Telehealth in MND-Research (TIM-R): A research database for MND Protocol

SHORT STUDY TITLE / ACRONYM

Telehealth in MND-Research / TIM-R

PROTOCOL VERSION NUMBER AND DATE

Version 1 – 12 March 2024

RESEARCH REFERENCE NUMBERS

IRAS Number:	340577
SPONSORS Number:	187038
FUNDERS Reference:	United2EndMND – Phase 1

Contents

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2. Protocol Summary

Title	Telehealth in MND-Research (TIM-R): A research database for MND Protocol
Acronym	TIM-R
Project Aims	The aim of this study is to implement the Telehealth in MND system (TiM) as a research database allowing for people with MND (pwMND) to take part in research and provide data remotely.
Project Design	TiM-R will act as a research database to allow for data collection from pwMND. The data will involve questionnaire responses relating to MND that will be completed remotely. Generic ethical approval will cover a range of prospective research regarding remote questionnaires that can be completed on TiM-R by pwMND. Researchers will be provided with access to anonymised data, dependent on approval from a data management committee.
Study Participants	PwMND.
Eligibility Criteria	Inclusion criteria: PwMND using TiM-Care as part of their clinical service or pwMND who opt-in to TiM-R.
Sample Size	All eligible participants who consent to TiM-R will be included. There is no upper restriction on sample size.
Project Duration	The TiM-R system will be available for pwMND for at least 50 years. Data collected will be stored and available in an anonymised format for researchers indefinitely.

3. Abbreviations

DPUK: Dementia Platform UK

HCPs: Healthcare Professionals

MDTs: Multidisciplinary Teams

MND: Motor Neuron Disease

pwMND: People with MND

TiM-C: Telehealth in MND-Care

TiM-R: Telehealth in MND-Research

TRE: Trusted Research Environment

TTP: Trusted Third Party

4. Background

Motor Neuron Disease (MND) is an incurable disease, causing progressive weakness of muscles involving the limbs, speech, and swallowing, leading to progressive disability and eventual respiratory failure. In the UK, there are approximately 5,000 people with MND (pwMND) at any one time (Opie-Martin et al., 2020). The average life expectancy following diagnosis is two to three years but the course of MND can vary from only a few months to over ten years. The distress and burden of the disease affects pwMND, their family, and carers and the relenting progression of disability causes social, emotional, and financial strain (O'Brien et al., 2012; Whitehead et al., 2012).

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5. TiM-Care

To provide more responsive care for pwMND and their carers, the Telehealth in MND-Care (TiM-C) on MyPathway system was developed. TiM-C is an online system that enables pwMND and their carers to report their symptoms to healthcare professionals (HCPs) from their homes using an app or via the online website (Hobson et al., 2018). Users are asked to complete symptom questionnaires (e.g., appetite, weight, functional rating, breathing, mental health), answers to which are securely sent to the clinical portal (see figure one).

TiM-C was co-developed with pwMND, carers, and HCPs (Hobson et al., 2019a; Hobson et al., 2019b). The system is easy to use, even for those with significant disabilities, acceptable, and low in burden, taking approximately five minutes per week to complete. 85% of pwMND would recommend TiM to others and 95% would use TiM if they could not travel to clinic. HCPs found it accurate and easy to use (Hobson et al., 2019a; Hobson et al., 2019b).

