

mnda

motor neurone disease
association



Research strategy

Foreword

Up to 5,000 people in the UK are living with motor neurone disease (MND) and around 1,200 die each year, more than half within two years of diagnosis.

The MND Association's vision is a world free from MND. We intend to be part of the history of ending the disease. Until then, we will strive to ensure that people with MND, their carers and families get what they need when they need it. Our 'Beating MND Together' document¹, developed in consultation with our membership, identifies the challenges we face and opportunities we must grasp in pursuit of our mission: to improve care and support for people with MND, their carers and families; to fund and promote research that leads to new understanding and treatments; and to campaign and raise awareness so the needs of people with MND and everyone who cares for them are recognised and addressed by wider society.

This Research Strategy outlines the mechanisms through which we will develop our research activities over the next four years, to continue to deliver measurable and significant advances in understanding and treating this complex and devastating disease.

In the past two decades, MND has moved from a relative scientific 'backwater' to the forefront of neurological disease research. We believe that there has never been a better opportunity to convert the unprecedented new knowledge of the disease and scientific momentum into potential diagnostics and treatments, so we intend placing greater emphasis on translational and patient-focused research in the coming years.



A handwritten signature in black ink, appearing to read 'Brian Dickie', written in a cursive style.

Dr Brian Dickie
Director of Research Development



¹ *Beating MND Together. MND Association 2022.*

Our research strategy

To achieve this we will fund a research programme that seeks to address four key strategic themes:

Identify therapeutic 'targets'

To understand the causes of MND and focus in on the pivotal biochemical processes involved in the disease that will provide a starting point for the development of new treatment strategies.

Understand clinical progression

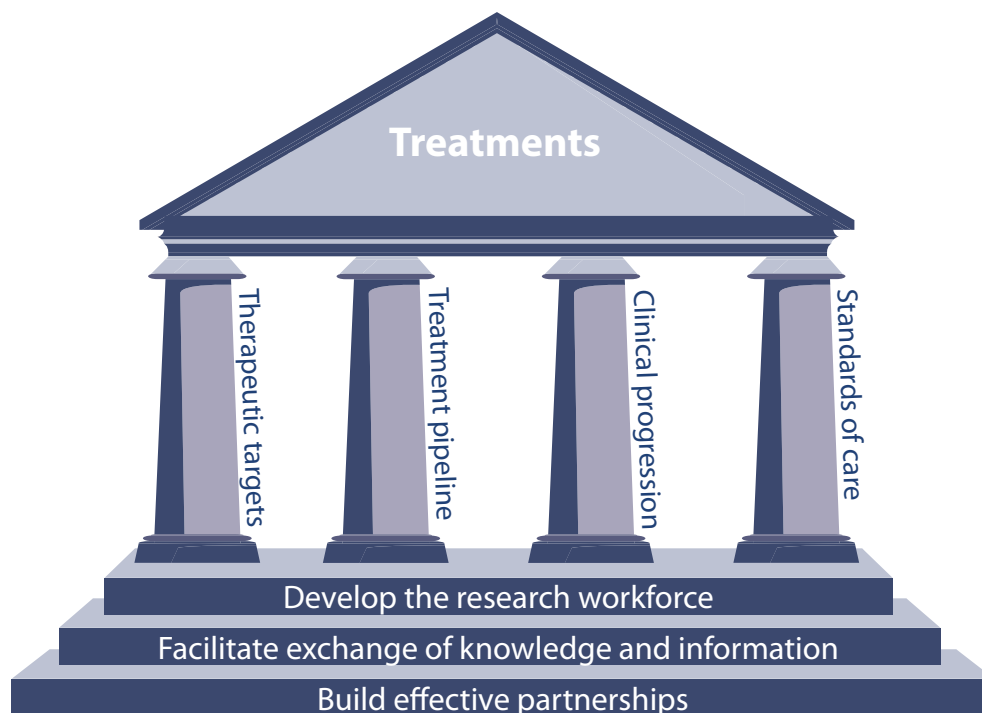
To develop a detailed understanding of how the disease manifests and progresses in humans, in order to ensure that fundamental laboratory research can be clearly linked to the 'real world' events occurring in people with MND.

Develop a treatment pipeline

To identify where directed investment can help drive these fundamental discoveries through the various stages of treatment development, from laboratory to clinic.

Improve standards of care

To ensure that the clinical management of MND is informed by the priorities of people with MND and their families and supported by a strong evidence base.



