MND Insights: **Perspectives from the MND Community to shape future drug treatments**

LifeArc

About LifeArc

LifeArc is a self-funded, not-for-profit, medical research organisation, and our ambition is to transform the way diseases are identified and treated.

Through our work and partnerships, we accelerate healthcare innovation by turning promising life science ideas into life-changing medical breakthroughs for the people who need them most.

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Background

Our vision is to create a world where Motor Neuron Disease (MND) is preventable and treatable. By leveraging our expertise in early translational science, we seek to advance discoveries that enable earlier interventions, deliver more effective treatments and improve the quality of life for people living with MND.

At LifeArc, we know from experience that for medical research to be most effective, it is vital that the people we are trying to benefit are involved throughout. That's why we created our MND Insights Group – a group of people with lived experience of MND – to better understand the most pressing challenges faced by those directly affected by the condition. Additionally, we're conducting surveys to capture perspectives from the wider MND community, ensuring that a broad range of voices shape our approach.

The invaluable insights shared by those affected by MND are essential for helping us to prioritise research aimed at finding new treatments and improving the quality of life for people living with the condition. By ensuring our technology solutions align with the real needs of the MND community, we aim to revolutionise how this disease is detected, treated and managed. We also recognise that these insights will be helpful to the wider community, and we are committed to sharing them to drive progress and foster collaboration.

In 2024, we conducted two workshops with the MND Insights Group and a community-wide survey, to explore treatment-related needs and priorities from people affected by MND. This report summarises the key findings from this research, identifying recurring themes that will directly help to inform our funding priorities and guide the overall direction of our MND Translational Challenge.

About MND

MND is a progressive condition that affects the specialist nerve cells in the brain and spinal cord that help tell muscles what to do.

This causes the muscles to gradually weaken, stiffen and waste, affecting a person's ability to walk, talk, eat, drink and breathe. Some people also experience changes in their thinking and behaviour, but the disease affects everyone differently and can be difficult to predict.

MND affects up to

5,000

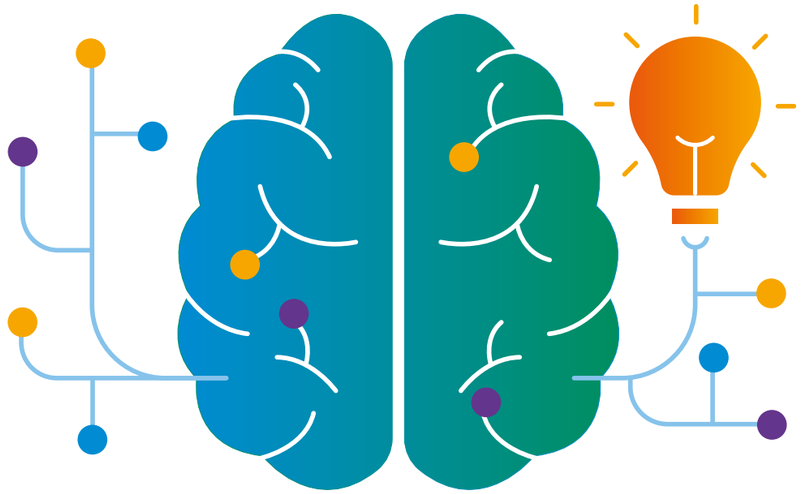
people in the UK at any one time

While MND/ALS is classified as a rare disease, 140,000 new cases are diagnosed worldwide each year. In the UK, MND affects up to 5,000 people at any one time. It can affect adults at any age, but is more likely to affect people over 50. While the causes of MND are largely unknown, in rare cases, it is due to a genetic fault that can be passed down through families.

MND is life-shortening and there is no cure. However, treatments are available that can help manage symptoms and achieve the best possible quality of life.

The main types of MND are:

- **Amyotrophic lateral sclerosis (ALS)**
  the most common form of MND, with weakness and wasting in the limbs, muscle stiffness and cramps.
- **Bulbar onset MND or progressive bulbar palsy (PBP)**
  affects a smaller number of people than ALS, and mainly affects the muscles of the face, throat and tongue.
- **Progressive muscular atrophy (PMA)**
  affects only a small proportion of people, with early signs often weakness or clumsiness of the hands.
- **Primary lateral sclerosis (PLS)**
  a rare form of MND, causing mainly weakness and stiffness that usually begins in the lower limbs.
- **ALS with frontotemporal dementia (ALS-FTD)**
  while ALS and frontotemporal dementia (FTD) often occur on their own, around 1 in 5 people with ALS will also develop FTD. They will experience mobility symptoms as well as cognitive symptoms simultaneously.



Foreword

At LifeArc, we are committed to making a meaningful difference in the lives of people living with Motor Neuron Disease (MND).

It's a mission grounded in our belief that those directly impacted by medical conditions must be at the centre of research efforts. Their insights and lived experiences are not just valuable—they are essential in shaping the path toward better diagnostics, treatments, and ultimately, a cure.

The creation of our MND Insights Group marks a pivotal step in this journey. This group brings together individuals diagnosed with MND, their loved ones, caregivers and includes a gene carrier, to collaborate with our researchers, providing first-hand perspectives that inform our priorities and ensure our work aligns with the real needs of the community. By listening to their voices and understanding their challenges, we aim to bridge the gap between scientific breakthroughs and solutions that truly matter in everyday life.

MND is an area of immense complexity and urgent need, yet also one of great potential. Science is advancing, and many promising discoveries are ready for translation.

Our MND Translational Challenge seeks to capitalise on these advancements with three key goals: facilitating earlier diagnosis, developing better treatments, and technology to improve quality of life. However, we know that scientific innovation alone is not enough. Success depends on engaging with the people whose lives we aim to change.

