



# **MND Australia Research Strategy 2018 - 2021**

# Investing in innovation, Partnering for progress

## VISION

To find effective treatments and ultimately a cure for motor neurone disease (MND).

## OBJECTIVES

- Promote research excellence by supporting only the best research that has the greatest chance of finding effective treatments and improving the care of people living with MND
- Attract and develop outstanding researchers by supporting researchers at all stages of their careers
- Partner for impact, drive collaboration and innovation along the research pipeline and the healthcare system
- Advance research evidence to inform healthcare policy and practice improvement.

## CONTEXT

There are currently more than 2,000 people living with MND in Australia. MND refers to a group of progressive neurological diseases in which motor neurones degenerate and die. Amyotrophic lateral sclerosis (ALS) represents 70 per cent of MND cases and with average survival of 2.5 years from disease onset, is the most malignant form of MND. MND occurs sporadically in about 90 to 95 per cent of cases, developing without any identifiable cause. Familial or inherited MND accounts for about 5 to 10 per cent of all MND cases. Clinically, the sporadic and familial forms of ALS are indistinguishable. Less common forms of MND include progressive bulbar palsy, pseudobulbar palsy, primary lateral sclerosis, progressive muscular atrophy, Kennedy's disease and spinal muscular atrophy.

### Research supported by MND Australia

MND Australia supports health and medical research through its research arm, the MND Research Institute of Australia (MNDRIA). Since awarding its first grant in 1987, MNDRIA has invested more than \$25 million to fund Australia's most comprehensive MND research program spanning a range of research, from discovery to healthcare. To recognise this achievement and the generosity of the many Australians who funded this research, Federal Assistant Minister for Health, the Hon. Dr David Gillespie MP, launched the *\$25 Million, 25 Milestones: Changing the future of motor neurone disease* report at the 13th MND Australia Research Conference in November 2017.

The landmark report details 25 high-impact, MNDRIA-funded advancements helping to change the future of MND. The 25 milestones include:

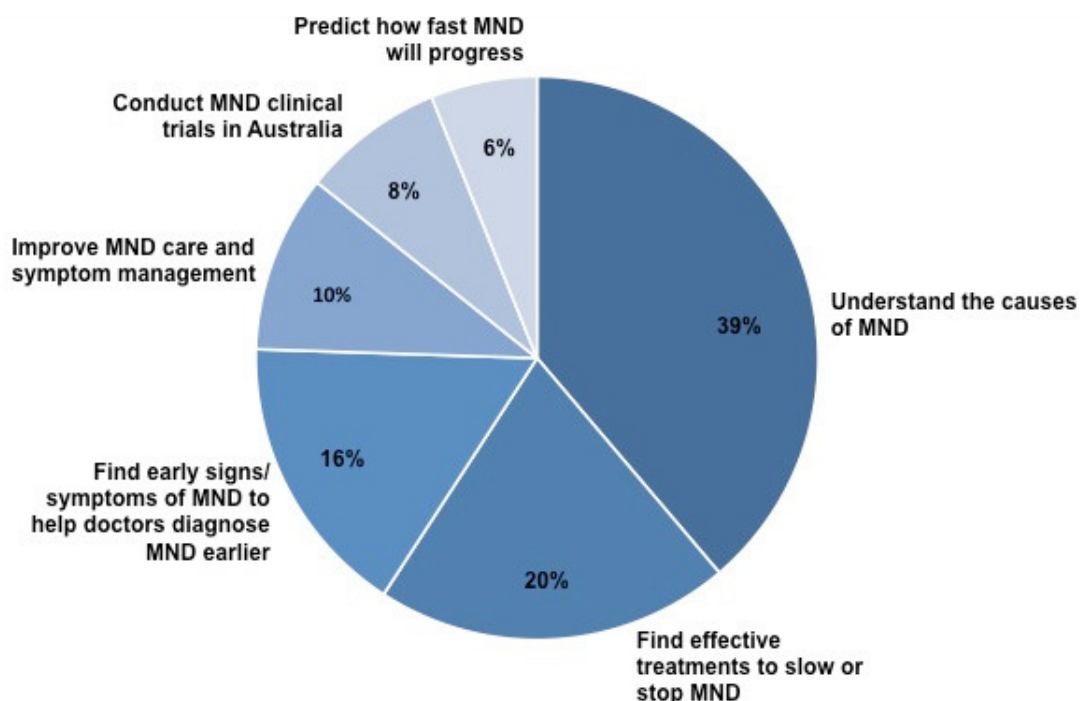
- The development of the MND research workforce in Australia with over \$5.3 million invested in a range of postdoctoral fellowships since 2002. Most fellowship recipients continue to work in MND and/or neurological diseases, with several rising to be among the world's leading MND researchers. MNDRIA PhD scholarships co-funded with the National Health and Medical Research Council (NHMRC) and MNDRIA PhD scholarship Top-up Grants have also helped to attract a number of early career researchers to the field.
- An important capacity-building initiative known as the SALSA-SGC, a national consortium of researchers at nine centres working together to find the genes involved in sporadic MND. This collaborative program was established in 2015 thanks to the generosity of the community participating in the 2014 ALS/MND Ice Bucket Challenge.