These activities are underpinned by three essential supporting themes:

Develop the research workforce

To attract, train and retain the 'brightest and best' laboratory and clinical researchers to work in the MND research arena.

Facilitate exchange of knowledge and information

To ensure that new data, ideas and discoveries are shared quickly and effectively, speeding up research progress and fostering a culture of collaboration.

Build effective partnerships

To maximise the impact of our research funding and influencing activities through close working relationships with leading research organisations - industrial, governmental and charitable - in the UK and beyond.

Key strategic themes

Identify therapeutic targets



Why is this important?

The development of effective treatments can be greatly aided if we know what causes the disease in the first place. We know that in most cases MND is likely to be caused by a complex combination of genetic and environmental factors. Considerable advances have been made in recent years (in particular our understanding of the genetic factors) but there is still much to do.

Whilst it is not nearly as simple a concept as 'Find the Cause, Find the Cure' this knowledge serves as an essential springboard for further research, such as the creation of better laboratory models and a greater understanding of the pivotal events that damage and ultimately kill motor neurons.

Finding these common pathways of degeneration, even when there are different factors causing the disease, will form the basis for new approaches to treatment – and possibly even prevention.

What we intend to do

- We will continue to operate at the forefront of genetic research, fulfilling our ongoing commitment of sequencing 2,200 genomes as part of the international Project MinE consortium. We will then consider whether further sequencing is required, or whether we need to prioritise investment in analysis of the unprecedented levels of data being generated;
- We will seek to use new genetic understanding as a foundation for more effective investigation of the interaction between environmental and genetic factors;
- We will support initiatives to generate better laboratory models that faithfully replicate the cellular events occurring in humans. Such work can be expensive and risky, so we must carefully consider the relative value of generating further models based on the progressively rarer MND genes being discovered;
- We will seek to support fundamental research studies that not only investigate pivotal cellular 'targets' associated with motor neuron degeneration and protection, but which also demonstrate therapeutic potential through inclusion of early stage *in silico* and *in vitro* screening programmes.

What we aim to achieve

- Our MND Collections (comprising DNA, cell lines and data) and funded research projects will contribute to a comprehensive understanding of the genetic component of MND, in turn shedding light on the environmental factors that contribute to the disease;
- New and better laboratory models of MND will be available to the research community;
- Our researchers will identify new disease pathways and confirmed their relevance to human MND.

"The amount of data is increasing exponentially, with 90% of the data that currently exists having been created within the last two years."

Dr Jackie Hunter, BenevolentBio

Develop a treatment pipeline

Why is this important?

Academic laboratories specialise in unpicking the basic chemical and biological events occurring in health and disease, but translating this knowledge into treatments has historically been the preserve of industry. Many promising treatment ideas have stalled in the gap between lab and clinic, often termed 'the valley of death' in drug development circles. This is especially true for neurodegenerative diseases, in particular the rarer conditions such as MND, where pharmaceutical companies face the conundrum of the high cost of drug development relative to a potentially low commercial return.

The task for the MND Association and related organisations is to identify and pursue ways in which we can reduce this risk and make MND drug development a more attractive proposition for investment, from both a scientific and a commercial perspective.

What we intend to do

- We will establish which laboratory models and analysis methods can best support the efficient large scale screening of compounds and other aspects of preclinical drug testing;
- We will identify opportunities to work with emerging academic drug discovery institutes, as well as industry, to help facilitate crucial stages of the drug development process, from compound discovery to clinical trials;
- We will explore opportunities to support 'drug repurposing' initiatives, which can bypass much of the lengthy and expensive testing process, in order to move directly to clinical studies at the earliest opportunity.

What we aim to achieve

- We will establish a research programme that provides targeted support to speed up the drug development process;
- We will deliver candidate drugs for testing in the clinic, collaborating with other funding bodies to spread the risk and cost associated with drug development and clinical trials.



“While investigation hums along at light speed, translation often does not. The good news is that obstacles to progress are tractable. The bad news, however, is that these problems are difficult.”

Dr Michael Emmert-Buck, Avonax Medical Institute

Understand clinical progression

Why is this important?

A more comprehensive understanding of the human disease will serve to confirm the relevance and importance of findings from laboratory studies. Our research, whether in the lab or the clinic, should be comparable with the 'real world' changes occurring in people living with MND.

A major advantage of laboratory models is that they allow the opportunity to study early disease states. In contrast, the diagnosis of MND is a lengthy and challenging process. The lack of a diagnostic test for MND prevents early diagnosis, resulting in uncertainty for the patients and delaying treatment options - including participation in therapeutic trials.