This inaugural report reflects the insights, experiences, and priorities of the MND community. It is a testament to the power of collaboration—where lived experience meets scientific expertise. By working together, we hope to accelerate the development of solutions that will bring real hope and transformative change to those affected by MND.

I am immensely grateful to everyone who has contributed to this report, from the dedicated members of the MND Insights Group to the wider community who have shared their thoughts through surveys. Your courage and generosity in sharing your experiences are shaping the future of MND research, ensuring it remains focused on what matters most.

Together, we are forging a path toward a future where MND is not only treatable but where lives are fundamentally improved by the innovations we help bring to life.

Paul Wright
Head of the MND Translational Challenge

Executive Summary

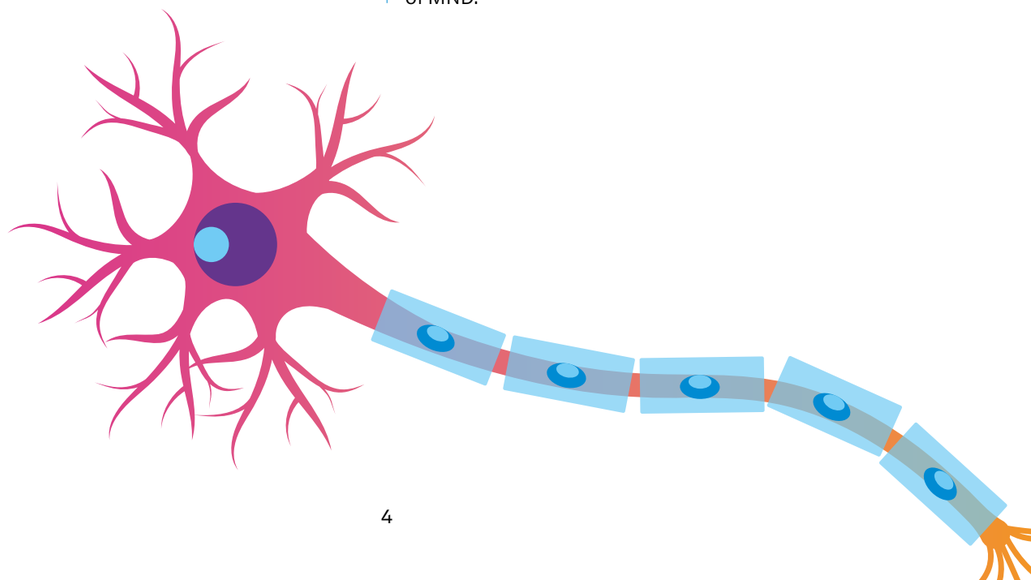
LifeArc is committed to revolutionising the detection, treatment, and management of MND, with the ultimate goal of making it a treatable condition. To achieve this, we recognise the importance of hearing from individuals and caregivers directly affected by this disease.

In 2024, we hosted two workshops with the MND Insights Group to explore the real-world impact of potential new treatments, focusing on the acceptability of different administration routes, side effects and measuring meaningful outcomes. We also conducted an online survey to capture perspectives from a broader cross-section of the MND community in the UK and abroad, including people living with the disease, current and bereaved caregivers, and those at high genetic risk.

Our findings reveal that those affected by MND want treatments that preserve a person's quality of life, maintain dignity, and are easy to administer, ideally in a home setting. People living with MND expressed a greater willingness than caregivers to tolerate side effects if they felt a treatment could significantly slow disease progression. However, the results also highlight the need for highly individualised treatment approaches, as preferences and needs vary widely and are likely to evolve as the disease advances.

These insights will be instrumental in guiding our MND Translational Challenge, shaping our efforts to develop effective new treatments that address the most pressing needs of those affected by this condition. Our key recommendations include the development of minimally invasive, home-based treatment options and the enhancement of patient-centred outcome measures that capture quality-of-life factors often missed by traditional assessment scales. This knowledge is already being used to inform our MND drug repurposing programme, which aims to boost preclinical discovery and development of repurposed drug candidates for treating the condition.

Looking ahead, a key priority is to continue our engagement with the MND community throughout the research and development process. Regular dialogue with people affected by the condition will ensure that new disease-modifying treatments (DMTs) align closely with their needs and preferences, ultimately leading to treatments that effectively address the unique challenges of MND.



Methodology

This report summarises the insights gathered from two sources: workshops conducted with our MND Insights Group and a community-wide survey.

1. Workshops with our MND Insights Group

We hosted two workshops with our MND Insights Group - a group of ten people affected by MND including people with MND and current and bereaved caregivers.

Workshop 1

Aimed to explore the burden of treatment and the acceptability of drug administration routes and side effects for potential future MND treatments. These discussions assumed that a potential new treatment could moderately to considerably slow MND progression.

Workshop 2

Aimed to identify the outcomes from treatment that people living with MND and caregivers consider most meaningful. Participants discussed which metrics should be used to assess the 'meaningful benefit' of potential treatments on symptoms and quality of life.

Both workshops were held with the facilitation of two experienced co-chairs: Roger Leek, a bereaved caregiver with extensive involvement in MND advocacy and research, and Emma Willey, a registered nurse with significant expertise in MND care and mental health programme management.

Emma Willey

Roger Leek

> "Members with lived experience generously share intimate personal experiences with honesty and fortitude. A bond has quickly developed and an empowered group dynamic is growing. Connecting shared experiences is powerful for us all and brings hope for tangible scientific and therapeutic advances.
>
> **Emma Willey**

> "I'm involved with MND research because I lost my wife, who was my best friend and love of my life, to MND. We now have granddaughters, who might be at risk of MND. I want MND research to progress and to make the world a better place for their future."
>
> **Roger Leek**

2. Community-wide survey

In May 2024, we conducted an online survey that aimed to capture perspectives from the wider MND community on drug administration routes and side effects.

