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Neuropsychological evaluation and rehabilitation in multiple sclerosis – definitive randomised controlled trial (RCT) and implementation study

Submission date
01/12/2023

Recruitment status
Recruiting

Registration date
11/03/2024

Overall study status
Ongoing

Last Edited
17/05/2024

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Problems with memory, attention, and problem solving (together known as 'cognitive' problems) affect up to 70% of people with multiple sclerosis (MS). These problems are distressing for people with MS, affecting their mood, ability to work, and enjoy social activities. Therefore, treating cognitive problems is a 'top 10' research priority for people with MS. The NEuRoMS (Neuropsychological Evaluation and Rehabilitation in Multiple Sclerosis) project aims to develop a clinical pathway, to routinely assess people with MS for cognitive problems using brief, online tasks (cognitive screening) and provide appropriate support to help them manage these problems. In this study, we will implement the pathway in seven study sites to evaluate the clinical and cost-effectiveness of the NEuRoMS rehabilitation intervention, and explore the process of implementation of the NEuRoMS screening and management pathway.

Who can participate?
Part 1: People diagnosed with multiple sclerosis who are aged 18 and above.

Part 2: People diagnosed with multiple sclerosis who are aged 18 and above that received cognitive screening and were identified with mild or moderate cognitive problems.

Part 3: People with multiple sclerosis who participated in Part 2 of the study; Intervention providers delivering the NEuRoMS pathway and intervention to people with MS in Part 1 and 2; Healthcare professionals (e.g., neurologists, MS nurse specialists, psychologists, occupational therapists, physiotherapists) delivering the NEuRoMS screening and management pathway to people with MS in Part 1.

Part 4: People with multiple sclerosis who participated in Part 2 of the study; Intervention providers delivering the NEuRoMS pathway and intervention to people with MS in Part 1 and 2; Healthcare professionals (e.g., neurologists, MS nurse specialists, psychologists, occupational therapists, physiotherapists) delivering the NEuRoMS screening and management pathway to

people with MS in Part 1; Service commissioners (or similar) working with the Clinical Commissioning Groups or Integrated Care Systems that commission new NHS services.

What does the study involve?
Using a mix of different methodological approaches, we will:
Part 1. Assess the frequency and severity of cognitive problems in people with MS using collected cognitive screening data.

Part 2: Recruit 478 people with MS with mild or moderate cognitive problems, who will either receive the NEuRoMS rehabilitation intervention plus usual care (intervention group) or receive usual care only (control group). The brief therapist-led, manualised intervention provides information and strategies to help people cope with their cognitive problems. We will evaluate the clinical and cost-effectiveness of the intervention to reduce the impact of cognitive problems amongst people with MS.

Part 3: Use observations, questionnaires, and interviews with Part 2 participants and healthcare professionals involved in delivering the pathway and the intervention to understand how the cognitive screening and management pathway and intervention work in practice (process evaluation).

Part 4: Conduct interviews with people with MS, healthcare professionals, intervention providers and service commissioners to understand the processes of implementation in 'real world' settings by exploring facilitators and barriers to implementation of the pathway and the intervention.

What are the possible benefits and risks of participating?
It is not known whether the study will have a direct benefit to participants, but participating means that they may help people with MS in the future. The information we get from this study will help us decide how to develop this screening and management pathway further in the hope of providing standardised screening and support for cognitive problems in MS.

When talking about experiences and issues associated with cognitive problems, participants may feel upset. This may also cause some concerns about their own cognitive abilities. If this happens during the cognitive management programme (including the feedback interviews), the clinician or researcher will be there to talk through these concerns. Participants will have their contact information in case they feel upset after the session for reasons associated with participation. The screening, cognitive management sessions, interviews and any other aspect of participants' involvement can stop at any time if they do not wish to continue.

Where is the study run from?
This is a multicentre study conducted across seven NHS sites in the UK with MS outpatient clinics.

