Countdown to a cure

How the MND Association is fighting MND

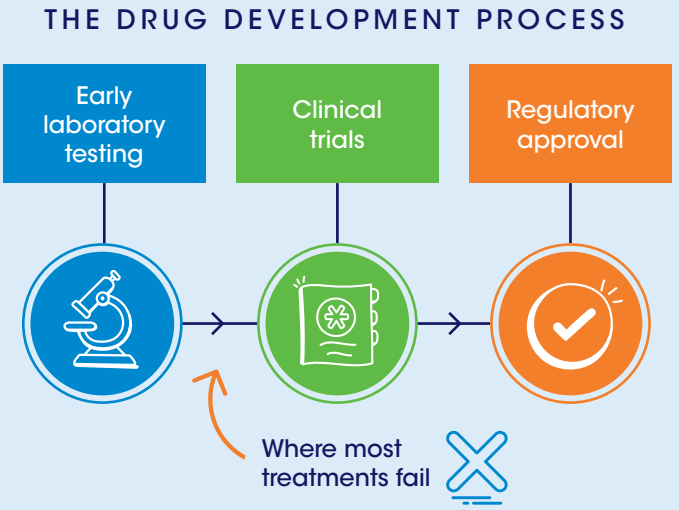
Translational research: new ways to tackle MND

The challenge

The process of developing a potential new treatment for MND is long, challenging and incredibly expensive.

First, a potential treatment must be identified and tested in the laboratory. Then it is tested in clinical trials to check it is beneficial and safe in people with MND.

Despite promising results in early laboratory tests, many potential new treatments often do not perform as well in people. This is where development of new treatments often fails.



A solution

Translational research bridges the gap between laboratory-based research and the testing of potential treatments in people through clinical trials.

The aim is to move research from the laboratory into clinics, such as hospitals.

Translational research can mean knowledge from the clinic and advances in technology are used much earlier in the drug development pathway. It also frequently includes a large multidisciplinary team, who work together to give a potential new treatment the best chance possible of making it through the drug development pathway, through clinical trials and into people with MND.

Our involvement

Countdown to a cure is a snapshot of the innovative research the MND Association is funding, showcasing how MND researchers are working together more than ever, and searching for new and better ways to carry out clinical trials.

Advances in technology, milestone discoveries and new partnerships are now helping us take what we have learned so far about what causes MND and translate that into potential treatments. This strongly indicates there is reason for cautious optimism.

Thank you to all the donors, funders and partners who have contributed to and supported our research. Together, we share common ground to understand, treat and - ultimately - defeat MND.

Stronger together
building partnerships

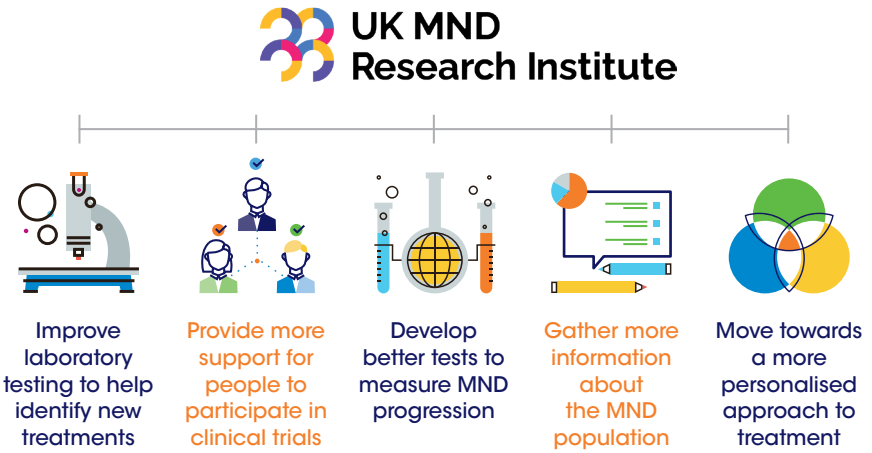
Finding new treatments for MND cannot be achieved by working in isolation. Work to tackle the disease needs to be coordinated. Most of the translational research initiatives the MND Association funds are partnerships with other charities or funders. Through these partnerships we will continue to strengthen and transform the world leading MND research carried out in the UK.

