therapy for glioblastoma Dr Lisa Ebert	University of South Australia		0.04		
	Research grant	Use of artificial intelligence to identify glioblastoma patients that respond favourably to therapy Dr Guillermo Gomez	University of South Australia		0.04		
	Research grant	FAPi-MRI towards better target delineation of high-grade gliomas Prof Benjamin Thierry	University of South Australia		0.03		
	Research grant	Initiation of the KARPOS clinical trial to treat GBM (CAR-T cells) A/Prof Lisa Ebert	University of South Australia		0.05		
	Research grant	Evaluating CD47 regulated mechanisms to treat GBM Dr Nirmal Robinson	University of South Australia		0.05		

					Funding o	contribution (\$m)	
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
	Research grant	A new approach to enhance immunotherapy for GBM Dr Melinda Tea	University of South Australia		0.05		
	Research grant	Roles of sphingosine kinase 1 and 2 in GBM Dr Briony Gliddon	University of South Australia		0.05		
	Research grant	Limiting invasive capabilities of GBM cells Dr Sunita Ramesh	Flinders University		0.03		
	Research grant	Membrane-cholesterol depleting agents o and anti- glioma cytolytic activity of GD2-specific CAR-T cells Dr Michael Brown	University of South Australia		0.04		
	Equipment grant	EVOS M5000 microscopic imaging system Prof Stuart Pitson	University of South Australia		0.02		
	Equipment grant	Tissue dissociator and stereotactic alignment and injection system Prof Stuart Pitson	University of South Australia		0.06		
	Equipment grant	GelCount equipment Dr Melinda Tea	University of South Australia		0.05		
	Research chairs	NRF Brain Tumour Research Chair Glioblastoma Prof Stuart Pitson	University of South Australia		1.00		
	Fellowships	Chris Adams Scholarship - Brain Tumour Research	University of South Australia		0.12		
	Fellowships	NRF Brain Tumour Chair Prof Stuart Pitson Scholarships	University of South Australia		0.03		
	Clinical Trial	CAR-T Cell Clinical Trial Developing new immune-based therapies for brain cancer. Assoc Prof Lisa Ebert	Royal Adelaide Hospital		0.10		
	Research Grant	Precision medical approaches for the treatment of gliomas with cannabinoids. Assoc Prof Simon Conn	Flinders University		0.10		
	Research Grant	Developing Advanced Pre-Clinical Models of Paediatric Brain Cancers. Prof Stuart Pitson	University of South Australia and SA Pathology		0.10		
	Equipment grant	VETSCAN HM5 Haematology Analyser Dr Briony Gliddon	University of South Australia and SA Pathology		0.01		

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					Funding o	contribution (\$m)	
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
	Other	South Australian Paediatric Brain Cancer Biobank A Prof Jordan Hansford	SAHMRI		0.10		
	Other	Establishment database management system for the South Australian Tumour Bank Dr Rebecca Ormsby	Flinders University		0.11		
Robert Connor Dawes Foundation	Clinical trial capacity	Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG)	Monash University	1.25		1.25	1.25
New South	Clinical trial	Multiple clinical trials	Multiple sites		0.51	9.50	7.50
Wales Government	Equipment grant	Research equipment: multiple grants	Multiple sites		0.24		
	Equipment grant	Research infrastructure: ACRF child cancer liquid biopsy program	Children's Cancer Institute		0.08		
	Research grants	Translational program grant: transforming protein quantitation technology to improve cancer diagnosis and treatment decisions	University of Sydney		0.18		
	Technology research	Cancer proteogenomics collaboration	Children's Medical Research Institute		1.02		
	Technology research	Zero Childhood Cancer	n/a		1.00		
	Centres of Excellence	Translational Cancer Research Centre: Centre for Oncology Education and Research Translation	University of New South Wales		0.46		
	Centres of Excellence	Translational Cancer Research Centre: Sydney Vital	University of Sydney		0.23		
	Centres of Excellence	Translational Cancer Research Centre: KIDS Cancer Alliance	University of New South Wales		0.23		
	Fellowships	Early career fellowship: eradication of neuroblastoma by targeting a novel long non-protein-coding RNA	University of New South Wales		0.34		
	Fellowships	Career development fellowship: towards a therapy for aggressive cancers that lack a telomere maintenance mechanism	University of Sydney		0.06		
	Fellowships	Career development fellowship: Investigation on MYCN- driven mitotic deregulation in neuroblastoma	University of New South Wales		0.34		