When is the study starting and how long is it expected to run for?
July 2017 to July 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Prof Roshan das Nair (Chief Investigator), roshan.dasnair@nottingham.ac.uk
Dr Gogem Topcu (Programme Manager), gogem.topcu@nottingham.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Gogem Topcu

ORCID ID
https://orcid.org/0000-0002-7400-5686

Contact details
Programme Manager
B Floor, Institute of Mental Health
Innovation Park
Triumph Road
Nottingham
United Kingdom
NG7 2TU
-
gogem.topcu@nottingham.ac.uk

Type(s)
Scientific, Principal investigator

Contact name
Prof Roshan das Nair

ORCID ID
https://orcid.org/0000-0001-8143-7893

Contact details
Programme Manager
B Floor, Institute of Mental Health
Innovation Park
Triumph Road
Nottingham
United Kingdom
NG7 2TU
-
Roshan.dasnair@nottingham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
325421

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 58780, IRAS 325421, NIHR PGfAR no. RP-PG-0218-20002

Study information

Scientific Title
Neuropsychological Evaluation and Rehabilitation in Multiple Sclerosis (NEuRoMS): A mixed methods pragmatic multicentre Randomised Controlled Trial (RCT) with nested health economic and process evaluations and an implementation study (Phase 3: Work Packages 4 and 5)

Acronym
NEuRoMS WP4 and WP5

Study objectives
The primary objective is to determine whether receiving the NEuRoMS rehabilitation intervention in addition to usual care is associated with reduced impact of cognitive problems, as measured on the MS Impact Scale (MSIS-Psych) when compared to usual care alone. The primary objective maps specifically onto Part 2, the definitive RCT.

The specific secondary objectives, mapped onto different parts of the study, are to:

Part 1:
1.a. Assess the frequency and severity of cognitive problems, based on Symbol Substitution Task (SST) and/or Word Colour Task (WCT).
1.b. Explore the relationship between the demographics, clinical features and screening usage data collected, and cognitive screening performance.
1.c. Explore whether there are different neuropsychological phenotypes (i.e., clusters of participants based on measurable traits such as self-reported cognitive problems, fatigue and mental health) based on the screening data.

Part 2:
2.a. Evaluate whether receiving the NEuRoMS rehabilitation intervention in addition to usual care results in significantly different outcomes in terms of participant's mood, objective and subjective cognitive impairment, quality of life, function, self-efficacy, fatigue, work/education related issues, Disease Modifying Therapy (DMT) adherence, and individual goal attainment compared to receiving usual care alone.
2.b. Evaluate cost-effectiveness of the intervention.

Part 3:
3.a. Explore how the cognitive screening and management pathway and the intervention was delivered.
3.b. Explore whether the pathway and the intervention were working in the ways which the logic model hypothesised.
3.c. Explore whether there were any unintended consequences of the pathway and the intervention.
3.d. Explore the level of satisfaction of the participants with the pathway and the intervention.
3.e. Assess the fidelity of the delivery of the intervention.

Part 4:
4.a. Explore the process of implementation in ‘real world’ settings.
4.b. Gain a deeper understanding of the complex contexts into which the NEuRoMS pathway is implemented.
4.c. Understand how the screening and management pathway is understood and implemented in differing contexts (in terms of service configuration, socioeconomic context, etc.).
4.d. Explore the commissioning of the screening and management pathway and the intervention.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 07/11/2023, North West – Greater Manchester West Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 207 104 8278; gmwest.rec@hra.nhs.uk), ref: 23/NW/0272

Study design
Randomised; Both; Design type: Treatment, Screening, Process of Care, Psychological & Behavioural, Complex Intervention, Management of Care, Qualitative, Validation of investigation /therapeutic procedures

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multiple Sclerosis

Interventions
Patient participants will receive the following interventions as part of this study:

Cognitive screening (Part 1): A new clinical procedure involving a self-administered, brief online screening tool (completed at home prior to clinic visit or completed in clinic prior to routine appointment) that can be administered with minimal support from clinical staff. The screen consists of computerised tasks and brief questionnaires that capture cognitive functions (information processing, attention and working memory), mood, fatigue, and self-reported cognitive function. This new clinical procedure will help identify cognitive problems and facilitate discussions about these between patients and clinicians, to encourage joint decisions about appropriate management for these problems.

