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# Practical Management of Behavioural Impairment in Motor Neurone Disease: MiNDToolkit Feasibility Study

## Study protocol (V9.0)

**STUDY PROTOCOL**
**MiNDToolkit Feasibility Study**


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# Contents

# 1. BACKGROUND & RATIONALE

Motor Neurone Disease (MND) has been known for a long time to affect the motor system and other circuitry in the central nervous system. It is now well established that up to 15% of people with MND can develop Frontotemporal Dementia (FTD), displaying complex changes in 'personality'/behaviour and cognitive functioning (i.e. planning, concentration and language ability). More recently, there has been increasing evidence that MND patients can also present with non-motor symptoms, which are defined as cognitive and behavioural changes or impairments, even without having full-blown MND-FTD (MND combined with FTD). Furthermore, the National Institute for Health and Care Excellence (NICE) MND guidelines published in February 2016, place an emphasis on the importance of non-motor cognitive and behavioural symptom assessment in the scope of disease management (NICE, 2016a). This is further supplemented with new publication of diagnostic guidelines for MND-FTD, there is a stronger emphasis on detection of cognitive and behavioural symptoms that could occur in up to 50% of MND patients (Strong et al., 2017), known as MND with cognitive impairment and/or behavioural impairment.

There are multiple, quick and effective screening tools/methods available for cognitive and behavioural impairment in MND, which have been recently noted in a systematic review of literature (Simon & Goldstein, In Press). Notably these include the Edinburgh Cognitive and behavioural ALS Screen (ECAS; Abrahams et al., 2014), ALS Cognitive Behavioral Screen (ALSCBS; Woolley et al., 2010), Mini-Addenbrooke's Cognitive Examination (Mini-ACE; Hsieh et al., 2015) and Motor Neuron Disease Behavioural Instrument (MiND-B; Mioshi et al., 2014). With these tools, there is increased awareness, more routine assessment and improved detection of cognitive and behaviour changes in MND for healthcare professionals (HCPs). Further, these cognitive and behavioural impairments have been associated with various practical impacts within the families of people living with MND. A recent systematic review of literature showed that behavioural impairment (such as lack of motivation or impulsivity) were associated with increased burden (de Wit et al., 2018). Earlier research has also shown that behaviour as well as cognitive impairment impacts burden in family members (e.g. Burke et al., 2015; Watermeyer et al. 2015). In dementia, impairments relating to cognition or behaviour are manageable through codes of practice applicable to specialist clinics and community teams (NICE, 2016b). Therefore, it is timely to explore tools that might help manage these impairments for both families and HCPs in MND.

We have created the MiNDToolkit for management of behavioural impairment in MND. This Toolkit was comprehensively created through surveying literature/research and multiple consultations with allied HCPs (e.g. Occupational Therapists, Speech and Language Therapists, Specialist Nurses), internationally expert clinicians, international expert researchers, family members of people living with MND-FTD and also people living with MND.

For carers, the MiNDToolkit comprises several psychoeducational online modules that are tailored for the symptoms they are dealing with. These have been added to the study due to the COVID crisis (please see 'study update' below).

For HCPs, the MiNDToolkit is a composition of tools inclusive of educational information, structured interactive clinical reasoning and techniques for management of behavioural change of people with such impairments or MND-FTD.

Before conducting any large randomized control trials of the MiNDToolkit as an intervention it is important to answer the question “Can this study be done?” (NIHR, 2019). Therefore there is need for a feasibility study for the design of future trials.

## 1.1 Study Update: COVID-19 Adaptations

The COVID crisis paused our study from March 2020. We explored a number of avenues to enable continuation of the MiNDToolkit intervention study, including novel ways to reach families that would not require face-to-face sessions. In addition, discussion with NHS managers who collaborate in the study, revealed that care provision offered by their specialist teams “would not go back to what it used to be before COVID”. They also reiterated the additional pressure and rapid changes in their services.

It is important to also note that people affected by MND are or have been shielding to reduce their risk of exposure to COVID. Nevertheless, issues related to behavioural changes continued and it was paramount to identify a new way to enable family and paid carers to take part in research that could lead to improvements in care management – while protecting them from unnecessary risk.

The content of the MiNDToolkit has been remodelled to be delivered via a bespoke online platform. Screening questions, online consent and post intervention follow-up measures are also collected through the platform. The most notable change is that the MiNDToolkit now targets primarily the management of behavioural symptoms, and recruits carers (e.g. family members, paid carers) directly, with additional engagement from specialised MND teams where possible. These are outlined below.

