

Changing the future of MND

This year marks a 30-year, \$25 million investment by the Motor Neurone Disease Research Institute of Australia (MNDRIA) in growing and sustaining Australia's world-class MND research. 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 MND* 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 and bringing hope to people living with MND. Among the accomplishments are MNDRIA's unparalleled contribution to developing the MND research workforce in Australia; the development of a genomics consortium, SALSA-SGC; 19 advances in research resulting in journal publications and four clinical trials.

While there is still much to learn about MND, understanding of this complex condition globally has transformed over the last decade. MNDRIA has played an integral role in this transformation by funding and promoting a comprehensive research program from discovery to healthcare. Continued investment in Australian scientists at the forefront of MND research is vital to understanding the causes, developing effective treatments and moving towards a cure for MND sooner. MNDRIA is indebted to the intellect and dedication of MND researchers across the nation as well as the generosity of donors and supporters who fund this research.

"Many parts of the MND puzzle are being put together and the \$25 Million, 25 Milestones report highlights just how much MND researchers have achieved."

Assistant Minister for Health,
Hon Dr David Gillespie MP



Photo: Philanthropist, John Laidlaw AO; Assistant Minister for Health, Hon. Dr David Gillespie MP and CEO of MND Australia, Carol Birks

The MND Research Institute of Australia (MNDRIA) has built and sustained MND research in Australia for the last 30 years.



Executive Director Research Report

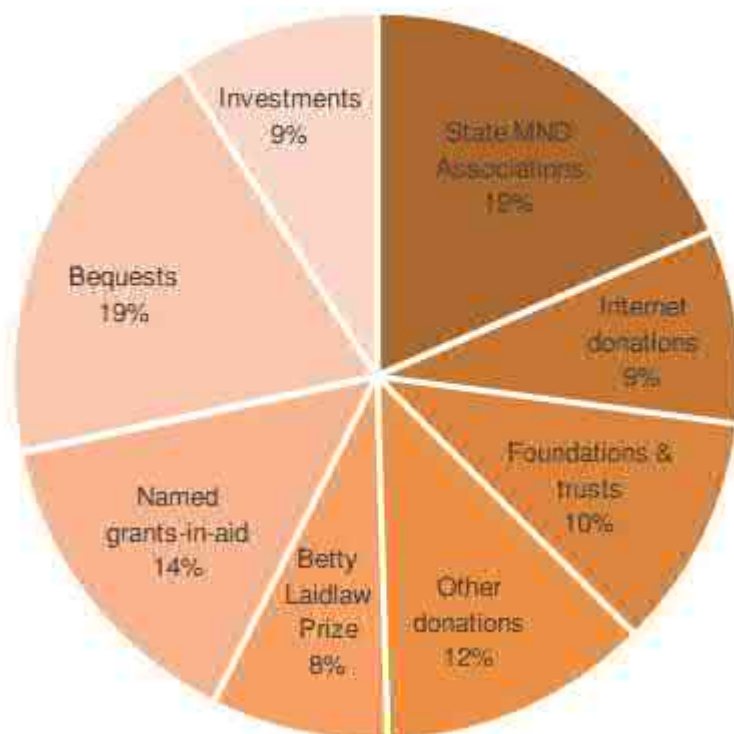
2016 – 2017

Thanks to generous donations from the State MND Associations, individuals and bequests, MNDRIA has had another strong year, with \$3.75 million awarded at the Grants Allocation Meeting in 2016 to fund 32 new research grants commencing in 2017. Two new grants were awarded in addition to two three-year fellowships and 29 grants-in-aid: the Betty Laidlaw Prize for an outstanding mid-career researcher and the Charcot Grant, to be awarded annually for the highest-ranking grant-in-aid. This year, outstanding donations were received from the MND and Me Foundation, the MonSTaR Foundation, Tom Barr Smith and his supporters, Peter Simko, the people of Benalla and the SuperBall X, Grant McKenzie, the family of David Flett and many others. Several significant bequests were also received for research.