Coordinating MND research in the UK

The virtual UK MND Research Institute (UK MND RI) was launched in 2023 after the United To End MND campaign, led by people with MND.

The research partnership enables clinicians, researchers and people with MND, together with charities, including the MND Association and other funders, to work together in a more coordinated way. Six participating centres around the UK, all leaders in MND research, currently make up the Institute.

Through the UK MND RI, MND research will be supported by national infrastructure, the sharing of information and internationally renowned expertise.



CO-FUNDERS:

mnda motor neurone disease association · My Name's Doddie Foundation · MND Scotland Making time count · LifeArc · UKRI Medical Research Council · NIHR National Institute for Health Research

"No other country has the leading institutes working together nationally like this"

Professor Ammar Al-Chalabi, Co-Director, UK MND Research Institute

A resource to help gather and store information

The MND Register gathers information on every person with MND in England, Wales and Northern Ireland.

As of 2023 over 6,000 participants have been recruited onto the Register. The Register is being integrated into the UK MND RI as a hub for research studies, to link data between different projects, and other large NHS datasets.

As well as helping researchers, this information can be used to help understand how many people have MND and where they live to allow for better care planning.

The MND Register team is currently working on an app, TiM (Telehealth in MND), that will allow people with MND to sign up and complete questionnaires, such as for symptoms, remotely.

The app will also act as a gateway to research and trial participation, for example it can send 'push' notifications to app users about clinical trials nearby that are recruiting.

The hunt for **biomarkers**

A multicentre biomarker resource strategy in ALS - AMBRoSIA

The standard method for measuring MND progression is the ALS Functional Rating Scale (ALSFRS-R), a questionnaire that records how well the muscles involved in movement, swallowing, speaking and breathing are functioning. The questionnaire, which is filled in by the person with MND and their healthcare professional, can be unclear and subjective.

Biomarkers are biological signals which can be measured in the body. These can help to more accurately measure MND progression, assess how beneficial a treatment is in clinical trials and potentially lead to faster diagnoses and earlier treatment.

In 2016, the MND Association funded Project AMBRoSIA, one of the world's largest MND sample collections focused on identifying effective biomarkers of MND.

PROJECT AMBRoSIA

AMBRoSIA was funded by the MND Association, with proceeds from the 2014 Ice Bucket Challenge and support from the London City Swim Foundation, The Linbury Trust, the Cook family and friends, and other generous donors. The project was only made possible by the selfless donation of samples from people living with MND.

"AMBRoSIA is proving the power of having a larger, multi-centre resource of samples collected over time. The lessons learnt have been pivotal in taking neurofilament light chain (NfL) to the next stage of development."

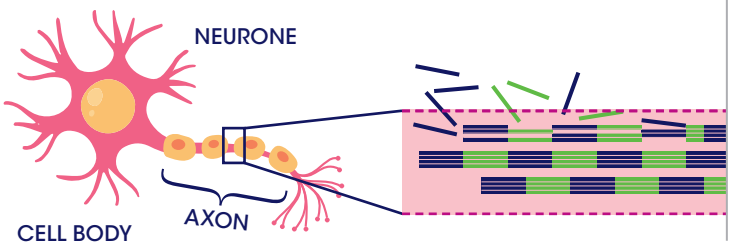
Professor Martin Turner,
Project AMBRoSIA co-lead, University of Oxford

A **biomarker** is a **unique biological fingerprint** that signals the presence of a disease and can be measured to give information on disease activity and progression

Neurofilament light chain (NfL)

As part of Project AMBRoSIA, researchers collected samples of blood, cerebrospinal fluid, urine and skin from both healthy people and several hundred people living with MND.

Neurofilament light chain (NfL), a breakdown product of damaged neurones, was found to be a powerful marker of disease activity that could be measured in the blood and used to determine the rate of neurodegeneration.

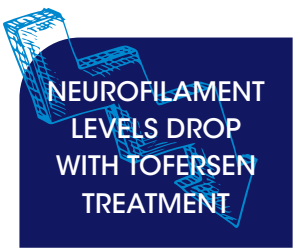


Using neurofilament light chain in clinical trials

Neurofilament light chain (NfL) can be used in MND clinical trials to help determine if a treatment is working. Lower levels suggest less damage is happening to motor neurones.