					Funding o	contribution (\$m)	
Funding partner	Category of funding	Activity	Institution	MRFF projects	Other projects	Committed to projects to date	Total committed to Mission*
	Fellowships	Career development fellowship: an anticancer chemically-modified natural compound targeting copper in neuroblastoma	University of New South Wales		0.09		
	Fellowships	Early career fellowship: improving brain cancer outcomes with MRI guided adaptive radiotherapy (INTREPID)	University of New South Wales		0.11		
	Fellowships	Career development fellowship: personalising cancer radiation therapy via dynamic MRI-based adaptation to changing tumour anatomy and biology	University of Sydney		0.23		
	Research grant	Translational program grant: experimental therapeutics for Myc-driven childhood cancer	University of New South Wales		1.18		
	Research grant	Translational program grant: cancer imaging and targeted radiation therapy: innovation, discovery and translation	University of Sydney		0.76		
	Research grant	Translation program grant: implementing novel therapeutic strategies for childhood brain cancer patients	University of New South Wales		2.44		
Victorian Government	Centres of Excellence	Centre of Research Excellence in adult brain cancer	ONJ Research Institute		2.00	24.00	2.00
	Centres of Excellence	Centre of Research Excellence in adult brain cancer	ONJ Research Institute		2.00		
	Centres of Excellence	The Brain Cancer Centre	WEHI		16.00		
	Equipment grant	Gamma Knife	Peter MacCallum Cancer Centre		4.00		
			Total	8.15	65.82		
			Total contribution all funding partners		\$73.97m	\$73.97m	\$76.40m

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Note: \* This figure represents the total the Funding Partner has allocated to the Mission (to 2027), some of which is not yet committed to specific projects.

NFP = Not for publication. Details on investments by the Cure Brain Cancer Foundation were not available at the time of publication.

As shown, some Funding Partners have invested more in the Mission than they had originally committed to.

## C Review method

## Scope of the environmental scan

The purpose of the Environmental Scan as set out in the Terms of Reference included:

- How does brain cancer research funded under the Mission and other MRFF initiatives compare with other national and international funded brain cancer research?
- Is it possible to assess whether brain cancer research funded under the Mission and other MRFF initiatives is ahead of, behind, or at a similar stage of progress compared to international research efforts that have been underway since the Mission was established?
- What are the key funding priorities for brain cancer research in Australia and overseas in terms of research areas as well as funding approaches? For example, is there an emphasis on collaborations, capacity building, consumer involvement, translation, etc?
- What are the key research strengths and evidence gaps in brain cancer research in Australia compared to overseas?
- For the Mission specifically, how do approaches, priorities, and research funded by the Mission compare nationally and overseas? What is unique about the Mission and the co-funding model with Funding Partners, and how does that model compare with other funding programs?
- For Funding Partner's research only, what are the research targets and how is funding prioritised? What are the different approaches to funding?

To achieve this, a literature review was undertaken using PubMed<sup>75</sup>, Embase<sup>76</sup>, and SCOPUS<sup>77</sup> and web-based searching, which focused on:

<sup>75</sup> The PubMed database contains more than 34 million citations and abstracts of biomedical literature. Citations in PubMed primarily stem from the biomedicine and health fields, and related disciplines such as life sciences, behavioural sciences, chemical sciences, and bioengineering. PubMed was developed and is maintained by the National Centre for Biotechnology Information (NCBI), at the U.S. National Library of Medicine (NLM)

<sup>&</sup>lt;sup>76</sup> Embase is a European-oriented biomedical and pharmacological bibliographic database of published literature. It contains over 32 million records from over 8,500 currently published journals from 1947 to the present. Embase's international coverage expands across biomedical journals from 95 countries.

<sup>77</sup> Scopus is an abstract and citation database of peer-reviewed literature including scientific journals, books, and conference proceedings. Scopus provides a comprehensive overview of worldwide research output in the fields of science, technology, medicine, social sciences, and arts and humanities. See https://www.scopus.com/home.uri

- who funds brain cancer research, types of funders, the funding model used, and the way that funds are allocated/prioritised
- typical features, or what might considered best practice when it comes to funded research, such as emphasis on consumer/patient input, multi-centre or international collaborations, infrastructure, capacity building, use of patient registries, translation, etc, and
- breadth of research in terms of research area and cancer type, and
- research endpoints (safety, efficacy, Health Related Quality of Life, etc), and stage on the pathway towards clinical translation (basic research, clinical trials by phase, observational studies etc).

Key cancer databases were also examined, including:

- the International Cancer Research Partnership (ICRP), which is an alliance of cancer research organisations from Australia, Canada, France, Japan, the Netherlands, United Kingdom, and the United States, which maintains the only public source, worldwide, of current and past grants, totalling over \$80 billion in cancer research since 2000 from 32 ICRP Partners and 156 international funding organisations<sup>78</sup>
- the 2023 Cancer Australia Audit of cancer research projects and programs in Australia over the last three triennia (2012-2014, 2015-2017 and 2018-2020)<sup>79</sup>
- the Australian New Zealand Clinical Trials Registry (ANZCTR), which is an online public registry of clinical trials, held at the NHMRC Clinical Trials Centre, University of Sydney, and
- ClinicalTrials.gov<sup>80</sup>, which is run by the United States National Library of Medicine at the National Institutes of Health, and is the largest clinical trials database. It holds registrations from over 425 000 trials from over 200 countries.

