

# Periodic Table of MND Research

## Perth 2019

In this document, you can find the complete Periodic Table of MND Research for the 30<sup>th</sup> International Symposium on ALS/MND in Perth, 2019.

Click on a tile below and read more about the content discussed at the Symposium or watch interviews (▶) with selected delegates and speakers. You can also scroll through this document to browse all topics within the Periodic Table. To get back to this page, click the 'back up' symbol (⬅) anywhere in the document.

For a current version of the Periodic Table, please visit  
[symposium.mndassociation.org/periodic-table](https://symposium.mndassociation.org/periodic-table)

### Key

■ Symposium   
 ■ People   
 ■ Biology   
 ■ Symptoms & disease management   
 ■ Causes   
 ■ Diagnosis & prognosis   
 ■ Treatments

<b>Sw</b> SympWatch								<b>Ct</b> Clinical trials
<b>Pe</b> Perth	<b>Pw</b> People with MND				<b>Jy</b> Justin Yerbury	<b>Md</b> Motor neurone disorders		<b>Pt</b> Platform trials
<b>Au</b> MND Australia & MNDWA	<b>Po</b> Poster presentations	<b>Nj</b> Neuromuscular junction	<b>Nu</b> Nutrition	<b>Re</b> Respiration	<b>Ge</b> Genetics	<b>Dd</b> Delivering diagnosis		<b>Gt</b> Gene therapy
<b>Gw</b> Global Walk to D'feet MND	<b>Pp</b> Platform presenters	<b>Mt</b> Mitochondria	<b>Sl</b> Swallowing	<b>Ph</b> Physical exercise	<b>Le</b> Lifestyle & environment	<b>Pr</b> Progression & prognosis		<b>Bc</b> Brain-computer Interface
<b>Aw</b> Awards	<b>Pl</b> Plenary speakers	<b>Mo</b> Modelling MND	<b>Cs</b> Caregiver support	<b>Pc</b> Palliative care	<b>In</b> Inflammation	<b>Bl</b> Biomarkers		<b>Cu</b> CuATSM
<b>Sm</b> Satellite meetings	<b>Hp</b> Healthcare professionals	<b>Rv</b> Retroviruses	<b>Cb</b> Cognition & behaviour	<b>Ac</b> Augmentative & alternative comms	<b>Ml</b> Microbiome	<b>Te</b> Telehealth		<b>Ds</b> Drug screening

## TOPICS

### Symposium ↑

Find out more about the International Symposium on ALS/MND, where is it held, how researchers present their work at the conference, other meetings that complement the Symposium, and an interactive session that everyone can take part in.

### People ↑

Read about the people coming to the Symposium this year, without whom the event wouldn't be possible.

### Biology ↑

The science of life. The main players involved in making us tick, from cells, molecules, nerves to the whole brain.

### Symptoms & disease management ↑

Understanding, managing and improving the care of people with MND and their supporters.

### Causes ↑

Read about the factors scientists study to find out more about what causes MND.

### Diagnosis & prognosis ↑

What is MND anyway? Find out about current status of diagnosis, the search for biomarkers to diagnose and measure disease progression, and how technology available now and in the future will impact MND.

### Treatments ↑

From bench to bedside. Covering medicines from those currently available to people with MND to those in development and into the future.

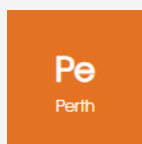
## SympWatch (Sw) ↑

For the first time, you can watch full presentations from the International Symposium on ALS/MND.

These SympWatch videos are a selection of presentations from the 30th Symposium in Perth, Australia. To help guide you through the talks, SympWatch videos include useful 'pop ups' explaining some of the scientific language used by the researchers.

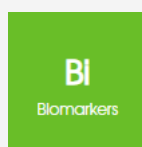
Here you can find a list of each SympWatch video, linked to the respective tile on the Periodic Table:

### SympWatch Videos



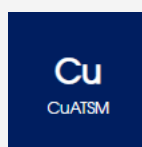
#### Welcome to the Symposium

Featuring a welcome to country performance



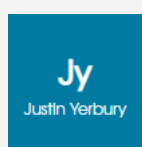
#### Professor Martin Turner:

The **Biomarker** Challenge: are we there yet?



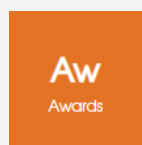
#### A/Professor Peter Crouch:

Relevance of the therapeutic **CuATSM** to sporadic ALS



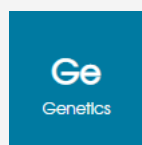
#### Professor Justin Yerbury:

The fine balance of **Proteostasis**



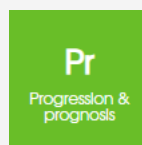
#### Dr Laura Ferraiuolo: 11th Paulo Gontijo award winner

Investigating the role of Astrocytes in ALS



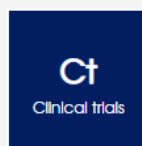
#### Professor Naomi Wray:

Future directions in ALS **genomics**



#### A/Professor Andrea Calvo:

How frequent are **pauses** in ALS progression? Results from a population-based cohort



#### Dr Ralph Kern:

Modulation of innate immunity by MSC-NTF cells  
(**NurOwn** correlates with ALS clinical outcomes)

## Perth (Pe) ↑

Organised by the MND Association, the International Symposium on ALS/MND is the largest medical and scientific conference specific to MND/ALS in the world. Held annually at venues around the world, this year's 30th Symposium sees us returning to Australia on 4-6 December 2019. This time, in the city of Perth.

Each Symposium is hosted by an ALS/MND Association from the home country, and this year's hosts are [MND Australia](#), the leading charity in Australia providing care and support to people affected by MND, as well as funding vital research into finding a cure. They will be hosting in partnership with [MNDAWA](#) (MND of Western Australia).

Combining big-city attractions with relaxed, informal surroundings, Perth has everything you need for an unforgettable visit. It boasts exciting architecture, inspiring museums and galleries, a diverse selection of shops, an abundance of restaurants and bars, a vibrant entertainment scene and wonderful open spaces.

Find out more about Perth – including what to do if you're interested in exploring the city either before, after or during the conference.

### SympWatch



**Opening session - Welcome to the Symposium**  
Featuring a welcome to country performance

### Video



Sally Light – Symposium 2019 Wrap Up

## MND Australia and MNDAWA (Au) ↑

[MND Australia](#) will be hosting the 30th International Symposium on MND/ALS this year in partnership with [MNDAWA](#) (Motor Neurone Disease Association of Western Australia).

**MND Australia** is a non-profit organisation that is the national voice representing all Australians who share the vision of a world without MND. Drawing on 35 years of experience, MND Australia works with a national network of State MND Associations to advocate, educate and raise awareness. Their goal is to empower Australians impacted by MND to live better for longer. Until there is a cure, MND Australia's research arm, the MND Research Institute of Australia, will promote and fund the best research with the greatest chance of making MND treatable.

**MNDAWA** is a non-profit organisation that is the specialist support organisation in Western Australia. It is committed to working with people living with MND, their carers and families, ensuring they will not be alone.





## Global Walk to D'feet MND (Gw) ↑

The first ever [Global Walk to D'feet MND](#) was held as part of the 30th International Symposium on ALS/MND this year to raise awareness of ALS/MND. The 5km, wheelchair accessible, walk occurred in the evening of the first day of the Symposium (Wednesday 4 December) along Perth's picturesque Swan River.

Following the walk, Cytokinetics warmly invited all delegates who took part in the walk to join them as they honoured and recognised the contributions of advocacy groups worldwide with local Australian barbecue food and refreshments served in the Summer Garden at the Perth Convention and Exhibition Centre.

We had an amazing turnout of over 400 people all wearing their respective country's ALS/MND association or institution T-shirts.



### Resources

- MND Research Blog: [Global Walk to D'feet: Highlights from Perth](#)
- MND Association Symposium website: [Global Walk to D'feet](#)
- MND Association website: [Organise your own Walk to D'feet MND](#)

### Video



FightMND - Drone footage



Time-lapse of the Global Walk to D'feet MND

## Awards (Aw) ↑

Various awards were presented at the 30th International Symposium in Perth.

The [International Alliance Humanitarian Award](#) is given annually to recognise an individual or group whose work has made a contribution of international significance to people affected by ALS/MND. This year, the Humanitarian Award was awarded to **Dario Ryba**, President of the ALS Association of Argentina (Asociacion ELA Argentina).

At the Allied Professionals Forum before the Symposium, the International Alliance of ALS/MND Associations [Allied Health Professional Award](#) is presented by the International Alliance of ALS/MND Associations to recognise an individual committed to providing exceptional care to people with ALS/MND. The recipient of the 2019 award was Rachel Marsden from Oxford MND Care Centre, UK.

Established in 2008, the **Paulo Gontijo Award** recognises researchers below 40 years of age who have dedicated their scientific work to investigate the causes and treatment of motor neuron disease. The [11th Paulo Gontijo Award](#) internationally recognised **Dr Laura Ferraiuolo**, from the Sheffield Institute of Translational Neuroscience ([SITraN](#)), for her investigation into the role of astrocytes (star-shaped cells that support neurons, particularly their secreted particles, as well as for her continued dedication to understand and find a treatment for MND.

The first annual [Healey Center Award for Innovation in ALS](#) was announced this year during the joint closing session of the Symposium. This was awarded to the team that brought to trial the first antisense oligonucleotide (ASO) therapy for ALS called Toferson for SOD1-mediated ALS.

Each year, the MND Association present **Biomedical and Clinical Poster Prizes** to celebrate the high quality of posters presented by early-career researchers during the symposium. The Clinical poster prize was awarded to **Ruben van Eijk** from University Medical Centre Utrecht, Netherlands – 'Optimising the ALSFRS-R as a clinical trial endpoint' ([CLT-14](#)). The Biomedical poster prizes were awarded to **Laura Reale** from University of Tasmania, Australia – 'Does mislocalised TDP-43 in excitatory neurons of the motor cortex cause ALS-like pathology in the spinal cord?' ([IVV-32](#)), and **Nora Markus** from University of Sheffield, UK – 'AI-led drug discovery identifies Nilotinib as a lead compound for ALS' ([TST-41](#)).