## 1.2 Study Objectives

1) To test the feasibility of the MiNDToolkit online intervention in MND Specialist Settings;

2) To explore the potential of several outcome measures for future evaluation studies (trials)

# 2. METHODS

## 2.1 Participants

The MiNDToolkit intervention will involve up to 30 carers (family carer/relative/live-in professional carer) of people with MND, with additional behavioural impairments.

Sample size revision dated 18/11/2020: based on COMMEND figures, another non-pharmacological feasibility trial on Acceptance and Commitment Therapy for MND patients funded by NIHR HTA, we would estimate a more realistic figure of recruiting 2-3 participants per site, instead of the original target of 60 that was based on observational studies.

## 2.2 Inclusion Criteria

1. Participants will be family carers, relatives or live-in professional carers of:

   - Patients with a diagnosis of MND with cognitive impairment or behavioural impairment, based on Strong et al. (2017) diagnostic criteria, or
   - Patients with a diagnosis of MND-FTD based on Strong et al. (2017) diagnostic criteria.
   - Carers will have at least 7 hours of contact with the person with MND per week and be willing to participate in research activities.
   - Carers must be aged 18 years or over

## 2.3 Exclusion Criteria

- Inability to read or communicate in English (with or without support)
- Participant is a carer of a patient who already has a carer recruited into the study.