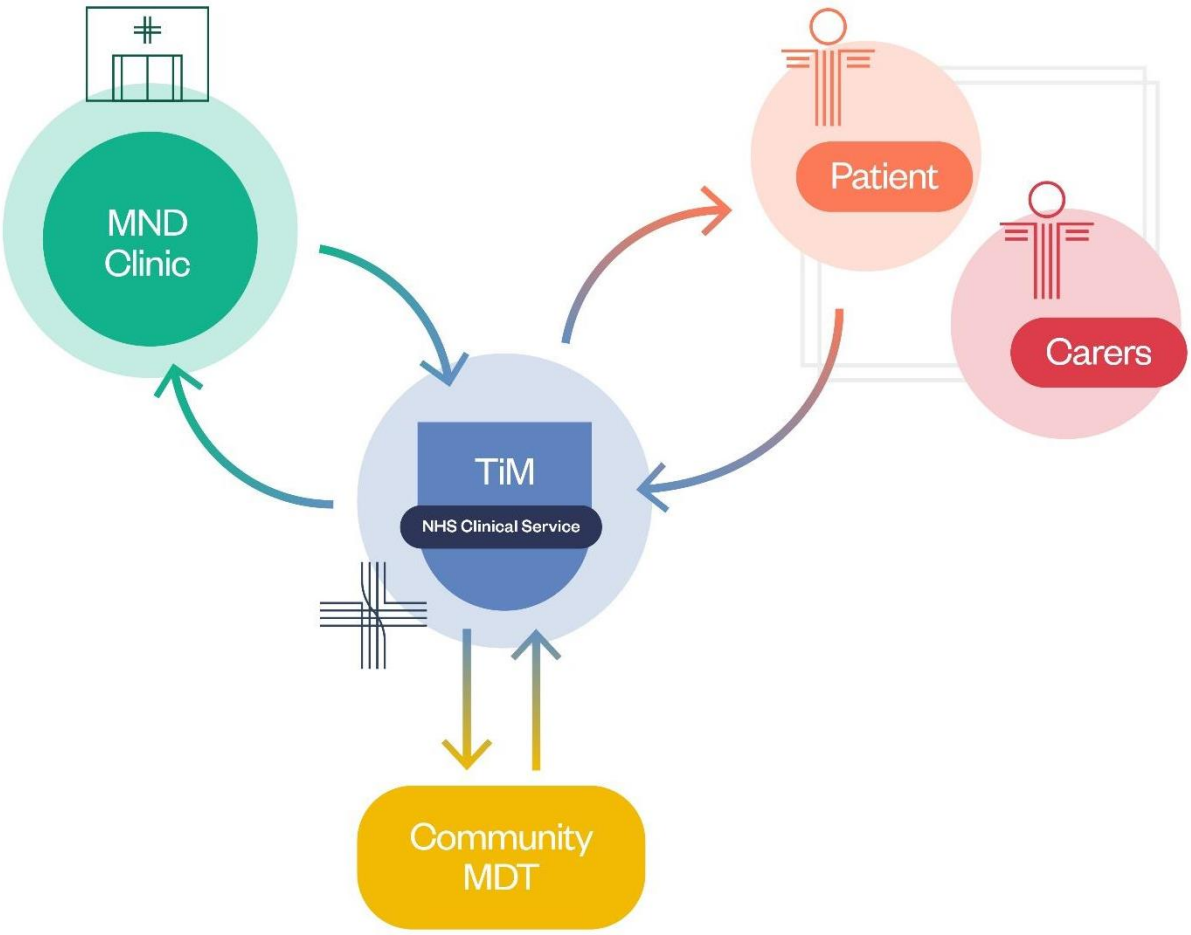

FIGURE 1: TIM-CARE AND INTERACTIONS WITH DIFFERENT USER GROUPS.

6. TiM-Research

To provide pwMND greater access to research from the comfort of their own homes, and collect longitudinal data relating to symptoms and treatment, we have created Telehealth in MND-Research (TiM-R). TiM-R will send regular symptom questionnaires to pwMND, whilst also enabling invitations to participate in future projects to be sent to those who are eligible. Results from research projects can then be sent back to participants (see figure 2). Anonymised data from the questionnaires will be made available to researchers in a controlled database.