A treatment for people with SOD1 MND, called tofersen, was found to reduce NfL in participants receiving the treatment, but not in the control group, in a phase 3 clinical trial.

The Food and Drug Administration (FDA) highlighted that the approval of tofersen, in the United States, was based on the reduction in NfL.



Is the answer to treating MND in our genes?

Armed with the increased knowledge of the genetics behind MND and the successful development of a treatment for people with a SOD1 gene change, MND Association funded researchers are **making great strides in the development of new potential gene therapies.**

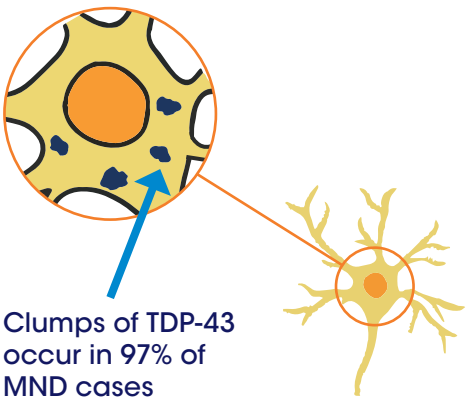
Developing a gene therapy for sporadic MND

In 97% of all MND cases a protein called TDP-43 is faulty and forms toxic clumps.

Research from Professor Pietro Fratta's lab, based at University College London, has shown that faulty TDP-43 causes a mistake in the genetic instructions for another protein called UNC13A. This leads to a reduction in the UNC13A protein which is vital to help keep neurones healthy.

Professor Fratta's lab is now making and testing small DNA-like molecules, called antisense oligonucleotides, to see how effective they are at correcting the mistake. It is hoped these potential treatments could benefit a large proportion of people with MND.

Professor Pietro Fratta, University College London



Clumps of TDP-43 occur in 97% of MND cases

CO-FUNDERS: mnda motor neurone disease association; MY NAME'5 DODDIE foundation; LifeArc

What is a gene therapy?

Our genes hold the instructions to all the biological processes that happen within our body.

Changes in genes can lead to changes to some of these processes, which can contribute to motor neurone damage and death in MND.

Gene therapies are designed to target changes in genes and correct the underlying genetic cause of the disease.

40 people out of 100 people with familial MND have a change in the C9orf72 gene

Targeting C9orf72 – the most common genetic form of MND

Professor Guillaume Hautbergue, Sheffield Institute for Translational Neuroscience

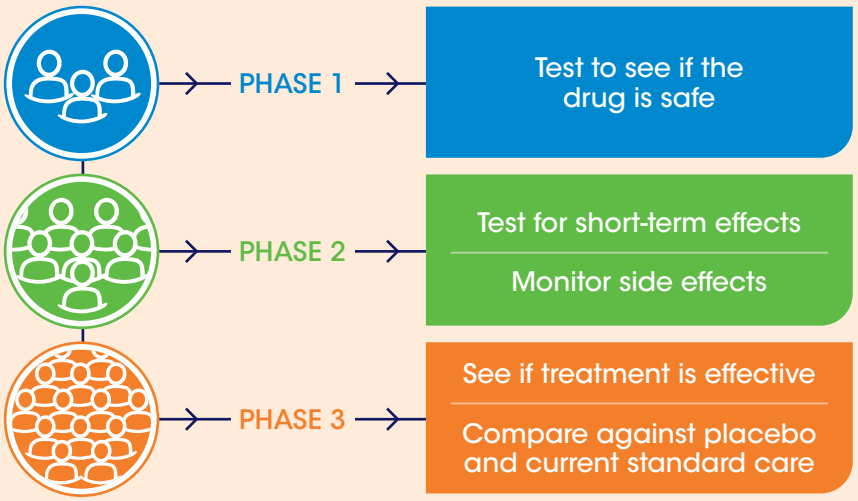
Other research is looking to design treatments for people who have a specific genetic change, such as C9orf72.

Professor Guillaume Hautbergue, from the Sheffield Institute for Translational Neuroscience (SITraN), has shown that a protein called SRSF1 plays a key role in the production of toxic proteins found in C9orf72 MND.