In October 2016, the 12th MND Australia Research Conference was held at the Queensland Brain Institute to foster information sharing and collaboration between Australia's leading researchers. Prize sponsor, John Laidlaw AO, presented the inaugural Betty Laidlaw MND Research Prize at the meeting to Dr Catherine Blizzard from the Menzies Research Institute. We hosted the 2nd MND Connect meeting the following day to inform the wider MND community about recent advances in research. Presenters included MNDRIA-funded researchers as well as MND community representatives. The majority of attendees were from the broader MND community (MND Queensland, MND and Me Foundation, people with MND and their families). Developed by University of Queensland researchers Drs Shyuan Ngo and Frederik Steyn, the forum was very well received with enthusiasm for continuing the concept in Sydney in 2017.

The past year has seen a number of significant research findings. Research led by Dr Mary-Louise Rogers at Flinders University has found a new and simple test to monitor disease progression in people with MND and evaluate drugs under investigation in MND clinical trials. University of Queensland scientists Associate Professor Trent Woodruff and Dr John Lee have found a drug "PMX205" extends the life of mice that have a SOD1 mutation. More studies are now underway to determine the safety of PMX205 before it can be tested in humans.

MNDRIA income for grants awarded in 2017
for new grants commencing in 2018



We are grateful for the time given by the expert MNDRIA Research Committee whose members continue to provide valuable advice and support around reviewing grants and grants allocation. Associate Professor Bradley Turner (Florey Institute of Neuroscience and Mental Health, Victoria) and Dr Shyuan Ngo (University of Queensland) joined the Research Committee this year. Their expertise will help with the clinical/basic science balance of the Committee. In addition, a Research Sub-committee chaired by Professor David Berlowitz reviewed the grants allocation process resulting in a number of recommendations and improvements to streamline the grants review process.

MNDRIA is indebted to many people who make its success possible. Janet Nash and Rachel Rizk are integral to MNDRIA's success, working tirelessly with passion and commitment. Special thanks also to volunteers Alan Hauserman, Maureen Burmeister and Clare Watson for donating their time and expertise this year. With the commitment of donors and supporters, the guidance of the expert Research Committee and the dedication of Australia's researchers at the forefront of MND research, we remain focused on working together for a world without MND.

Dr Stephanie Williams
Executive Director Research
MND Australia

2018 MNDRIA grant recipients

The MNDRIA Research Committee met in November at the annual grants allocation meeting to determine allocation of available funds for new grants commencing in 2018. \$3.31 million was awarded to the Betty Laidlaw MND Research Prize, two 3-year postdoctoral fellowships for early career researchers and 25 innovative 12-month research projects (grants-in-aid). Provision was included for two PhD top-up grants and two travel grants to be awarded in January. Grants were awarded to research projects ranging from genetics to healthcare. [Read full project descriptions](#)

Betty Laidlaw MND Research Prize
A/Prof Justin Yerbury, University of Wollongong

Beryl Bayley MND Postdoctoral Fellowship 2018 – 2020
Dr William Huynh, University of Sydney

Bill Gole MND Postdoctoral Fellowship 2018 – 2020
Dr Nirma Perera, Florey Institute of Neuroscience and Mental Health

Charcot Grant
Dr Mary-Louise Rogers, Flinders University

David Flett Memorial MND Research Grant
A/Prof Julie Atkin, Macquarie University

MNDRIA Grant-in-aid
A/Prof Mark Bellingham, University of Queensland

Superball X MND Research Grant
Prof Roger Chung, Macquarie University

Jenny Simko MND Research Grant
Dr Dominic Hare, Florey Institute of Neuroscience and Mental Health

Peter Sterne Familial MND Research Grant
Prof Lars Ittner, University of NSW

MonSTaR Foundation MND Research Grant
A/Prof Anna King, University of Tasmania

MNDRIA Grant-in-aid
Dr Angela Laird, Macquarie University

MNDRIA Grant-in-aid
Dr John Lee, University of Queensland

Lady (Mary) Fairfax MND Research Grant
Dr Edwin (Chai) Lim, Macquarie University

Fat Rabbit MND Research Grant
Prof Pamela McCombe, University of Queensland

MNDRIA Grant-in-aid
Dr Marco Morsch, Macquarie University

MonSTaR Foundation MND Research Grant
Dr Shyuan Ngo, University of Queensland

MND and Me Foundation Research Grant
A/Prof Peter Noakes, University of Queensland

Benalla Act to d'feet MND Research Grant
Dr Lezanne Ooi, University of Wollongong

Grant McKenzie MND Research Grant
Dr Thomas Oxley, University of Melbourne

Mavis Gallienne and Graham Lang MND Victoria Research Grant
A/Prof Gail Robinson, University of Queensland

Dr Paul Brock MND NSW Research Grant
Prof Dominic Rowe, Macquarie University

Jenny Simko MND Research Grant
A/Prof Justin Rubio, University of Melbourne

Marie McGrath MND Research Grant
Dr Frederik Steyn, University of Queensland

MNDRIA Grant-in-aid
Dr Lachlan Thompson, Florey Institute of Neuroscience and Mental Health

MNDRIA Grant-in-aid
A/Prof Bradley Turner, Florey Institute of Neuroscience and Mental Health

Col Bambrick Memorial MND Research Grant
Prof Anthony White, QIMR Berghofer

Jenny Barr Smith MND Research Grant
Dr Kelly Williams, Macquarie University

Charles and Shirley Graham MND Research Grant
A/Prof Trent Woodruff, University of Queensland

Of the 86 applications for research grants commencing in 2018, the MNDRIA Research Committee awarded the top accolades to Associate Professor Justin Yerbury and Dr Mary-Louise Rogers.

The Betty Laidlaw MND Research Prize was awarded at the 13th MND Australia Research Conference to Associate Professor Justin Yerbury from the Illawarra Health and Medical Research Institute, University of Wollongong. The Prize was presented by John Laidlaw AO in honour of his wife Betty who has lived with a slowly progressive form of MND for over 30 years.

The Prize rewards an outstanding mid-career researcher with a demonstrated background of excellence in neuroscience research with a grant to enable an innovative project with the potential to lead to effective treatments for MND. The \$250,000 grant will fund

Associate Professor Yerbury's latest project investigating the dysfunction of proteins in nerve endings as a cause of MND.



Dr Mary-Louise Rogers

The Charcot Grant is given annually for the highest ranking grant-in-aid project. The Charcot Grant 2018 was awarded to Dr Mary-Louise Rogers from Flinders University for her project titled *Pre-clinical validation of growth factors delivered to motor neurones by non-viral gene therapy as a treatment for MND*.

"I am very honoured to receive this award on behalf of our laboratory. It is confirmation that our team is heading in the right direction – looking at both treatments and biomarkers," says Dr Rogers.



A/Prof Justin Yerbury

Research Conference wrap-up

Associate Professor Bradley Turner (Florey Institute of Neuroscience and Mental Health) reports on the 13th MND Australia Research Conference held at the University of Sydney in November 2017.

This year's Conference showcased major research achievements funded by the MNDRIA coinciding with the \$25 Million, 25 Milestones report (cover story), a Roadmap for the future and research outcomes from MNDRIA-sponsored projects. The Conference was launched by The Hon. Dr David Gillespie MP, Federal Assistant Minister for Health, who remarked on the recent significant investment of Government and MNDRIA funding for MND. Associate Professor Justin Yerbury (University of Wollongong) was awarded the Betty Laidlaw MND Research Prize and Dr Mary-Louise Rogers (Flinders University) received the Charcot Grant (page 3). Janet Nash (MND Australia) was presented with a trophy for her many years of service to the MNDRIA and her extraordinary contributions to building and sustaining MND research in Australia. Thank you Janet for your limitless energy and patience!