The survey was structured into five separate streams, with the wording of questions adapted to accommodate the following groups of participants:

- people living with MND
- current caregivers responding on behalf of the person with MND
- current caregivers expressing their own views
- bereaved caregivers
- people at a high genetic risk of MND

The survey was open for 3.5 weeks and promoted online as well as through direct contacts of LifeArc, UK-based MND charities, and other health research organisations in the UK and abroad. Data visualisation was used as the primary tool for data analysis, with AI employed to support the qualitative analysis of free-text responses by identifying and categorising common themes.

Insights from workshops

Through facilitated discussions, the workshops provided a qualitative foundation for understanding treatment expectations and quality-of-life priorities among people affected by MND.

1. Routes of administration

We explored different methods of treatment administration and which frequency could be acceptable for people living with MND and caregivers.

Impact of disease stage

Several people living with MND, particularly those at the earlier stages of the disease, expressed a willingness to accept any route of administration if it held the promise of slowing disease progression. However, their acceptance of high-burden routes (like spinal injections) decreased at later stages of the disease.

> "Even if I had to go into hospital every day, if that slowed my progression and gave me a relatively normal life expectancy, I personally would do it."
>
> **Person living with early MND**

> "It's how much you are willing to put up with for an unknown possibility of whether it will stop progression. [...] You have to go through all of this pain and difficulty; and it's not just you, but all of your family and the people supporting you."
>
> **Person living with advanced MND**

Challenges with oral medications

Although frequently considered to be the most convenient route of administration in general, oral medications can be problematic for people with MND, especially for those with swallowing difficulties. Several people reported having to crush tablets so they could be swallowed. The process of crushing, weighing and administering medications can take up to what feels like the entire day for caregivers, especially during the final stages of the disease. When swallowing is an issue, liquid administration may be preferred over taking multiple daily tablets/capsules at home.

Perspectives on injections

Views on the acceptability of injections varied based on personal preferences, frequency of injections and perceived benefits. While some caregivers were happy to administer injections at home, other caregivers and people living with MND would prefer these to be administered by healthcare professionals locally. People living with MND were generally averse to lumbar punctures, but those who had experienced them had found them to be less painful than anticipated.

Oral medications versus injections

Receiving a medication as a monthly or bi-weekly injection at a hospital by a healthcare professional may be preferred to administering a large number of oral medications at home. However, as MND progresses, reduced mobility may make travelling to the hospital more difficult.

> If there was some facility that you could go once a month and have the necessary injections that would help you for the following month, then I would pursue that avenue rather than having my wife crush tablets with a pestle and mortar."

Person living with MND

PEGs and cannulas

Some people living with MND did not consider PEGs[1] as an option for themselves, but some caregivers saw them as a useful tool for medications that were otherwise hard to administer. Some caregivers suggested cannulas[2] may be acceptable if they were required.

Home versus hospital administration

Views varied about treatments that could be administered at home or in a hospital, such as an intramuscular (IM) injection, depending on individual circumstances. It was generally agreed that different routes of administration should be offered because every person living with MND has different needs and preferences. Caregivers emphasised that care for people with MND should be shifted from the hospital to the community as much as possible, to reduce the need for travel.

> The hospitalisation element, for Dad, would have definitely encroached on his quality of life, and it is that balance."

Bereaved caregiver

Hardships of treatment

Sometimes, people living with MND have considerable costs or out-of-pocket expenses when receiving treatment, which is made worse by the fact that they can often no longer work. It was also pointed out that not all people living with MND have family support to enable home administration of medications. Approaches could benefit from learning in other therapy areas, such as diabetes.

2. Side effects

We explored the manageability and acceptability of potential side effects of treatments, focusing on key considerations for people affected by MND.

Acceptable side effects

Opinions on the acceptability of side effects varied considerably. Some people were willing to tolerate almost any side effect if it helped slow their disease progression, but others prioritised 'life quality over quantity'.
An important decision point is when the person with MND is no longer able to communicate. Some people living with MND and caregivers expressed that side effects that were manageable with other medications would be acceptable.

> MND will have a terminal impact on my life. I will therefore tolerate any side effects if the drug demonstrably slows or stops progression of MND. The only prerequisite for me is being able to communicate with others in whatever way possible."

Person living with MND

Unacceptable side effects

People living with MND highlighted certain side effects they felt would be unacceptable, including those that increased the risk of chest infections or worsened breathing difficulties. Preserving their sense of identity, cognition and ability to communicate were also highlighted as key priorities. Side effects that impacted energy levels or reduced independence were widely regarded as unacceptable.

Maintaining a person's independence and dignity was emphasised as important, particularly regarding side effects that might cause incontinence or interfere with their ability to maintain personal care. These concerns were especially pronounced when such side effects would have a significant impact on their immediate family and caregivers, such as bowel issues that required more assistance with using the bathroom.

[1]Feeding tubes, or percutaneous endoscopic gastrostomy (PEG) tubes, allow a person to receive medications directly into their stomach.
[2]A small, thin, plastic tube inserted into a vein to deliver medications directly into the bloodstream.

> One of the last things to go is your mind and identity and who you are; if there was a side effect that took that away from me, I wouldn't want to continue."

Person living with MND

Informed decision-making

People acknowledged that side effects vary from person to person and there is uncertainty around them. Providing clear information about potential side effects is essential, allowing each person living with MND to make informed decisions about their treatment options.

> It would be about that balance of side effects and quality of life, and still maybe being able to do A, B and C and that'll be different for everyone at different stages."

Caregiver

Symptom or side effect?

Distinguishing side effects from MND symptoms was a common challenge, particularly for changes in mood and fatigue, and this uncertainty can result in people reconsidering whether or not to continue with their medication.

> It's being able to work out precisely what's causing the problems, and if the side effects are similar to MND symptoms I think that's a consideration as well."