Professor Hautbergue is developing a gene therapy to lower levels of the SRSF1 protein. By lowering SRSF1 levels, the researchers hope that the levels of toxic proteins will also be reduced.

CO-FUNDERS: mnda motor neurone disease association; LifeArc

The end of the **translational journey**



Once a potential new treatment has been shown to be beneficial in laboratory testing, it is then tested in clinical trials.

The process of taking a potential treatment through clinical trials, to make sure it works and is safe, can be time-consuming and expensive. There have been hundreds of clinical trials over the past several decades, but unfortunately, their success rate has been very low.

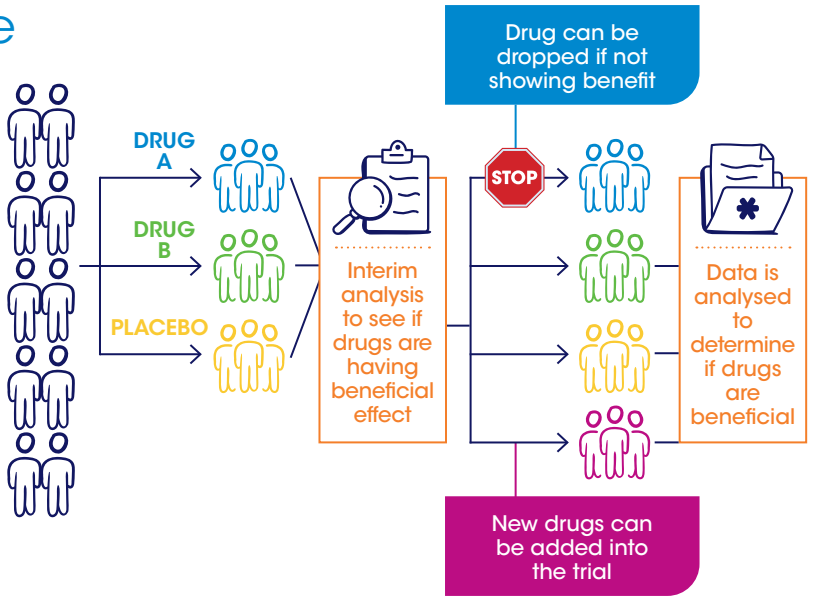
MND Association researchers are now using new, innovative trial designs in the hope of increasing the chance of success.

Building the infrastructure to keep trials running

Often clinical trials only investigate one treatment at a time. Setting up each of these clinical trials is time-consuming, taking precious time away from other research.

Researchers investigating other diseases, such as cancer, developed the concept of testing multiple treatments at the same time in one trial. These types of trials are called platform clinical trials.

The overall infrastructure is set up, allowing new treatments to be added more easily. Regular examination of the data means that treatments that aren't working can be dropped.



MND–SMART
Clinical trials for MND

MND-SMART is the first UK wide platform clinical trial for MND. With sites across the UK the trial gives more people with MND an opportunity to take part.

In 2023, the MND Association joined together with MND Scotland, the primary funders, and the Alan Davidson Foundation to provide funding to secure the future of the platform trial.

This funding is essential to:

- maintain the existing trial infrastructure
- open up more trial sites to increase opportunities for people with MND
- increase the number of treatments tested

CO-FUNDERS:

MY NAME'5 DODDIE foundation

mnda motor neurone disease association

MND Scotland Making time count

Alan Davidson Foundation

EUAN MACDONALD CENTRE Vital research into motor neuron disease

Trialling a **new approach**

EXPERTS-ALS
EXPErimental medicine Route To Success in Amyotrophic Lateral Sclerosis

"We will be able to screen drugs faster and prioritise those with the best chance of success"