## Survey of grant recipients

The purpose of the survey of grant recipients was to:

- assess the extent to which MRFF grants aligned with the Mission Roadmap
- assess the progress that MRFF have made towards achieving the MRFF 'Measures of Success' and MRFF 'Impact Measures' as set out in the MRFF Monitoring, Evaluation and Learning Strategy 2021-22 to 2023-24 (the Evaluation Strategy), and
- provide insights into other matters relevant to the review of the Mission, including whether MRFF grants enabled research institutions to undertake more brain cancer research, whether MRFF grants encouraged collaboration with researchers within Australia and internationally, and the extent of engagement with consumer groups.

<sup>78</sup> https://www.icrpartnership.org/

<sup>&</sup>lt;sup>79</sup> Cancer Australia (2023), Cancer Research in Australia: An overview of funding for cancer research projects and programs in Australia, 2012 to 2020, Cancer Australia, Surry Hills, NSW.

<sup>80</sup> https://clinicaltrials.gov/

## Stakeholder engagement process

A list of stakeholders involved in the review is provided in table C.1 below.

#### C.1 Consultation list

Organisation/Affiliation
Brain Tumour Alliance Australia
Canadian Institute of Cancer Research/Canadian Institutes of Health Research
Cancer Council SA
Cancer Institute NSW
Cancer Voices Australia
Carries Bickmore's Beanies 4 Brain Cancer Foundation
Children's Hospital Foundation Queensland
Cure Brain Cancer Foundation
Department of Health and Human Services, State Government of Victoria
Financial Markets Foundation for Children
Former MSAG
Group of Eight
Mark Hughes Foundation
Medicines Australia
Minderoo Foundation
National Cancer Institute/National Institutes of Health (US)
Patient representatives
NeuroSurgical Research Foundation
Rare Cancers Australia
Rare Disorders NZ
RCD Foundation
Tessa Jowell Brain Cancer Mission
The Kids' Cancer Project

Source: CIE.

An overview of the themes explored by stakeholder group is provided in table C.2.

-	Research on unmet need/ survivorship/ innovations	Pathway to translation/ embed in clinical practice, and adoption	Capacity/ capability for translational research	Key Mission achieve- ments	Commercial- isation of research	Funding model options	Consumer involvement, access to trials, and adoption	Future prioritis- ation
Mission grantees	$\checkmark$	✓	✓	✓	$\checkmark$		✓	$\checkmark$
Non-Mission brain cancer research grantees	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$		$\checkmark$	$\checkmark$
Other Australian brain cancer researchers	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$		$\checkmark$	$\checkmark$
Clinicians participating in research	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$		$\checkmark$	$\checkmark$
Stakeholders that can identify research groups (AAMRI, Go8, Brain Cancer Biobanking Australia)	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$			
Mission Funding Partners	$\checkmark$			$\checkmark$		$\checkmark$	$\checkmark$	$\checkmark$
Research bodies - Australia	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Research bodies – International	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Consumer representatives - Australia	$\checkmark$			$\checkmark$			$\checkmark$	$\checkmark$
Consumer representatives - International	$\checkmark$						$\checkmark$	$\checkmark$
Cancer Australia	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Medicines Australia	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$		$\checkmark$	$\checkmark$
Sister brain cancer missions	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
International research organisations	$\checkmark$	✓	$\checkmark$		✓	$\checkmark$	✓	$\checkmark$

### C.2 Themes explored by stakeholder group

Source: CIE.

# D Key areas of brain cancer research and treatments

## Key areas of Australian brain cancer research

Key areas of brain cancer research<sup>81</sup> and Australian examples of their application include:

- Enhanced imaging tests new techniques for imaging scans that are being researched to track how well treatment is working, and watch for possible tumour recurrence or growth, such as:
  - Flinders University research to develop a novel technique for defining brain tumours on MRI<sup>82</sup>, and
  - University of South Australia research to develop better imaging of high-grade glioma towards enabling the delivery of more accurately targeted treatment including proton therapy and MRI-Linac technologies<sup>83</sup>
- Biomarkers examining biomarker tests to more accurately predict prognosis, identify high-risk patients, or to characterise the tumour's genetic markers, which may inform treatment selection. An example includes the University of Melbourne research into a non-invasive blood test for diagnosis and monitoring of brain cancer<sup>84</sup>
- Immunotherapy/biological response modifier (BRM) therapy boosting the body's natural defences to fight tumour using materials made by the body or in a laboratory to improve, target, or restore immune system function. Examples highlighted by researchers from the WEHI include chimeric antigen receptor T cell (CAR-T) therapy, vaccine therapy, and checkpoint inhibition.<sup>85</sup> Australian examples include:
  - University of Queensland research into using immunotherapy to improve glioblastoma treatment<sup>86</sup>, and
  - Monash University research into novel targets for paediatric brain tumour immunotherapy<sup>87</sup>