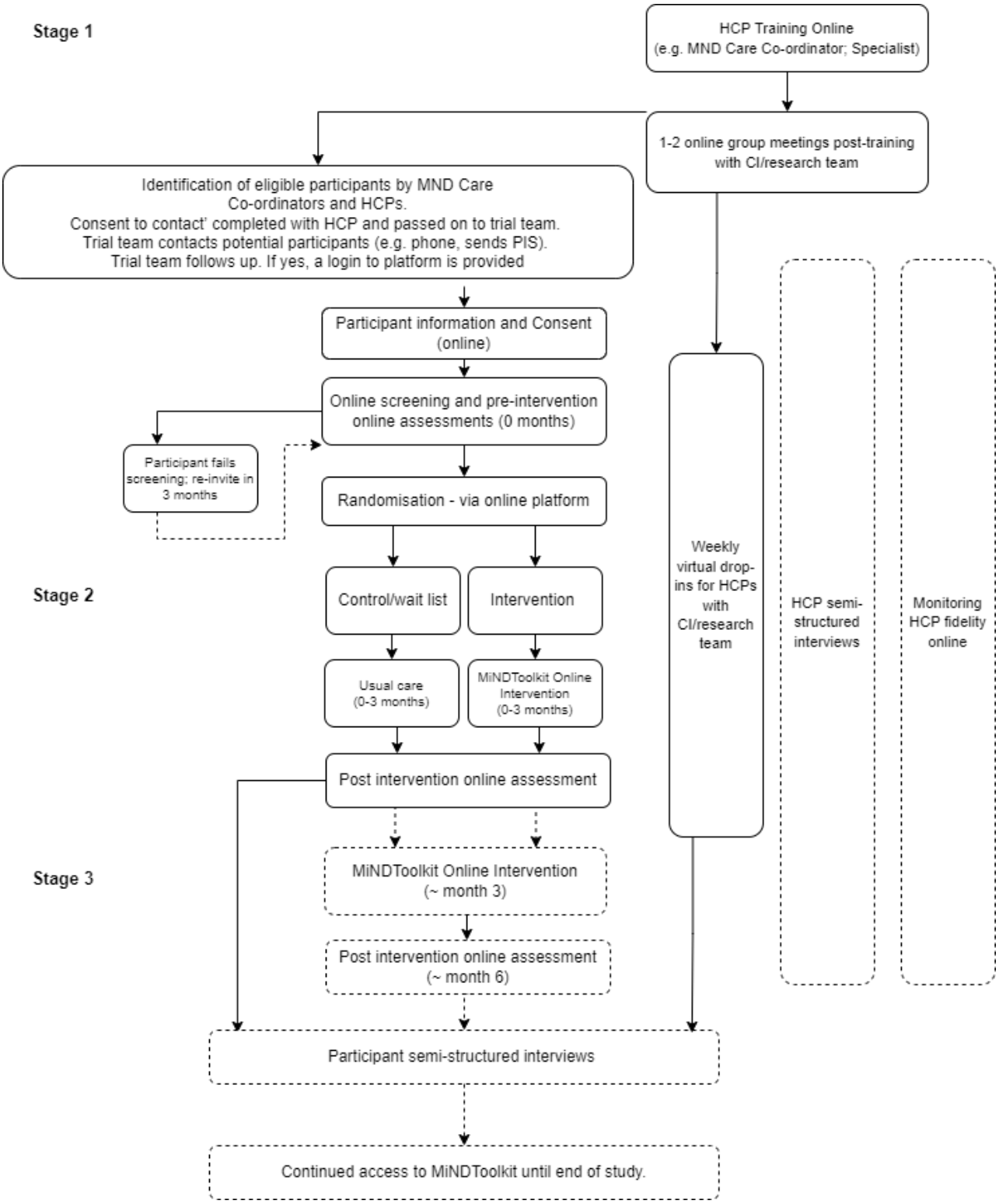
## 2.4 Study Design

The study is a pilot, small, open-label, randomised controlled design to determine feasibility of the MiNDToolkit for use by carers (family carer/relative/live-in professional carers) with optional support from HCPs.

The principle of the MiNDToolkit is to recommend individually tailored techniques to carers for management of behavioural symptoms in MND. These are based on current literature, experts in the field (MND and FTD) as well as techniques reported by current and former carers.

The REC had originally suggested a cross-over design, which was not feasible initially due to the involvement of HCPs and limited resources in our collaborating teams. However, as the MiNDToolkit will be now delivered online, we are able to deliver the intervention to the control group (wait list control) after the post-intervention assessment, as shown on the revised Figure 1. Although the control group will crossover and have access to the intervention after the post intervention timepoint, the intervention group will not crossover to act as controls, which occurs under a normal crossover study design.

Figure 1. Flowchart illustrating participants' pathway from recruitment to completion of the study.



## 2.5 Procedures

The online platform will have a three-way access: 1) research administrator; 2) participant (carer); 3) HCP. This will ensure the HCP can use the portal for training and to utilise the Toolkit in their regular appointments for the period of study.

***Stage 1: Health Care Professional Training***

At least 2 HCPs per site (e.g. Nurses, Occupational Therapists, Speech and Language Therapists) will be invited to an online training session on use of the MiNDToolkit, followed by 1-2 follow-up training meetings in groups with the CI. Group supervisions will be offered weekly during the intervention phase (telephone or via Voice over Internet Protocol systems, e.g. Skype, Zoom). At this early stage, engagement with clinical teams is necessary not only for fidelity but also to gather important information from trainees and users that can improve the training package itself, in preparation for larger future studies. Indeed, preliminary test training has highlighted the need to deliver shorter and intensive training to fit with NHS demands, which has been addressed.

The online training session will involve modules with an overview of behavioural symptoms, assessments and strategies, and how to use the MiNDToolkit online.

***Stage 2: Feasibility Intervention study***

***a) Identification of Eligible Participants***

Potential participants will be identified through a number of clinical teams associated with the MND Care and Research network, such as the Norfolk and Norwich University Hospital (NNUH) NHS Foundation Trust, James Paget University Hospitals NHS Foundation Trust, The Queen Elizabeth Hospital Kings Lynn NHS Trust and Norfolk Community Health and Care NHS Trust. The NNUH clinical team has a current caseload of approximately 46 MND families, and we will also be working with the Norfolk Neurology Community Nurses and other HCPs, who see 50-100 families on average.

Initial approach will be as follows:

- Carers of people with MND attending routine appointments at MND Clinics will be informed about the study by their clinician or supporting HCP, either in person, by telephone or post. Carers who are interested in joining will be asked for consent to share their contact details with the trial research team. This may be done verbally, with site staff completing an electronic or paper consent to contact form on behalf of the potential participant.
- Upon receipt of referrals, a research team member (from CTU/UEA) will telephone potential participants to explain the study. Following this, the team will send an information sheet to potential participants. The trial researcher will contact the carer again within 1week, however the potential participant can confirm sooner than this second contact from the CTU team that they would like to participate. If the participant would like to join the study, a unique login to the online platform (including electronic consent) and password will be sent to them by email).