Person living with MND

3. Meaningful benefit of treatments

We set out to understand what people affected by MND consider as the meaningful benefits of disease-modifying treatments (DMTs) and how these should be measured.

Each participant had unique perspectives, highlighting how diverse feelings on the meaningful benefit of a DMT may be across the MND community. We have grouped the topics covered in these discussions into three overarching themes:

Symptoms affecting quality of life

Overall, the impact of symptoms on quality of life is different for everyone and is often tied to their self-expression and identity. A person's age at diagnosis, as well as their stage of MND, is also likely to influence the impact of symptoms, with their priorities changing as their disease advances. Some specific symptoms mentioned include:

- **Extreme fatigue:** People living with MND emphasised that extreme fatigue had a significant impact on their lives, limiting their ability to undertake physical activities, causing anxiety, and forcing them to rest for extended periods after even minor physical exercise.

> I have started using the example of it [the fatigue] feels like I am walking with divers' lead boots that are having more and more weight added during the day."

Person living with MND

- **Bulbar symptoms:** Difficulties with salivation, swallowing and speech are among the most challenging symptoms – and can lead to social isolation due to embarrassment.

- **Self-expression and identity:** Maintaining a sense of identity is very important for people living with MND. For some, continuing to do the things they enjoy (e.g. work or hobbies) was important, as these activities supported their sense of identity.

- **Speech and mobility:** For people with MND, both speech and mobility are deeply tied to their sense of identity, though the relative importance of these symptoms varies between individuals. For some, speech is crucial to maintaining their identity while others prioritise mobility, viewing it as essential to their independence and ability to participate in meaningful activities. For those who previously led active lives, the loss of mobility can feel particularly disheartening, as it restricts them from engaging in the work or hobbies that once defined them.

> “For me it’s all about mobility. I would be happy to lose what little speech I have left if I could mobilise easier, preferably without the use of mobility aids. I was a volunteer archaeologist before I developed MND.”
>
> **Person living with MND**

Meaningful treatment benefit

People living with MND and their caregivers expressed varied perspectives on what they consider meaningful benefits of treatment. People with MND valued extended life expectancy and an improvement in their extreme fatigue, alongside reductions in fasciculations (involuntary muscle twitches) and improvements in breathing and nutrition. However, caregivers placed high importance on preserving communication abilities, as well as improvements in sleep, mood, mental well-being and bulbar symptoms.

Both people living with MND and caregivers highlighted the importance of seeing clear signs of slowed disease progression, but many stressed it was difficult to know what this might look like. Despite not being able to see a noticeable effect of treatment, most people were generally unwilling to stop taking MND medications and risk losing any potential benefits.

Perspectives on what makes treatment ‘worthwhile’ varied based on a person’s age and life circumstances at diagnosis. Many people living with MND emphasised the importance of balancing quality of life with side effects. However, some expressed a willingness to compromise their quality of life and accept a degree of difficulty (such as the need to travel to a hospital to receive the medication) if the treatment offered a real chance of slowing disease progression.

> “If we’re up against it, and we always talk about ‘We wouldn’t want this and we wouldn’t want that’, but when it’s right in your face and you’ve got an opportunity, then you tend to compromise quite a lot for that opportunity.”
>
> **Person living with MND**

Measuring meaningful benefit

The ALS-FRS-R was used as a framework to guide discussions on assessing the meaningful benefits of DMTs. The overall consensus from the group was that measuring meaningful treatment benefits should reflect a holistic view of MND, addressing physical, cognitive, and emotional symptoms to better reflect the broader impact of MND on individuals and their families.

What is the ALS-FRS-R?

The Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALS-FRS-R) is an internationally recognised and validated tool used to measure the physical progression of MND. It is considered one of the gold standard outcome measures in clinical trials to assess treatment efficacy. However, as it focuses on physical aspects of MND, such as motor, bulbar and respiratory function, it is acknowledged that this tool does not fully capture all symptoms that can affect a person’s quality of life.

Key points included:

- **Differing impact of ALS-FRS-R domains on life**

  Some ALS-FRS-R domains were considered more important for measuring meaningful treatment benefits than others, as certain symptoms have a greater impact on the daily life of people affected by MND than others. For example, one person living with MND expressed that they would find changes to their breathing or speech a lot more distressing than challenges with fine movement.

- **Specificity of ALS-FRS-R subgroups**

  Participants suggested that the existing subgroups could be further broken down to better reflect the varied experiences of those living with MND, enabling more personalised assessments of treatment impact.

- **Gaps in symptom coverage**

  The ALS-FRS-R does not include symptoms such as fatigue, spasticity, leg cramps, sleep quality, and problems with muscle control, all of which were seen as important indicators of treatment benefit.

- **Emotional lability**

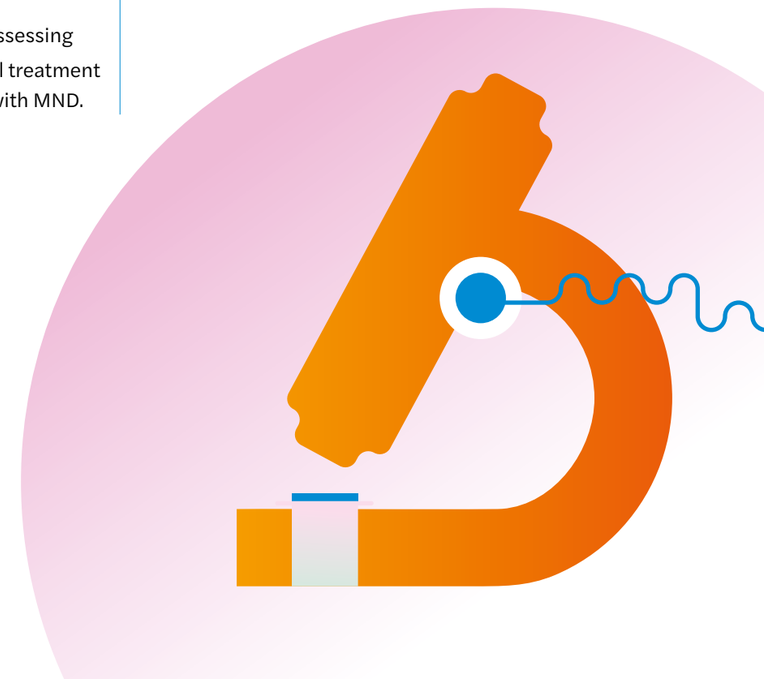
  Emotional lability (rapid and extreme changes in mood) is a frequent symptom of MND and is considered to be an important quality-of-life factor. The group noted the link between emotional lability and dementia among people affected by MND, making its evaluation particularly relevant for those with ALS-FTD.