In addition, the heterogeneity of disease progression can make personalised care planning more challenging, as well as distorting the findings of clinical trials. The identification of biomarkers that help predict the course of the disease, together with more rigorous functional assessment, is fundamental to more accurate evaluation of therapeutic outcomes. Moreover, if combined with the opportunity to demonstrate that a drug is hitting its target, it should be possible to run shorter, smaller and significantly cheaper trials in the future.

What we intend to do

- We will support the development of the AMBRoSIA initiative to create a world- leading clinical biomarker resource, using this and linked collections (including presymptomatic cohorts) to identify and validate markers for use in clinical practice and clinical trials;
- We will fund studies that incorporate new methods and technologies to improve clinical phenotyping, stratification and disease staging, with the ultimate aim of enhancing clinical management and research.

What we aim to achieve

- Through our support for biomarker collections and associated research studies, we will help to identify and validate markers that help speed up diagnosis, accurately predict disease progression and improve the design and execution of future clinical trials;
- We will contribute to advances in disease classification, stratification and clinical staging, creating a platform for more personalised approaches to medical treatment.

The diagnosis [of MND] is still clinical and there is a pronounced delay between the onset of symptoms and diagnosis, possibly beyond the therapeutic window.

*Prof Martin Turner,
University of Oxford*



Improve standards of care

Why is this important?

Statutory providers face ever-increasing demands on finite resources, with evidence-based decision-making on healthcare replacing decisions informed by fashion or vested interest. Ensuring that MND is treated as a priority requires us to champion changes in care provision at all levels, but we need to do so with the support of a strong evidence base and with the confidence that our priorities are aligned with and informed by people living with MND, their families and carers.

The NICE Guideline on MND incorporates many findings arising from previous healthcare research we have supported - in themes such as respiratory management, nutritional support and cognitive and psychological change - but it has also identified areas where significant knowledge gaps remain. Addressing these gaps through high quality research and implementing findings into clinical practice will improve the quality and consistency of care: locally, nationally and internationally.

What we intend to do

- We will use research recommendations from the NICE Guideline, together with findings from the 2015 Palliative Care and End of Life Priority Setting Partnership, to help guide our healthcare research funding programme and provide an evidence base to support our care and campaigning activities;
- We will establish the National MND Register as a key foundation for our activities, providing vital information on the demographics of MND and identifying areas where disparity in healthcare provision exists;
- We will continue to build upon the successes of our MND Care Centres and Networks in creating a vibrant and sustainable research environment, partnering with other funders to support multi-centre studies.

What we aim to achieve

- Findings from our healthcare research programme will inform management guidelines and clinical practice;
- The National MND Register will deliver relevant data to improve care service delivery - locally and nationally - and inform clinical trial design;
- We will contribute a much greater understanding – and be able to demonstrate the impact – of specialist multidisciplinary care as well as specific interventions.



Our cross-cutting themes

Develop the research workforce

Why is this important?

In order to carry out the best research, we need the best researchers. MND is a complex disease and modern biomedical research is so highly specialised and multi-faceted that scientists and clinicians will need to collaborate more effectively and in greater numbers if we are to understand this complexity and turn knowledge into treatments.