Carers of people with MND taking part in other research studies, such as the FACTOR-MND (REC 20/WM/0185) or CHANGE-MND study (REC 17/LO/1820) may be invited to the present study. These ongoing projects are led by the CI of the current study at the University of East Anglia. Carers of people with MND taking part in these studies will already have given their consent to be further contacted about participation in other research.

### *b) Participant Information and Consent*

After being given access to the consent form on the platform, participants will be able to complete this in their own time.

All participants will be given up to 48 hours (standard practice) to read the information sheet and consent form before being re-contacted by the research team. This will allow potential participants time to consider whether they wish to be included in the study or not.

If there is no response, potential participants will be contacted again to see if they are still interested, have further questions, have decided not to take part, or need any assistance with the electronic consent process. Reasons for deciding not to take part will be captured where possible.

### *c) Screening/Baseline measures (0 months)*

If consent is provided, participants will then be asked to complete the screening and baseline assessment questionnaires online. Of note, some measures (e.g. ALSFRS-R adapted) were modified in terms of sentence construction, as they are being completed by the carer. For example, instead of 'normal speech processes', it now reads 'They have normal speech processes. Sentences became longer to ensure they were clearer for the carer, following feedback from PPI test users and clinicians. Additionally, some questions were further explained to help carer in completing the information. For example, please enter month and year. We also had to break down questions set up as tables on paper, as they are now presented as separate questions due to the online nature of the questionnaire where only one question is presented at a time. This was a point raised by PPI members, who asked for a simple view of the questionnaires, e.g. not presented as pages (as in paper questionnaires), but as one question at a time.

This assessment will include the following (in **bold** are domains assessed by each instrument):

#### *Screening measures*

- **Carer socio-demographic, medical history proforma.**
- ALS-Functional Rating Scale Revised (ALSFRS-R; Cedarbaum et al., 1999) is an interview-based assessment of progression of **functional disability** in people with MND. Adapted for completion by carer.
- Motor Neurone Disease Behavioural Instrument (MiND-B; Mioshi et al., 2014) is a multiple domain carer-rated short form measure of **changes in the behaviour of the**

**person with MND**. For the purposes of this study, we will also ask carers to rate the distress caused by the behaviour.

The screening assessment will be automatically scored by the online platform. If the screening criteria are not met, the carer will be contacted again in approximately three months for a repeat screening assessment, when symptoms of the person with MND may have changed.

***Baseline measures***

*Outcome measures being tested:*

- The Patient Health Questionnaire 9 (PHQ-9; Kroenke et al., 2003) is a very brief multipurpose self-rated instrument for screening, diagnosing, monitoring and measuring the severity of **depression** for the carer.
- The Generalized Anxiety Disorder Questionnaire 7 (GAD-7; Kroenke et al., 2007) is a very brief self-rated questionnaire measuring for symptoms of generalized **anxiety** disorder for the carer.
- The Adapted Client Service Receipt Inventory (CSRI; Beecham & Knapp, 2001) is a tool to collect information on the range of **services and supports** currently being utilised by the person with MND.
- The Carer Experience Scale (CES; Al-Janabi et al., 2008) is a short, self-report measure for the carer of their **caring experience** for use in economic evaluation that assesses care-related quality of life in multiple domains including activities outside caring, fulfilment from caring, and relationship with the care recipient.
- ICEpop CAPability measure for Adults (ICECAP-A; Al-Janabi et al., 2012) is the short measure of **wellbeing** for the carer. The ICECAP-A is a measure of capability of the general adult (18+) population for use in economic evaluation.
- Acceptance and Action Questionnaire II (AAQ-II; Bond et al., 2011) is a 7-item self-report questionnaire assessing people's general levels of **psychological flexibility**, the ability to be open, present-focused, and to change or persist in behaviour according to changing internal and external circumstances.

*Measures that trigger modules in intervention:*

- Adapted Frontotemporal Dementia Rating Scale (FRS; Mioshi et al., 2010) is a 30-item, carer interview-based measure of **disease severity** in FTD and has been validated in MND.
- MiND-B (from screening)

*Other relevant assessments*

- Person with MND brief proforma including clinical MND phenotype and other questions relevant to the care provided by the carer, e.g. does the person with MND receives other support that may alleviate carer work

The baseline assessment will be automatically scored by the online platform. Please see Appendix 1 for table of Schedule of Assessment.