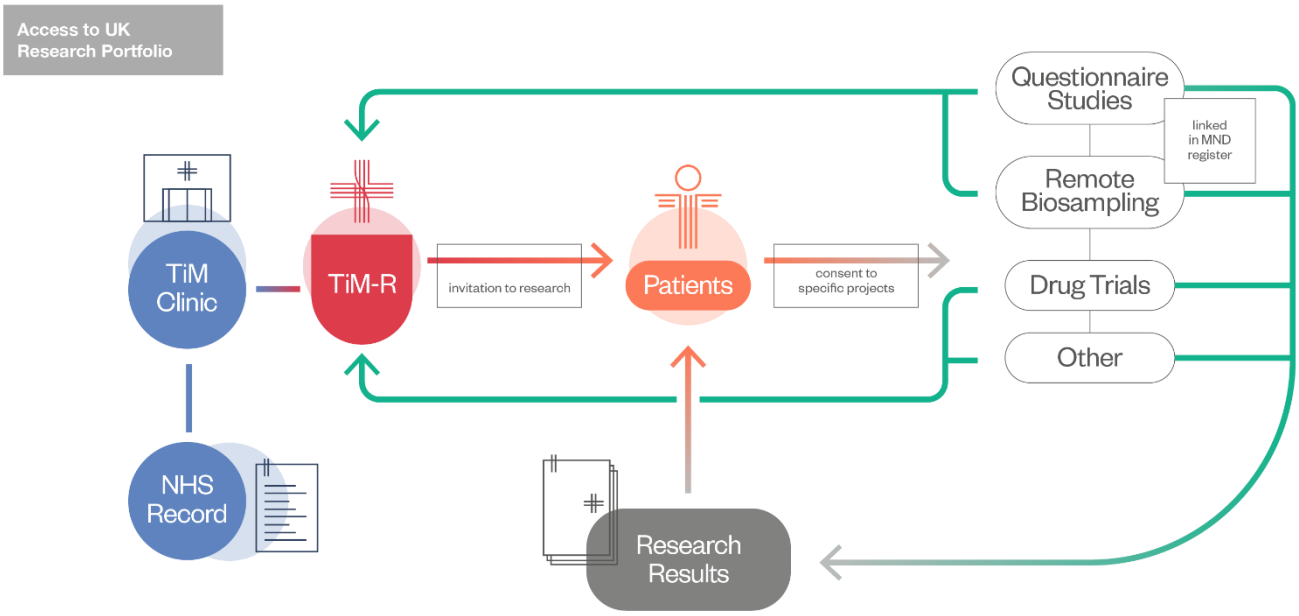

FIGURE 2: TIM-RESEARCH PROVIDING PWMND ACCESS TO RESEARCH.

7. Aim of the project

The aim of this project is to create a research database that pwMND can be invited to and submit regular data (i.e., TiM-R). Users can then be invited to research projects and notified of results. Researchers can apply to a Research Management Committee for access to anonymised data.

8. Project Design

PwMND will be invited to TiM-R through two methods.

If they are using TiM-C as part of their clinical care, a notification will appear on their account describing the purposes of TiM-R and providing the participant information sheet (PIS). They can then provide consent if they are willing to join TiM-R. If the individual does not want to join TiM-R, they can still use TiM-C to receive clinical care.

If the individual is not using TiM-C as part of their clinical care, they may still join TiM-R by responding to a study advert, which will describe the purposes of the study and a link to the PIS. Advertisements will be distributed through social media, relevant charities (e.g., MND Association), and patient support groups. If willing, the participant can follow links on the PIS to create their TiM-R account, part of which will include providing consent for the purposes of this study.

Regardless of the invitation method, once the participant has consented, they will have access to TiM-R and will start to receive regular research questionnaires (see section 9). They may also receive invitations to other research projects for which they are eligible. For each of these future projects the user can choose whether to participate.

The participant can choose to withdraw from TiM-R at any time without having to give a reason by contacting the Research Management Committee. Contact details will be available through TiM-R. Any withdrawal from TiM-R will not affect participants' ability to use TiM-C.

Researchers can contact the Research Management Committee to gain access to anonymised data collected through TiM-R. The exact process is described in section 12. Providing that the reason for this data usage falls under one of the topics covered by this generic ethical approval (see section 11), researchers will not require their own NHS ethical approval to use this data. If the Research Management Committee agrees access to anonymised data, the researcher will be provided with log in details to a Trusted Research Environment (TRE), where they can perform analyses and write up necessary reports.