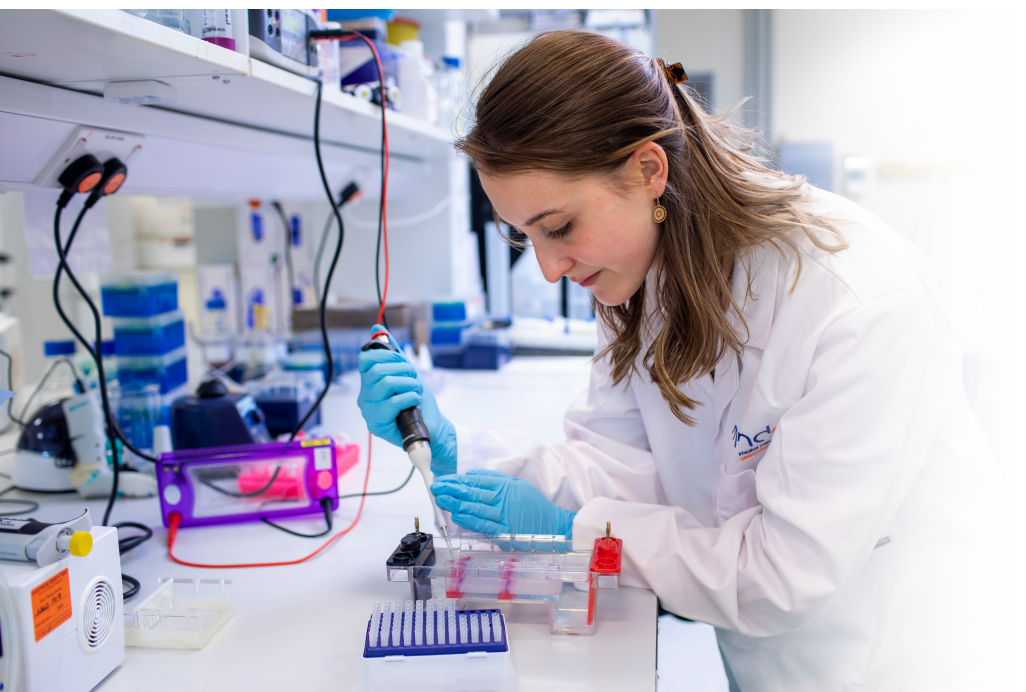
The Association has a longstanding track record of supporting the careers of researchers. We need to continue to strengthen UK MND research capacity by encouraging young investigators to embark on a career in MND research and supporting established scientists from other disciplines in applying their knowledge and skills to MND.

What we intend to do

- We will continue to develop our PhD Studentship and Fellowship programmes, to attract, train and retain the brightest and best young researchers, creating future international leaders;
- We will seek to identify and exploit opportunities to support senior investigators where targeted funding helps to secure long-term leadership, collaboration and multidisciplinary 'critical mass' within leading research institutions.

What we aim to achieve

- Greater numbers of researchers and institutes working on MND, with dedicated career development opportunities at key stages of career progression.



“Without the Association’s support at a crucial early stage in my career, I doubt if I would have been able to continue in MND research. Since then I have been able to train over 20 students and postdoctoral fellows, drawing a new generation of scientists into the field.”

*Prof Janice Robertson,
University of Toronto*

Facilitate exchange of knowledge and information

Why is this important?

A key component in the fight to defeat MND lies with greater collaboration and the sharing of new understanding of the disease, which requires both organisational and cultural change. A particular challenge for the MND research community is how to deal with the unprecedented quantity of information emerging from labs and clinics around the world.

Whilst traditional 'face to face' meetings such as the annual International Symposium on ALS/MND will continue to play an important role in networking and information exchange, the increasing use of computer technology and web-based media is revolutionising the speed of – and ease of access to – new scientific information on the disease. In the past quarter of a century, MND research output has grown almost 6-fold, with an average of 40 new papers currently published every week .

As a principal funder of MND research, we seek to ensure that new findings arising from our funding programmes are disseminated to the international research community with as little delay as possible. As a patient representative organisation, we also aim to ensure that research advances are communicated to people with MND and their families in an accessible, accurate, up-to-date and honest fashion.

What we intend to do

- We will continue to develop the International Symposium as a catalyst for collaborative research activity, whilst also supporting focused 'hothouse' workshops to draw together key players in relevant subfields of research;
- We will maximise the scope and impact of our MND Collections, providing researchers with appropriate access to Association samples and data, underpinned by robust governance processes;
- We will explore how online tools and resources can support scientific networking, information exchange and faster access to new research findings;
- We will seek to ensure that all new research papers arising from our funding programmes are made rapidly and freely available to the international research community;
- We will develop our science communication activities, taking advantage of new media to help bridge the gulf between those performing the research with those living with MND.

What we aim to achieve

- The International Symposium continues to develop its role as the premier annual international meeting for research and care;
- We will be a leading participant in international initiatives, through provision of Association-sponsored samples, data and funding;
- By taking advantage of advances in Information and Communication Technology, we will facilitate information between researchers, funders and people affected by MND;
- All new MND Association-funded research papers are available 'Open Access'.

Build our partnership and influencing activities

Why is this important?

The Association's combined roles of Patient Association and Research Funder provide us with opportunities to engage and influence a wide variety of organisations and institutes, across academia, industry and government, to focus on our common aim of defeating MND. We can be more effective working together.

In order to maximise these opportunities, we must continue to develop our reputation within these circles. We must be able to demonstrate that our understanding of the disease and the current state of play in international research is matched by high standards of research governance in supporting research of the highest scientific merit and greatest relevance.