### *d) Randomization*

After completion of pre-intervention assessments, eligible recruited participants will be randomized by the CTU, using a randomisation table provided by the study statistician. The participant will be allocated to either the MiNDToolkit intervention group (described below in section e) or wait list control/usual care group. Those allocated to usual care will serve as a control group. The platform will automatically notify MiNDToolkit-trained HCPs at sites of participants assigned to the MiNDToolkit intervention group.

For participants assigned to the usual care group, there will be no change to the care and support provided to the carer or the person with MND who they care for during the control period.

### *e) MiNDToolkit Intervention (0 - 3 months)*

The new online intervention comprises: modules that (1) target symptoms identified in the screening data; (2) suggest which strategies the person with MND and carer would benefit from; (3) utilise these techniques during each week. In addition, (4) if the HCP of the person with MND has also been trained, they will demonstrate those techniques for the carers during consultations.

Each week, the carer will be given modules with information on behavioural symptoms as well as strategies to apply, tailored to the issues identified during the screening assessment. It is expected that the carer will apply these techniques in their daily routine after the modules for a week. At any following MND consultation with a HCP trained in the MiNDToolkit, a *review* of strategies utilised will be recorded and the HCP will discuss with the carer what may have worked or not, and examples of context. The HCPs will then record this information on the platform.

An automatic email/text reminder will be provided when a new module starts and when participants have not accessed any learning resources for a few days since the first reminder.

### *Post-intervention assessment (within 1 month after the end of the intervention)*

After the three-month intervention or usual treatment period, participants will be notified of the post-intervention assessment to complete via the platform.

Participants will be asked to complete the same assessments to that of the screening/pre-intervention assessment minus the socio-demographic, medical history questionnaires. In summary, the post-intervention assessment will include the following:

- About the person with MND: ALSFRS-R, MiND-B; FRS adapted, CSRI
- Carer questionnaires: PHQ-9, GAD-7, CES, ICECAP-A, CSRI, AAQ-II (six outcome measures being tested)

If post-intervention assessments are not completed after one week of the notification, a reminder will be sent. After a further week, participants will be contacted by telephone and given the option to complete the questionnaires over the phone with a researcher.

***Stage 3: Opportunity for wait list controls to join the MiNDToolkit intervention platform***

After the equivalent period of intervention (post-intervention assessment, 3 months), participants allocated to control will be given access to the MiNDToolkit Intervention Platform. This step had originally been suggested by the REC; given that now the intervention does not require intensive time from the HCP teams, we are able to offer this opportunity to all participants (See Fig 1). A post-intervention assessment will be issued following three months of using the toolkit, as per section f above.

The additional 3-month intervention and post-intervention assessment will also be made optionally available to participants originally randomised into the intervention group.

*Monitoring and Semi-structured Interviews*

1. Platform Monitoring

As shown in Figure 1, there will be continued monitoring of delivery of the MiNDToolkit to ensure its acceptability, feasibility and treatment fidelity. The following will be recorded:

- Numbers of potentially eligible participants
- Number of participants subsequently recruited into the study
- Number of withdrawals, and reason for withdrawal
- Use of the MiNDToolkit by carers: engagement with the platform, feedback on implementation and acceptability.
- Use of the MiNDToolkit by HCPs: frequency of use, duration/time taken.

These will be recorded through the MiNDToolkit platform. If HCPs or participants decide to continue accessing the platform after the end of the trial, these data relating to their use of the MiNDToolkit will continue to be collected. Access to the platform will be allowed for as long as there are adequate funding and resources to maintain the website, however data will only be collected for the purposes of analysis until the end of the ethical approval for the study.

2. Semi-Structured Interviews

In addition to platform monitoring, (1) HCPs will undergo a semi-structured interview on their utility and experience using the MiNDToolkit; (2) carers will be interviewed on their utility and experience using the MiNDToolkit, and in relation to barriers for implementation of strategies advised. The interviews will be optional for both HCPs and carers. As the MiNDToolkit is a new intervention we will be considering themes generated in the interviews and observations of delivery to inform minor edits of the MiNDToolkit and its online training for HCPs.

**Sample Size and Selection**
Participating HCPs will be invited to take part, up to a maximum of 20 HCPs. Purposive sampling will be used to select HCPs with the greatest experience and engagement with MiNDToolkit, across a range of study sites.

Carers who have been exposed to the intervention will be invited to take part, up to a maximum of 20 carers.