- <sup>85</sup> See Wang, S., Bandopadhayay, P, and M, Jenkins 2019, 'Towards Immunotherapy for Pediatric Brain Tumors', *Trends in Immunology*, August 2019, Vol. 40, No. 8.
- <sup>86</sup> See https://brainfoundation.org.au/research-grants/2017/brain-tumours-8/
- 87 See https://markhughesfoundation.com.au/news/novel-targets-for-paediatric-brain-tumourimmunotherapy/

<sup>&</sup>lt;sup>81</sup> Cancer.Net 2022, Brain Tumor: Latest Research, Approved by the Cancer/Net Editorial Board September 2021, see <u>Brain Tumor: Latest Research | Cancer.Net</u>, Accessed 5 July 2022.

<sup>&</sup>lt;sup>82</sup> See https://www.nrf.com.au/current-brain-tumour-research, Accessed 20 August 2022.

<sup>83</sup> Ibid.

<sup>84</sup> See https://brainfoundation.org.au/research-grants/2019/brain-tumours-12/, Accessed 20 August 2022.

- Oncolytic virus therapy using a virus that infects and destroys tumour cells while sparing healthy brain cells<sup>88</sup>
- **Targeted therapy** medication therapy that targets faulty genes or proteins that contribute to a tumour's growth and development (different ways to target how a tumour grows, spreads, or can be destroyed), such as:
  - Children's Cancer Institute research into novel therapeutic approaches for children participating in the ZERO national clinical trial, which utilises the database of genomic and drug screening data being generated by ZERO to investigate novel therapies for all high-risk childhood brain tumours<sup>89</sup>, and
  - Olivia Newton-John Cancer Research Institute research into Therapeutic Targeting of the Tumour Microenvironment in Glioblastoma<sup>90</sup>
- Blood-brain barrier disruption temporarily disrupting the brain's protective barrier to allow chemotherapy to more easily enter the brain from the bloodstream, such as University of South Australia research into the potential repurposing of FTY720 to allow the entry of existing anti-cancer drugs across the blood-brain barrier and into brain tumours<sup>91</sup>
- New drugs, new combinations of drugs, and repurposed drugs using drugs currently available for other types of cancer as treatment for a brain tumour, and/or combinations of drugs that target the different ways a tumour grows and spreads, such as:
  - the University of Sydney based Multi-Arm GlioblastoMa Australasia (MAGMA) Trial that aims to assess several options in standard of care for the management of glioblastoma<sup>92</sup>
  - WEHI research into using systems pharmacogenomics to identify novel targets and clinically actionable therapeutics for medulloblastoma<sup>93</sup>
  - Children's Cancer Institute research into dual targeting of the epigenome via Facilitates Chromatin Transcription (FACT) complex and histone deacetylase is a potent treatment strategy for DIPG<sup>94</sup>

- 90 See https://markhughesfoundation.com.au/news/therapeutic-targeting-of-the-tumourmicroenvironment-in-glioblastoma/, Accessed 10 August 2022.
- <sup>91</sup> See https://www.nrf.com.au/current-brain-tumour-research.
- <sup>92</sup> See https://ctc.usyd.edu.au/our-research/research-areas/cancer/cancer-divisions/braincancer/open-trials/magma/.
- <sup>93</sup> Wang, S., Bandopadhayay, P, and M, Jenkins 2019, 'Towards Immunotherapy for Pediatric Brain Tumors', *Trends in Immunology*, August 2019, Vol. 40, No. 8
- <sup>94</sup> Ehteda A, Simon S, Franshaw L, Giorgi FM, Liu J, Joshi S, Rouaen JRC, Pang CNI, Pandher R, Mayoh C, Tang Y, Khan A, Ung C, Tolhurst O, Kankean A, Hayden E, Lehmann R, Shen S, Gopalakrishnan A, Trebilcock P, Gurova K, Gudkov AV, Norris MD, Haber M, Vittorio O, Tsoli M, Ziegler DS. Dual targeting of the epigenome via FACT complex and histone deacetylase is a potent treatment strategy for DIPG. Cell Rep. 2021 Apr 13;35(2):108994. doi: 10.1016/j.celrep.2021.108994. PMID: 33852836.

<sup>&</sup>lt;sup>88</sup> At this stage, only international examples of published work have been identified.

<sup>89</sup> See https://www.ccia.org.au/about-the-institute/our-research/molecular-targets-and-cancertherapeutics/brain-tumours, Accessed 10 August 2022.

- Kids Cancer Alliance research of PLK1 inhibition on a panel of DIPG cultures to identify the most promising combinatorial strategies, and test the most effective combinations in two robust animal models of DIPG<sup>95</sup>
- Gene and cell therapy replacing or repairing abnormal genes that are causing or helping tumour growth, such as:
  - Diamantina research into stem cell factor SOX9 as a potential therapeutic target for the treatment of Sonic Hedgehog medulloblastoma<sup>96</sup>
  - University of Melbourne research into how specific alterations in lipid accumulation can lead to the pathogenesis of gliomas, showing glioblastoma cells use differences in metabolic processes driven from fats (called lipids) allowing tumour cells to advantageously grow at greater rates to normal brain cells
  - University of South Australia research into inhibiting ER-phagy to kill Glioblastoma Multiform (GBM) cells and reduces the expression of 'don't eat me' signals which further promotes GBM clearance<sup>97</sup>, and
  - WEHI research using genetically engineered blood cells from the patient's blood designed to specifically kill cancer cells. The work has led to the 2021 publication of 'Novel high-affinity EGFRvIII-specific chimeric antigen receptor T cells effectively eliminate human glioblastoma<sup>'98</sup> and the 2020 publication of 'De novo designed receptor transmembrane domains enhance CAR-T cell cytotoxicity and attenuate cytokine release'<sup>99</sup>
- Genetic research seeking more information about specific gene mutations and how they relate to the risk and growth of a brain tumour so that precision medicine approaches that target tumour-specific mutations can be explored. For instance,
  - ZERO is the most comprehensive precision medicine program for children and young people with cancer in the world, designed to fast-track children with high-

- 97 See https://www.nrf.com.au/current-brain-tumour-research, Accessed 20 August 2022.
- <sup>98</sup> Abbott RC, Verdon DJ, Gracey FM, Hughes-Parry HE, Iliopoulos M, Watson KA, Mulazzani M, Luong K, D'Arcy C, Sullivan LC, Kiefel BR, Cross RS, Jenkins MR 2021, Novel high-affinity EGFRvIII-specific chimeric antigen receptor T cells effectively eliminate human glioblastoma. Clin Transl Immunology. 2021 May 9;10(5):e1283. doi: 10.1002/cti2.1283. Erratum in: Clin Transl Immunology. 2021 Jul 18;10(7):e1317. PMID: 33976881; PMCID: PMC8106904

<sup>99</sup> Elazar, A., Chandler, N., Davey, A., Weinstein, J., Nguyen, J., Trenker, R., Jenkins, M., Call, M., Call, M., Fleishman, S. 2020, 'De novo designed receptor transmembrane domains enhance CAR-T cell cytotoxicity and attenuate cytokine release', bioRxiv 2020.07.26.221598; doi: https://doi.org/10.1101/2020.07.26.221598.

<sup>&</sup>lt;sup>95</sup> Inducing DNA lethality in DIPG' (2017-2019), which involved comprehensive analysis of PLK1 inhibition on a panel of DIPG cultures to identify the most promising combinatorial strategies, and test the most effective combinations in two robust animal models of DIPG, see Our Research - Kids Cancer Alliance (kca.org.au)

<sup>&</sup>lt;sup>96</sup> Adolphe, C., Millar, A., Kojic, M., Barkauskas, D., Sundström, A., Swartling, F., Hediyehzadeh, S., Tan C. W., Davis, M., Genovesi, L., Wainwright B., 2021, SOX9 Defines Distinct Populations of Cells in SHH Medulloblastoma but Is Not Required for Math1-Driven Tumor Formation' *Mol Cancer Res* 1 November 2021; 19 (11): 1831– 1839. https://doi.org/10.1158/1541-7786.MCR-21-0117

risk, aggressive cancers into treatment with new drugs specifically tailored for their unique disease. The Australian program is led by Children's Cancer Institute and Kids Cancer Centre at Sydney Children's Hospital, Randwick<sup>100</sup>

- the German INFORM2 platform is being brough to Australia to enable Australian children with brain cancer to access the benefits of the INFORM registry study. The purpose of the INFORM registry is to establish a technical, structural and genetic information base for future clinical trials (AMG) in the field of personalised paediatric oncology. In Australia, Sydney Children's Hospital, Royal Children's Hospital, Perth Children's Hospital, Children's Hospital Westmead are participating sites<sup>101</sup>
- the brain cancer element of the US 'Count Me In' program enables patients to share their medical information, tumour, saliva, and/or blood samples with researchers who combine data with that of other patients for transformative genomic studies to expediate advances in the treatment of brain cancer<sup>102</sup>, and
- The (United States bases) Cancer Genome Atlas Program to find out more about the link between genetics and glioma. Recent results include the discovery of three specific genetic mutations not previously linked to glioblastoma: NF1, ERBB2, and PIK3R1,<sup>103</sup>
- The Garvin Institute and the Charlie Teo Foundation Brain Cancer Seq. project The research team is using a technique called 'single-cell RNA sequencing' to understand the behaviour of individual cells within GBM brain tumours, an extremely aggressive type of brain cancer, and the most common. Researchers are analysing the individual cells in a tumour to produce the first real picture of everything that's in one cancer. This information will be used to develop new ways to better diagnose and treat GBM and provide an unprecedented look into brain cancer<sup>104</sup>, and