It will also be necessary to influence the wider environment within which MND research takes place, in particular the UK and European landscape, which may undergo considerable change in the coming years. We will use our influencing and campaigning capacity to exert leverage where policy changes affect us uniquely or as a joint voice in partnership with others to create the best conditions in which scientific research can flourish.

What we intend to do

- We will engage with the research community and funding agencies to promote the priorities of people with MND and their families;
- We will identify strategically relevant partnership funding opportunities and pursue the most productive initiatives, in order to support research programmes that may otherwise not occur due to cost and/or risk;
- We will recognise those areas in which we are not specialists and seek opportunities to expand research understanding and capacity.

What we aim to achieve

- We are recognised by statutory providers and research funders as a leading authority in MND, promoting the needs and priorities of people affected by MND;
- We can demonstrate the impact of our funding partnerships with multiple agencies in the UK and beyond.

“New funding partners such as the MND Association have allowed us to broaden the scope of our research and ultimately result in better care for more people living with a terminal illness.”

Dr Sabine Best, Marie Curie

Our funding programmes

In order to maximise our impact on MND research within the biomedical and healthcare research communities, the strategy is designed, where practicable, to complement and build upon the strategic aims, priorities and funding arrangements of the statutory funders and relevant medical research charities in the UK and abroad. Our principal award schemes are outlined in the table below and are administered as two funding programmes, supported by specialist Research Advisory Panels.

The **Biomedical Research Programme** aims to create an environment within the UK where new scientific understanding of the disease generates therapeutic strategies that can be effectively translated from lab to clinic. As such, we intend to focus our resources on biomedical research that seeks to offer a stepwise progression of activity from lab to clinic and/or links directly to the clinical manifestation of the disease in humans.

Whilst we will remain sufficiently flexible to be able to respond to and promote the testing of novel interventions, the main thrust of the Association's **Clinical & Healthcare Research Programme** will be principally dictated by identified priority 'knowledge gaps' where research could make a significant impact on disease management. A targeted approach to Clinical and Healthcare funding has distinct advantages to the response-mode 'scatter-gun' approach, in that it will be possible to support longer-term development of major themes of interest, fostering collaborative ventures between researchers and ensuring that appropriate expertise is available and that qualitative and quantitative research will be conducted to appropriate standards.

Grant funding for researchers will be provided through the following schemes:

Project grants

Awards for up to three years, will be available to researchers through our existing grant schemes. Funding for biomedical research will be based on broad criteria of relevance to classical MND, scientific merit and novelty. However, applicants must also demonstrate a potential therapeutic route from lab to clinic and/or the clinical relevance of their proposed research (for example, linking genotype, pathology or biomarkers with phenotype). Studies will generally be anticipated to relate to human MND, but research linked to phenotype in animal models will also be considered if the research is likely to significantly advance understanding or treatment of the human condition.

Clinical & Healthcare project grants will seek to address knowledge gaps identified by the Association, taking into account information obtained from the PSP on Palliative and End of Life Care (2015) and the NICE Guideline on MND (due to be published in 2016). We will also seek to build on studies already incorporated within the DenDRON portfolio. In addition to research merit, applicants must be able to explain how the anticipated findings will be incorporated into clinical practice.

Small Grants/Meeting grants

In order to assist with the generation of new ideas and pilot data for larger scale applications, or to facilitate the rapid follow-up of important new findings, small pump-priming grants will be considered on an 'ad-hoc' basis.

Programme Grants

Support will be provided for strategic priorities (such as maximising the use of our National DNA Bank and establishing new resources to support the research community) where collaboration by several groups is required, or for clinical projects requiring multicentre collaboration and/or large population cohorts. Projects will usually be pursued as collaborative funding partnerships with other grant awarding bodies.

Clinical Research Fellowships

Support to develop the research careers of clinicians will be made available through the Medical Research Council (MRC)/MND Association Lady Edith Wolfson Clinical Research Fellowship Programme, administered by the MRC.

PhD Studentships

Research awards for three-year projects will be based upon similar criteria for grants, with the additional criterion of quality of the research environment and training for the student.

Non-Clinical Research Fellowships

Awards to support outstanding basic science researchers at early and intermediate stages of their postdoctoral career.



THANK YOU FOR YOUR SUPPORT

www.mndassociation.org • 01604 250505 • enquiries@mndassociation.org

Motor Neurone Disease Association, Francis Crick House, 6 Summerhouse Road, Northampton, NN3, 6BJ
Registered charity No. 294354

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