**Recruitment and Consent**
All HCPs participating in MiNDToolkit will consent to the collection of the platform utility data above and to being approached to participate in the voluntary semi-structured interviews via the platform. Carer participants also consent to their general participation in the study via the platform, including being approached to take part in an optional interview. In both cases, the participant information sheet will contain information relating to the optional interviews.

HCPs and carers who are approached to take part in the interviews will be asked to complete an interview consent form by email or post. HCPs may be interviewed at any

time during the intervention delivery period. Carers will be interviewed after their final post-intervention assessment.

Those who express an interest will be contacted to arrange a mutually convenient time to conduct the interview. Interviews will be conducted via telephone or video call (approximately 30 minutes). Prior to conducting the interview, verbal consent will be re-confirmed. The interview will then follow a semi-structured, open-ended question schedule using an interview topic guide.

The audio and video recordings from interviews will be transcribed verbatim by an external company. Identifiable data will be removed from the transcripts and the recordings will be filed using study ID only.

## 2.6 Data Analysis Plan

### *1. To examine the feasibility of the MiNDToolkit for use with health professionals and carers of people with MND*

Feasibility and acceptability will be evaluated by:

- Numbers of potentially eligible participants who meet the inclusion criteria
- Number of participants subsequently recruited into the study
- Attrition rate, and reason for withdrawal (e.g. families do not like the novel approach; professionals may have concerns about the tools)

The feasibility of participant recruitment will be examined. This will include examining numbers assessed for eligibility from each recruitment strategy, numbers eligible, and reasons for ineligibility or non-participation. Attrition rates, and time needed to collect data will be recorded throughout the study. How helpful the intervention has been to the carer will also be recorded at the post-intervention assessment.

Data analyses: we will compare our rates of eligible participants, recruitment, and attrition rates with those of published studies in MND interventions, to evaluate if the MiNDToolkit was well accepted by families and professionals, and feasible for professionals. Formally, we will estimate each rate with an associated 95% confidence interval. Of note, current published studies may not provide the ideal estimates for comparison to our proposed study, given the differences in the nature of the intervention. For this reason, we will have a cautious approach in the interpretation of attrition rates for the MiNDToolkit.

We will also collate any feedback that professionals trained and using the MiNDToolkit may have, in order to review the toolkit for the feasibility trial.

### *2. To preliminarily explore the impact of the MiNDToolkit intervention on relevant carer variables, such as wellbeing, distress, quality of life.*

Data analyses: the data analyses will be used to assess: (i) the degree of completion of each outcome measure and (ii) potential impact of the intervention on each.

(i) We will provide an estimate of the number of individuals completing each outcome measure and provide a 95% confidence interval with each estimate. We will also assess the number of missing items and for each with attention to any particular pattern. The distribution of each measure will be inspected to assess the possibility of 'ceiling' or 'flooring' effects. which would make an outcome inappropriate for a trial.

(ii) A comparison will be made between the MiNDToolkit and treatment as usual group with respect to each of the above outcome measures. Assuming a Normal distribution (or after an appropriate transformation) the difference in means will be estimated with a 95% confidence interval. The difference will also be expressed as a 'generic' (or Cohen's) Effect Size in order to assess the relative impact on each measure. The within group standard deviation will also be estimated, with 95% confidence intervals, which will be useful for future studies.

# 3. ETHICAL CONSIDERATIONS

## 3.1 Research Ethics

The research clinic will be run in compliance with the principles of the Declaration of Helsinki (1996) and Good Clinical Practice (GCP-ICH 1997). All researchers working in the clinic will receive training in GCP-ICH guidelines and any relevant future acts and regulations.

Participant information sheets, consent forms, and the study protocol (created with reference to the National Research Ethics Service guidance and input from Patient and Public Involvement) will make it clear that participation is voluntary and participants can withdraw at any time without giving a reason and without the care they receive from the NHS being affected.

Some of the measures used are either routine in the NHS clinics or have been validated for the neurodegenerative conditions involved in this project. Withdrawal may occur for several reasons, including change in circumstances (e.g. health status of person with MND), intolerance of the assessments/intervention by the carer, or a change of carer. If a participant moves out of the area, participation can still continue with their consent. If the person with MND passes away, the carer will be automatically withdrawn from the study and a condolence letter will be sent via post or email from the central team informing them that their account will be inactivated so that they no longer receive notifications sent from the platform. Participant assessments will be tracked by the MiNDToolkit platform to prevent unnecessary repetition of tests or questionnaires. Furthermore, following input from the trial management group and PPI, participants and HCPs will be allowed continued access to the MiNDToolkit following the end of the trial while funds are available for running costs enabling the platform to be open.