- Advances in our understanding of the causes of MND e.g. the discovery of the *TDP-43* and *CCNF* genes.
- Significant insights into many clinical aspects of MND e.g. how MND spreads, metabolic changes in people with MND.
- Identification of new diagnostic and prognostic tools e.g. the discovery of the P75ECD biomarker, threshold tracking TMS.
- Identification of potential MND treatments now undergoing further testing e.g. copper-ATSM, PMX205.
- Clinical trials e.g. The Diet and Exercise in ALS Study (DEALS), Breath-stacking in Neuromuscular Disease.
- Care improvement e.g. Decision-making about care, breathing support improves care and survival in MND.

These findings are pivotal to the incremental progress of MND research with implications for people with MND, their families and clinicians. Each milestone highlighted in the report is another step forward in defeating MND.

MNDRIA has supported only the best applicants to its funding program through a competitive peer review process. It has supported a comprehensive research program from discovery, to testing potential treatments, clinical research, clinical trials and healthcare. Special grants to support major initiatives have been provided from time to time when exceptional funds became available through large donations. These include the MND Australia Leadership Grant (2013 – 2016), the MND Australia Ice Bucket Challenge Grant (2015 – 2018) and the Betty Laidlaw MND Research Grant (2016 – 2018). Currently, there are approximately 100 active MND researchers in Australia. In 2017, MNDRIA supported more than 40 individuals via fellowships, scholarships and grants-in-aid.

## Projects supported by MND Australia in 2017, by research goal



While understanding of MND has transformed over the last decade, there is still much to learn about MND. Genetic factors are implicated in both familial and sporadic MND. Protein aggregation or misfolding, glutamate toxicity, mitochondrial dysfunction, oxidative stress (free radical damage), immune-mediated damage, and dysfunctional signalling pathways are all linked to MND. Physical trauma and exposure to environmental toxins and chemicals are also implicated. Research into the incidence of MND in populations suggests a multi-step process leading to MND. The heterogeneity of the disease remains a major challenge, making it difficult to identify treatment strategies that could work for a significant proportion of people with MND. Disease models have not been effective in translating potential treatments. There have been more than 50 failed phase 2 and 3 MND clinical trials, despite positive studies in animal models. An international ALS clinical trials guidelines workshop, attended by more than 140 delegates from around the world, was held in March 2016. The meeting reviewed lessons learned from ALS clinical trials to date and discussed ways to improve the design of clinical trials in future.

## METHODOLOGY

The process to develop the MND Australia Research Strategy 2018 – 2021 consisted of:

- i) An analysis of research activities supported by MNDRIA and other research organisations in June 2017.
- ii) Internal and external consultations to identify views and practical challenges to the MND research effort in Australia.

### Research activities analysis

Analysis of research supported by MNDRIA found the current research program had been a productive means of providing support for MND research, resulting in almost 200 journal publications in the last five years (2012 – 2017). The *\$25 Million, 25 Milestones: Changing the future of motor neurone disease* report demonstrated significant advances in MND research. Australian research strengths were noted around research into the causes of MND, testing potential treatments as well as some clinical research areas, including diagnosis and disease spread.

A review of several major research organisations (The Heart Foundation, Multiple Sclerosis Research Australia and the National Breast Cancer Research Foundation) and MND Associations (the MND Association of England, Wales & Northern Ireland, the ALS Association (US) and ALS Canada) was conducted in June 2017. Findings included:

- i) The identification of research themes e.g. identifying causes of MND.
- ii) A range of competitive funding for PhD scholarships, fellowships, project grants and small grants for new ideas.
- iii) Funding for priorities identified by the organisation (sometimes referred to as ‘platform projects’) to support DNA and tissue banks, clinical trials networks, clinical trials, registries and the development of clinical practice guidelines.
- iv) Funding to support partnerships – driving collaboration among non-profits, academia and government.