### SympWatch



Paulo Gontijo award and Humanitarian award presentation



Dr Laura Ferraiuolo: 11th Paulo Gontijo award winner - Investigating the role of Astrocytes in ALS

## Satellite meetings (Sm) ↑

Whilst the main Symposium runs over three days, Wednesday to Friday, there are also several smaller satellite meetings in the days before as well as during the Symposium itself. These cover several subject areas that delegates can attend, encouraging further knowledge sharing.

The [International Alliance of ALS/MND Associations](#) organise meetings to serve the broader ALS/MND community: The **Annual International Alliance Meeting**, on the 1-2 December 2019 and **Allied Professionals Forum (APF)** on the 3 December.

The **Alliance Meeting** is attended by representatives of ALS/MND associations from around the world and provides the opportunity for these associations to meet and share knowledge of supporting people living with ALS/MND. It is also an opportunity for representatives from around the world to discuss developments and planning from their organisations, patient care and funding, and the role and activities of the Alliance and its Board of Directors. [View the 2019 agenda here.](#)

Every year the International Alliance invite the host association to organise a free ALS/MND Connect session (formerly called Ask the Experts), as an addendum to the Alliance meeting. It is designed specifically for people living with MND and their caregivers to attend an afternoon of presentations by neurologists and researchers, then participate in a 'question and answer' session afterwards. This session was chaired by **Professor Merrilee Needham** (Fiona Stanley Hospital, Australia) and we heard from **Professor Matthew Kiernan** (The University of Sydney, Australia), **Professor Ammar Al Chalabi** (King's MND Care and Research Centre, United Kingdom), and **Professor Leonard Van den Berg** (University Medical Center Utrecht, Netherlands). The session was live streamed on Facebook, so anyone from around the world could take part.

The **APF** is for healthcare professionals, such as physiotherapists, nutritionists, speech-language therapists and more, who specialise in ALS/MND. It is an educational and training forum and offers healthcare professionals from around the world an opportunity to share ideas about good practice in the daily care management of people living with ALS/MND.

### Video



Scientific Update from the Scientific Advisory Council of the International Alliance of ALS MND Associations



ALS/MND Connect Facebook live stream 2019



Allied Professionals Forum recordings 2019



Dr Nick Cole - Satellite meetings 2018



## People with MND (Pw) ↑

People living with MND, their carers and families are at the heart of everything we do, and our reason for organising the Symposium every year. Whilst the event is aimed primarily at scientists and healthcare professionals, there is an opportunity for people with MND to attend, via the [Patient Fellows Programme](#) managed by the ALS Therapeutic Development Institute (**ALSTDI**). This allows some people with MND to be funded to attend the Symposium and then share their experiences via an article or social media.

This year's patient fellows were Ed Buckingham (US), Sunny Erasmus (US), Philip Green (US), Dave Healey (Australia), Jonathan Jenson (US), and Gwen Petersen (US).

### Video



Philip Green – Symposium Patient Fellow



Ed Buckingham – Symposium Patient Fellow



Sunny Erasmus – Symposium Patient Fellow

### Resources

- MND Research Blog: [MND Engage - collaboration, engagement and communication](#)
- From 2018 Symposium: [Catherine Collet - Patient Fellows Programme](#)

## Poster presenters (Po) ↑

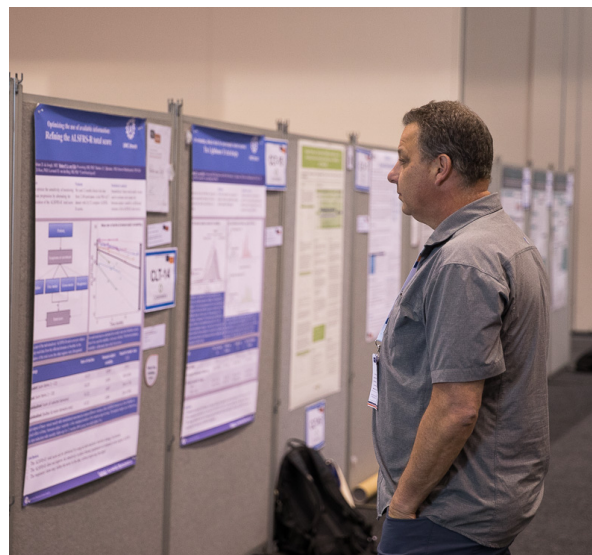
Researchers who would like to present at the Symposium must submit an abstract – an overview of their research and findings. A Programme Committee then decides who will be given the chance to present to an audience from the stage (oral presentations) and who will be offered a poster – the chance to display their work in the form of a poster at a dedicated session. Some submissions do not get offered either.

This year, as well as having 110 speakers, we also have **over 420 poster presentations**. Giving researchers the opportunity to talk about their work with the wider MND research community with a poster, means that even more exciting and innovative work can be shared than would be possible with just oral presentations. The poster sessions encourage networking and collaboration, bringing together researchers, clinicians, neurologists and other healthcare professionals. The poster sessions also give researchers who are still in the early stages of their work, and don't yet have any results, to present in the Work in Progress section.

You can read all the [abstracts online](#). Where we have mentioned a specific poster in a tile on the periodic table, we have included the code for that poster, for example RNM-03. This tells you that the abstract for that poster can be found in the Respiratory and Nutrition Management section and it is abstract number three.

### At the Symposium

**Ruben van Eijk** from University Medical Centre Utrecht, Netherlands, won the **2019 Clinical poster prize** for his work on '*Optimising the ALSFRS-R as a clinical trial endpoint*' ([CLT-14](#)). Ruben demonstrated a great attempt to improve the known drawbacks of the ALSFRS-R tool which could mean treatment effects could be identified faster or with less patients on placebos required for measurement of clinical trial outcomes. You can watch Ruben sum up his poster this year below:



### Videos



Ruben van Eijk - Optimising the ALSFRS-R as a clinical trial endpoint poster

## Platform presenters (Pp) ↑

Researchers who would like to present at the Symposium must submit an abstract – an overview of their research and findings. A Programme Committee then decides who will be given the chance to present to an audience from the stage – platform presentations and who will be offered a poster – the chance to display their work in the form of a poster at a dedicated session. Some submissions do not get offered either.

Platform presentations are prestigious, and Perth will hear **110 speakers** over the three days of the Symposium. These talks will be split between three sessions Biomedical (A), Clinical (B), and Alternative mixed (C). Each session is organised by specific themes such as genetics, clinical trials or neuroimaging. See the [full programme](#) for this year's Symposium.

Alongside these presentations we also invite several **plenary (keynote) speakers** who are the world experts in their respective fields. Their talks complement the Symposium sessions by providing an overview of a variety of topics across the ALS/ MND research and clinical management spectrum.

You can read all the [accepted abstracts online](#). Please note, the page may take a couple of minutes to load. All platform presentations have a code beginning with 'C' followed by a number (e.g. C50). This will help you locate the specific abstract mentioned throughout the periodic table topics.



## Plenary speakers (PI) ↑

Every year we invite a number of plenary speakers who are experts in their respective fields. Their talks complement the Symposium sessions by providing a coherent overview on a variety of topics across the ALS/MND research and clinical management spectrum. This year's 22 plenary speakers were:

- **Dr Jeffrey J Iliff** (USA) – 'Glymphatic system dysfunction as a driver of protein mis-aggregation in neurodegenerative disease' ([C1](#))
- **Professor Martin Turner** (UK) – 'The biomarker challenge: What is it, and are we there yet?' ([C2](#))
- **Professor Justin Yerbury** (Australia) – 'The fine balance of proteostasis and its implications for ALS' ([C3](#))
- **Associate Professor Kenneth Rodgers** (Australia) – 'Non-protein amino acids and neurodegenerative disease' ([C7](#))
- **Dr Hiroshi Nishimune** (USA) – 'Neuromuscular degeneration in ALS and SMA' ([C19](#))
- **Professor Nortina Shahrizaila** (Malaysia) – 'ALS phenotypes, demographics and clinical management in Asia' ([C23](#))
- **Professor Naomi Wray** (Australia) – 'Future direction in ALS genomics' ([C27](#))
- **Professor Don W Cleveland** (USA) – 'Designer drug therapy for human neurodegenerative disease' ([C32](#))
- **Professor Steven Finkbeiner** (USA) – 'iPSC-derived models for genetic and compound screening in ALS' ([C33](#))
- **Professor Erik P Pioro** (USA) – 'Pseudobulbar effect in ALS: Not (only) a laughing matter' ([C37](#))
- **Professor Samar Aoun** (Australia) – 'Supporting MND family carers from diagnosis to bereavement: The palliative approach to care' ([C52](#))
- **Dr Melinda S Kavanaugh** (USA) – 'Research and support for young caregivers in families with ALS' ([C53](#))
- **Dr Gen Sobue** (Japan) – 'Lessons from SBMA study: Pathophysiology, clinical characteristics and treatment strategies' ([C56](#))
- **Professor Shigeki Kuzuhara** (Japan) – 'ALS-PDC of the Kii Peninsula, Japan: Clinical and neuropathological features and epidemiology' ([C57](#))
- **Dr Arindra Nath** (USA) – 'Investigating the role of endogenous retroviruses in ALS' ([C60](#))
- **Professor Luc Deliens** (Belgium) – 'Palliative care and healthcare utilisation at the end of life in people with ALS' ([C65](#))
- **Dr Julian Grosskreutz** (Germany) – 'Is ALS a network disease?' ([C68](#))
- **Dr Susan E Mathers** (Australia) – 'Progressive neurological diseases: Modelling care' ([C77](#))
- **Associate Professor Bradley Turner** (Australia) – 'Mouse models of ALS: Past, present and future' ([C90](#))
- **Professor Capucine Morelot-Panzini** (France) – 'The multidimensional nature of respiratory failure in ALS' ([C105](#))
- **Professor David J Berlowitz** – University of Melbourne (Australia) – 'The management of disordered breathing in MND' ([C106](#))
- **Associate Professor Thomas J Oxley** (Australia) – 'The dawn of brain computer interfaces' ([C110](#))

## Healthcare professionals (Hp) ↑

As well as researchers, many healthcare professionals attend the Symposium to help expand their existing knowledge of MND. All fields are represented at the Symposium from respiratory experts to physiotherapists. It is a chance for them to hear innovative talks from experts in their field from nutritional support to quality of life and learn about new techniques and ways to improve their practice.