## 3.2 Safety

The risk of a serious adverse event arising from any of the research activities involved in this study is extremely low. Patients with MND about whom data is being anonymously collected are under the care of specialist clinics for their condition during the period of the study. The main focus of the study is on the health and wellbeing of the carer, and the intervention aims to provide psychoeducation and patient management suggestions to the carer rather than offering a clinical intervention to the person with MND.

The Trial Management Group (TMG) will assist with developing the design, co-ordination and strategic management of the trial. They will oversee any safety issues that arise during the trial. The membership, frequency of meetings, activity (including trial conduct and data review) and authority will be covered in the TMG terms of reference.

Carers will be given the opportunity to report any adverse events that they feel are related to the intervention at the post-intervention assessment, and this will be monitored by

the CI and site PI. If a researcher becomes concerned about the safety or welfare of a carer or the person they care for during the study period, they will encourage the carer to contact their GP, and sign-post them to local sources of support. If a carer indicates on the online platform that they are experiencing thoughts of self-harm (Patient Health Questionnaire 9 – item 9), the CTU and linked HCPs will be automatically notified and a list of contact details for support and crisis lines will appear for the carer at the end of the testing battery.

## 3.3 Trial Management Group (TMG)

| Name | Affiliation | Role and responsibilities |
|---|---|---|
| Professor Eneida Mioshi | School of Health Sciences, University of East Anglia | Chief Investigator |
| Professor Michael Hornberger | Norwich Medical School, University of East Anglia | Professor of Dementia Research |
| Helen Copsey | Norfolk and Norwich University Hospital | Principal Investigator - MND Care and Research Network Coordinator, Norfolk |
| Prof Lee Shepstone | Norwich Medical School, University of East Anglia | Professor of Medical Statistics |
| Dr Polly-Anna Ashford | University of East Anglia & NCTU | CTU Senior Trial Manager - operational oversight |
| Martin Pond | University of East Anglia & NCTU | Head of Data Management - data management oversight |
| Emma Flanagan | University of East Anglia & NCTU | Trial Manager |
| Danelle Breach | University of East Anglia | Sponsor representative |
| Sue Heal | | PPI |

# 4. DATA MANAGEMENT, CONFIDENTIALITY AND DATA STORAGE

Essential trial issues, events and outputs, including defined key data points, will be detailed in the MiNDToolkit trial Data Management Plan.

We follow standard good research practices within our departments, to ensure confidentiality of electronic and hard copy data, in keeping with most recent data protection regulations. All data will be handled in accordance with the Data Protection Act (2018) and the EU GDPR. Participants will be assured that confidentiality will be maintained unless there is evidence of risk of harm to self or others.

Any paper copies of personal trial data will be kept at the participating site in a secure location with restricted access. Following consent, identifiable participant data will be kept on the trial database to allow authorised members of the trial team to contact participants in order to arrange appointments and assessments. Only authorised trial team members will have password access to this part of the database. At trial enrolment the patient will be issued a participant identification number and this will be the primary identifier for the participant and their study data.

The participant's consent form will contain their name. These will be primarily stored in the online database, but will also be kept and will be archived at the trial site, and copies may also be accessed and stored at NCTU for monitoring purposes. Consent forms will not be kept with any additional participant data.

Data will be entered under the participants' platform PID number onto the central database stored on the servers based in Amazon Web Services' London EU Region. This will also include personally identifiable data including names, email addresses and contact phone numbers. Access to the database will be via unique, individually assigned (i.e. not generic) usernames and passwords, and only accessible to members of the MiNDToolkit trial team at UEA, and external regulators if requested. Each participant's data will also be accessible to the specific site team responsible for their recruitment and delivery of the intervention. The servers are protected by firewalls and are patched and maintained according to best practice. The physical location of the servers is protected physically and environmentally in accordance with University of East Anglia's General Information Security Policy 3 (GISP3: Physical and environmental security).

The database and associated code have been developed by AAH Software Limited, in conjunction with the MiNDToolkit trial team. The database software provides a number of features to help maintain data quality, including; maintaining an audit trail, allowing custom validations on all data, allowing users to raise data query requests, and search facilities to identify validation failure/ missing data.