- **Mental health**

  Many people emphasised the importance of assessing mental health as part of evaluating meaningful treatment outcomes, as it affects so many people living with MND.

> “Prior to diagnosis, I had a lot of emotional instability. I was going through highs and lows and I couldn’t understand why...prior to being diagnosed with MND I didn’t know emotional instability was part of the disease. So, I do believe mental [symptoms] are part of it and needs to be confronted on the [ALS-FRS-R] scale.”
>
> **Person living with MND**

> “My speech is starting to be affected now and to me that’s much more distressing and worrying [than fine movements]. Speech is such a big part of our identity....Of the [ALS-FRS-R] categories some are so much more impactful on life than others.”
>
> **Person living with MND**



Insights from the community survey

158 complete responses

Our analysis of survey data provided wider perspectives from the MND community about what potential new treatments should look like.

The survey collected 158 complete responses, 64 incomplete[3] responses and 2 disqualified[4] responses.

Data from all participants who answered at least one question were included. Responses from caregivers reporting on behalf of people with MND were combined with those from those living with the condition. The findings in this report reflect responses from:

66 People living with MND

40 Current caregivers

88 Bereaved caregivers

19 People at high genetic risk of MND

Participant demographics

Respondents were predominantly middle-aged, with ~75% aged between 40-69 years of age. The majority (~87%) identified as White British, more than 71% were female, and ~37% reported living with a disability. Around 44% identified as Christian while ~50% reported they had no religion. Most participants (~87%) identified as heterosexual. Around 40% described themselves as unpaid carers and ~7% as paid carers.

Most participants were based in different geographical locations across the UK, with an additional 12 international respondents (7 from the USA and 1 each from Australia, France, Ireland, Italy and the Netherlands).

Respondents were affected by various types of MND, including ALS, PLS, PMA, PBP and ALS-FTD. The length of time since diagnosis ranged widely, from less than six months to five years or more.

[3]Responses were marked 'incomplete' if the participant had only partially completed the survey and not pressed 'submit' at the end.
[4]Responses were disqualified if the participant either did not agree to the terms and conditions, or if they indicated that they had no connection to MND.

Q1. What are the most important factors to consider when taking medicines for MND?

Participants were asked to select the three most important factors from a multiple-choice list:

- For people living with MND, 62% prioritised the location of administration (e.g. at home or in a hospital), 55% selected the route of administration, and 53% were concerned about drug-drug interactions.
- Both current and bereaved caregivers prioritised the same top three factors (location of administration, route of administration and drug-drug interactions) as people living with MND. For current caregivers, the route of administration was the top factor, selected by 67%. Bereaved caregivers placed equal importance on the route and location of administration, each selected by 69% of participants.
- Among people at high genetic risk of MND, 92% highlighted the location of administration as most important, followed by 67% prioritising the route of administration.
- Factors that were considered less important (20% or fewer responses) across groups were regularity of administration (same time each day), medication storage considerations, timing with food and drink and inconvenience of administration when away from home.

> "I cannot take tablets due to no longer being able to swallow. I could not use an inhaler due to my reliance on a ventilator. Whether or not I would undergo spinal injections would depend on the potential impact of the drug."
>
> **Survey participant**

> "I am happy to take a drug in any form other than a suppository as this mentally for me would be undignified."
>
> **Survey participant**

Q2. Which routes of drug administration are acceptable?

Participants were asked to rate different drug administration methods as either 'acceptable', 'unacceptable' or 'unsure' and could also share the reasons for their choices in a text box:

- For people living with MND, the most acceptable routes were skin patches (96%), liquid administration (89%) and oral gels (89%). The least acceptable options were suppositories (50%), lumbar puncture (39%) and intravenous (IV) injection (22%).
- For people at high genetic risk of MND, the most acceptable routes were skin patches, liquid administration and intramuscular (IM) injection (all 92%). They deemed suppositories, lumbar punctures and inhalers as the least acceptable options.
- Current and bereaved caregivers also emphasised methods that balanced ease of use with patient comfort. Skin patches (current, 93%; bereaved, 91%), liquid administration (current, 87%; bereaved, 88%) and oral gels (current, 77%; bereaved, 83%) were the top choices. The least acceptable routes were suppositories (current, 53%; bereaved, 57%), lumbar punctures (current, 60%; bereaved, 59%) and oral tablets (current, 41%; bereaved 41%).

In free text responses, people living with MND cited concerns about swallowing difficulties, which may explain their preference for options like patches, liquids or gels. Concerns about dignity may explain the low acceptability of suppositories, while concerns about invasiveness and ease of use reduced support for lumbar punctures and IV infusions. One person at high genetic risk of MND noted living alone as a factor that could affect their ability to manage complex administration methods.