The Conference commenced with two excellent keynote presentations highlighting the significant impact of MNDRIA-funded research on a global scale. Associate Professor Ian Blair (Macquarie University) summarised the staggering progress in genetic discovery in MND. While it took over a century to find the first culprit gene for MND, recent next-generation DNA screening technology has narrowed this gap to years. As a result, 10 MND genes have been discovered from MNDRIA-funded projects. Aside from shedding light on the causes of MND, these genes have revealed shared molecular origins of MND and frontotemporal dementia, dissolved barriers between inherited and sporadic MND, and inspired a generation of innovative experimental models to tackle MND in the laboratory. Next, Professor Steve Vucic (University of Sydney) summarised over a decade of clinical research by Professor Matthew Kiernan and their team, providing compelling evidence that MND is fundamentally a disorder of electrical circuits in the brain, leading to subsequent spinal cord and muscle damage. Importantly, electrical overload in the brain of MND patients can be detected by a sensitive and non-invasive technique called "TMS" that Professor Vucic and colleagues have recently commercialised, which may provide a powerful tool to diagnose and track MND in the clinic.

Associate Professor Tracey Dickson (Menzies Institute for Medical Research) opened the *Roadmap for the Future* session, outlining the important contribution of experimental model systems such as flies, worms, fish and mice to MND research. Although these simple organisms have obvious inherent limitations, their implementation and interpretation in MND research is continually improving. Human-based models of MND were presented, ranging from stem cell reprogramming to mini-brains "on-a-chip", suggesting we are at an exciting advent of highly relevant and digital models for rapid drug screening in MND. Dr Peter Crouch (University of Melbourne) summarised his team's 10-year journey in the making with positioning CuATSM as a possible therapeutic option for MND which is currently under clinical trial in Australia. Dr Michelle Farrar (University of NSW) provided an overview of *Spinraza*, the first approved therapeutic for the fatal childhood motor neurone disease, spinal muscular atrophy (SMA), recently approved in Australia. While *Spinraza* continues to demonstrate unprecedented and remarkable benefits in children affected by SMA, this was tempered by the future realities of implementing such an expensive drug and its challenging route of delivery directly into the spine. Lastly, Dr Anne Hogden (Macquarie University) provided insights into how we can best translate research into practice, reminding us that making research useful to MND patients and their families is the big picture goal of research.

After lunch, several current MNDRIA-funded projects were highlighted. While MND typically presents in late-life, the disease process may span years and decades before symptom onset. Associate Professor Brad Turner (Florey Institute) outlined his team's approach to understand the molecular processes of this critical early time period which could provide fresh insights into motor neurone vulnerability. Dr Chris Bye (Florey Institute) presented evidence for spread of pathology in brains of MND mice which received healthy nerve cell grafts, suggesting a biological mechanism for the characteristic spread of pathology, and perhaps symptoms, in MND. "Could MND result from accelerated ageing of chromosomes?" was a question posed by Associate Professor Julie Atkin (Macquarie University) who found the ends of chromosomes, called telomeres, were shorter in MND affected cells. This suggests DNA instability and damage may contribute to the disease process in MND.



Next, Associate Professor Anna King (Wicking Dementia Research and Education Centre) showed TDP-43 triggered abnormal branches and connections in motor neurones, reinforcing the notion that MND is a disorder of connectivity in the nervous system. Associate Professor Trent Woodruff (University of Queensland) provided an update on targeting the blood-related complement system in MND, revealing a novel role for the "C5aR1" molecule in muscle and extending the role of the complement system to muscle. Lastly, Dr Albert Lee (Macquarie University) summarised his efforts to understand the biology of CCNF mutations, a newly identified gene responsible for MND, revealing these mutations interfere with self-cleansing of damaged proteins in motor neurones which is a pathological pathway in MND.

In the final session, Dr Adam Walker (Macquarie University) presented his findings on protein signatures detected in affected tissues of a novel TDP-43 mouse model of MND, revealing widespread protein disturbances that may point to early disease pathways. Associate Professor Ron Sluyter (University of Wollongong) reported on effects of targeting the "P2X7 receptor" linked to inflammation and motor neurone death in MND mice using an improved brain-penetrating drug. Dr Shyuan Ngo (University of Queensland), revealed new insights into the link between abnormal whole body and muscle metabolism occurring in MND patients. Ashley Crook (Macquarie University) highlighted current issues and dilemmas with genetic testing in inherited MND, weighing up costs and benefits and existing barriers in the event of mutation detection. Lastly, Dr Mehdi Van den Bos and Dr Nimeshan Geevasinga (University of Sydney) summarised encouraging progress with developing and enhancing TMS with MRI to probe brain dysfunction in MND.

The evening Poster Session provided an engaging mix of clinical, healthcare and scientific research presentations and discussions inspiring collaboration outside the platform communications and the best Poster Prize was awarded to PhD student Samantha Levin (University of Queensland).

Conference and MND Connect presentations will be online in December: facebook.com/MNDAustralia
youtube.com/user/MNDAust

MND Connect

Isabella Lambert-Smith (University of Wollongong) reports on highlights from the 3rd MND Connect held at the University of Sydney in November 2017.

November 11 marked a highlight event of the MND calendar; the 3rd MND Connect, a day when people impacted by MND come together with healthcare professionals and researchers to reach better outcomes for the MND community, now and in the future.

"There is always something that can be done", multidisciplinary care is available for all who are living with MND."

Carmen Sanchez, Calvary MND Service

Dr Frederik Steyn, who chaired the first session of presentations, voiced the sentiments of all of us who research MND: "We may not have all the answers but we're a reminder – you're not alone. There's a research community who serve you." And that sums up the most valuable outcomes of this day of connection.

From a researcher's perspective, one of the most insightful presentations was given by Lynda Legradi. Lynda, diagnosed with MND in 2016, emanated spirit and vibrance as soon as she started speaking. She described her family's history of MND and shared her own experiences of living with MND, enlightening the audience with the wisdom she has gained. "Dum spiro spero", "While I breathe, I hope". Words of strength that we could all do with remembering.

"While I breathe, I hope"

Lynda Legradi



- updates on the latest research discoveries in understanding the causes of MND and the development of potential treatments for MND
 - updates on clinical trials in progress and possible future trials
 - examples of how people with MND can be involved in research
 - an update on research into respiratory management in MND
 - tips on where to go and who to contact for support and multidisciplinary care.
- Following Lynda's presentation, there were two sessions that continued with respiratory management in MND.

World-first clinical trial of anti-retroviral therapy

Professor Julian Gold from The Albion Centre is chief investigator of *The Lighthouse Project*, the first clinical trial in the world to use modern combination anti-retroviral therapy in people with MND.

Approximately 8 per cent of human genes have retroviral origins. Human endogenous retroviruses (HERVs) infected animals and humans over millions of years of evolution and eventually became part of our genetic makeup. HERVs were only discovered about 20 years ago and it is still not known exactly how they may be related to causing human diseases. However, there is very good evidence that in animals these viruses are associated with a number of neurological conditions. HERV-K has been directly linked to motor neurone damage and has been found in the brain tissue of patients with MND.

The Lighthouse Project is a Phase 2 open-label clinical trial conducted at four centres in Australia. It is partly funded by MNDRIA through the Cure for MND Collaboration Initiative Grant. The study aims to determine the safety and tolerability of an anti-retroviral therapy known as *Triumeq* in 40 people with MND and provide preliminary data on whether it is able to slow down the progression of MND. *Triumeq* is already used to treat HIV infection safely and effectively.

All participants have been recruited and more than 60 per cent have completed the study. Analysis of data from the trial will give researchers a clearer picture on whether *Triumeq* should be tested in larger studies to further investigate its potential.