Helping to educate healthcare professionals is a priority for the MND Association as this will help those affected by MND have a better multi-disciplinary care plan, as well as improving their quality of life. As part of this education the Association runs conferences, study days and online learning for professionals on a range of topics. Find out more about these [events for healthcare professionals](#).

View this year's Allied Professional Forum (APF) agenda [here](#). Our previous Head of Education and Information, Rachel Boothman, joint-hosted the session and gave a presentation on 'Let's talk about end of life in ALS/MND - a masterclass for professionals'.

### Videos



Recordings from the 2019 APF



Rachel Boothman – Let's talk about end of life in ALS/MND - a masterclass for professionals

## Neuromuscular junction (Nj) ↑

The neuromuscular junction (**NMJ**) is a chemical synapse formed by the contact between a motor neuron and a muscle fibre. It is at the NMJ that a motor neuron can transmit a **signal** to the muscle fibre, causing **muscle contraction**.

Muscles require innervation (literally meaning 'to put nerves into', so when nerves go into muscle fibre, they innervate that muscle) to function and even just to maintain muscle tone to avoid the muscle from wasting away. In the NMJ nerves from the central nervous system and peripheral nervous system are linked and work together with muscles. Motor neurons release a **neurotransmitter** called acetylcholine which crosses the synapse at the NMJ and binds to receptors on the muscle fibre which results in a muscle contraction.

Studies have revealed the important involvement of muscles and NMJs in the initial stages of MND. It is acknowledged that degeneration to the NMJ, leading to skeletal muscle wasting, is a key point in MND clinical symptom onset and disease progression.

### At the Symposium

Plenary speaker Dr Hiroshi Nishimune opened [Session 3A: Synaptic Pathology](#) with his presentation 'Neuromuscular degeneration in ALS and SMA' ([C19](#)). MND patient and animal models show signs of degeneration of NMJs prior to the degeneration of motor neuron cell bodies. In a SOD1 mouse model, this degeneration still occurred when apoptosis (the death of a cell as part of the natural progression of the cell's life) of motor neuron cells was suppressed. This suggests a mechanism that actively degenerates NMJs separately from cell body deterioration. Dr Nishimune discussed these mechanisms and the development of novel approaches to stop degeneration of NMJs.

Posters focusing on this topic included a presentation which investigates synaptic dysfunction in a C9orf72 zebrafish model ([IVV-04](#)).

Recent data revealed an alteration of synaptic transmission and inappropriate repair in NMJs in a SOD1 mouse model prior to motor symptoms, which are known to be regulated by perisynaptic Schwann cells (PSCs), suggesting that the alteration of PSC function may contribute to NMJ vulnerability. Researchers from Canada aim to determine if PSC functions at NMJs contribute to the resistance to disease progression ([IVV-24](#)).

Researchers from Japan and the USA presented their work about a novel treatment using human mesenchymal stem cells to treat degeneration of NMJs in a mouse model of MND ([TST-22](#)).

Dr Tosolini presented a poster which discusses axonal transport, the movement of proteins and other substances through a neuron that is vital for neuronal function and survival ([IVV-28](#)).

### Videos



Dr Andrew Tosolini – Neuromuscular Junction



## Mitochondria (Mt) ↑

Mitochondria are organelles – specialised units within a cell that have a specific function – and are essential for a variety of cellular processes including providing **energy** for the cell (bioenergetics, calcium homeostasis – which regulates the concentration of calcium ions in the fluid outside the cell, lipid biosynthesis – the production of lipids (fats which are the main form of stored energy in most organisms, and apoptosis – normal and controlled cell death.

Mitochondrial dysfunction is a common feature of many neurodegenerative diseases including MND. Disruption of mitochondrial structure, bioenergetics and stabilisation of calcium ions has been widely reported in people with MND and models of the disease and has been suggested to be directly involved in the development of MND.

### At the Symposium

Researchers from the USA have studied the bioenergetics of platelets (which are involved in blood clotting) in a group of people with MND over time and compared them with healthy controls, looking at differences, changes and correlations with clinical measures of disease progression. Recent studies have suggested that these bioenergetic profiles can reflect mitochondrial dysfunction in skeletal muscle making them a possible biomarker for neuromuscular defects in MND ([C85](#)).

### Resources

- MND Research Blog: [Focusing on mitochondria: a potential target for early MND treatment](#)

## Modelling MND (Mo) ↑

In order to understand what goes wrong in MND, researchers need to study 'something' that, to all intents and purposes, mimics the biology of the disease. Ideally that 'something' has to be readily available, tangible, accessible, and available with a large enough number of samples so that any findings can be reproduced and confirmed.

There is currently no way to visualise all the complex interactions that happen in MND. For example, observing all of the biology of motor neurones in living people is impossible, and so researchers use models of the disease.

There are generally three types of models that are used to research MND:

- ***In vitro*** (meaning 'in the glass') models use isolated cells in a lab dish, with the most widely used being induced pluripotent stem cells (iPSCs). These are skin cells taken from people with MND that are transformed into stem cells – cells with the potential to turn into different types of cells, including motor neurones.
- ***In vivo*** (meaning 'within the living') models include testing in living organisms, with the most widely used animals being zebrafish, fruitflies, worms or mice.
- ***In silico*** (meaning 'in silicon' as in silicon microchips) modelling, while not as common, is used to perform a computer simulation.

### At the Symposium

Plenary speaker **Professor Bradley Turner** opened [Session 8A: Disease Models](#) by talking about '*Mouse models of ALS: Past, present and future*'. Even though advances in the development of induced pluripotent stem cell (iPSC) models of MND have been made, animal models, particularly those using mice, provide useful tools to study disease progression and test potential new therapies for MND. In the 25 years since the first mouse model of MND was generated (the SOD1 mouse model, and despite its limitations in predicting effective drugs for MND to date, the SOD1 mouse model has provided important insights into key mechanisms of the disease. In the past decade, more diverse mouse models have been developed, largely based on TDP-43, FUS and C9orf72 mutations. Prof Turner discusses the strengths, limitations and potential of traditional and emerging mouse models of MND, with particular emphasis on relevance and translational validity for MND ([C53](#)).

Models of MND are also discussed in [Session 4A: Therapeutic Strategies](#). Researchers in the USA have developed human models of MND using iPSCs, and Steven Finkbeiner will discuss their experience and how they have used their models to conduct genetic screens and develop potential therapies ([C53](#)).

Elsewhere in the USA, researchers have used 'machine learning' (using algorithms and statistical models) to accelerate drug discovery in pre-clinical models ([C35](#)).

More presentations on how models of MND are being used in MND research were presented in poster themes [In Vivo Experimental Models](#) and [In Vitro Experimental Models](#).

## Video



Dr David Gordon (University of Oxford) talks about modelling MND



Dr Rickie Patani (University College London) on using stem cells to model human MND



Dr Clive Svendsen talk about modelling MND in a chip

## Resources

- Website resource: [Understanding animal research](#)
- MND Research blog: [iPSC collection of blogs](#)

## Retroviruses (Rv) ↑

There is evidence to suggest that **Human Endogenous Retroviruses (HERVs)** may be involved in MND. Endogenous means 'within the body' and HERVs are genes that are found in our genome. Our genome contains all our genetic material, in the form of DNA, and is stored in the nucleus of all cells in our body. HERV-K has been directly linked to MND and has been found in the brain tissue of people with MND.

For a long time, HERVs were believed to be 'fossil viruses' or 'junk' DNA, rendered inactive as they became defective or mutated as they were passed through generations over millions of years. They comprise up to 5-8% of the human genome and there is now evidence to suggest that they are not inactive.

HERVs are a type of gene called a **retrotransposon** which can 'jump' from one part of the genome to another. They contain DNA and use a 'copy and paste' mechanism which enables them to integrate themselves into the genome at a different place. In a process called transcription, the viral DNA sequences are converted into RNA, a short section of genetic code which, in normal cells, encodes for the proteins that make up the building blocks of our bodies. In virus-infected cells, the RNA is moved out of the nucleus into the cytoplasm. Using an enzyme called reverse transcriptase, the RNA is then 'copied' to make identical DNA sequences, moved back into the nucleus and 'pasted' back into the genome near another gene. This can cause disease if too many copies of the gene are made.

Using antiretroviral therapies, it may be possible to stop the malformed proteins being made.

### At the Symposium

'Investigating the role of endogenous retroviruses in ALS' ([C60](#)) is the topic of the talk being given by plenary speaker **Dr Avindra Nath** and opens [Session 6A: Human Cell Biology and Pathology](#). He discusses the activation of HERV-K and how strategies are being developed to block the unique enzymes encoded by the virus, to develop antisense molecules to block the expression of the protein and two clinical trials investigating the effect of available antiretroviral drugs on HERV-K.

We also hear about '*An antiretroviral response as a trigger of FUS proteinopathy*'. Proteinopathy is any disease, particularly neurodegenerative disease, caused by a malformed protein. Mutant FUS, which is responsible for around 5% of inherited MND cases, is found in the cytoplasm where it aggregates (forms sticky clumps) marking the onset of FUS proteinopathy. Researchers from the UK are hoping to establish the most likely stressor(s) which can trigger persistent aggregates containing mutant FUS ([C61](#)).

In the supporting poster theme [Pre-Clinical Therapeutic Strategies](#), researchers from Australia compare different viral delivery methods using a TDP-43 mouse model of MND, which will guide pre-clinical testing of potential therapies for MND ([TST-28](#)).

### Resources

- MND Research Blog: [Lighthouse Project shines a beacon on HERVs and their role in ALS](#)
- MND Research Blog: [Could MND be treated by HIV drugs?](#)

## Nutrition (Nu) ↑

With MND, the way a person eats and drinks may need to be adapted to help them get the nutrition and fluids their body needs. They may experience difficulties with chewing and swallowing (see tile [Sw](#) for more information on swallowing), problems with hand and arm control, reduced mobility (making food preparation difficult) and fatigue, which can make the effort of eating and drinking tiring in itself.

Weight loss in MND is associated with faster disease progression and shorter survival and has several possible causes. These include loss of appetite, difficult in swallowing and hypermetabolism, which is an increase in the rate at which energy is burned – even though mobility may be limited, a person 'burns off' more calories than they consume.

Some people with MND choose to have a **gastrostomy** – a surgical opening through the abdomen into the stomach. This allows tube feeding – a way of passing specially prepared food and fluids straight into the stomach.

### At the Symposium

[Session 9B: Dysphagia and Nutritional Management](#) opened with a presentation that discussed the frequency and impact of loss of appetite on change in body weight and composition in people with MND compared to health controls ([C95](#)).

This was followed by a talk that addressed the fact that hypermetabolism is not always associated with greater weight loss. Dietary intake of people with MND is compared to healthy controls to determine whether hypermetabolic MND patients consume more calories to offset higher resting energy expenditure – the energy cost of involuntary functions such as breathing, cardiac output and regulation of body temperature ([C96](#)).

In the corresponding poster theme: [Respiratory and Nutritional Management](#), researchers from the UK present their findings from a review of the literature to identify the key factors associated with nutritional behaviours and outcomes in people with MND ([RNM-03](#)). Nutrition was also covered in several 'work in progress' posters – [CP-04](#), [CP-06](#) and [CP-07](#).

### Video



Dr Fredrick Stein – Weight loss in MND



Professor Chris McDermott – Nutrition session summary

### Resources

- MND Research Blog: [Dysphagia and nutritional management: Highlights from Perth](#)
- Information sheet: [Eating and drinking with MND](#)
- Information sheet: [Tube feeding](#)
- MND Research Blog: [Tackling weight loss in MND - from ProGas to PostGas](#)

## Swallowing (SI) ↑

Swallowing problems, known as **dysphagia**, affect at least two-thirds of people with MND during their illness. This is due to a weakening of the muscles in the mouth and throat. If MND affects a person's ability to swallow, it becomes harder for them to eat and drink. As a result, they are likely to experience dehydration and weight loss.

### At the Symposium

Our platform presentations included a talk about a pilot trial to assess the feasibility and effect of swallowing exercises and diet in people with MND. Presented by **Professor Victoria Flood**, this work followed promising results from two trials looking at exercises for the strengthening of the expiratory muscles, and a study using a mouse model in which 20% of calories came from extra virgin olive oil, leading to increased survival rate, improved motor co-ordination and less muscle atrophy compared to controls ([C97](#)).

Another presentation, given by **Dr Emily Plowman**, addressed the need for a standardised swallowing screening test for use in MND clinics and identifying simple clinical markers to reliably detect swallowing impairment in people with MND ([C98](#)). Check out her summary of this model, called **PRISIM** (Physiologic Risk Index of Swallowing IMpairment) in the video interview.

In the corresponding poster theme [Clinical Management and Support](#), Rebecca Francis presented her review of the evidence to address the question 'How do cognitive and/or behavioural changes impact on a person with MND's ability to recognise, understand and manage dysphagia?' ([CMS-18](#)).

One of the main symptoms of dysphagia is the occurrence of choking with thin liquids. Because of this, there is an increased risk of dehydration which, in turn, affects health and performance. Researchers from Brazil have evaluated the level of functional hydration according to dysphagia in people with MND and present their findings in poster [RNM-07](#).

### Video



Dr Emily Plowman – PRISIM

### Resources

- MND Research Blog: [Dysphagia and nutritional management: Highlights from Perth](#)
- Information sheet: [Swallowing difficulties](#)
- Webpage: [Managing dysphagia](#)
- Webpage: [Swallowing, eating and drinking](#)



## Caregiver support (Cs) ↑

When someone is diagnosed with MND, the changes affect not only the person with the disease but also those close to them. Becoming a carer for someone with MND can be very challenging and, over time, the level of care needed will increase – sometimes rapidly.

Supporting someone with MND can often feel emotionally overwhelming but there can be many positive emotions, such as satisfaction when a task or challenge is successfully completed, especially if this has involved both the carer and the person with MND. It is important that the carer takes time to look after their own needs, even if this feels impossible when facing the challenges of supporting someone with MND.

### At the Symposium

In [Session 5B: Carer and Family Support](#), plenary speaker Professor Samar Aoun talks about a number of evidence-based initiatives to support carers from diagnosis to bereavement, that need to be implemented or strengthened in standard practice in order to improve the health and social well-being of family carers ([C52](#)).

Our second plenary speaker in this session, Dr Melinda Kavanaugh discusses current research on children and youth caregivers in ALS/MND, perspectives of the person with MND, how research has been used to inform evidence-based interventions and supports, and a roadmap for future inclusion of children and youths in caregiving research, programming and support worldwide ([C53](#)).

In the supporting poster themes we learn how the unique insight that people living with MND and their caregivers give can help design clinical trials that are more patient-centred, and how their experience of the disease impacts on their expectations and concerns regarding clinical trial participation ([CLT-02](#)). Researchers from Ireland look at how the quality and role of relationships, and social support, impacts on caregivers' psychological wellbeing ([COG-12](#)), and how the needs of caregivers might be identified to inform the development of interventions ([COG-13](#)).

Researchers in Switzerland are carrying out a systematic review of evidence to establish the needs of caregivers of people with MND at different stages of the disease ([CP-13](#)) and, in Denmark, researchers are reviewing the evidence that addresses the ongoing needs and psychological consequences experienced by family caregivers after the death of the person with MND, with the aim of providing information on the long-lasting impact of MND and the need for continued support ([CP-20](#)).

Posters [CP-14](#), [CP-17](#) and [CMS-14](#) also cover this topic.

### Video



Samar Aoun - Caring for the Carer



Melanie Kavanaugh - Role of a Young Carer

## Resources

- MND Research Blog post: [Carer and family support: Highlights from Perth](#)
- MND Research Blog: [Recognising and supporting the role of informal carers](#)
- Guide: [Caring and MND: support for you guide](#)
- Guide: [So what is MND anyway?](#) (for young carers)
- Website resource: [Support for carers](#)
- Website resource: [Children and young people](#)

## Cognition & behaviour (Cb) ↑

Up to half of people with MND experience changes to how they think and behave, and these affect people in different ways. For some they will have little effect on daily life, while others will need significant day-to-day support. In a small number of cases, people with MND develop **frontotemporal dementia** (FTD).

People with MND may experience changes to their thinking and learning, language and communication, and behaviour and emotions. It may become more difficult for them to make and carry out plans, process information and solve problems. They may find it harder to recognise words when reading or writing, have difficulty spelling or find it hard to follow conversations. They might also begin to lack enthusiasm, find it difficult to manage emotions and behave inappropriately in social situations.

If a person is affected by FTD they will experience symptoms similar to those already described but with greater severity. With FTD, memory is not usually affected although it may appear that it is due to difficulties with concentration and taking in new information.

### At the Symposium

We heard about how hyperexcitability (an excessive reaction to stimuli) of the motor cortex could be a reliable diagnostic marker of MND from an early stage and that features of cortical hyperexcitability precede the development of cognitive dysfunction. The motor cortex is the part of the brain that nerve impulses that initiate voluntary muscular activity originates from ([C13](#)).

It is traditionally believed that eye motor function is preserved in MND but abnormalities in eye movements have been described in people with MND. Researchers in Italy have assessed whether some eye movement abnormalities represent a good marker of the presence of cognitive and/or behavioural deficits in people with MND ([C40](#)).

Researchers in Ireland investigate the earliest cognitive changes that occur in pre-symptomatic C9orf72 carriers because, with the arrival of potential genetic therapies targeting C9orf72 carriers, definition of onset of disease is important ([C41](#)).

Many more presentations on how cognitive and behavioural changes affect different aspects of MND occurred in the poster theme: [Cognitive and Psychological Assessment and Support](#).

Hear Ratko Radakovic talk about the MiND Toolkit below ([C79](#)), a method of structuring decision-making and giving techniques of how to manage cognitive and behavioural changes that can occur in around 50% of people affected by MND.

## Video



Ratko Radakovic – MiND Toolkit

## Resources

- Webpage: [Cognitive change, frontotemporal dementia and MND](#)
- Webpage: [Emotions, thinking and behaviour](#)
- Information sheet: [Changes to thinking and behaviour with MND](#)
- Information sheet: [Emotional and psychological support](#)
- MND Research Blog: [MND and the mind - who is affected?](#)
- MND Research Blog: [Cognition and FTD: Highlights from Glasgow](#)
- MND Research Blog: [Are there differences between FTD alone and FTD-MND?](#)

## Respiration (Re) ↑

MND can affect the way a person breathes by weakening the muscles that control breathing. Although this cannot be reversed, there are treatments that can help reduce symptoms such as disturbed sleep, fatigue and anxiety, and enable the person to breathe more effectively.

When breathing becomes weaker a machine may be used to support breathing. This is known as assisted ventilation. There are two types of assisted ventilation: non-invasive ventilation, where a machine supports breathing by boosting the intake of normal air through a mask, and tracheostomy ventilation, where a tube is inserted into the windpipe through the front of the neck, which enables a ventilator to support breathing.

The use of ventilation may not be suitable for everyone. If appropriate, it may help to relieve breathing problems but will not stop the progress of the disease.

### At the Symposium

Plenary speaker Professor Capucine Morelot-Panzini opens [Session 9B: Respiratory Support](#) and talks about the '**Multidimensional nature of respiratory failure in ALS**'. Respiratory muscle weakness impairs quality of life in relation to sleep-related respiratory disorder and dyspnea (shortness of breath), and respiratory failure is the most common cause of MND-related death. Using a questionnaire, dyspnea was assessed in people with MND requiring non-invasive ventilation (NIV) to try to provide new ways in which to manage dyspnea ([C105](#)).

The second plenary speaker in this session, Professor David Berlowitz, talks about 'The management of disordered breathing in MND'. He addresses the evidence for respiratory support in ALS/MND and outlines opportunities to increase the evidence base for this important supportive therapy ([C106](#)).

Many more presentations on respiration will be given in the corresponding poster theme [Respiratory and Nutritional Management](#) ([RNM-05, 10, 15-18, 20, 26](#)).

### Resources

- Information sheet: [Support for breathing problems](#)
- Information sheet: [Ventilation for motor neuron disease](#)
- Information sheet: [Withdrawal of ventilation with MND](#)
- MND Research Blog: [Choices around tracheostomy ventilation](#)
- MND Research Blog: [Withdrawing ventilation support at the request of the patient: the clinical, moral and legal issues](#)

### Video



Dr Esther Hobson on gastrostomy, non-invasive ventilation, and utilising telemedicine in MND care

## Physical exercise (Ph) ↑

The stories about MND and physical activity that make it into the media feature prominent sports people who have been very active for a number of years. While this is good for raising awareness of the disease, it also raises concerns for people living with MND.

Most concerns fall into two categories: did the amount of physical activity I undertook **before my diagnosis** cause my MND and can I continue with physical activity **after my diagnosis**, or will this make my MND worse?

Physical activity ranges from gentle exercise, like walking, to more vigorous daily activity like working out at a gym, to the levels achieved by professional sportspeople and elite athletes.

Exercise is widely recommended to the general population due to its benefits to health and wellbeing. It improves the cardiovascular, respiratory, musculoskeletal, and endocrine functions and leads to psychological wellbeing. Many people with MND specifically ask whether they can safely continue to exercise regularly without fear of accelerating their disease. At present, there is no firm evidence that exercise exerts a harmful effect, although avoidance of very strenuous activity would seem to be sensible. Low-grade, managed exercise programmes may even be of benefit.

For many people with MND, exercise played an integral role in their pre-diagnosis lives. A wish to continue exercising, in the hope it will have positive effects on endurance and strength, is understandable. While pre-diagnosis exercise is likely to have involved aerobic training and strengthening programmes, research has shown that moderate exercise can slow functional decline whereas high intensity training can be detrimental.

### At the Symposium

In [Session 6B: Palliative Care](#), Dorothy Lull discusses the effect that physical exercise and physical therapies have on patients' quality of life and affective state ([C67](#)). In the poster presentations, researchers in Australia are carrying out a systematic review of clinical trials investigating diet and exercise interventions in people with MND, to identify effective treatment options and assist multidisciplinary teams to better support people living with the disease. It will also help to identify current gaps in knowledge and will inform the direction of future research ([CP-04](#)).

### Resources

- MND Research Blogs:
  - [Does physical activity cause MND? A fresh look at the evidence](#)
  - [Exercise after diagnosis - a closer look at the evidence](#)
  - [What's going on inside? Possible mechanisms associated with physical activity and MND](#)
  - [Physical activity and the odds of developing MND](#)
  - [Professional football and MND - looking at the evidence](#)
  - [Physical activity and MND. Is there a link?](#)
- Information sheet: [Physiotherapy](#)



## Palliative Care (Pc) ↑

**This section talks openly about death and end of life decisions.**

The aim of hospice and palliative care is to give the best possible quality of life with a life-shortening illness. For maximum benefit to people with MND, this type of care is recommended from the point of diagnosis onward.

Palliative care refers to specialised care services that focus on quality of life and symptom control when an individual has an illness that can't be cured. This includes practical help, medication to ease symptoms and support for the individual and their family. Palliative care isn't just for end of life. It may be given earlier in a person's illness in conjunction with other therapies treating the condition.

Palliative care is of utmost importance in MND and focusing on managing symptoms and improving quality of life of people living with the disease is a priority of healthcare professionals. Because of the nature of the disease, it is important for those affected by MND to know about the symptoms they should expect as the disease progresses, and how best to manage them. Research is always ongoing to find out how best to manage symptoms and when to utilise life-sustaining measures.

Thinking about end of life is rarely an easy task. Some of the decisions that need to be made are very difficult and everyone's experience will be different. People may have troubling thoughts such as 'what will happen?', 'will it hurt?' and 'will I lose control?'. It is normal to expect heightened emotions when facing end of life decisions, but it has been reported that people feel relieved and much calmer having made their plans and knowing what is likely and less likely to happen. Every individual's needs and preferences will be personal to them but can be influenced by those around them, leaving them feeling angry, guilty, sad and even relief. These are all normal and expected reactions to challenging circumstances. With support from health and social care professionals, and family and friends, difficult feelings usually become more manageable over time.

### At the Symposium

**Akshay Kulkarni** talked about how by alleviating psychological distress and managing symptoms with the appropriate palliative care, over 90% of people with MND can achieve a peaceful death. He discussed the evaluation and management of patients in the last seven days of life (the terminal phase) and provided new information about the management of the terminal phase for people diagnosed with MND ([C80](#)).

In the supporting poster theme – **Clinical Management and Support** – researchers from the USA presented their work looking at incorporating end of life discussion into all aspects of the multidisciplinary care given to people living with MND and their caregivers ([CMS-32](#)).

## Video



Rachel Boothman at the Allied Health Professional Forum 2019 – How to discuss end of life

## Resources

- Guide: [Palliative and end of life care guide for professionals](#)
- Guide: [End of Life guide for people with MND](#)
- Information sheet: [Hospice and palliative care](#)
- MND Research Blog: [New research projects agreed to help improve palliative and end-of-life care](#)
- From 2018 Symposium: Listen to Prof Carolyn Young give an [overview of the TONiC project](#) (the largest study in the UK examining the factors that influence quality of life in people with neurological conditions)

## Augmentative & alternative comms (Ac) ↑

Augmentative and alternative communication (AAC) tools are vital for people living with MND. As their disease progresses, they may experience slurred speech or even completely lose the ability to speak (dysphasia). To ensure that people with MND can continue to have a voice in making decisions regarding their care, technology can facilitate communication when speech is impaired. AACs can be as simple as using hand gestures, facial expression and writing, but can also include using high tech devices to communicate.

### At the Symposium

A comprehensive review of the literature available on AAC in MND was carried out by researchers in Brazil with the aim of identifying types of AAC and its purpose, to assess how it might be best used by people with complex communication needs ([COG-14](#)).

Researchers from India present their bespoke solution for people with MND who are reliant on voice-output communication aids (VOCAs). VOCAs that are currently available generate synthetic voices, but this new-generation technology will use the patient's own voice and speech patterns which helps them to maintain a sense of identity ([EPI-19](#)).

Some patients may not receive enough information and support to adapt to using communication aids because medical professionals do not have enough knowledge of the technology to provide this. Researchers from Japan are presenting two posters, [CMS-21](#) and [CMS-22](#), discussing their training programmes for healthcare professionals – teaching them to use the technology so they may better understand the difficulties experienced by people in their care.

### Resources

- MND Research Blog: [Technology and MND: Highlights from Glasgow](#)
- Information sheet: [Speech and communication support](#)
- Information sheet: [Voice banking](#)
- Website resource: [Introducing AAC to people with MND](#)

## Justin Yerbury (Jy) ↑

Justin is a Professor of neurodegenerative disorders at the [University of Wollongong \(UOW\)](#) and the Illawarra Health and Medical Research Institute (IHMRI) in Australia, who has earned a reputation as an internationally renowned MND researcher. His research focus lies in molecular biology – studying how proteins in MND can be dysfunctional through protein misfolding and aggregation. His research into the causes and potential effective treatments of MND is made even more remarkable with he himself living with an inherited form of MND, caused by a faulty SOD-1 gene, which has left him paralysed, unable to speak or breathe independently. As well as all of this, Prof Yerbury is actively involved in MND advocacy and fundraising.

As a result of thorough planning and co-operation of QANTAS airlines with the Yerbury family, Justin was able to travel to Perth and present his current research on the fine balance of proteostasis (the process that regulates proteins within the cell) and its implication for ALS at the 30th International Symposium on ALS/MND in December 2019 ([C3](#)).

Justin was recently awarded the '[MND Australia Betty Laidlaw MND Research Prize](#)' for 2017, the '[Wollongong's Citizen of the Year](#)' at the Australia Day Awards 2019, and was made a [Member of the Order of Australia](#) in the 2020 Australia Day Honours for 'significant service to education and research in the field of biological sciences'.

### SympWatch



Professor Justin Yerbury – The fine balance of proteostasis

### Resources

- Review based on the research presented in his talk, published in [Cell Trends in Neuroscience, April 2020](#).
- According to [Pubmed](#), Justin has over 70 publications to date.
- MND Research Blog: [Do the eyes have it? Could Resistant Nerves See Our Way to a Treatment?](#)

## Genetics (Ge) ↑

Around 5-10% of people with MND have a family history of the disease known as **familial or inherited MND**. This is caused by a mistake in the genetic code that holds the instructions for making every protein in our bodies. This mistake may be passed down from parent to child.

There are a growing number of genes which have been associated with MND. The most common of these are **SOD1, TARDBP, FUS** and **C9ORF72**. Other extremely rare causative genes have also been identified. These discoveries represent major breakthroughs because they can provide important clues as to how motor neurones are damaged in MND and may advance our understanding of all types of the disease.

### At the Symposium

**Professor Naomi Wray** from The University of Queensland, Australia, gave a talk on the future directions of ALS genomics ([C27](#)) with a comparison to other diseases and disorders.

#### SympWatch



Professor Naomi Wray – Future directions of ALS genomics

Several researchers presented their work about how structural variants (variation in the structure of an organism's chromosome) in genes associated with the development of MND may impact survival or act as a biomarker for disease survival ([C72](#), [C73](#), [C74](#)).

People with familial MND are likely to develop the disease at a younger age than those with sporadic MND because of Mendelian gene variants lowering the age of onset. As gene therapies are now being developed, and because about 15% of people with apparently sporadic MND carry a Mendelian gene variant, gene testing is likely to become more frequent regardless of family history. Researchers from the UK sought to develop a clinical tool to determine the probability of having a positive MND gene test, given the age of onset of the person being tested ([GEN-02](#)).

Researchers from Ireland and the Netherlands aimed to determine whether there are shared genetic factors between MND and other neuropsychiatric disorders, such as bipolar disorder and schizophrenia, as around 30% of people with the disease experience cognitive and behavioural changes, and these disorders seem to be more common in families that have a history of MND ([GEN-04](#)). There were also several posters looking at different aspects of the MND-causing genes:

## Video



Tobias Moll, PhD student, presented a poster on mutations in the GLT8D1 gene ([HCB-16](#)). Watch him discuss the genetic research project called **Project MinE**.



Ashley Crook, PhD student and genetic counsellor – genetic testing for familial ALS/MND ([CMS-01m CMS-02, CP-12](#)).



Dr Emily McCann, post-doctoral research fellow – The sporadic basis of MND

## Resources

- MND Research Blogs:
  - [New gene therapy targeting C9orf72-ALS begins Phase 1 clinical trial in the UK](#)
  - [Tofersen - antisense oligonucleotide drug shows promising results in Phase 1/2 trial](#)
  - [Highlight the MND researchers of the future - Tobias Moll](#)
- Information sheet: [Introduction to inherited MND](#)
- Website resource: [What causes inherited MND](#)
- From 2018 Symposium: Watch Dr Russel McLaughlin talk about [Project MinE Understanding of MND genetics](#)
- From 2018 Symposium: Watch Professor Christopher Shaw talk about [MND gene testing](#)



## Lifestyle & environment (Le) ↑

The causes of MND are still not fully understood. Around 90% of people with MND have a sporadic form of the disease – when the disease appears for no apparent reason and with no known familial link. Sporadic MND is thought to be caused by a combination of genetic, environmental and lifestyle influences.

Exposure to these factors has been extensively studied. This is known as **epidemiology**. Epidemiological studies have identified possible links with prior exposure to mechanical and/or electrical trauma, military service, high levels of physical activity, agricultural chemicals and a variety of heavy metals. However, these are all only suspected contributory risk factors and the evidence from studies is often circumstantial or conflicting and offers no clear conclusions.

Understanding the causes and mechanisms of motor neurone degeneration is essential to the development of new treatments. Only by understanding what goes wrong in MND can scientists identify potential drug targets and other therapies.

### Highlights from the Symposium

There are several researchers who presented posters about possible environmental contributions to the development of MND. There is a follow-up to previous research that investigates if Italian football players are at an increased risk of developing MND. The research team used data collected on a large group of players over a long period of time ([EPI-02](#)). Another poster looks at the hazards posed by residential exposure to environmental risks using location data for approximately 34,000 people with MND ([EPI-03](#)). Using post-mortem tissue from people with MND, [EPI-04](#) looks for evidence and degree of cyanobacterial (blue-green algae found in bodies of water) exposure, neurodegeneration and residential proximity to water.

**Sarah Opie-Martin** presented a poster ([EPI-09](#)) on the MND Register which is designed to serve as a tool to build an accurate picture of how many people are living with MND, as well as their disease characteristics and regional distribution of MND in the UK. This information will give an insight into any potential geographical risk factors and will evaluate the distribution of health and social care resources in relation to the distribution of people living with MND. Several posters investigate the impact of using large patient databases and 'machine learning' (using algorithms and statistical models) to help predict diagnosis and survival.

### Resources

- Information sheet: [Introduction to MND research](#)
- MND Research Blogs:
  - [Physical activity blog collection](#)
  - [Epi epi epi, oi oi oi](#)
- Website resource: [MND Register](#)
- Interviews from the 2018 Symposium:
  - Dr Roger Mills – [Smoking history and MND \(TONiC study\)](#)
  - Prof Ammar Al-Chalabi – [Physical activity and MND](#)
  - Prof Ammar Al-Chalabi – [Smoking and MND](#)

## Inflammation (In) ↑

Although MND is not a disease of the immune system, there is evidence from studies of patients that the levels of some types of immune cells in the blood can play a role in the speed at which the disease progresses.

Neuroinflammation is commonly seen in neurodegenerative diseases, including MND, and animal studies have shown active roles of glial (support) and immune cells in the development of MND.

Neuroinflammation is an inflammatory process thought to originate primarily from central nervous system (CNS) cell types such as microglia and astrocytes. Both cells have pro- and anti-inflammatory functions meaning that they can offer protection against cell injury or can become destructive.

For example, astrocytes are key homeostatic cells (they have the ability to maintain internal stability) that play numerous supportive roles in maintaining the brain environment. In MND, astrocytes change their shape and molecular expression patterns, and are referred to as reactive or activated astrocytes. Reactive astrocytes in MND lose their beneficial functions and gain detrimental roles. In addition, interactions between motor neurons and astrocytes are impaired in MND.

### At the Symposium

In [Session 9A: Immunity and Inflammation](#) we heard presentations about how a SOD1 mouse model has helped us further understand the relationship between the immune system and the neuroinflammation that affects the disease process in MND ([C99](#)), how effectively reproducing microglia cells in vitro using patient-derived microglia may present an effective model for testing new microglia-targeted drugs ([C103](#)) and how developing a new nanoparticle may enable the delivery of a therapy across the blood-brain barrier (BBB) to affected regions of the brain and spinal cord (nanoparticles are molecules that are small enough to cross the BBB ([C104](#))).

Posters [WP-07](#) and [TST-19](#) also looked at the role of inflammation in MND.

### Video



Dr Hande Ozdinler – Neuroinflammation modulation

### Resources

- Information sheet: [MIROCALS clinical trial](#)

## Microbiome (Mi) ↑

Recent studies have found that microbes living in our gut (microbiome) might have an effect on the rest of the body, including the immune and nervous systems. It is possible that the microbiome may be able to communicate with and affect the immune cells in the brain and spinal cord, the microglia.

Microglia have a naturally protective effect on motor neurones and the rest of the nervous system. Therefore, if the microbiome has the potential to affect the way microglia are behaving in the brain and motor neurones of people with MND (and other neurodegenerative diseases such as Parkinson's and Alzheimer's disease), the microbiome could become an important treatment target.

Researchers are currently focusing on the possible differences in the gut microbes of people with MND compared to people without the disease, in order to establish the possible connection between gut microbes and MND (and other neurodegenerative diseases).

### At the Symposium

Researchers from the USA present their poster reporting their findings from an open-label clinical trial looking at the safety and effectiveness of a new probiotic compound, given as a dietary supplement, on the gut microbiome of people with MND ([CLT-33](#)).

### Video



Dr Nik Sharma – Microbiome study (2018 Symposium)

### Resources

- MND Research Blog: [Microbiome: is the answer in our guts?](#)

## Motor neurone disorders (Md) ↑

It has long been debated whether ALS/MND is one disease, or whether we should look at it as a collection of multiple conditions with similar symptoms and disease mechanisms. We are observing a large amount of variation in terms of speed of disease progression, length of survival, type of onset (bulbar or limb), absence/presence of frontotemporal dementia and its degree, as well as cause of the disease (e.g. involvement of specific genes).

This is especially important when investigating the effectiveness of a new drug in clinical trials, which might not work in the same way across all MND subgroups. A good example is the drug lithium, which was found not to be effective in treating MND, until the data re-analysis found that there was an improvement in people with a specific genetic variation (UNC13A).

### At the Symposium

**Session 5C** focused on the Spectrum of Motor Neurone Disorders including two plenary talks: **Dr Gen Sobue** discussed spinal and bulbar muscular atrophy (SBMA) ([C56](#)), and **Professor Shigeki Kuzuhara** will discuss ALS and parkinsonism-dementia complex (PDC) ([C57](#)). The rest of the session discusses: Hereditary spastic paraplegia (HSP) and primary lateral sclerosis (PLS) ([C58](#)), and a patient case of an infant with MND caused by the inheritance of two SOD1 mutations ([C59](#)).

Further studies on disease subgroups will be discussed at the poster sessions, including: [CLT-11](#), [TST-02](#), [TST-03](#), [GEN-30](#), [CMS-19](#), [DSP-13](#).

### Video



Prof Jeffrey Rosenfeld - Defining ALS/MND: The Big Debate (2018)



Professor Ammar Al-Chalabi – Progress in understanding and treating of MND in the last few decades (2018)

### Resources

- MND Research Blogs:
  - [Kennedy's Disease vs ALS: How muscle patterns can aid diagnosis and perform as a novel biomarker](#)
  - [Kennedy's Disease: focus on muscle damage reveals key biomarker](#)

## Delivering diagnosis (Dd) ↑

Breaking the news of the diagnosis of MND can be challenging for most healthcare professionals. As well as this, most people affected by MND are dissatisfied with their experience. Could there be room for improvement in the practice of delivering diagnosis and policies? More integration across care sectors and a more person-centred approach to care from the beginning could be the way forward.

### At the Symposium

Delivering diagnosis will especially be discussed for healthcare professionals in two talks and several poster presentations at the Symposium this year. This includes a talk on modelling care for progressive neurological diseases ([C57](#)) and a discussion on the gap between standards and actual practice of delivering diagnosis ([C78](#)).

A poster presentation within [Theme 13: Clinical management and support](#) will discuss the diagnostic experience in MND through a UK survey ([CMS-04](#)).

Another poster in [Theme 1: Epidemiology and Informatics](#) will discuss the use of machine learning methods to help shorten the time to diagnosis ([EPI-10](#)). Machine learning methods are based on predicting future ALS diagnosis by using pre-diagnosis histories of ALS patients in a large insurance claims database.