After completion of the trial the database will be retained on the servers of AAH Software Limited and the dataset for analysis will be transferred to servers at UEA for on-going analysis of secondary outcomes.

The identification, screening and enrolment logs will be held locally by the trial site. This will either be held in written form in a locked filing cabinet or electronically in password protected form on hospital computers. De-identified participant data including screening logs and

withdrawal forms may be shared between sites and the central NCTU team via a secure Microsoft OneDrive folder hosted by NCTU. After completion of the trial the identification, screening and enrolment logs will be stored securely by the sites for 5 years unless otherwise advised by NCTU.

In accordance with good practices locally we will hold non-identifiable data for a minimum of 10 years within the Faculty of Medicine and Health Sciences, UEA. Individual data will be anonymised and indexed by an alphanumeric reference code, which is kept separately from other data and retained only by the study team. It will not be possible to identify participants' individual data without this code. All non-identifiable data will be kept within a locked building with keycard access doors. Anonymised electronic data will be stored and managed using databases encrypted with industry standard cryptographic methods and protected by passwords. Hard copy data will be stored in a locked cabinet in a locked room to which only the study team have access.

Relevant information will be shared between other members of the department (of the participants who will be seen in departmental clinics), and UEA collaborators, and with researchers undertaking other ethically approved research including national and international collaborations, who all adhere most recent data protection regulations and confidentiality. This information will be anonymized prior to sharing. If participant identifiable data is required (for example to contact participants regarding upcoming research projects), their identifiable information will not be linked to the current research project but rather stored on the clinic databases for which consent has previously been sought.

## 5. COMPLAINTS

A system is in place that enables complaints to be directed either the Head of School, where the Chief Investigator is based, or the respective NHS Trust independent patient liaison service (PALS). Contact details for all of these sources are provided on the participant information sheet.

## 6. SPONSORSHIP AND INDEMNITY

This study will be sponsored by UEA. UEA has appropriate insurance policies in place to provide professional indemnity and public liability cover. Medical personnel on the study are also advised to have additional personal medical indemnity.

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# Appendix 1. Schedule of Assessment: MiNDToolkit Feasibility Study

| | **Consent + Screening measures**<br><br>**(0 months)** | **Baseline measures**<br><br>**(0 months)** | **MiNDToolkit Intervention**<br><br>**(0 – 3 months)** | **Post-intervention Assessment**<br><br>**(within 1 month after end of intervention)** | **Second post-intervention assessment**<br>**(0-6 months)**<br>***For intervention group participants who continue to use modules or cross over from control group*** |
|---|---|---|---|---|---|
| Online session length (minutes approx.) | **15** | **30** | **10 to 20** | **30** | **30** |
| ***Carers (about MND patients)*** | | | | | |
| MiND-B | ☑ | | | ☑ | ☑ |
| ALSFRS-R | ☑ | | | ☑ | ☑ |
| FRS adapted | | ☑ | | ☑ | ☑ |
| CSRI adapted | | ☑ | | ☑ | ☑ |
| Socio-demographic, medical history | | ☑ | | | |
| ***Carers (self)*** | | | | | |
| Informed Consent | ☑ | | | | |
| Socio-demographic, medical history | ☑ | | | ☑ | ☑ |
| PHQ-9 | | ☑ | | ☑ | ☑ |
| GAD-7 | | ☑ | | ☑ | ☑ |
| CES | | ☑ | | ☑ | ☑ |
| ICECAP-A | | ☑ | | ☑ | ☑ |
| AAQ-II | | | | ☑ | ☑ |
| Semi-structured Interview | | | | ☑ | |
| MiNDToolkit Intervention | | | ☑ ☑ ☑ | | |
| ***HCP*** | | | | | |
| Fidelity Monitoring | | | ☑ | ☑ | ☑ |
| Semi-structured Interview | | | | ☑ | |

PHQ = Patient Health Questionnaire, GAD = Generalize Anxiety Disorders scale; MiND-B = MND Behavioural Instrument; ALSFRS-R = ALS Functional Rating Scale-Revised; CES = Carer Experience Scale; ICACAP-A = ICEpop CAPability measure for Adults; AAQ-II = Acceptance and Action Questionnaire II; CSRI = The Client Service Receipt Inventory; FRS = Frontotemporal Dementia Rating Scale