**Palliative care/supportive care** — we found limited research and clinical trials under way to find better ways of reducing symptoms and side effects of current brain tumour treatments to improve comfort and quality of life for patients<sup>105</sup>. Some relevant research is not specific to brain cancer, such as the UTS's Cancer Symptom Trials<sup>106</sup> and PaCCS programs<sup>107</sup>.

- 106 See https://www.uts.edu.au/research-and-teaching/our-research/impacct/cancer-symptomtrials/cstprojects.
- 107 See https://www.uts.edu.au/research-and-teaching/our-research/impacct/palliative-careclinical-studies-collaborative/about-paccsc/paccsc-team.

<sup>100</sup> See https://www.zerochildhoodcancer.org.au/about/what-we-do, Accessed 20 August 2022.

<sup>101</sup> See INFORM2-NivEnt in detail (dkfz.de), Accessed 17 August 2022.

<sup>102</sup> See Brain Tumor Project, Accessed 17 August 2022.

<sup>103</sup> See https://www.genome.gov/Funded-Programs-Projects/Cancer-Genome-Atlas.

<sup>104</sup> See https://www.garvan.org.au/research/collaborative-programs/brain-cancerseq/about/, accessed 10 February 2023

<sup>&</sup>lt;sup>105</sup> Whittle JR, Williams M, Eisenstat DD. 2021, 'Medical Assistance in Dying (MAiD) in Brain Cancer: Whose Autonomy Are We Respecting?' Can J Neurol Sci. 2021 Nov;48(6):747-749. doi: 10.1017/cjn.2021.198. Epub 2021 Aug 20. PMID: 34412718.

## Key brain cancer treatments

The goal of brain cancer research is to improve treatment and patient outcomes.

The aim of treatment may be to remove the tumour completely, slow its growth, or relieve symptoms by shrinking the tumour and reducing swelling, depending on:

- the size, type, and grade of the tumour
- whether the tumour is putting pressure on vital parts of the brain
- if the tumour has spread to other parts of the central nervous system or body
- possible side effects, and/or
- the patient's preferences and overall health.

Direct treatment options include surgery, radiation therapy, chemotherapy, chemoradiotherapy, immunotherapy and targeted therapy. Cancer.net<sup>108</sup> provides a detailed overview of the brain cancer treatment pathway and options, which is summarised in the sections below.

#### Surgery

Surgery is usually the first line treatment used for a brain tumour. It is often the only treatment needed for a low-grade brain tumour. Removing the tumour can improve neurological symptoms, provide tissue for diagnosis and genetic analysis, help make other brain tumour treatments more effective, and, in many instances, improve the prognosis of a person with a brain tumour.

There have been rapid advances in surgery for brain tumours, including the use of cortical mapping, enhanced imaging, and fluorescent dyes.

- Cortical mapping allows doctors to identify areas of the brain that control the senses, language, and motor skills.
- Enhanced imaging devices give surgeons more tools to plan and perform surgery. For example, computer-based techniques, such as image guided surgery, help surgeons map out the location of the tumour with increased accuracy. However, as this is a very specialised technique, it may not be widely available.
- A fluorescent dye, called 5-aminolevulinic acid, can be given by mouth the morning before surgery which is then taken up by tumour cells. Doctors can then use a special microscope and light to see the cells that have taken up the dye.

For a tumour that is near the brain's speech centre, it is increasingly common to perform the operation when the patient is awake for part of the surgery. Special electrical stimulation techniques are used to locate the specific part of the brain that control speech, which can help avoid causing damage to the speech centre while removing the tumour.

<sup>108</sup> Cancer.Net, accessed (14 November 2022) https://www.cancer.net/cancer-types/braintumor/types-treatment

#### **Radiation therapy**

Radiation therapy is the use of high-energy X-rays or other particles to destroy tumour cells, which are used to slow or stop the growth of a brain tumour. It is typically given after surgery and possibly along with chemotherapy.

The most common type of radiation treatment is external-beam radiation therapy (EBRT), which is radiation given from a machine outside the body. Alternatively a radiation treatment given using implants is called internal radiation therapy or brachytherapy.