### Resources

- Website resources: [Professionals](#)
- Website resource: [How can I check if my treatment and care are appropriate?](#)

## Progression & prognosis (Pr) ↑

A prognosis is defined as a likely course of a medical condition. ALS/MND is a progressive and fatal neurodegenerative disease, with an average life expectancy of two to three years. However, individual prognosis can be highly variable – from weeks to decades. Several prognostic factors are known, such as site of onset (bulbar or limb), age at symptom onset, delay from onset to diagnosis, and the use of riluzole and non-invasive ventilation (NIV).

While we wait for an established tissue biomarker (a signature of a biological change), measures of clinical progression are currently the standard for monitoring disease progression. The most widely used measure is the revised ALS Functional Rating Scale (ALSF<sub>RS</sub>-R), which is a 12-item clinical chart assessing patient's functional abilities. Each item asks about specific abilities (such as speech, swallowing, dressing, or walking) and is rated on a 5-point scale from '0' (severe disability) to '4' (normal functioning). A cumulative score gives a physician a considered view on the person's disease status (where 48 marks means normal functioning).

Other measures focus on more specific symptoms of the disease, including motor neurone loss, reduced breathing ability, or assessment of behaviour and thinking abilities.

### At the Symposium

Is the incidence of ALS/MND higher in some regions than others? Are there differences in phenotype (observable characteristics) between areas, for example a younger age of onset or more pronounced cognitive dysfunction? Does the incidence rate or prognosis vary amongst different ethnic populations? [Session 3B: Demographics and Clinical Features](#) highlighted the variance in MND diagnosis across the world ([C23-26](#)). [C107](#) discussed the ability of respiratory function, during the disease course, to predict survival in ALS patients (a possible prognostic factor).

**Associate Professor Andrea Calvo** from University of Turin, Italy, discussed how frequent pauses in ALS progression are using results from a population-based cohort ([C26](#)). For diagnosis of ALS to be confirmed, a 'progressive spread of symptoms or signs within a region or to other regions' should be present. However, it is scarcely documented whether ALS progression could show any pause.

### SympWatch



A/Professor Andrea Calvo: How frequent are pauses in ALS progression? Results from a population-based cohort

A poster within [Theme 1: Epidemiology and informatics](#) discussed a probabilistic model of disease progression which would be helpful for both clinical and research purposes ([EPI-15](#)). [EPI-16](#) considered whether the use of needle EMG, an invasive diagnostic procedure, is an effective tool in the diagnosis of ALS and prediction of disease prognosis.

A poster within [Theme 13: Clinical management and support](#) presented the development of a guide to support neurologists and rehabilitation physicians in discussing personalised prognosis with people affected by ALS ([CMS-31](#)).

A work in progress poster will discuss the use of machine learning for novel prognosis prediction and ALS patient stratification ([WP-19](#)). Machine learning methods look at the underlying patterns in data to predict future outcomes. For example, predicting future ALS diagnosis by using pre-diagnosis histories of ALS patients in a large insurance claims database.

## Resources

- Website resource: [Care information sheets](#)
- MND Research Blog: [Can the progression of MND pause or reverse?](#)



## Biomarkers (Bi) ↑

There is currently no diagnostic test for MND. Because of its relatively rare nature and non-specific symptoms, it is currently being diagnosed by an exclusion method, whereby clinicians have to rule out a whole range of other neurological and muscular conditions before giving a diagnosis of MND.

Finding a simple and pain-free test that would make this process easier and faster, would likely increase the effectiveness of existing and emerging treatments. These tests require searching for what is called a 'biomarker' – a signature of a biological change occurring in a specific disease (or a group of diseases). Some biomarkers have been identified for MND and are being tested to develop them into clinical tests.

Another reason to look for biomarkers is to keep track of the progression of the disease. Researchers are now testing various measures to see how biomarkers might change as the disease progresses, and whether these differ in people with rapid progression from those with a slower progression rate. However, due to the current lack of biomarkers, other measures of functional ability are used in clinics instead. While these are informative and provide us with a good estimate of the disease progression, they are not as accurate as biological markers.

### At the Symposium

In the opening session, **Prof Martin Turner** gave a plenary talk on the biomarker challenge ([C2](#)). A lack of biomarkers has prevented therapy development from reproducing the model of trials that has been so successful in other diseases such as cancer. With a decade of global research focused on MND biomarkers, are we there yet?

#### SympWatch



Professor Martin Turner: The Biomarker Challenge: are we there yet?

Other talks about biomarkers included [Session 4C \(C42-46\)](#) and posters within [Theme 6: Tissue Biomarkers](#).

### Resources

- Information sheet: [Biomarkers](#)
- From 2018 Symposium: Dr Hande Ozdinler talk about [Testing biomarkers specific to site of onset](#)

## Telehealth (Te) ↑

Telehealth, or telemedicine, involves the use of technology to allow healthcare professionals to monitor an individual's health and deliver care remotely. For example, they could assist in the diagnosis and management of a condition. The ultimate goals of using this technology are to increase access to care for people, decrease the frequency of clinical visits and reduce clinical costs.

For people with reduced mobility, telehealth means no long commutes to short, but critical, assessments and no waiting around. From previous studies, people taking part in remote assessments expressed higher satisfaction with the overall care they were given and appreciated remaining in the comfort of their own homes. People living long distances away from services or with increasing disease related disability are usually most likely to utilise Telehealth.

### At the Symposium

Kelly Atkins discussed how telehealth provides a meaningful contribution to patient care in ALS within [Session 7B: Improving care practice \(C81\)](#) – read our summary blog post [here](#). The research sought to review the Telehealth services offered at a state-wide ALS clinic in Melbourne, Australia, and examine the clinical outcomes. A six-month audit carried out in Australia identified that telehealth was used by both medical and allied professional staff to deliver care remotely. This meant patients did not need to come into the clinic and could discuss care needs from their own homes. They estimated telehealth had saved 9,000 km of travel and \$6,000 for people with MND. Bringing care closer to home can be especially important for those with more advanced disease who find it difficult to travel.

### Videos



Dr Ruben van Eijk – Remote monitoring of disease progression using accelerometry (2018)

### Resources

- MND Research Blog: ['There is an app for that' - the wonders of technology in ALS](#)
- MND Research Blog: [Technology and MND: Highlights from Glasgow](#)
- Video: [Dr Esther Hobson on gastrostomy, non-invasive ventilation, and utilising telemedicine in MND care](#)

## Clinical trials (Ct) ↑

Clinical trials are research studies in human volunteers that determine whether potential treatments are safe and effective. All clinical trials have strict guidelines about who can take part (factors that allow inclusion criteria). Clinical trials are usually conducted in four progressive phases which check for safety and efficacy, establish the correct dosage and method of delivery, and assess the drug's ability to treat the condition it is designed for.

Clinical trials take many years to complete and are often extremely costly. At any stage the drug can be deemed too dangerous, or inefficient, to take into the next phase. To speed up the process, clinical trials are beginning to incorporate a biomarker element (a biological characteristic) into their design. Monitoring levels of specific biomarkers during a trial will help establish if the drug or intervention being tested is influencing disease progression. Researchers are also looking to 'repurpose' drugs that have showed an effect for other diseases and have already been shown to be safe in humans, as potential treatments for MND.

Several clinical trials of potential new treatments for MND have been completed and some are still in progress. So far, only one drug, riluzole, has been proven to have enough of an impact on the disease to warrant its licensing for general use in the UK. For a list of MND clinical trials taking place in the UK and around the world, please visit [www.mndassociation.org/treatment-trials](http://www.mndassociation.org/treatment-trials). For a complete list, see [www.clinicaltrials.gov](http://www.clinicaltrials.gov), which gives updated information on clinical trials.

### At the Symposium

**Session 2B: clinical trials** included a talk on phase 2 trial of MN-T66 (**lbudilast**), which Canada recently approved a new patent for use in ALS treatment (**C9**). Ibudilast is an anti-inflammatory drug currently used to treat asthma and tested for the treatment of neurodegenerative diseases by Medicinova. It is thought to suppress inflammation, activate neuronal function and reduce the number of toxic glial (support) cells.

**NurOwn®**, Brainstorm-Cell Therapeutics, is an investigational therapy which reprogrammes bone marrow-derived stem cells into neurone-supporting cells (**C10**). These are then transplanted back to the same patient so that they can secrete neurotrophic factors to protect and promote growth of neurones. The Phase 3 trial has fully enrolled 200 participants across centres in the USA to investigate its effectiveness, and treatment is now underway. Results are expected by the end of 2020.

The Phase 2 clinical trial results of **tofersen**, an antisense oligonucleotide (ASO) therapy to reduce SOD1 as a potential treatment for SOD1-mediated MND was also presented this year (**C11**). Results supported the continued development of tofersen for treatment and is currently being recruited for Phase 3, **VALOR**.

Within [Theme 9: Clinical trials and trial designs](#), [CLT-16](#) presented information on [TUDCA](#) (Tauroursodeoxycholic Acid), a novel European-run clinical trial design for disease progression, that recently began recruiting for Phase 3 in the UK and Ireland. [CLT-24](#) presented the clinical trial design for a Phase 2 trial, **CENTAUR**, of **AMX0035**, which is Tauroursodeoxycholic Acid (TUDCA) and Sodium Phenylbutyrate. The study of 132 participants over 24 wks administration showed significantly slowed progression in people with ALS, but Phase 3 results are required to see how the treatment pans out in a longer term.

## SympWatch



Dr Ralph Kern: Modulation of innate immunity by MSC-NTF cells (NurOwn) correlates with ALS clinical outcomes

## Resources

- MND Research blog:
  - [Clinical trials \(Part 1\) - Platform Presentations: Highlights from Perth](#)
  - [Clinical Trials \(Part 2\) - Posters: Highlights from Perth](#)
- Research Information sheet D: [Clinical trials](#)
- Research Information sheet DB: [TUDCA](#)
- Website resource: [Take part in research in the UK](#)
- Website resource: [Treatment trials](#)

## Platform trials (Pt) ↑

There is an urgent need for innovative clinical trial designs to accelerate the drug development process to test awaiting candidate therapies and develop new therapeutics for ALS/MND. A potential solution is an adaptive platform trial which allows multiple drugs to be tested and evaluated for each drug's efficacy simultaneously, and with fewer participants required.