NEuRoMS rehabilitation intervention (Part 2): A therapist-led, manualised psycho-education programme to teach people with MS about cognitive problems and how to manage them. Up-to 6 sessions (4 hours in total over 2-3 months period), which can be delivered in-person or remotely over videoconferencing or telephone (or in hybrid mode).

Intervention Type
Behavioural

Primary outcome(s)

Self-reported psychological impact of MS on everyday life, measured using the Psychological Subscale of the Multiple Sclerosis Impact Scale (MSIS-Psych; Hobart et al., 2001) at baseline, 3, 6 and 12 months post randomisation. The primary endpoint is at 3 months post-randomisation.

Key secondary outcome(s))

Outcomes for secondary objectives 1a and 1b:
1.1. Participant scores from cognitive screening measures (completed at a single time-point at screening) including an online, self-administered: Symbol Substitution Task (SST), and Word Colour Task (WCT).
1.2. Demographic, clinical features and screening usage information (e.g., time taken to complete the screening, type of device used to complete screening, setting the screening completed at, number of patients who required reminders and extra support, etc.) will be collected as part of cognitive screening (at a single-time point at screening).

Outcomes for secondary objective 1c:
1.3. Clinical data collected as part of usual care: Patient scores from the three measures from the Multiple Sclerosis Quality of Life Inventory for self-reported cognitive problems, fatigue and mental health (Ritvo et al., 1997), measured during screening as part of usual care.

Outcomes for secondary objectives 2a and 2b:
The following secondary outcome measures will be used to capture information about the patient at baseline and to assess outcomes at 3, 6 and 12 months after randomisation:
2.1. Self-reported (subjective) cognitive impairment as measured using the Perceived Deficits Questionnaire – 20-items (PDQ-20) (Sullivan et al., 1990).
2.2. Objective cognitive impairment as measured using the Symbol Substitution Task (SST). Participants' Part 1 SST scores will be used as baseline, and SST will be repeated at 3-, 6- and 12-month follow-ups.
2.3. Quality of life as measured using the Multiple Sclerosis Impact Scale (MSIS-29; Hobart et al., 2001) and EQ-5D-5L (Herdman et al., 2011).
2.4. Mood as measured using the Patient Health Questionnaire 9-items (PHQ-9; Kroenke et al., 2001); Generalized Anxiety Disorder-7 (GAD-7; Spitzer et al., 2006).
2.5. Function as measured using the Nottingham Extended Activities of Daily Living Scale (Nicholl et al., 2002).
2.6. Self-efficacy as measured using the Multiple Sclerosis Self-efficacy Scale (Rigby et al., 2003).
2.7. Fatigue as measured using the Modified Fatigue Impact Scale-5 item version (MFIS-5; Fisk et al., 1994; D'Souza, 2016).
2.8. Work-related issues as measured using the Multiple Sclerosis Work Difficulties Questionnaire short form (Honan et al., 2014) and a bespoke single item question asking to what extent work has been impacted by cognitive problems. For participants who are in education, a bespoke single item question will be asked to measure to what extent education has been impacted by cognitive problems.
2.9. Medication adherence as measured using a bespoke single-item question asking to what extent medication adherence has been impacted by cognitive problems.
2.10. Cost-effectiveness as measured by the:
2.10.1. Service-use questionnaire, based on a measure used in other MS trials (Lincoln et al., 2020) adapted for use in the NEuRoMS project and refined in WP3 feasibility study.
2.10.2. EQ-5D-5L (Herdman et al., 2011).
2.10.3. MSIS-8D (using MSIS-29) to derive utilities.
2.10.4. ICECAP-A (ICEpop CAPability measure for Adults; (Al-Janabi, N Flynn, & Coast, 2012)) measure of capability and wellbeing for health economic evaluation.
Please note: MSIS-29 and EQ-5D-5L will be collected only once per time point, but will be used for two purposes: 1) for clinical evaluation, and 2) for cost-effectiveness evaluation.