Professor Chris McDermott,
EXPERTS-ALS co-lead investigator

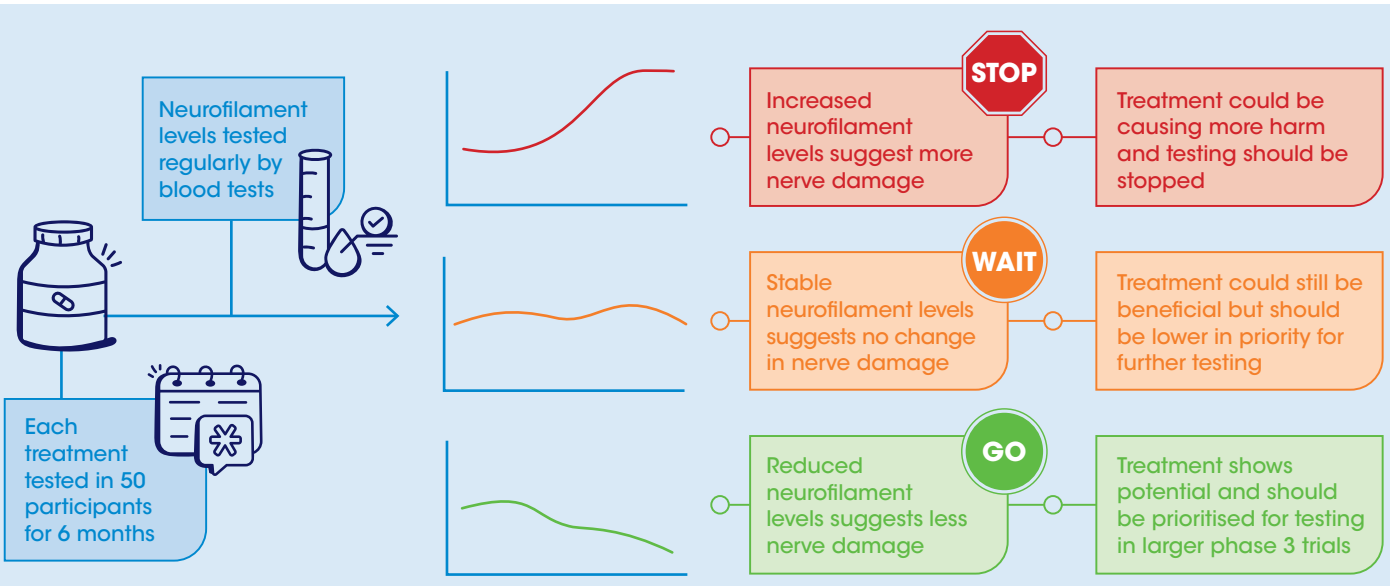
Choosing the right drug candidates to test in trials

Potential new treatments for MND are currently chosen based on data from laboratory studies. While these studies are vital in identifying promising treatments, the success rate of the treatments in clinical trials is currently low.

Building on the discovery that neurofilament light chain is a biomarker for MND, researchers believe they can use this marker of nerve damage to rapidly test treatments in people with MND. Researchers will then be able to prioritise which treatments go into clinical trials and hopefully offer a higher chance of finding drugs that actually work.

A five year programme, called EXPERTS-ALS, will initially test drugs which have already been approved for other diseases and have shown signs they could also work in MND in the lab. The EXPERTS-ALS platform will involve 11 MND centres across the UK.

Each drug will be tested in people with MND for six months. During the study, participants' neurofilament light chain levels will be monitored through simple blood tests. Researchers will then use the neurofilament levels to make a 'go' or 'no-go' decision and these successful drugs can be prioritised for testing in larger phase 3 trials.



CO-FUNDERS:

EXPERTS-ALS is primarily funded by money pledged by the Government as part of a £50 million commitment to targeted MND research following the United To End MND campaign. The MND Association, LifeArc and My Name'5 Doddie Foundation are contributing to extend the length of the platform.

mnda motor neurone disease association
LifeArc
MY NAME'5 DODDIE foundation
NIHR | National Institute for Health Research

Our research

Hear how our researchers are fighting MND by visiting **mndassociation.org/research**

Research blog

Stay up to date with the latest MND research at **mndresearch.blog**

@mndresearch

Follow us **@mndresearch**

If you would like to donate to MND research, contact us at **fundraising@mndassociation.org**

mnda
motor neurone disease association

Motor Neurone Disease Association
Francis Crick House, 6 Summerhouse Road,
Moulton Park, Northampton, NN3 6BJ
Tel: 01604 250505

www.mndassociation.org

Registered with FUNDRAISING REGULATOR