Importantly, it was noted the research strategy should have some flexibility to allow for opportunities as they arise. Other considerations for a not-for-profit organisation research strategy include:

- i) Level of community support for MND research. To date, all research supported by MNDRIA has been as a result of community donations.
- ii) A suitable funding structure that recognises a) the capacity and capability of the research workforce locally and internationally b) the knowledge base of the research field. The reality is we still do not really know enough about what causes MND or how best to treat it. The research strategy should consider the clinical trials environment given the large number of failed clinical trials in the past and limited number of potential participants in Australia.

## Consultations

Following the review of other research organisations, a draft research strategy was developed in 2017 for internal review between July and November 2017 by i) the MND Australia Board ii) the State MND Associations and iii) the MND Australia Research Committee. Feedback was taken into account where possible and appropriate.

A session called “Roadmap to the Future” at the 13th MND Australia Research Conference in November 2017 asked speakers to consider the challenges and opportunities they faced in their research at various stages of the research pipeline.

MND Australia also undertook extensive community consultation to inform the research strategy. An online questionnaire about MND research was developed and implemented on Survey Monkey. It was advertised via email and social media between 4th December 2017 and 2nd February 2018. The questionnaire asked people about their views on research goals and the types of research needed to achieve those goals. A total of 567 people took part in the survey. One half of participants (49%) had a personal connection to MND i.e they had a family member or friend with MND. One quarter of participants (25%) had a professional connection to MND. Almost one fifth of participants (18%) were diagnosed with MND.

## FUTURE DIRECTIONS

MND Australia will continue to drive collaboration and develop capacity and capability in MND research. The organisation will support the best research through a competitive peer review process. Community consultation shows particularly strong support for research to i) find effective treatments to slow or stop MND ii) find the early signs of MND to help doctors diagnose MND earlier iii) improve MND care and symptom management and iv) clinical trials. MND Australia will continue to support outstanding research applications that aim to achieve these goals through its annual funding round.

The MND research field in Australia is still relatively small. MND Australia will continue to develop the Australian health and medical research workforce through fellowships, PhD Top-up Grants, PhD scholarships co-funded with NHMRC and travel grants. Notably, Australia has particularly strong capability around research into the causes of MND, testing potential treatments and clinical research including diagnosis and disease spread.

There is an opportunity to strengthen the conduct of clinical trials in Australia. Clinical trials networks help to facilitate investigator-led clinical trials and also provide a single interface to attract industry studies. They foster and promote multidisciplinary and international research collaboration. Notably, in February 2018, MND Australia has supported three MND management and care clinical trials underway (BreatheMND-1, Breath-stacking in Neuromuscular Disease, DEALS (Diet and Exercise in ALS) Study) and one drug clinical trial (The Lighthouse Project) as well as laboratory research to inform the Phase I Copper-ATSM drug trial (2016 – 2018).

There will be increased emphasis in developing partnerships. From time to time, MND Australia will consider participating in research that leverages funding from other sources and promotes collaboration and cross-disciplinary research e.g. NHMRC Partnership Grants. There may also be opportunities for more international alignment. MND Australia has strong linkages to several sister organisations internationally particularly the MND Association (England, Wales & Northern Ireland), the ALS Association (US) and ALS Canada. MND Australia is an active member of the International Alliance of ALS/MND Associations and connected to the Pan-Asian Consortium for Treatment and Research in ALS (PACTALS).

## STRATEGIC RESEARCH PRIORITIES

### 1. Advance MND research to understand its causes

This priority covers research that improves our knowledge of the underlying disease mechanisms causing MND and the development of representative laboratory models.

### 2. Foster the drug development process and clinical trials

MND Australia will work with partners to develop initiatives that support the drug development process. There are relatively few compounds ready to be tested in humans. Representative animal models and properly conducted pre-clinical studies are vital to assist translation into treatments.

### 3. Enhance clinical research and the evidence-base for clinical practice

MND Australia will invest in clinical and healthcare research to promote innovation and best practice to improve quality of life for people living with MND and their families and carers. Following community consultation, the following have been noted as the highest MND management and care research priorities: i) Breathing problems and respiratory management ii) Swallowing problems iii) Speech and communications iv) Walking and mobility v) Pain management vi) Hand function vii) Upper limb function viii) Depression ix) Cognitive function x) Nutrition.