MNDRIA and the MND Association of England, Wales and Northern Ireland are now funding the analysis of two recently discovered biomarkers in people who have completed the trial. This will help to assess whether *Triumeq* has had a positive effect on people with MND. Blood and urine samples were taken from each participant before, during, and after treatment and stored. Analysis of a biomarker called p75^{ECD}, which is found in urine, will be supervised by Dr Mary-Louise Rogers from Flinders University. Dr Andrea Malaspina from the Blizard Institute in London will oversee analysis of a neurofilament light-chain biomarker found in blood.

Find Professor Gold's MND Connect presentation online in December:

facebook.com/MNDAustralia
or
youtube.com/user/MNDAust



MND Fact

Each day in Australia two people are diagnosed with MND and two people die with MND

Stronger together

When Dr Shyuan Ngo (Shu) and Dr Frederik Steyn (Derik) are not busy in their labs at the University of Queensland, you'll find them at the MND clinic, getting to know people living with MND to fast-track their understanding of the disease. The dedicated duo has made a promise to "never give up" on finding answers to MND.

Their research partnership emerged while working together on studies in MND mouse models. "At first, we were testing the hypothesis that an increase rate of metabolism causes weight loss, leading to faster decline and earlier death in MND. Our studies found that this is not always the case, rather weight loss is caused by a loss of appetite," says Dr Steyn.

One of Drs Ngo and Steyn's research strengths is their holistic approach. Their independent but complementary research builds from the same foundation of studying how people living with MND use energy at the whole-body level, including energy expenditure, dietary intake, gut function and physical activity.



"Together, we can look at things as a whole but also intricately at the cellular level. As a neuroscientist, I get to ask questions about how the nervous system forms and what happens when things go wrong. I hone in on the effects of MND on muscle and neurones, with the goal of slowing and halting disease progression and improving quality of life by reducing disability and fatigue," says Dr Ngo.

While investigating metabolic changes in MND, Dr Steyn has turned his focus to the neuroendocrinology of MND, meaning he studies how the nervous and endocrine systems are impacted by MND. He is particularly interested in studying the effects of MND on appetite. "My projects seek new information on why some people with MND lose their appetite. While disability and depression are factors, it is clear that loss of appetite for some patients is due to changes in how the brain controls appetite," says Dr Steyn.

"We made a promise to each other to never give up"

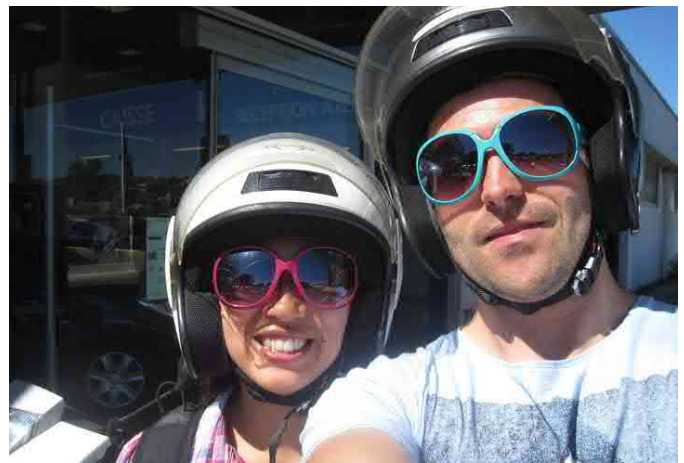
Loss of appetite can occur very early in disease, with some patients losing their appetite before they show motor signs. This indicates widespread changes in the brain that could provide critical information to help us understand how MND is spread between neurones.

Despite their strong partnership, Drs Ngo and Steyn do not work in isolation. "We surround ourselves with inspirational people. We have great mentorship and fantastic research support. It really aids our research to be able to move between the lab and the MND clinic at the Royal Brisbane and Women's Hospital. For that, I value my relationships with the clinical support staff, geneticists, physiologists, neuroscientists and stem cell biologists with whom we work," says Dr Steyn.

Dr Ngo adds, "We work with many people living with MND and I always want to do more and to do it faster. I find it difficult that there are only so many hours in a day during which I can look for answers. Talking to people living with MND and having them so intricately involved in our research is the most rewarding part of the research."

Drs Ngo and Steyn's commitment to the MND cause runs to the core. "I once did a half marathon after training a total of one single two kilometre run ... that wasn't a good idea. I also swung off the Goodwill Bridge to raise funds for MND. I am not as hardcore as Derik," jokes Dr Ngo.

"We have done nothing that people with MND haven't already done," says Dr Steyn. "I'm going to volunteer Shu for the next challenge ... she can't say no."



Get involved

28th International Symposium on ALS/MND

The International Symposium on ALS/MND is the largest medical and scientific conference on ALS/MND. It brings together leading international researchers, and health and social care professionals to present and debate key innovations in their respective fields.

When: 8 – 10 December 2017

Where: Boston, USA

More information: mndassociation.org/symposium

Participate in research

Onset and progression of MND (nationwide)

People living with MND and their carers are invited to participate in this Australia-wide project looking to understand the onset and progression of MND. Both sporadic and familial MND will be studied. Contact Anjali Henders: a.henders@uq.edu.au, 07 3346 6474 or your local SALSA clinic: hsu.imb.uq.edu.au/contact

Research project targeting swallowing exercises and diet change (Sydney)

Professor Vicki Flood from the University of Sydney is currently recruiting people living with MND to take part in a pilot study running from Westmead Hospital in Sydney. The study will evaluate the effects of an extra virgin olive oil enriched diet and active swallowing exercises on swallowing ability, speech, and weight status of people with MND. More information: vicki.flood@sydney.edu.au

Do regular breathing exercises help breathing function? (Melbourne)

Respiratory physiotherapist Nicole Sheers from the Victorian Respiratory Support Service is currently seeking volunteers to take part in a randomised controlled trial at Austin Health in Melbourne. This three-month study will evaluate whether performing daily breathing exercises helps breathing symptoms and lung function of people living with MND. More information: nicole.sheers@austin.org.au

Governance

MND Australia is the principal member of the MND Research Institute of Australia.

The governance and operations of both organisations are the responsibility of MND Australia.

Directors

The board of MND Australia consists of an independent elected President and a nominated representative from each member MND Association board, the chair of the MNDRIA Research Committee and up to three independent directors.

Research Committee

The MNDRIA Research Committee reviews research grant applications and determines the distribution of available funds within the set policies and criteria for scientific assessment.

Research Committee Members

Chairman: Professor Matthew Kiernan, NSW

Professor David Berlowitz, VIC

Associate Professor Ian Blair, NSW

Associate Professor Tracey Dickson, TAS

Professor Simon Foote, ACT

Professor Glenda Halliday, NSW

Dr Susan Mathers, VIC

Professor Pamela McCombe, QLD

Dr Shyuan Ngo, QLD

Professor Dominic Rowe AM, NSW

Professor Dominic Thyagarajan, VIC

Associate Professor Bradley Turner, VIC

Professor Steve Vucic, NSW

Professor Naomi Wray, QLD

MND Fact

More than 2,000 people have MND in Australia of whom 60% are male and 40% are female

Donations

Research funded by the MND Research Institute of Australia is dependent on donations. To contribute to this vital work, please send your gift to:

MND Research Institute of Australia
PO Box 430, North Sydney, NSW 2059

Donations can be made by cheque (payable to MND Research Institute of Australia). Visa or MasterCard donations can be made via phone (02 82874989) or online (mndresearch.org.au)

All donations of \$2 and over are tax deductible.

ABN: 46 789 710 580

Bequests

Your Will can provide an important way of making a gift that can have lasting influence on MND research and give hope for the future.

If you would like to consider the MND Research Institute of Australia in your Will by providing a Bequest from your Estate, please contact your solicitor.

For more details on how your bequest can help MND research

Phone Dr Stephanie Williams, Executive Director Research on 02 8287 4988 or email stephaniew@mndaustralia.org.au

Thank you