9. Clinical Data collection

Once pwMND have created their TiM-R account, they will be asked to complete regular questionnaires. These are listed in table 1. Additional questionnaires may occasionally be added, either by a researcher request or to update the system in line with literature and patient reported outcome measure development. No questionnaire will ask sensitive questions relating to protected characteristics. The addition or removal of a questionnaire will be dependent on a majority decision of the Research Management Committee, who will consider user burden and justification of need for any adaptations.

Questionnaire name	What it measures	Frequency
Demographics	General participant information	Once
Coping Index-ALS (Young et al., 2021)	Coping strategies	Once every 2 months
ALSFRS-r (Cedarbaum et al., 1999)	Functional rating	Once every month
EQ-5D-5L (Herdman et al., 2011)	Quality of Life	Once every 2 months
Dyspnoea-12 (Yorke et al., 2011)	Breathlessness	Once every 2 months
M-HADS-D (Gibbons et al., 2011b)	Anxiety and depression	Once every 2 months
Neurological Fatigue Index-MND (Gibbons et al., 2011a)	Fatigue	Once every 2 months
WHOQoLB (Group, 1994)	Quality of life	Once every 2 months
MND-Social Withdrawal Scale (Gibbons et al., 2013)	Social withdrawal	Once every 2 months
WHODAS (Üstün, 2010)	Disability	Once every 2 months
Rosenberg Self-Esteem Scale (Rosenberg, 1965)	Self-esteem	Once every 2 months
General Self-efficacy Scale (Schwarzer & Jerusalem, 1995)	Self-efficacy	Once every 2 months

Table 1: TiM-R questionnaire schedule.

PwMND who also have a TiM-C account complete regular symptom questionnaires. We will ask these users to consent to the questionnaires to also be uploaded to the research database and used for research purposes, after they have been anonymised. This will be included in the PIS. The questionnaires include the SNAQ, PHQ-8, and GAD-7 (Kroenke et al., 2001; Rolland et al., 2012; Spitzer et al., 2006); however, these may change over the course of this project, depending on the needs of clinical teams using TiM-C.

10. Research Project Overview

The database will support MND researchers inside and outside of the UK and their collaborators. Any outcomes of the research will provide information to improve the care, quality of life, and treatment of pwMND. All academic outputs will be publicly available on a dedicated website.

Only staff and researchers who have completed relevant research data security training will be granted access to TiM-R. The Research Management Committee will be responsible for ensuring that all participant-identifiable data is excluded from available datasets.

11. Areas of research covered by generic ethical approval.

The areas of research that are covered under this protocol and ethical approval are:

- MND-related studies that will facilitate and support the development of clinical care and advance the knowledge of HCPs and researchers in attempting to find new treatments and methods of improving quality of life for pwMND and carers.
- Studies looking for specific trends or correlations in the data, aiding in understanding of the disease progression and investigating potential therapeutic benefits or targets for future therapies.

12. Access to Data for Research Purposes

The process for all researchers wishing to request access to data from the clinical database for research purposes is:

- Read the online information regarding what data is available and for what purposes it can be used for
- Use the online application to provide a description of the project, what data is requested, and for what purposes
- The Research Management Committee will respond to the application within 90 days
- If approved, the researcher will be asked to accept the terms and conditions of using TiM-R data
- The researcher will then be provided with log in details for the TRE, where they can access and analyse the data

Access may be provided to researchers within universities and commercial companies both inside and outside of the UK. We may charge a small fee to researchers for the use of data to support the upkeep of TiM research.

13. Data storage and access

Data will be stored on Dementia Platform UK (DPUK) Secure eResearch Platform, hosted by Swansea University. DPUK acts as an enabling infrastructure, working with data owners to facilitate the curation and storage of data and access to that data.