External-beam radiation therapy can be directed at a brain tumour in the following ways:

- Conventional radiation therapy is a treatment where location is determined based on anatomic landmarks and X-rays.
- 3-dimensional conformal radiation therapy uses images from CT and MRI scans to create a 3-dimensional model of the tumour and healthy tissue surrounding the tumour.
- Intensity modulated radiation therapy (IMRT) is a type of 3D-CRT that can more directly target a tumour. It can deliver higher doses of radiation to the tumour while giving less to the surrounding healthy tissue.
- Proton therapy is a type of external-beam radiation therapy that uses protons rather than X-rays. Proton beam therapy is typically used for tumours when less radiation is needed because of the location, such as the base of skull, and those near the optic nerve.
- Stereotactic radiosurgery is the use of a single, high dose of radiation given directly to the tumour and not healthy tissue. It works best for a tumour that is only in one area of the brain and certain noncancerous tumours. There are many different types of stereotactic radiosurgery equipment, including:
  - A modified linear accelerator is a machine that creates high-energy radiation by using electricity to form a stream of fast-moving subatomic particles
  - A Gamma Knife is another form of radiation therapy that concentrates highly focused beams of gamma radiation on the tumour
  - A Cyber Knife is a robotic device used in radiation therapy to guide radiation to the tumour, particularly in the brain, head, and neck regions
- Fractionated stereotactic radiation therapy which is delivered with stereotactic precision but divided into small daily doses called fractions and given over several days or weeks, in contrast to the 1-day radiosurgery. This technique is used for tumours located close to sensitive structures, such as the optic nerves or brain stem.

Depending on the size and location of the tumour, the radiation oncologist may choose any of the above radiation techniques. In certain situations, a combination of multiple techniques may work best and is also sometimes used in conjunction with drug therapies.

#### Therapies using medication

Medication given through the bloodstream to reach cancer cells throughout the body is called systemic therapy. This can be achieved through chemotherapy, immunotherapy or targeted therapy.

Chemotherapy is the use of drugs to destroy tumour cells, usually by keeping the tumour cells from growing, dividing, and making more cells.

A challenge for using drugs to target cancer cells is permeating the blood-brain barrier, which is both a structural and functional roadblock to microorganisms, such as bacteria, fungi, viruses or parasites, that may be circulating in the bloodstream.

Some drugs are better at going through the blood-brain barrier. These are the drugs often used for a brain tumour chemotherapy and chemoradiotherapy, and include:

- Gliadel wafers are a way to give the drug carmustine. These wafers are placed in the area where the tumour was removed during surgery.
- For people with glioblastoma and high-grade glioma, the latest standard of care is radiation therapy with daily low-dose temozolomide.
- A combination of three drugs, lomustine, procarbazine, and vincristine, have been used along with radiation therapy. Clinical trials on the use of chemotherapy to delay radiation therapy for patients with low-grade glioma are ongoing.

Targeted therapy is a treatment that targets the tumour's specific genes, proteins, or the tissue environment that contributes to a tumour's growth and survival. This type of treatment blocks the growth and spread of tumour cells and limits the damage to healthy cells.

For a brain tumour, there are two types of targeted therapy that may be used:

- Bevacizumab is an antiangiogenesis therapy used to treat glioblastoma multiforme when previous treatment has not worked. Antiangiogenesis therapy is focused on stopping angiogenesis, which is the process of making new blood vessels. Because a tumour needs the nutrients delivered by blood vessels to grow and spread, the goal of antiangiogenesis therapy is to 'starve' the tumour.
- Larotrectinib and entrectinib are examples of targeted therapy that are not specific to a certain type of tumour but focus on a cancers with specific genetic change called an NTRK fusion.

The latest research is developing immunotherapy, also called biological response modifier (BRM) therapy. Immunotherapy is designed to boost the body's natural defences to fight the tumour. It uses materials either made by the body or in a laboratory to improve, target, or restore immune system function. Different methods are being studied for brain tumours, such as the use of dendritic cells or the use of vaccines aimed against a specific molecule on the surface of the tumour cells. Several methods are currently being tested in clinical trials.

#### Alternating electric field therapy

This type of treatment uses a non-invasive portable device that interferes with the parts of a cell that are needed for tumour cells to grow and spread. It is given by placing electrodes that produce an electric field on the outside of a person's head.

Alternating electrical field therapy may be an option for people newly diagnosed with glioblastoma or for those with recurrent glioblastoma. Researchers have found that people with recurrent glioblastoma who used the device lived as long as those who received chemotherapy. In addition, they had fewer side effects.