TRICALS, the world's largest network of trained specialised ALS centres, has just launched to collect and combine patient data in the UK and Europe. The clinical trial design, which will start with lithium, will be expanded and improved, targeted more precisely, and carried out more quickly.

### At the Symposium

First to present in [Session 2B: Clinical trials](#) were **Sabrina Paganoni**, MD, PhD, a faculty member at the Healey Center, and **Ben Saville** (USA) who discussed the **Healey ALS Platform Trial** which aims to accelerate the process of drug development and the path for effective treatment by testing multiple drugs simultaneously and adaptively as has been done in cancer trials and other diseases ([C8](#)). It was also presented within Theme 9 of poster presentations ([CLT-05](#)).

Incredibly, it has only been one year from concept to launch of this large-scale trial, with enrolment due to begin in early 2020 across 54 sites in the US. With multiple drugs tested at once, shared controls would be used across regimens meaning the platform trial would cut the number of placebo participants down to a third. The trial will continue to test more interventions until cures are found for all people with ALS.

As well as being able to find an effective therapy more quickly, the platform trial could drive the development of novel outcome measures and biomarkers (biological signatures of disease) and provide data for future discovery. Just recently, five 'promising' candidate treatments from among 30 applications had been chosen to test in its first platform trial for ALS.

### Resources

- MND Research Blogs:
  - [Clinical Trials \(Part 1\) - Platform Presentations: Highlights from Perth](#)
  - [Paving the way towards better clinical trials](#)

## Gene therapy (Gt) ↑

There are a growing number of genes which have been associated with MND. The most common of these are **SOD1**, **TARDBP (TDP-43)**, **FUS** and **C9ORF72**. Other extremely rare genes have also been identified to be causative. There are currently no treatments to prevent the effects of the gene damage that is being passed from one generation to another. However, research is underway to find such treatments. An emerging innovative approach has been gene therapy.

Gene therapy is designed to introduce genetic material into cells to alter how faulty/missing genes work in order to correct genetic disorders. It is expected at the very least to alleviate the symptoms and slow the progression of MND. Hopefully, gene therapy could even prevent the disease when a faulty gene is diagnosed and treated at an early-enough stage.

Just recently, researchers at King's College Hospital, London, embarked on the first gene therapy called [BIIB078](#) targeting C9orf72, the most common type of MND. It is a short DNA molecule called an **antisense oligonucleotide (ASO)** which is capable of selectively binding to and degrading toxic products made from the C9orf72 mutation. The Phase 1 clinical trial is now active to test its potential across multiple sites in the USA, Canada and Europe. The study aims to recruit up to 80 patients to test the safety and tolerability of the ASO, with an expected completion date in 2021. The first dose for the study at King's College Hospital was successfully delivered in September 2019.

### At the Symposium

Within [Session 2B: Clinical trials](#), **Dr Timothy Miller (C11)** discussed the safety, tolerability, pharmacokinetics (what the body does to a drug), and pharmacodynamics (effects of drugs and the mechanism of their action) of **Tofersen** in people with SOD1-mediated ALS. The gene therapy could, if successful, silence the faulty SOD1 gene that is associated with 20% of inherited MND cases (~2% of all MND cases). It uses an approach uses antisense oligonucleotides (ASOs), in which the drug directly interferes with the faulty instructions for making SOD1 protein, thus stopping the production of the disease-causing substance. The Phase 3 trial, **VALOR**, is currently active and recruiting ([BIIB067](#)).

During [Session 4A: Therapeutic strategies](#), there was another talk on ASOs, also known as 'designer DNA drugs', in neurodegenerative diseases ([C32](#)).

At the poster session, within [Theme 7: Pre-clinical therapeutic strategies](#), [TST-06](#) will highlight the use of artificial microRNA (used to regulate gene expression) to target a protein called AT N2 as a gene therapy for sporadic ALS. [TST-27](#) will present pre-clinical test of a gene therapy approach for familial ALS with SOD1 mutations. At [Theme 4: In vivo experimental models](#), [IVV-35](#) will discuss the investigation of HSF1 gene therapy on TDP-43 pathology in a mouse model of ALS/ frontotemporal dementia (FTD).

## Video



Prof Ammar Al Chalabi - Gene therapy

## Resources

- Thumbprint article: [What s next for gene therapy?](#)
- MND Research Blogs:
  - [New gene therapy targeting C9orf72-ALS begins Phase 1 clinical trial in the UK](#)
  - [Tofersen: antisense oligonucleotide drug shows promising results in Phase 1/2 trial](#)
- Website resource: [Treatment trials](#)



## Brain-computer interface (Bc) ↑

A brain-computer interface (BCI) is a direct communication pathway between an enhanced or wired brain and an external device.

Research has shown that brain signals can be recorded using electrical sensors implanted onto the brain. Signals could be used by the individuals to control assistive technology (e.g. spelling devices) to help with daily life, just by thinking. Implanting these electrical sensors often requires open brain surgery. Although this is technically not considered a treatment yet, implantation of a BCI system in patients could have potential to restore communication in people with severe paralysis, similar to the procedure utilised for implantation of cardiac pacemakers. A new medical device and surgical technique has been developed to allow implantation without open brain surgery.

### At the Symposium

The topic of the joint closing session discussed the dawn of brain computer interfaces. Thomas Oxley, University of Melbourne, discussed the potential of Stentrode®, a minimally invasive and wireless technology, with data from one patient that was late breaking news at the time of the Symposium ([C110](#)).



Stentrode® is a small metallic mesh tube (stent), with electrode contacts (small metal disks). He discussed the potential of incorporating the system inside a blood vessel of the brain located in the motor cortex (area that controls movement). By recording and decoding the signals from the brain, speech would be synthesised.

This is now being trialed in people with loss of motor function from Sept 2019 in an early feasibility study, called [SWITCH](#) (Stentrode With Thought Controlled Digital Switch) – making a preliminary step on the approval pathway. This research will be the first of its kind to be performed in humans and may help find safer, more effective ways to introduce electrical sensors in patients' brains.

### Resources

- Interesting article: [Terminally ill scientist 'transforms himself into world's first full cyborg'](#)

## CuATSM (Cu) ↑

Copper ATSM (CuATSM) is a small, orally administered, man-made compound that can deliver copper to cells where the cell's energy batteries, mitochondria, have been damaged. Damaged mitochondria are considered a hallmark of several neurodegenerative disorders, including MND/ALS, Parkinson's disease, and Alzheimer's disease. CuATSM allows for selective delivery of the drug (i.e. to only those cells that have been damaged) and it is blood-brain barrier permeable.

CuATSM is being investigated for its effects of slowing down disease progression and improving respiratory and cognitive function. After it was observed to be safe and well-tolerated with some beneficial effect in the Phase 1 trial. The Phase 2/3 study started in Australia to explore whether the drug is beneficial to people with MND, in a larger cohort of people. This trial will help determine the optimal dose size, timing of doses and drug delivery route (e.g., by mouth, or injection) for the next phase of testing.

Please note: CuATSM is a specialised compound and is not the same as taking copper supplements, which can be poisonous in high doses.

### At the Symposium

Associate Professor Peter Crouch from Melbourne University discussed the relevance of the candidate MND drug, Copper ATSM, to sporadic MND, and the therapeutic potential for this compound to extend to all forms of MND and other neurodegenerative disorders ([C36](#)).

#### SympWatch



A/Professor Peter Crouch: Relevance of the therapeutic CuATSM to sporadic ALS

Two posters were displayed within [Theme 9: Clinical trials and trial design: CLT-35](#) highlighted the design of the Australian multicentre study of CuATSM for the treatment of ALS. [CLT-36](#) evaluated whether the CuATSM capsule formulation (from phase 1 study) and oral suspension formulations (to facilitate dosing to patients with PEG or swallowing difficulty) are of bioequivalence, i.e. the same, to be used in the phase 2 trial.

[TST-12](#) within [Theme 7: Pre-clinical therapeutic strategies](#) discussed a potential therapeutic target for CuATSM. This target is associated with an iron-dependent form of cell toxicity (ferroptosis) inducing neurotoxic astrocyte activation. Astrocytes normally regulate transmission of electrical signals within the brain, but toxic versions could contribute to neuronal death in ALS.

## Resources

- MND Research Blog: [What 's the story with CuATSM](#)
- ALS News Today: [First patient enrolled in phase 2/3 trial of CuATSM](#)
- MND Research Information Sheet: [D - Clinical trials](#)
- ALSUntangled Report: [#43 - Copper](#)
- Clinicaltrials.gov: [NCT04082832 CuATSM trial](#)

## Drug screening (Ds) ↑

Before a drug can be tested in clinical trials (in humans), it first must be examined in a lab to provide an insight into its mechanism (how it is likely to work in the body), safety, and preliminary effectiveness. These studies can be done in cells in a lab dish (in vitro), in animals (in vivo), or using computer modelling (in silico).

While there is only a limited number of clinical trials, there are many compounds currently being investigated that could have the potential to be developed into ALS/MND treatments.

In general, only an extremely small proportion of compounds tested in pre-clinical studies get to the final drug approval stage, reflecting the rigorous and strict process assuring that only safe drugs of good quality are tested in clinical trials and approved.

### At the Symposium

Various talks within [Session 4A: Therapeutic strategies](#) discuss the use of modern technology to establishing new drug candidates – **BenevolentAI** and **SITraN** demonstrated how the use of artificial intelligence (AI) has the potential to increase the efficiency of the drug discovery process ([C34](#)), and **Verge Genomics** discussed how machine learning helps to accelerate drug discovery with their finding of a novel small molecule that rescues ALS phenotypes in preclinical models ([C35](#)). Machine learning methods are based on predicting future data by using determining patterns seen in existing and past data.

A work in progress was also presented ([WP-24](#)).

### Resources

- MND Research Blogs:
  - [Journey of a drug](#)
  - [How animals are helping to improve our understanding of MND](#)