### 4. Build research capacity

MND Australia will continue to develop the research workforce, an area in which MNDRIA has a strong track record. The goal is to continue to encourage promising young scientists to MND, foster early and mid-career researchers, as well as established scientists from other fields of research, to apply their knowledge and skills to MND.

### 5. Working together and inspiring partnerships

This priority promotes networking, communication, collaboration and cross-disciplinary research. It includes fostering national and international partnerships. Investment in research will be maximised where possible by leveraging funding from other sources.

### 6. Facilitate information exchange

MND Australia will continue to improve and facilitate knowledge and information sharing and collaboration between researchers internationally. The benefits of research and outcomes of research supported by MNDRIA will be communicated to the MND community and the broader general public. MND Australia will continue to hold the MND Australia Research Conference and MND Connect as annual events. In addition, MND Australia will continue to support attendance of researchers to the International Symposium on ALS/MND and act as host from time to time when the meeting is held in Australia.

### Research focus areas

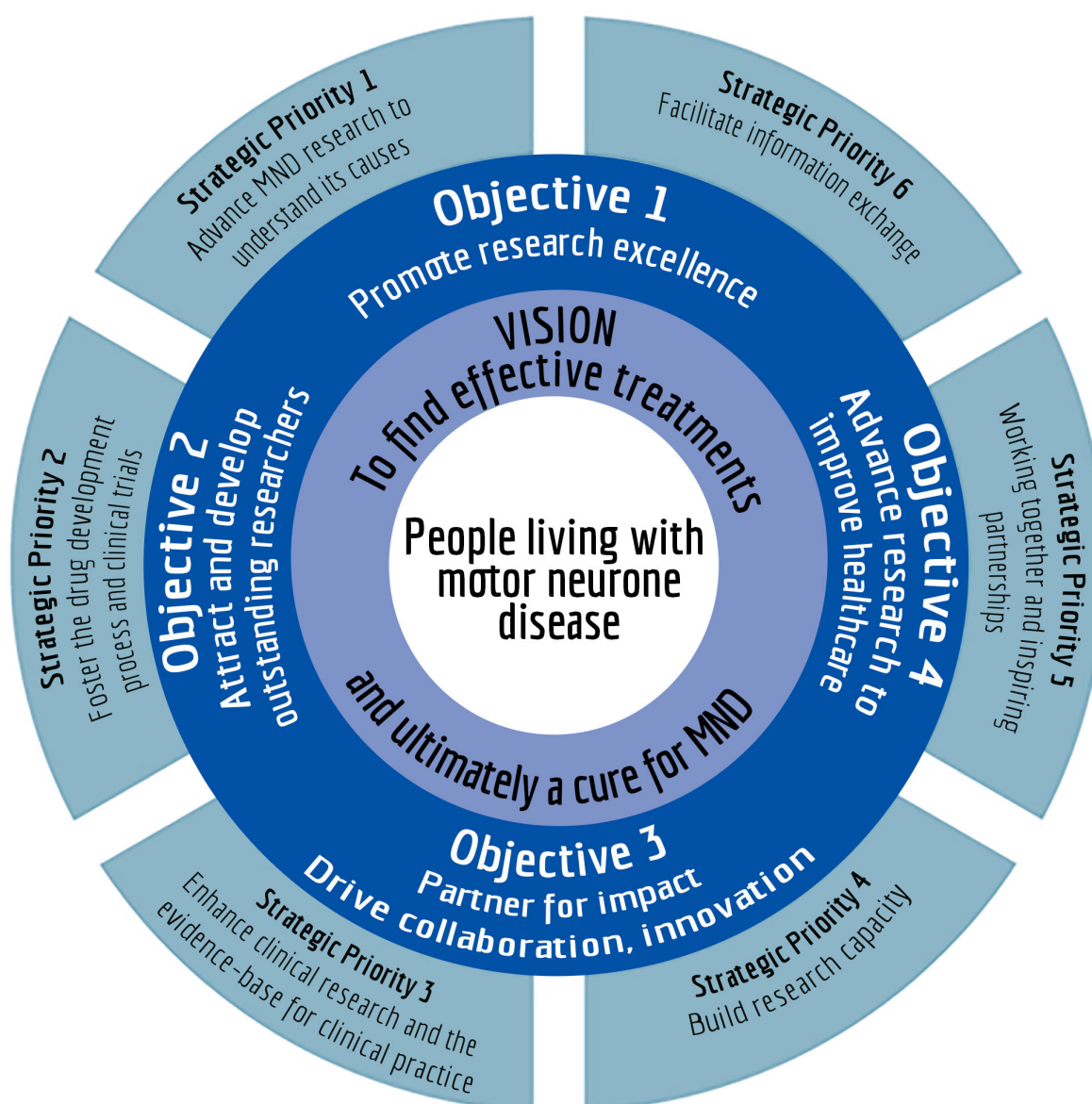
MND Australia supports a broad range of research areas along the research pipeline. Each research area is critical to advancing MND research. Focus areas include:

- Biomarkers
- Cell biology
- Clinical research
- Cognitive studies
- Diagnosis and progression
- Disease models
- Drug development
- Environmental factors / epidemiology
- Genetics
- Healthcare research
- Immunology
- Metabolism and nutrition
- Skeletal muscle
- Social research
- Stem cells.



# MND Australia Research Strategy 2018 - 2021

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## RESEARCH PROGRAM

### 1. Competitive research initiatives

Competitive funding will continue to support research into the classical forms of MND (amyotrophic lateral sclerosis, progressive bulbar palsy, pseudobulbar palsy, primary lateral sclerosis and progressive muscular atrophy). Research into Kennedy's disease and spinal muscular atrophy must show a potential benefit to the classical forms of MND to be considered for funding.

From 2018, "grants-in-aid" will be replaced by "Innovator Grants" to better reflect their purpose around seed-funding new ideas. Annual funding rounds will continue to develop capacity, capability and collaboration, and include support for:

- i) Fellowships, PhD Scholarship Top-up Grants, NHMRC/MNDRIA postgraduate awards and travel awards under Strategic Priority 4: Build research capacity.
- ii) Up to \$100,000 Innovator Grants for new research that:
  - a) Advances MND research to understand its causes (Strategic Priority 1)
  - b) Fosters the drug development process and clinical trials (Strategic Priority 2)
  - c) Enhances clinical research and the evidence-base for clinical practice (Strategic Priority 3).

Naming rights for Innovator Grants will be considered for donations of \$50,000 or more.

Large donations of more than \$300,000 may enable a special grant to be awarded competitively to outstanding researchers in a prescribed research area seen as highly relevant at the time the donation is made (Strategic Priority 1-5).

A Practice Improvement Projects (PIP) program to complement competitive funding awarded by MNDRIA for healthcare and social research will be piloted in 2018. This program will align with Strategic Priority 3: Enhance clinical research and the evidence-base for clinical practice.

### 2. Strategic partnerships and initiatives

MND Australia will foster national / international partnerships and initiatives to maximise impact and leverage funding. Initiatives will include:

- Strategic partnerships that leverage funding from other sources as well as promote collaboration and cross-disciplinary research e.g. Co-partner on NHMRC Partnership Grants (Strategic Priority 5).
- Support and facilitate multi-centre MND clinical trials in Australia (Strategic Priority 2).
- Continued support of the Australian MND Registry (Strategic Priority 3).
- Commissioned healthcare research projects to improve the quality of life and care of people with MND and their families. Such projects will align with Strategic Priority 3: Enhance clinical research and the evidence-base for clinical practice.



## FUNDING PROGRAM

### Competitive research initiatives



#### Innovator Grants for new research

- Advance research to understand the causes of MND
- Foster the drug development process and clinical trials
- Enhance clinical research and the evidence-base for clinical practice



#### Capacity building

Fellowships, NHMRC/MNDRIA postgraduate awards, MNDRIA PhD Top-up Grants and travel awards to develop research capacity



#### Special Grants Scheme

Major competitive initiatives when extensive funds are available



#### Practice Improvement Projects Program

Complement competitive funding awarded by MNDRIA for healthcare and social research

### Strategic partnerships and initiatives



#### Strategic partnerships

Leverage funding from other sources as well as promote collaboration and cross-disciplinary research



#### Support development of clinical trials

Facilitate multi-centre MND clinical trials in Australia



#### Australian MND Registry

Continued support of the Australian MND Registry



#### Healthcare research projects

Commission healthcare projects to improve the quality of life and care of people with MND and their families