Caregivers consistently highlighted concerns around dignity, practicality, ease of access, and minimising discomfort and pain. They also frequently highlighted swallowing difficulties as an issue. Bereaved caregivers also mentioned the importance of adapting treatment methods as MND progresses.

Q3. Which places and types of support are acceptable when receiving treatment, and why?

Survey participants rated the acceptability of four potential options for locations and types of support for receiving drug treatments as 'acceptable', 'unacceptable' or 'unsure', with an option to provide a free text response to explain their reasons.

A clear preference for home-based treatment emerged across all groups. Over 90% of respondents, whether people living with MND, caregivers, or those at high genetic risk, deemed receiving treatment at home as acceptable, whether administered independently, with caregiver support, or by a healthcare professional. Hospital visits were less favoured, especially among current and bereaved caregivers (50% and 33% acceptability, respectively).

In free text responses, people cited the home environment as the most convenient and relaxing setting for treatment, with many noting the challenges of travelling to hospital appointments as a significant factor in their preference. However, others stated they would happily receive treatment anywhere if it would help slow MND progression.

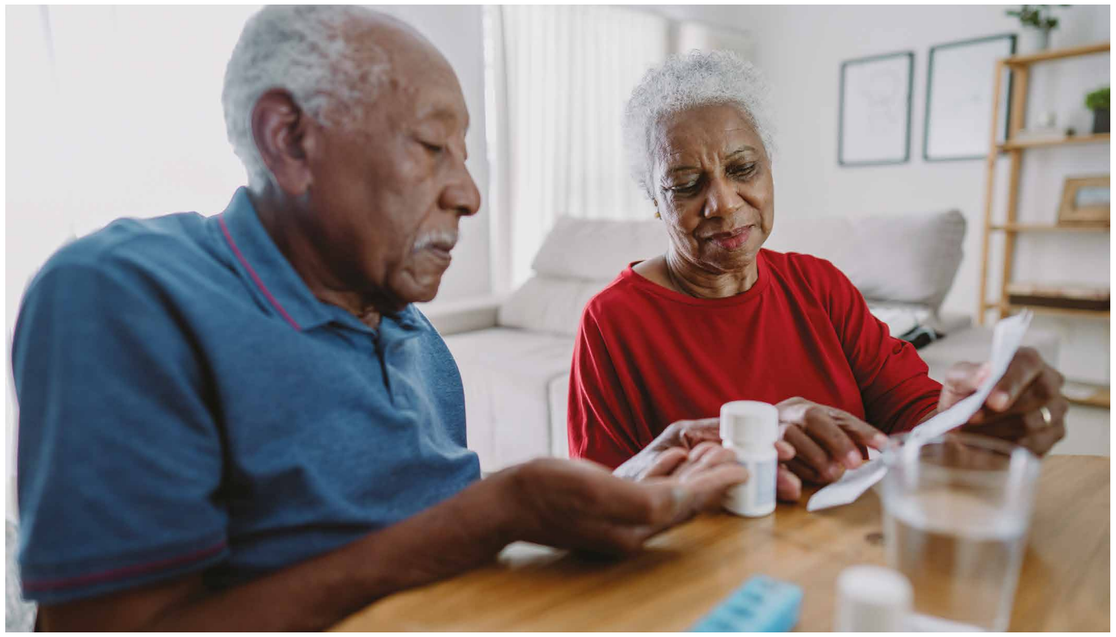
> "Being able to administer medication at home is convenient for me and also places less burden on my primary carer."
>
> **Survey participant**

Q4. How regularly are hospital visits acceptable to receive treatment?

Participants were asked to rate the acceptability of different frequencies for visiting a hospital for treatment, ranging from weekly to fewer than four times a year.

Overall, the most acceptable frequency across all groups was every two months or less frequently. However, preferences varied by group. People living with MND and those at high genetic risk were more open to more frequent visits, while caregivers, especially bereaved ones, preferred less frequent visits. For example, 50% of people living with MND felt weekly appointments were acceptable, and 62% every other week – whereas only 20% of bereaved caregivers felt weekly hospital appointments were acceptable and 33% every other week.

The greater acceptability of more frequent visits among people living with MND and those at high genetic risk may reflect a willingness to pursue any potential treatment, especially at the early stages of the disease. For caregivers, particularly bereaved ones, frequent hospital visits may be seen as burdensome, which may reflect their experiences of managing MND as it progresses.



Q5. How regularly is it acceptable to take oral medications or injections at home?

Participants were asked about the maximum acceptable frequency for taking oral medications and administering subcutaneous injections at home, with options ranging from multiple times a day to once a week:

Oral medications

- The most common maximum acceptable frequency for people living with MND was four times a day (35%). For current caregivers, it was three times a day (37%), while for bereaved caregivers it was once a day (28%), and for people at high genetic risk of MND it was two times a day (50%).
- Bereaved caregivers were the least likely to accept four doses a day, with only 21% finding it acceptable, compared to 30% of current caregivers, 35% of people with MND, and 34% of people at high genetic risk.

Subcutaneous injections

- The most common maximum acceptable frequency was once a day for people living with MND (33%), current caregivers (36%), and bereaved caregivers (38%). People at high genetic risk showed more varied preferences, with 34% indicating that four injections a day would be acceptable, and 25% each finding either once or twice a week acceptable.

Overall, people with MND and current caregivers were generally more open to frequent dosing for both oral medications and subcutaneous injections, potentially reflecting their willingness to try more intensive treatment options that could offer benefits. In contrast, bereaved caregivers seem to prefer less frequent dosing, possibly due to the burden they had experienced while managing high-frequency treatments for individuals with advanced MND.

Q6. How regularly are hospital visits acceptable to receive treatment?

Participants were asked to assess the difficulty of tolerating or managing various side effects of treatments. People living with MND and those at high genetic risk were asked about tolerability, while caregivers were asked about manageability.