Cohort data will be housed in its own dedicated area of the UKSeRP (https://serp.ac.uk/serp-uk/), readily accessible by cohort permitted persons, and upon request and subject to access procedures by the Research Management Committee. This system uses two vendor firewalls, two factor authentication for data analysts, weekly vulnerability scanning, annual penetration testing, and meets ISO27001 accreditation. All data is in File Store. Backups are done via VMBackups and backed up daily.

Upon uploading of data, a dataset will enter into a split-file anonymisation process, to reduce the risk of identifying individuals. This process is undertaken with NHS Wales Informatics Service (NWIS), a Trusted Third Party (TTP) of Swansea University, who are contracted to perform one half of the split-file anonymisation.

Data held by DPUK will only be made available to researchers who have successfully completed the DPUK Study Application process (described in section 12).

14. Terms and Conditions of Access for Research

Researchers provided with anonymised data will be required to complete and sign a data use agreement to confirm they agree with the terms and conditions of receiving the data. These are:

- Any data provided will not be used for anything other than this research project, as described in the Project Summary.
- If additional uses for the data emerge, the data is required for longer, or the project develops such that other data from the database would be of use, a request for extension of data use will be submitted and must be approved before this additional research takes place.
- Any data provided will be used appropriately, and as stated in the Application for Access to Data.
- Contribution of data from the TiM-R Database will be acknowledged in the authorship of all publications (i.e. papers, presentation at symposia etc.) that arise from use of the data.
- If any issues arise surrounding this agreement, the Research Management Committee will be notified as soon as possible.

15. Research Management Committee

Name	**Project Role**
Professor Christopher McDermott (CI)	Chief Investigator, Consultant Neurologist
Dr Esther Hobson	Consultant Neurologist
Dr Liam Knox	Study Coordinator, Research Fellow
Dr Alys Griffiths	Senior Research Fellow
Dr Yasmin Ali	Research Associate

The DPUK team	Technical support

The project will be coordinated and managed by the Research Management Committee. In addition to providing overall project coordination, the CI and clinical team will assist in ensuring the documentation is maintained and the database is kept up to date, complying with relevant ethical and regulatory standards, and that all aspects of the database entry and analysis are performed to the highest quality.

16. Regulatory issues

16.1. Project site

All data will be collected from pwMND across the UK. Although this will predominantly be users based in the UK, there is the possibility that pwMND outside of the UK create TiM-R accounts.

16.2. Clinical Data collection

PwMND are responsible for responding to questionnaires on the TiM-R system, therefore any data on the database will be directly inputted by participants themselves. TiM-R users will be made aware that they do not have to answer any of the questionnaires they are sent and can withdraw entirely if they wish. The data is inputted by users at a time and place of their choosing.

Each record holds a database-specific identity number which could then be traced back on the database to identify the participant. All data will be anonymised before access is provided to researchers.

16.3 Data linkage

Participants will be asked to provide broad consent so that data from this project can be made available to researchers to answer scientific questions beyond the scope of the primary outcomes specified.

In order to update clinical outcome data and to leverage data collected by other research studies and routinely collected datasets, identifiable data will be made available to link the TiM-R dataset to other sources such as the ALS Biomarkers study, NHS databases, hospital, GP, local authority records, national registries, and other research studies.

Where data sharing requires identifiable data to be transferred outside of the project database the minimum data necessary will be shared to achieve linkage and the data will be shared using secure transfer methods.

16.4. Investigators' Responsibilities

Investigators are responsible for performing the project in accordance with the NHS Research Governance, Guidelines for Good Clinical Practice and the Declaration of Helsinki guidelines (www.wma.net). Investigators are required to ensure compliance to the protocol. Investigators are required to allow access to project documentation or source data on request for monitoring visits and audits performed by any regulatory authorities.

16.5. Project Funding & Oversight

This research is funded by the medical research charity LifeArc. The University of Sheffield will provide project oversight.

16.6. Ethics

This research database will conform to the Declaration of Helsinki guidelines (http://www.wma.net/) on research involving human subjects. The project protocol will be submitted to the NHS Research Ethics Committee for approval before commencing research activities.

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