2.11. Goal attainment, measured using the Goal Attainment Scale at 3, 6 and 12 months after randomisation for goals set at baseline.

Outcomes for secondary objectives 3a, 3b, 3c and 3d:
Process evaluation is assessed throughout the screening pathway and intervention delivery and Part 3 data collection period by:
3.1. The qualitative data collected through interviews with patients, healthcare professionals and intervention providers, audio-/video-recordings of intervention sessions and session record forms, and notes from monthly teleconferences/videoconferences with study site teams and supervision sessions with intervention providers on: a) Experiences of cognitive screening and management pathway and the intervention, b) Factors facilitating or hindering engagement with the pathway and the intervention, c) Resources and mechanisms considered important in delivering key outcomes, d) Experiences of how the pathway and the intervention were delivered /received and they are working, e) Any unintended consequences/outcomes of the pathway and the intervention, f) Acceptability of the intervention, g) Content of usual care, h) Intervention providers' readiness to deliver the NEuRoMS rehabilitation intervention following training.
3.2. The level of satisfaction with the pathway and intervention, measured using the NEuRoMS pathway satisfaction questionnaire at Part 3 interview.
3.3. Intervention record forms completed by intervention providers for each intervention session to describe the number of intervention sessions, frequency, and duration.

Outcomes for secondary objective 3e:
Fidelity of the intervention, measured throughout intervention delivery, as assessed by:
3.4. The content of intervention sessions and quality of intervention delivery, through intervention record forms, audio-/video-recordings of intervention sessions, and case notes of interventions
3.5. Contextual and process issues related to intervention delivery, assessed by a review of case notes, intervention record forms, audio-/video-recordings of intervention sessions, and through monthly supervision sessions with the NEuRoMS therapists and the Part 3 and Part 4 interviews with intervention providers.

Outcomes for secondary objectives 4a, 4b, 4c and 4d
4.1. Process of implementation measured by the qualitative data collected through interviews with patients, HCPs, intervention providers and service commissioners (or similar), observations, and notes from monthly teleconferences/videoconferences with study site teams and supervision sessions with intervention providers on: a) Facilitators and barriers to implementation of the pathway and the intervention, and b) Views and experiences of how the intervention is understood and implemented in differing contexts (in terms of service configuration, socioeconomic context, etc.).

Completion date
31/07/2027

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 17/05/2024:
All individuals: Able and willing to give consent and able to communicate in English. Participant information sheets can be provided in Welsh upon request but the standardised materials and tests to be used require communication in English since these have not yet been developed for other languages.

Part 1: People with MS:
1.1. Diagnosis of MS
1.2. Aged 18 years or above

Part 2: People with MS:
2.1. Aged 18 years or above
2.2. Diagnosis of MS
2.3. Received cognitive screening, and mild or moderate cognitive problems identified (Part 1):
Mild or moderate problems will be identified by the clinical team based on the screening scores, the clinical and contextual information collected as part of the cognitive screening, and the patient-clinician conversations on cognitive problems experienced.
Thresholds for mild and moderate cognitive problems in people with MS will be defined based on norms (WP6: compared to control participants (people without MS)) and based on previous research (van Dongen et al. 2020) and recommendations on classifications and labelling of neuropsychological assessments (Lezak 1996; Guilmette et al. 2020)*:
-Mild cognitive problems: Scores of 1 SD below the mean or lower, and higher than 2 SD below the mean;
-Moderate cognitive problems: Scores of 2 SD below the mean or lower, and higher than 2.5 SD below the mean.
*People with scores in mild or moderate ranges in either cognitive test (SST and/or WCT) would be considered eligible to participate.