The responses highlighted significant differences in the perceived impact of side effects, reflecting participants' experiences living with MND themselves and providing support in a caregiving role:

- For people living with MND, the most challenging side effects were vomiting (48.2%), breathing difficulties (46.3%), diarrhoea (28.3%), and abdominal pain (28.3%).
- Current and bereaved caregivers also highlighted vomiting (current, 66%; bereaved 74%), breathing difficulties (current 79%: bereaved 78%) and diarrhoea (current 76%; bereaved 67%) as the most unmanageable side effects.
- People at high genetic risk of MND indicated breathing difficulties 58%, muscle weakness (42%), vomiting (33%) and diarrhoea (33%) as the most intolerable side effects.

Some other types of side effects were considered to be more tolerable or manageable:

- People living with MND generally found sleepiness (44%), fatigue (39%), and rash (39%) more tolerable.
- Caregivers found fatigue (current, 86%; bereaved 57%), lack of energy (current 83%; bereaved 63%) and sleepiness (current 79%; bereaved 69%) to be more manageable.
- People at high genetic risk tended to find rash (58%), muscle aches (50%), and tingling sensations (45%) as the most tolerable.

Free-text responses revealed deeper insights into why certain side effects were more challenging. People living with MND expressed a willingness to trade off certain side effects for an effective drug, but quality of life was a major concern.

They emphasised that side effects worsening existing symptoms – particularly breathing difficulties – were especially intolerable, as well as those that are hard to manage with limited mobility, like diarrhoea.

Current caregivers also highlighted quality-of-life concerns. They were worried that certain side effects might worsen existing symptoms and the impact of mobility challenges, making side effects like vomiting and diarrhoea more challenging to manage. Specific concerns included the risk of choking due to vomiting and the impact of incontinence on dignity. The emotional and psychological toll on the person they cared for was also frequently mentioned.

Bereaved caregivers also highlighted the difficulties of managing additional symptoms alongside MND. They emphasised safety risks from certain side effects, such as those affecting breathing and choking, as well as concerns related to quality of life, communication challenges, and the potential for side effects to worsen a person's mobility and independence.

Q7. Would it be acceptable to have severe side effects for a brief time after treatment, if it would mean feeling better for the remainder of time until the next dose?

Survey participants were asked whether they would accept severe side effects for a brief period after treatment, provided it would result in feeling better until the next dose.

The responses varied significantly among different groups, with people living with MND, those at high genetic risk, and caregivers showing varying levels of acceptance:

- Among people at high genetic risk of MND, there was complete acceptance, with 100% agreeing that they would tolerate severe side effects for a short time if it led to feeling better until the next dose. A majority of people living with MND (72.22%) also expressed a willingness to endure short-term severe side effects for longer-term benefits.
- However, caregivers were less likely to accept such side effects. Only 31% of current caregivers found it acceptable, with 41% deeming it unacceptable. Bereaved caregivers showed slightly more tolerance, with 41.79% considering the brief period of severe side effects acceptable, while 26.87% still found them unacceptable.

These results highlight how perspectives on the acceptability of side effects are shaped by each group's unique experience with MND, with a clear divide between those directly affected by the disease or at risk of it and those providing care.

Combined analysis

Insights from the workshops and the survey revealed common themes in attitudes toward DMTs among people affected by MND, highlighting shared values as well as distinct priorities across participant groups.

Overarching themes included a strong preference for non-invasive, home-based treatments, along with a focus on quality of life and manageable side effects. While caregivers tended to prioritise a person's quality of life and dignity, people living with MND or at a high genetic risk of the condition were often more willing to tolerate short-term side effects or treatment burdens if it offered the promise of slowing their disease progression.

Routes of drug administration

Workshop participants highlighted challenges with administering solid oral medications, particularly for those with swallowing difficulties, and opinions about the acceptability of injections varied depending on personal preferences, frequency of administration and perceived benefits. The survey supported these findings, highlighting skin patches, liquid administration and oral gels as the most acceptable administration methods. More invasive options like suppositories, lumbar punctures, and IV infusions were broadly rejected, especially by caregivers. People living with MND, especially those in the earlier stages of the disease, expressed a greater willingness than caregivers to accept any route of administration if it offered potential benefits.

Preferred treatment locations and frequency of visits

Workshop discussions reflected diverse preferences for treatments that could be administered at home or in a hospital, acknowledging individual needs and practical limitations, particularly at the later stages of disease when mobility is reduced. The survey indicated a strong preference for home administration, which was valued for its convenience and comfort.

Most participants favoured hospital visits no more than every two months, with caregivers less open to frequent hospital appointments compared to those living with or at risk of MND.

Acceptability of side effects

Views on side effects varied considerably among workshop participants, with some people living with MND willing to tolerate almost any side effect if it could help to slow their disease progression, while others prioritised maintaining their quality of life.

Survey data provided more detailed insights, revealing vomiting, breathing difficulties, diarrhoea and abdominal pain as the least acceptable side effects. In contrast, fatigue, sleepiness, and rashes were generally considered more tolerable or manageable. Caregivers were generally more reluctant than people with MND or at high genetic risk of the condition to accept severe short-term side effects for longer-term benefits.

Concerns on treatment burden and practicality

Workshop participants highlighted concerns about the physical and emotional burden of treatment, especially related to administration and managing challenging side effects. Caregivers expressed concerns about treatments that compromised the dignity and independence of their loved ones, emphasising a need for practical and easy-to-administer treatments. Survey responses echoed these themes, with caregivers rating certain administration methods, like suppositories and lumbar punctures, as unacceptable. They were also less willing to accept high-frequency dosing, reflecting concerns about the burden of managing complex treatment schedules.

Recommendations

The insights from people affected by MND captured in this report have informed our following recommendations:

1. Prioritise minimally invasive administration methods

Researchers should focus on developing MND treatments that can be administered via skin patches, liquid formulations, or oral gels, which offer ease of use and help maintain patient dignity. Avoid solid oral medications, particularly if they require high-frequency dosing.

2. Consider the location and frequency of treatment administration

Develop medications that can be administered at home, or no more than every two months in a hospital setting, to reduce the burden of treatment. Investigate long-acting formulations or less frequent dosing regimens to reduce complexity for people living with MND and their caregivers.

3. Prioritise side effect profiles that maintain quality of life

Minimise side effects that interfere with a person's identity, mental health, communication, and mobility. If possible, side effects that exacerbate swallowing or breathing difficulties should be avoided as they may impact treatment adherence.

4. Ensure clear communication

Transparency about any potential side effects of treatment, especially those affecting mobility and independence, is crucial to enable informed decision-making by people affected by MND.

5. Use comprehensive outcome measures

Assessing meaningful treatment outcomes should ideally reflect a holistic view of MND – capturing physical, cognitive and emotional symptoms – to better reflect the broader impact of MND on people's lives.

6. Ensure dignity and independence for people living with MND

Develop treatment approaches that respect and maintain a person's dignity and independence.

7. Be aware there is no 'one size fits all'

Listen to what individuals and their families want and tailor treatment to meet their circumstances and preferences, as perspectives on treatment and acceptability of side effects can vary widely among those affected by MND.

> "These recommendations aim to respect the needs and preferences of both people living with MND and their caregivers, supporting quality of life, reducing treatment burden, and encouraging personalised approaches in treatment development and administration."
>
> **Paul Wright, Head of MND Translational Challenge, LifeArc**

Implications for MND research

Future MND research should focus on treatments that prioritise a person's quality of life, minimise physical and emotional burdens, and respect the dignity of people living with MND. By addressing gaps in minimally-invasive administration methods, holistic quality-of-life measures, and side effect management, researchers can move closer to developing meaningful, patient-centred treatments. Early and sustained engagement with people affected by MND will be key to ensuring that research remains aligned with the values, needs, and preferences of those affected by the disease.

Conclusion

This report has provided new and valuable insights into the perspectives of people affected by MND, highlighting key considerations for future DMTs.

By engaging with our MND Insights Group through workshops and conducting a broader community survey, we have developed a deeper and up-to-date understanding of the diverse needs, preferences and priorities that must be carefully balanced when developing new MND treatments.

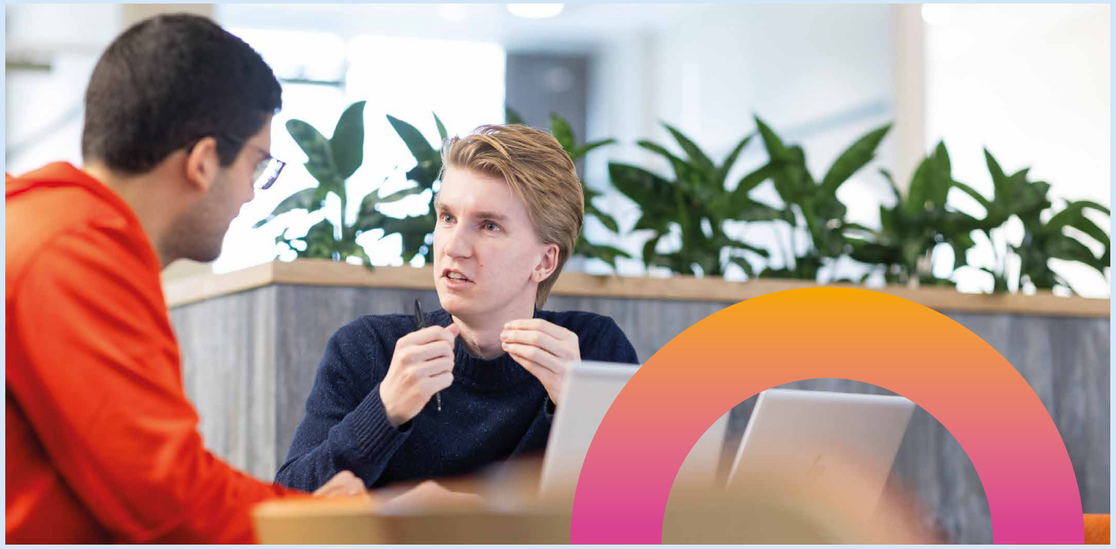
A clear theme emerging from this research is the strong emphasis on preserving a person's quality of life. Across all participant groups, there was a resounding preference for minimally-invasive, home-based treatment administration methods that minimise disruption to daily living. Opinions on the acceptability of side effects varied widely, with people living with MND often more willing to tolerate short-term discomfort if it promised meaningful long-term benefits, while caregivers tended to prioritise maintaining dignity and independence.

Importantly, the findings highlight the complex, variable and highly individualised nature of the MND experience. Perspectives on meaningful treatment outcomes, acceptable trade-offs, and ideal administration methods differed significantly based on a variety of factors including disease stage, age, and personal circumstances.

This emphasises the need for a personalised approach to MND care, with treatments tailored to address the unique needs and preferences of each individual.

Moving forward, these insights will be instrumental in guiding LifeArc's MND Translational Challenge. By prioritising the development of patient-centred therapies that minimise treatment burden, preserve a person's quality of life, and capture meaningful outcomes, we aim to revolutionise the way MND is detected, treated and managed.

Continued engagement and collaboration with the MND community will be crucial to these efforts. Regularly seeking input from people living with MND, current and past caregivers, and those at high genetic risk of the condition will ensure that the research agenda remains closely aligned with their needs and preferences. Only through this sustained partnership can we hope to create a world where MND is truly preventable and treatable.



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