#### Metastatic cancer

Brain metastases from non-CNS cancers have traditionally been treated with surgery or radiation therapy. Chemotherapy is not often used because the blood-brain barrier keeps many drugs from reaching the brain, however other medications like targeted therapy and immunotherapy (which has been proven to work for metastatic melanoma) are options for certain people. Below is a general summary of when and how surgery and radiation therapy are used to treat brain metastases:

- People with up to four brain metastases generally receive stereotactic radiosurgery
- Treatment for people in relatively good health and with more than four tumours that cannot be removed with surgery or more than two tumours that were removed surgically may include stereotactic radiosurgery or whole brain radiation therapy
- People who also have metastatic cancer in parts of the body other than the brain usually continue their treatment regimen if disease outside the brain is not worsening.

#### Palliative or supportive care

A brain tumour and its treatment cause physical symptoms and side effects, as well as emotional, social, and financial effects. Managing all these effects is called palliative care or supportive care. It is important that this care is included along with treatments intended to slow, stop, or eliminate the tumour.

Palliative treatments vary widely and often include medication, nutritional changes, relaxation techniques, emotional and spiritual support, and other therapies.

Supportive care for people with a brain tumour includes corticosteroids which are used to lower swelling in the brain, and antiseizure medicines which help control seizures. Furthermore, there are various treatments for functional loss, such as speech therapy or physiotherapy.

# *E* US style cradle to grave research grants

The United States Department of Defence grant funding structure provides funding from a concept stage through to translation.

Each stage is presented in table E.1. The structure of this funding is unique in that it does not require preliminary data until the idea development award stage, which creates opportunities for funding ideas at a concept.

Award Mechanism	Key Mechanism Elements	Funding
Concept Award	<ul> <li>Supports highly innovative, non-incremental, high risk/potentially high-reward lung cancer research.</li> <li>Emphasis on innovation.</li> <li>Clinical trials are not allowed.</li> <li>Preliminary data are not required.</li> <li>Relevance to military health is strongly encouraged.</li> <li>Care Delivery and Health Disparity category must address one or more of the Disparities, Health Outcomes, and Survivorship Areas of Emphasis.</li> <li>Cancer Research Continuum category must address at least one or more of the nine cancer continuum-focused Areas of Emphasis.</li> </ul>	<ul> <li>Maximum funding of \$100,000 in direct costs (plus indirect costs).</li> <li>Period of performance should not exceed 1 year</li> </ul>
Career Development Award	<ul> <li>Supports early-career, independent researchers to conduct research under mentorship of an experienced lung cancer researcher.</li> <li>Clinical trials are not allowed.</li> <li>Preliminary data are not required.</li> <li>Relevance to military health is strongly encouraged.</li> </ul>	<ul> <li>Maximum funding of \$375,000 in direct costs (plus indirect costs).</li> <li>Period of performance should not exceed 3 years.</li> </ul>
ldea Development Award	<ul> <li>Supports new ideas in the early stages of development representing innovative, high-risk/high-gain research.</li> <li>Emphasis on innovation and impact.</li> <li>New Investigator category supports applicants early in their faculty appointments or in the process of developing independent research careers.</li> <li>Clinical trials are not allowed.</li> <li>Preliminary data are required.</li> <li>Relevance to military health is strongly encouraged.</li> </ul>	<ul> <li>Maximum funding of \$525,000 in direct costs (plus indirect costs).</li> <li>Period of performance should not exceed 3 years.</li> </ul>

#### E.1 US Department of Defence grant funding structure

Award Mechanism	Key Mechanism Elements	Funding
Translational Research Award	<ul> <li>Supports advanced translational research that will foster transformation of promising ideas in lung cancer into clinical applications. Translational research may be defined as an integration of basic science and clinical observations.</li> <li>This mechanism is intended to fund a broad range of translational studies including, but not limited to, the following:</li> <li>Advanced preclinical studies aimed at translating results from animal studies to applications with human samples/cohorts</li> <li>Late-stage preclinical work leading to/preparing for a clinical trial, e.g., Investigational New Drug application submission</li> <li>Correlative studies that are associated with an open/ongoing or completed clinical trial</li> <li>Projects that develop endpoints for clinical trials</li> <li>Pilot clinical trials where limited clinical testing (e.g., small sample size) of a novel intervention is necessary to inform the next step in the continuum of translational research</li> <li>Preliminary lung cancer relevant data are required.</li> <li>Relevance to military health is strongly encouraged.</li> <li>Level 1</li> <li>Clinical trials are not allowed.</li> <li>Level 2</li> <li>Supports translational studies that include a pilot/proof-of-principle clinical trial.</li> </ul>	Level 1 Maximum funding of \$900,000 in direct costs (plus indirect costs). Period of performance should not exceed 3 years. Level 2 - Clinical Trial Option Maximum funding of \$1,200,000 in direct costs (plus indirect costs). Period of performance should not exceed 4 years.

Source: US Department of Defence – Congressionally Directed Medical Research Programs, https://cdmrp.health.mil/pubs/press/2023/23lcrppreann



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