Part 3:
3.1. People with MS: People with MS who participated in Part 2.
3.2. Intervention providers: AP/Research Nurses/Assistant OT delivering the NEuRoMS pathway and intervention to people with MS in Part 1 and Part 2.
3.3. Healthcare professionals (HCPs): Healthcare professionals (e.g., neurologists, MS nurse specialists, psychologists, occupational therapists, physiotherapists) delivering the NEuRoMS screening and management pathway to people with MS in Part 1.

Part 4:
4.1. People with MS: People with MS who participated in Part 2
4.2. Intervention providers: AP/Research Nurses/Assistant OT delivering the NEuRoMS pathway and intervention to people with MS in Part 1 and Part 2
4.3. HCPs: Healthcare professionals (e.g., neurologists, MS nurse specialists, psychologists, occupational therapists, physiotherapists) delivering the NEuRoMS screening and management pathway to people with MS in Part 1
4.4. Service commissioners: Service commissioners (or similar) working within the Clinical Commissioning Groups or Integrated Care Systems that commission new NHS services.

Previous participant inclusion criteria:
All individuals: Able and willing to give consent and able to communicate in English. Participant information sheets can be provided in Welsh upon request but the standardised materials and tests to be used require communication in English since these have not yet been developed for other languages.

Part 1: People with MS:
1.1. Diagnosis of MS
1.2. Aged 18 years or above

Part 2: People with MS:
2.1. Aged 18 years or above
2.2. Diagnosis of MS
2.3. Received cognitive screening, and mild or moderate cognitive problems identified (Part 1): Mild or moderate problems will be identified by the clinical team based on the screening scores, the clinical and contextual information collected as part of the cognitive screening, and the patient-clinician conversations on cognitive problems experienced.
Thresholds for mild and moderate cognitive problems in people with MS will be defined based on norms (WP6: compared to control participants (people without MS)) defined by Lezak (1996) on the level of performance on SST and/or WCT*:
-Mild cognitive problems: Scores of 1 SD below the mean or lower, and higher than 2 SD below the mean;
-Moderate cognitive problems: Scores of 2 SD below the mean or lower, and higher than 2.5 SD below the mean.
*People with scores in mild or moderate ranges in either cognitive test (SST and/or WCT) would be considered eligible to participate.

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4.2. Intervention providers: AP/Research Nurses/Assistant OT delivering the NEuRoMS pathway and intervention to people with MS in Part 1 and Part 2
4.3. HCPs: Healthcare professionals (e.g., neurologists, MS nurse specialists, psychologists, occupational therapists, physiotherapists) delivering the NEuRoMS screening and management pathway to people with MS in Part 1
4.4. Service commissioners: Service commissioners (or similar) working within the Clinical Commissioning Groups or Integrated Care Systems that commission new NHS services.

Participant type(s)
Patient, Health professional

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

1. All participants: Do not have mental capacity to consent to participate in the study.

Part 2 participants only:
2.1. Currently receiving neuropsychological intervention for cognitive problems
2.2. Received NEuRoMS intervention during WP2ii or WP3.

Part 3 patient participants only:
3.1. Participated in Part 4 interviews.

Part 4 patient participants only:
4.1. Participated in Part 3 interviews.

Date of first enrolment
01/06/2024

Date of final enrolment
30/04/2027

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Nottingham University Hospitals NHS Trust - Queen's Medical Centre Campus
Nottingham University Hospital
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
80 Newark Street
London
United Kingdom
E1 2ES

Study participating centre

Cardiff and Vale University Health Board
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
The Leeds Teaching Hospitals NHS Trust
Leeds General Infirmary
Great George St
Leeds
United Kingdom
LS1 3EX

Study participating centre
United Lincolnshire Hospitals NHS Trust
Lincoln County Hospital
Greetwell Road
Lincoln
United Kingdom
LN2 5QY

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2JF

Sponsor information

Organisation
Nottinghamshire Healthcare NHS Foundation Trust

ROR
https://ror.org/04ehjk122

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes