A real-world longitudinal study to implement digital assessment and treatment for psychological distress in multiple sclerosis (MS): The COMPASS-MS study protocol

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Submitted to: JMIR Research Protocols
on: September 02, 2025

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Emma Jenkinson[1] MSc, PhD; Yasmin H Ali[1] MSc, PhD; Rona Moss-Morris[1] MSc, PhD; Natasha Seaton[1] MSc, PhD; Eli Silber[2] MBBCHIR, FCPS, MD, FRCP; David Okai[2] MD, MBBS, BMedSci, PGD; Abigail Wroe[1] DClinPsy; Simon Brodie[3]; Sam Norton[1, 4] MSc, PhD; Joanna L Hudson[1] MSc, PhD

[1]Department of Psychology Institute of Psychiatry, Psychology & Neuroscience King's College London London GB
[2] Neurology Department King's College Hospital London GB
[3] Lead Patient and Public Involvement Representative London GB
[4]Department of Inflammation Biology Faculty of Life Sciences and Medicine King's College London London GB

Corresponding Author:
Natasha Seaton MSc, PhD
Department of Psychology
Institute of Psychiatry, Psychology & Neuroscience
King's College London
Guy's Hospital
London
GB

Abstract

Background: Comorbid anxiety and depression in Multiple Sclerosis (MS) are common, and confer greater risk of poorer outcomes and increased healthcare utilisation and costs. Currently, few MS services include scalable treatment pathways for psychological distress. This real-world longitudinal study evaluates the implementation of a new integrated pathway including digital screening for psychological distress and COMPASS-MS and a therapist-guided, digital cognitive behavioural therapy (CBT) tailored to challenges of living with MS.

Objective: This protocol describes a mixed-methods, observational, real-world, longitudinal study in the UK (Trial registration: NCT06222359).

Methods: This protocol describes a mixed-methods, observational, real-world, longitudinal study in the UK (Trial registration: NCT06222359). Routine mental health screening in the MS clinic will identify patients with distress (using pre-defined clinical cut-offs), who will be assessed for eligibility for psychological treatment, including the COMPASS-MS programme. Participants will receive COMPASS-MS online over approximately 12 weeks (including up to 6 × 30-min therapist sessions). The implementation, reach and adoption of the treatment pathway within a specialist MS service will be assessed using aggregate data on uptake of mental health screening, eligibility, and consent rates for COMPASS-MS, and the number of COMPASS-MS sessions completed. Interviews with patients and healthcare professionals will primarily assess the scalability and potential or actual barriers and facilitators of the new pathway. Potential effectiveness will be assessed using participant questionnaires at pre-intervention and 12 weeks (post-intervention). The primary effectiveness outcome will be pre-post changes in distress (PHQ-ADS scores). Quantitative data will be summarised using descriptive statistics and mixed effects models. Qualitative data will be analysed using reflexive thematic or framework analysis.

Results: Patient recruitment was completed by September 2025, while recruitment of healthcare professionals is expected to be completed by August 2026.

Conclusions: Study findings will inform treatment pathways that can be incorporated into MS clinics, and highlight adaptations or implementation protocols required to increase future scalability and effectiveness. Clinical Trial: ClinicalTrials.gov Trial registration: NCT06222359

(JMIR Preprints 02/09/2025:83416)
DOI: https://doi.org/10.2196/preprints.83416

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[1]Health Psychology Section, Department of Psychology, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK
[2]Neurology Department, King's College Hospital, London, UK
[3]Lead Patient and Public Involvement Representative
[4]Department of Inflammation Biology, Faculty of Life Sciences and Medicine, King's College London, London, UK

Keywords: multiple sclerosis, cognitive behavioural therapy, digital intervention, psychological distress, depression, anxiety, implementation

Abstract

Introduction. Comorbid anxiety and depression in Multiple Sclerosis (MS) are common, and confer greater risk of poorer outcomes and increased healthcare utilisation and costs. Currently, few MS services include scalable treatment pathways for psychological distress. This real-world longitudinal study evaluates the implementation of a new integrated pathway including digital screening for psychological distress and COMPASS-MS and a therapist-guided, digital cognitive behavioural therapy (CBT) tailored to challenges of living with MS.

Methods. This protocol describes a mixed-methods, observational, real-world, longitudinal study in the UK (Trial registration: NCT06222359). Routine mental health screening in the MS clinic will identify patients with distress (using pre-defined clinical cut-offs), who will be assessed for eligibility for psychological treatment, including the COMPASS-MS programme. Participants will receive COMPASS-MS online over approximately 12 weeks (including up to 6 × 30-min therapist sessions). The implementation, reach and adoption of the treatment pathway within a specialist MS service will be assessed using aggregate data on uptake of mental health screening, eligibility, and consent rates for COMPASS-MS, and the number of COMPASS-MS sessions completed. Interviews with patients and healthcare professionals will primarily assess the scalability and potential or actual barriers and facilitators of the new pathway. Potential effectiveness will be assessed using participant questionnaires at pre-intervention and 12 weeks (post-intervention). The primary effectiveness outcome will be pre-post changes in distress (PHQ-ADS scores). Quantitative data will be summarised using descriptive statistics and mixed effects models. Qualitative data will be analysed using reflexive thematic or framework analysis.

Results. Patient recruitment was completed by September 2025, while recruitment of healthcare professionals is expected to be completed by August 2026.

Conclusion. Study findings will inform treatment pathways that can be incorporated into MS clinics, and highlight adaptations or implementation protocols required to increase future scalability and effectiveness.

Introduction

Multiple Sclerosis (MS) is a chronic, incurable neurological condition characterised by the demyelination of the central nervous system. The majority of people living with MS (pwMS) are diagnosed with relapsing-remitting MS (RRMS, approximately 85%), which involves intermittent relapses or 'flares' of new or existing symptoms, followed by periods of recovery or 'remission' [1] . A smaller proportion, approximately 15%, have primary progressive MS [1]. Many with RRMS eventually transition to secondary progressive disease, after a median of 20 years (range 1-51), in untreated cases [2]. PwMS commonly experience diverse and unpredictable symptoms, including fatigue, mobility issues and cognitive impairments. Unsurprisingly, psychological distress, including symptoms of depression and/or anxiety, is amongst the most common comorbidities in pwMS [3]. Prevalence is estimated at 31% for depression and 22% for anxiety [4].

Psychological distress is associated with poorer clinical outcomes, including increased disease severity and disability [5, 6], poorer quality of life [7] and reduced adherence to disease-modifying therapies (DMTs) [8]. It is also linked to increased healthcare utilisation and costs for health services [9]. Despite these consequences, psychological support remains a substantial unmet need for pwMS [10, 11] with long-standing evidence suggesting that distress is often undetected or under-treated [12-14]. In a recent UK-wide survey, approximately 40% of pwMS reported that their mental wellbeing needs were not being met [15].

While both pharmacology and psychotherapy show promise for treating distress in pwMS [16], evidence suggests that pwMS prefer psychotherapy, demonstrating an inclination to receive proactive support and acquire skills to manage their wellbeing in the context of living with MS [10]. Cognitive Behavioural therapy (CBT) is recommended by the National Institute of Health and Clinical Excellence (NICE) for treating mild to severe depression and anxiety in the context of Long-Term Physical Health Conditions (LTCs), including MS [17, 18]. CBT treatment protocols that are tailored to the challenges of living with MS appear to demonstrate larger treatment effects than traditional CBT [19]. This concurs with other LTC populations, with studies showing that LTC-tailored CBT increases treatment effect sizes for psychological distress alongside patient acceptability [20, 21]. However, providing tailored CBT presents challenges for MS clinics and other healthcare services due to cost, time and workforce constraints.

Digitally delivered CBT presents a scalable solution. Digital CBT achieves similar effect sizes as face-to-face treatment, while reducing costs and therapist time, as well as improving accessibility [22-25]. Given this need and opportunity, Researchers at Kings College London developed COMPASS, a therapist guided, web-based CBT programme designed to treat depression and/or anxiety in patients living with LTCs. COMPASS was based on the transdiagnostic model of adjustment to LTCs (TMA-LTC), so targets mechanisms known to maintain depression/anxiety and prevent optimal psychological adjustment in LTCs [26].

The original transdiagnostic version of COMPASS was tested in a randomised controlled trial (RCT) compared with standard charity support [27]. This RCT, involving four distinct LTC populations (MS, Inflammatory Bowel Disease, psoriasis, and kidney disease), demonstrated medium to large treatments effects on self-reported psychological distress, depression, anxiety and illness related distress across all LTCs at 12 weeks post-randomisation [28]. However, exploratory moderation analysis suggested smaller effects for anxiety and illness-related distress in the MS subgroup compared with LTCs, indicating scope to further tailor the intervention for pwMS and potential to boost the efficacy of COMPASS. The qualitative findings also highlighted that pwMS generally

approved of COMPASS but desired more MS-specific content [29]. To address this, COMPASS was adapted for the MS population (COMPASS-MS) using the person-based approach [30] and extensive patient and public involvement [31]. A separate manuscript will detail the adaptation process [29].

While COMPASS shows promise, evidence of intervention effectiveness rarely translates to successful implementation: only 50% of psychological interventions from clinical research are embedded into routine usage [32], typically 17 years after they have been developed [33]. An existing service improvement project has investigated the implementation of a transdiagnostic version of COMPASS into a primary care, a UK National Health Service (NHS) Talking Therapy setting [34]. However, the unique context and specific challenges for implementing COMPASS posed by a secondary care service for MS have not been explored. Digital health tools are viable in MS care; however, they are often evaluated based on their clinical effectiveness, overlooking their implementation success, and barriers and facilitators to reach, adoption, and acceptability and/or scalability [35]. Currently treatment in MS is largely focused on treating the biological disease, with far less attention paid to psychological comorbidities, with evidence suggesting that two thirds of MS patients meeting criteria for depression receive no medication or psychological support [36]. This gap persists despite the availability of reliable and brief screening tools and recommendations from expert consensus panels advocating for routine distress screening in MS clinics [37, 38]. There is a need to explore how integrated psychological care pathways, such as COMPASS-MS, can be successfully integrated into clinical care for pwMS.

Qualitative research with pwMS and healthcare professionals [39] suggests that effective mental health care in MS requires both internal service improvements (e.g., better pathways for identifying and treating psychological distress) and external changes (e.g., increased local funding). Developing and testing integrated pathways that include routine mental health screening and scalable low-cost psychological support is an important step towards addressing these longstanding service gaps.

Study aims and objectives

The overall aim of this mixed-methods study is to evaluate the implementation and potential effectiveness of an integrated care pathway for treating psychological distress within one NHS neurology service for pwMS. The integrated pathway includes routine mental health screening and COMPASS-MS, a digital therapist-supported CBT programme adapted for MS. A nested qualitative study will additionally explore the barriers and facilitators to scaling the integrated pathway within and beyond the study site. In-depth interviews with stakeholders from the study site and approximately 6-8 additional neurology services will be conducted.

The study objectives were defined using four components of the RE-AIM framework [40] (Reach, Effectiveness, Adoption and Implementation). The specific objectives are as follows:

- **Reach**: To assess the socio-demographic and clinical reach of the new integrated care pathway in the MS clinic.
- **Effectiveness**: Establish the potential effectiveness of the treatment pathway for MS patients and the service.
- **Adoption**: To qualitatively explore the barriers and facilitators to adopting the integrated pathway from the perspective of patients and healthcare professionals (study site) and stakeholders in other NHS neurology services.
- **Implementation**: To explore the potential implementation of COMPASS-MS in routine practice, including engagement, adherence and therapist fidelity.

Methods

Study design and ethics.

This real-world longitudinal single-arm study includes two nested qualitative studies. Quantitative data will be collected at pre-treatment and post-treatment (12 weeks). This protocol is aligned with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist, adapted for single-arm, non-randomised studies.

Study setting.

This study will be conducted within a London-based outpatient Neurology MS clinic. The MS clinic is a specialist service and cares for <1500 adults with MS aged ≥18 years and employs 5 consultants, 55 nurses and 4 community MS nurses. Currently, psychological provision is limited in the service, however the medical team liaise with a neuropsychiatrist who advises the team on mental health needs.

Study participants.

Patients with a diagnosis of MS, aged ≥18 years old who are experiencing psychological distress will be eligible for inclusion. Mental health screening and treatment will be available to patients who have an appointment at the MS clinic during study implementation.

Routine care: Screening and treatment of psychological distress.

Psychological screening

In current standard care, psychological distress is identified through informal conversations between patients and clinicians during consultations. This may result in a direct referral.

The novel pathway introduced as part of the current study will include routine screening for depression and anxiety, delivered via MyChart. MyChart is a mobile app that is integrated into the hospital's electronic health records. MyChart digitally collects patient-reported outcome measures (including depression and anxiety) within outpatient services. Therefore, all patients who have downloaded the MyChart app will be prompted to complete digital mental health screening prior to their appointment. Patients will not be able to complete screening if they do not have a registered MyChart account accompanying their patient record. MyChart screening results appear in patients' electronic health records so that clinicians can review them, discuss and refer as appropriate.

For the implementation of this pathway, the clinical team will utilise trainee psychologists and therapists to complete psychological assessments, supervised by a clinical and health psychologist (AW) and a consultant neuropsychiatrist and CBT therapist (DO). All patients who demonstrate mild symptoms of distress (scores above ≥5 on the Patient Health Questionnaire-8 [PHQ-8] [41] for depression or Generalised Anxiety Disorder Scale-7 [GAD-7] [42] for anxiety) through MyChart and all patients directly referred by clinicians will be assessed over the telephone.

Utilising a trainee psychologist model within the service will enable the new pathway to be delivered with minimal additional resource and cost. The assessment process aims to identify six key aspects:

- Whether the patient is interested in receiving psychological support

- Levels of anxiety and/or depression (if directly referred and this data is not already known from MyChart)
- Whether active suicidal risk is present
- Whether distress is related to MS
- Whether the patient self-reports any significant diagnosed mental health conditions including such as Schizophrenia or posttraumatic stress disorder (PTSD)
- Whether the patient is currently receiving any other psychological therapies

As shown in Fig. 1 these six aspects determine the treatment pathway within the MS service. If patients are interested in receiving therapy, exceed distress cut-offs (see below), experience distress related to MS and show no active suicidal ideation, they will be suitable for COMPASS-MS. If they are not eligible for COMPASS-MS, but are interested in psychological support, offerings within the service will be assessed for relevance on a case-by-case basis and offered to the patient. Alternatively, referrals and signposting to other services may be made, e.g., to Talking Therapy services.

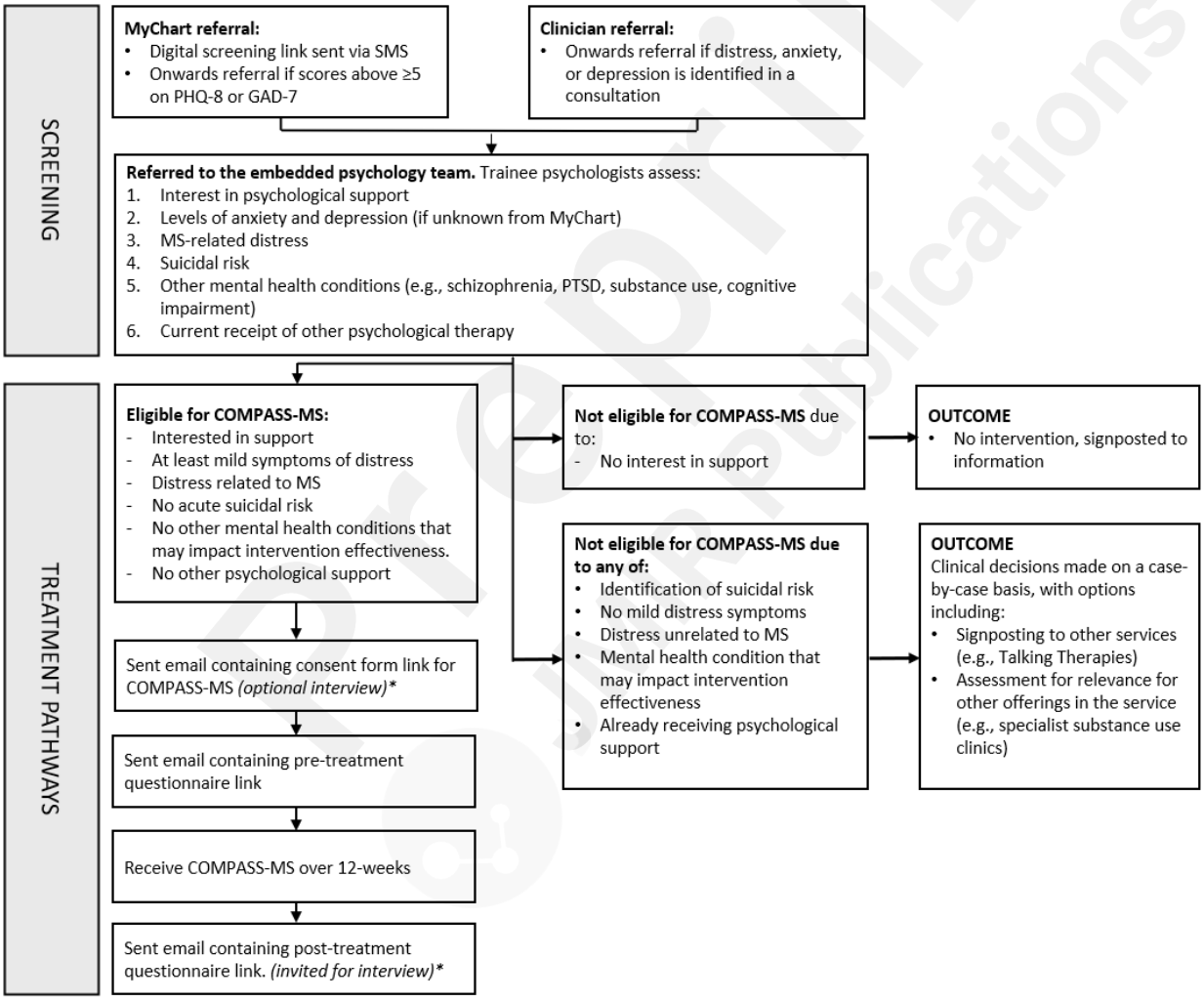

Fig. 1. Referral, screening and treatment pathway overview. *Note*. *The consent form will allow participants to opt in to a post-treatment interview. Participants were purposively sampled for the post-treatment interviews to capture the range of sociodemographic diversity and engagement with COMPASS-MS.

COMPASS-MS treatment

The theoretical underpinnings and full description of the original COMPASS intervention are reported elsewhere [26, 27]. In brief, COMPASS is a web-based, therapist-supported CBT intervention delivered over 12 weeks. Patients can complete 11 online modules and receive up to 6 x 30-minute therapist support sessions delivered over the telephone, videoconferencing, or in-site messaging. The online modules comprise of psychoeducation, patient stories, goal setting, and interactive tasks which utilise evidence-based CBT techniques. The modules explore a range of topics such as managing the uncertainty of living with an LTC, managing unhelpful thoughts and symptoms and utilising social and professional support. In COMPASS-MS, certain aspects, such as the patient stories, have been adapted to include lived examples of common challenges experienced by pwMS [29]. However, the basic components, delivery, and CBT techniques are the same as the original COMPASS intervention. Therapists will be clinical/health psychology trainees and will have at least basic CBT training, alongside COMPASS-specific training, an intervention manual, therapeutic guidance for the digital platform and standard operating procedures for suicidal risk (see Supplement 2 for service procedures). Therapists will receive weekly supervision with a clinical and health psychologist (AW) and/or a neuropsychiatrist (DO).

COMPASS-MS intervention inclusion criteria

Patients will be eligible for COMPASS-MS if they: are ≥18 years old; have a diagnosis of MS; sufficient English language skills to interact with digital CBT; have access to a computer or device to complete the intervention; present with at least mild symptoms of distress and demonstrate evidence of illness-related distress.

Patients will not be eligible if they have active suicidal risk (recent suicidal intent and/or plans); are currently receiving psychological treatment; have a mental health presentation that is not related to MS; have a health issue, identified by a clinician that may be a barrier to using COMPASS-MS, such as substance dependency, severe mental health condition (such as PTSD) or severe cognitive impairment.

Study procedures

The route of routine screening (MyChart versus clinician referral) and whether a patient completes a psychological assessment will be pseudo-anonymised, recorded and shared with the research team. For patients who complete a psychological assessment, demographic (age, gender, ethnicity, index of multiple deprivation) and clinical (depression, anxiety, cognitive impairment, disability) information will be collected to determine the appropriate treatment pathway (more details in measures).

Following patient screening and assessment, eligible and interested patients who have consented to have their contact details shared will be contacted by the research team. Patients will be emailed the information sheet and link to the informed consent form. On receipt of consent, a link to the baseline questionnaire (pre-treatment) will be sent. Following completion, patients will be enrolled onto COMPASS-MS. Patients will complete a follow-up questionnaire at 12 weeks after baseline (posttreatment). All recruitment procedures will be completed remotely via telephone or on the Qualtrics online platform (https://www.qualtrics.com/). Pre- and post-treatment questionnaires will also be administered through Qualtrics. These questionnaires will assess the potential effectiveness

of COMPASS-MS. Additionally, eligible patients will have the option to consent to take part in a qualitative interview study. A sub-group, purposively sampled to capture sociodemographic diversity and different levels of engagement with COMPASS-MS, will be invited to take part in an interview about their experience of the integrated pathway.

Nested study procedure: interviews with stakeholders and healthcare professionals

Stakeholders within the NHS trust of the study site will be approached to take part in the qualitative interview study via email. The email will include a study information sheet and a link to a consent form to be filled in online via Qualtrics. Stakeholders outside of the study site will be identified based on their services' geographic location. This will enable a representative understanding of the challenges experienced across the country. The site principal investigator (ES) and senior author (RMM) will identify appropriate services. Following this, the research team will approach the services with information about the study and will direct any potential stakeholder participants with interest back to the central research team.

Nested qualitative interview study inclusion criteria

Eligible stakeholders will be those who engaged with the new care pathway in the study site, specifically those who have been involved in: 1) routine mental health screening, 2) direct referrals to psychology, 3) assessing patients as part of the new pathway 4) providing COMPASS-MS therapist support. Furthermore, other stakeholders who work with pwMS in the study site (e.g. physiotherapists, occupational therapists or commissioning bodies) will be eligible for inclusion.

Additionally, individuals who work with pwMS in NHS trusts outside of the study site will also be eligible, including doctors, nurses, psychologists, occupational therapists, physiotherapists, and members of commissioning bodies. This will broaden the scope to barriers and facilitators to implementation outside of the study site.

Outcomes

Co-primary objectives are to explore the real-world implementation and effectiveness of a new integrated care pathway (mental health screening and COMPASS-MS treatment) in a specialist MS service (treating ~1000 pwMS). Our outcomes were defined using four components of the RE-AIM framework [40] (Reach, Effectiveness, Adoption and Implementation). The specific outcomes are as follows:

1. **Reach:** What number, percentage and characteristics of pwMS who:
    a. Complete routine screening and psychological assessment?
    b. Report clinical levels of psychological distress at assessment? Associations between distress and demographic/clinical characteristics will also be assessed.
    c. Meet the inclusion criteria for COMPASS-MS, and consent to the COMPASS-MS study? Reach will also be assessed by comparing the demographic characteristics of patients who were referred and those who consented for COMPASS-MS.

2. **Potential effectiveness**
    a. Patient level
        i. What are the changes pre-post COMPASS-MS treatment for self-reported

clinical outcomes (primary outcome is psychological distress, an anxiety and depression composite)? Additionally, depression, anxiety, illness-related distress, functioning, and quality of life) will be assessed.

ii. What are the changes pre-post COMPASS-MS in healthcare utilisation to explore potential cost-effectiveness?

iii. What are the potential mechanisms of change pre-post COMPASS-IBD (cognitive and behavioural responses to symptoms, acceptance of illness, intolerance of uncertainty, expression of emotion, health behaviours)?

b. Service level

i. How many pwMS receive COMPASS-MS who are subsequently identified as requiring more intensive treatment input and what are their demographic and clinical characteristics?

3. **Adoption:** Adoption will be explored **qualitatively** through themes on barriers/facilitators from patient and stakeholder interviews:
   a. What are the barriers and facilitators to **screening** and **treating distress using COMPASS-MS** from the **perspective of pwMS and stakeholders** exposed to the care pathway?
   b. What are the barriers and facilitators of **scaling the pathway** to sites outside the study site?

4. **Implementation:**
   a. What are the rates of adherent users, non-engagers and dropouts. For adherence, we will report percentages of those adhering to the online component, the therapist component and meeting the composite adherence definition (see below).
   b. What is the therapist fidelity to the COMPASS-MS treatment?

Implementation Measures.

Reach

Data collected during screening and triage to determine appropriate treatment pathways will include the number, percentage and characteristics of patients who:

a. Agree to and complete routine screening for psychological distress via MyChart
b. Receive a direct clinician referral for psychological distress following identification of distress during a consultation
c. Complete psychological assessment
d. Interested in receiving psychological support
e. Report clinical levels of psychological distress, depression or anxiety at assessment. Sociodemographic predictors of these outcomes will be assessed.
f. Report their distress as related to their MS
g. Report presence of active suicidal risk
h. Express interest in participating in the COMPASS-MS study
i. Meet the inclusion criteria for COMPASS-MS, and consent to the COMPASS-MS study. Differences in demographic characteristics between this sub-group and those who were referred will be statistically assessed.
j. Receive COMPASS-MS but are subsequently identified during treatment as requiring

more intensive treatment input

The characteristics that will be evaluated are as follows:

- *Demographics* (Age, Gender, Ethnicity, Index of Multiple Deprivation)
- *Depression and Anxiety* measured using the Patient Health Questionnaire 8-item version for depression (PHQ-8) [41], and the Generalised Anxiety Disorder Scale (GAD-7) for anxiety [42].
- *Mild cognitive impairment* using the Montreal Cognitive Assessment (MoCA) telephone version [43, 44].
- *Expanded Disability Status score (EDSS)* [45]. EDSS scores are clinician reported and are based on an examination by a neurologist. Scores range from 0 to 10 and increase in 0.5 unit increments. Higher scores represent higher levels of disability.

For those who consent and complete the pre-treatment questionnaire, data will be gathered on sociodemographic (age, gender, ethnicity, index of multiple deprivation) and clinical (MS type, year of diagnosis, co-morbidities, commonly occurring MS symptoms, relapse history in the last 12 weeks and medication to treat relapses.

Adoption

Patient interviews will be conducted remotely and will follow a semi-structured interview guide. The interviews will focus on pwMS's experience of 1) MyChart mental health screening and clinician referral for support, 2) study participation, and 3) using COMPASS-MS.

Stakeholder interviews will assess perceptions of mental health screening and treatment of psychological distress in MS and any barriers and facilitators to this. Additionally, for those exposed to MyChart screening and COMPASS-MS treatment, the interviews will explore the perception of implementing the integrated care pathway. The interview guide will be informed by Normalisation Process Theory [46] and the Non-adoption, Abandonment, and challenges to Scale-up, Spread, and Sustainability (NASSS-CAT) tool [47]. Stakeholder interviews will be conducted in-person or remotely.

Implementation

To explore the potential implementation of COMPASS-MS, we will record:

- The number of patients requiring digital support to use COMPASS-MS.
- The number of online sessions completed and time spent engaging with COMPASS-MS sessions (minutes). This usage data will be collected and automatically recorded on the COMPASS-MS web platform.
- The number attended, length (minutes) and mode of session delivery of therapist sessions. This data will be recorded manually by the therapist.
- Health service outcome on completion of COMPASS-MS, e.g. drop-out.
- Therapist fidelity to the COMPASS-MS treatment. Telephone and video-conferencing therapist sessions will be audio-recorded, and assessed by the clinical and health psychologist supervisor (AW). A bespoke fidelity scale will be used to check that therapists are using the relevant CBT skills and adhering to the protocol. This fidelity scale has been used previously [27]. Regular supervision (AW, DO) will support therapist fidelity to the treatment.

We will report rates of engagement and adherence as well as the demographic and clinical

characteristics of the following groups:

1) Non-engagers (those who are enrolled, but never use COMPASS-MS).
2) Less-adherent users (those who use COMPASS-MS but do <5 online sessions and receive <3 support session).
3) Those adherent to the online component (≥5 online sessions).
4) Those adherent to the therapist component (attend ≥3 appointments).
5) Fully adherent users (≥5 online sessions and attend ≥3 appointments).

to check therapist fidelity. To assess fidelity to the COMPASS-MS treatment,

Effectiveness Measures

Primary patient effectiveness outcome

Psychological distress will be measured pre- and post-treatment using the PHQ Anxiety and Depression Scale (PHQ-ADS) [48], which combines the PHQ-9 (9-item version) [49] and GAD-7 [42] into a 16-item measure of distress. A decrease of ≥4 on the PHQ-ADS is considered a minimum clinically important difference (MCID) [50], and total score cut-offs of 10, 20, and 30 indicate mild, moderate, and severe levels of distress, respectively [50].

Secondary patient effectiveness outcome

a. **Anxiety** will be measured using the GAD-7 [42], a seven-item self-report anxiety questionnaire. The questionnaire has a scale range of 0-21; high scores indicate increased anxiety symptoms.
b. **Depression** will be measured using the nine-item self-report Patient Health Questionnaire (PHQ-9) [49]. This questionnaire has a scale range of 0-27; high scores indicate increased depressive symptoms.
c. **Illness-Related Distress** will be measured with the Illness-Related Distress (IRD) scale [51]. The IRD scale is composed of two 7-item subscales (*interpersonal* and *intrapersonal* distress) answered on a 4-point scale. Each subscale ranges from 0-21, with higher scores indicating greater distress.
d. **Social functioning** will be measured by the Work and Social Adjustment Scale (WSAS), a five-item measure of functional impairment [52]. The WSAS has a scale range of 0-40; high scores indicate greater functional impairment.
e. **Health-related quality of life** will be measured using the European Quality of Life Scale (EQ-5D-3L) [53]. The EQ-5D-3L includes five items (item scores range from 1 to 3) which assess mobility, self-care, usual activities, pain/discomfort, and anxiety and depression. High item scores indicate poorer quality of life. The EQ-5D-3L also includes a visual analogue rating scale (range, 0-100), whereby higher scores reflect better global health.

Moreover, to assess potential cost-effectiveness, patients will be asked to self-reported healthcare utilisation:

f. **Health Service usage** will be explored through the 4 service use items from the Client Service Receipt Inventory (CSRI) [54]. These ask participants to self-report whether they have visited their GP, accessed psychologist/therapist support (outside of the study), visited a secondary care service, and accessed emergency care in last three months**.**

Process variables

Additionally, secondary outcomes will include process variables as potential mechanisms of change, to understand the underlying intervention effects. These will include the following measures:

g. **Cognitive and behavioural responses to symptoms** will be measured using the Cognitive and Behavioural Responses Questionnaire short-version (CBRQ-SF). The current study will use an adapted version of the CBRQ-SF [55] including 5 subscales from the CBRQ-SF, *symptom focusing* (3 items), *damage beliefs* (3 items), *embarrassment avoidance* (3 items), *all-or-nothing behaviour* (3 items) and *fear avoidance* (3 items) subscales. Additionally, we will include the *catastrophising* subscale (4 items) from the original Cognitive and Behavioural Responses Questionnaire (CBRQ) [56]. Items are rated on a 5-point Likert scale ranging from 'strongly disagree' to 'strongly agree'. Each of the subscales in the shortened and original CBRQ have been shown to be reliable and valid [55, 56].

h. **Acceptance of illness** will be measured using the Acceptance of Chronic Health Conditions Scale, which has demonstrated reliability and validity in chronic conditions [57]. This 10-item scale scores items on a 5-point Likert-scale from 'strongly agree' (1) to 'strongly disagree' (5). Items were adapted to include 'MS' in the wording. Items pertaining to positive attitudes toward the condition are reversed scored. Higher scores therefore indicate higher levels of acceptance of the condition.

i. **Intolerance of uncertainty** will be measured using the Intolerance of Uncertainty Scale-12 item [58]. The 12-item scale is rated on a five-point Likert scale ranging from 1= 'not at all characteristic of me' to 5= 'entirely characteristic of me'. Items on the questionnaires are summed and can therefore scale scores range from 12- 60.

j. **Expression of emotion** will be measured using the Beliefs about Emotions Scale [59]. This twelve-item scale assesses beliefs about the unacceptability of expressing and experiencing negative emotions. Each item is responded to on a 7 – point Likert scale ranging from "totally agree" = 6 to "totally disagree" = 0. The scale is scored by summing items and thus the total scores can range from 0 to 72. High scores on the scale represent a greater belief that it is unacceptable to express emotions.

k. **Health-related behaviours** such as smoking status and alcohol use (average weekly consumption) will also be recorded.

Sample size

The target patient sample size for the study (n=75) is based on the number of pwMS attending the MS service. The objective of the mental health screening is to assess all eligible pwMS attending the MS clinic during the study period. However, we conservatively estimate a 50% consent rate for screening, resulting in 500 out of 1000 patients completing the screening. Based on findings from Boeschoten, Braamse [4], we anticipate that 30% of these screened patients (n=150) will experience distress. If 50% of these distressed patients find the treatment acceptable, we will achieve our target sample size of 75.

Statistical methods and data analysis

Most Reach and Implementation outcomes will be summarised descriptively. Categorical variables will be summarised with frequencies and percentages, while continuous variables will be reported as means and standard deviations or as medians with interquartile ranges, depending on distribution.

Where relevant, rates (e.g., eligibility, adherence) or mean differences (e.g., change from baseline) will be presented alongside 95% confidence intervals (CIs) to quantify uncertainty in estimates. In the screened sample, differences in psychological distress, depression and anxiety between key demographic characteristics (age, gender, and ethnicity) and any interaction effects will be examined using linear regressions. For between-group comparisons (e.g., demographic and clinical differences between referred patients and those who consent to COMPASS-MS), chi-square, Mann-Whitney U, and independent sample *t*-tests will be conducted, depending on the distribution of the variable.

Potential effectiveness will be assessed using mixed-effects linear regression, including a random intercept to account for repeated measurements within participants. Assessment time points will be modelled as dummy-coded covariates to estimate change from baseline, adjusting for demographic and relevant clinical variables. Interaction terms between time and covariates will be tested to explore whether the change from baseline differs across subgroups. Effect sizes will be reported as standardised mean differences (SMD), using the adjusted mean change from baseline from the mixed-effects models and the pooled standard deviation (treating baseline as the control). Missing item-level data within self-report measures will be handled using proration when at least 50% of items are completed. A per-protocol sensitivity analysis will be undertaken for potential effectiveness outcomes, restricted to participants who fully adhered to the treatment protocol. Moreover, moderator analyses will be conducted for the primary effectiveness outcome with the intention-to-treat sample to examine the heterogeneity of the treatment effect across age, gender, ethnicity and education level.

Qualitative data will be analysed using an inductive thematic analysis for the interviews with stakeholders, incorporating an iterative constant comparison approach. Conversely, patient interviews will be analysed with a framework technique to enable comparisons with other COMPASS studies (e.g., Jones, Harding [60]). Coding will be completed line-by-line by members of the research team, with regular discussions to refine coding frameworks and record analytic reflections. Interviews with patients and healthcare professionals will be analysed and reported separately. Data collection and analysis will occur concurrently to allow emerging insights to inform subsequent interviews. NVivo software will be used to facilitate data management and analysis.

Patient and public involvement (PPI)

The Person-Based Approach [30] was central to the original development of COMPASS, as described in detail elsewhere [26, 27]. Patient and Pubic Involvement (PPI) continues to play a central role in the current project, with our lead PPI representative actively contributing to study design, intervention development, data analysis, interpretation of findings, and dissemination activities.

To support the MS-specific adaptation of COMPASS, we convened a PPI advisory group comprising 10 members: 8 people living with MS (including the lead representative) and 2 healthcare professionals. This group contributed to the co-design process through structured workshops and targeted consultations, ensuring that intervention content and delivery were relevant to the lived experiences of pwMS. Clinicians within the MS service were also regularly consulted to refine the integrated treatment pathway during the study's planning and implementation phases. Further details of the PPI activities undertaken in this project, including the impact of patient and public contributions, will be reported in subsequent publications.

Ethical approval

The study has been approved by the Health Research Authority and Health and Care Research Wales (HCRW) (REC reference: 24/WM/0085). All participants will provide written informed consent.
COMPASS-MS has been developed in accordance with the Kings Digital Therapies Quality Management System, ensuring compliance with the Medical Devices Directive 93/42/EEC for class I medical devices. It adheres to all clinical safety and quality management protocols, including supervision by a digital clinical safety officer.

Dissemination

The results from the study will be published in peer review journals and will be presented at relevant conferences. Additionally, the findings may be disseminated through social media, web posts and live events. A newsletter summarising the study findings will be disseminated to participants who indicate a wish to receive this.

Results

Study status

The study has been registered on ClinicalTrails.gov (registration number: NCT06222359). Recruitment of both patients and healthcare professionals began in June 2024. For patients, recruitment was complete as of September 2025, including 82 participants. For healthcare professionals and stakeholders, as of September 2025, 7 had consented and completed interviews and 13 more were expected to be recruited by August 2026. Data analysis has not yet started, however, quantitative results are expected by March 2026.

Discussion

This protocol outlines the rationale, design, and methods for evaluating the implementation of a new integrated care pathway through which psychological distress is digitally screened, and then treated with a digital CBT programme adapted for MS (COMPASS-MS), within an NHS neurology service. The study will gather data from both patients and healthcare professionals to examine the reach, adoption, and implementation of this integrated care pathway, as well as its potential effectiveness of COMPASS-MS in real-world practice. This will be the first study to assess the delivery of COMPASS-MS in routine clinical care, evaluating both patient-level changes in psychological distress and broader service-level outcomes.

Findings from this research will inform how such a pathway could be embedded into other NHS MS services. By increasing access to low-cost digital CBT, this model has potential to expand psychological support provision without substantial additional resource demands. The results will generate practical recommendations for future roll-out, while recognising that each service context will present its own challenges, in relation to workforce capacity and access to psychological supervision.

Moreover, this study may have important implications regarding the introduction of routine mental health screening via software such as MyChart. While screening is intended to ensure that those with psychological needs are identified and supported, it may also uncover unmet demand, increasing the number of patients requiring intervention. However, incorporating lower-intensity, scalable options

such as COMPASS-MS could help address this by providing timely support to patients with moderate distress, while reserving more resource-intensive face-to-face therapy for those with greater clinical need.

Insights from this single-site study will be valuable in planning a larger, multi-centre implementation trial. For example, a centralised "hub" model, where specialist therapists provide support across multiple NHS sites, may facilitate equitable access and consistent delivery. It will also be important to explore how the pathway can be adapted to settings with varying levels of existing psychological provision, including those with limited capacity for digital screening or in-house supervision.

Finally, beyond the immediate MS context, the findings from this study have potential relevance for integrating mental health screening and digital psychological interventions into other long-term condition outpatient pathways. Disseminating the results to national and local stakeholders will be critical for identifying opportunities to scale and sustain this model of care across the NHS.

Declarations

This project was funded by the MS Society (grant number: 2250). King’s College London and the NHS trust in which the study took place acted as the Trial Sponsor. The funder had no authority or oversight of the design, conduct, analysis and reporting of the trial. The authors report no conflict of interests. Data will be shared to other researchers upon reasonable request.

Author contributions

EJ: Investigation, Methodology, Project administration, Writing – original draft; YA: Investigation, Methodology, Project administration, Writing – original draft; RMM: Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – review & editing; NS: Investigation, Writing – original draft, review & editing; ES: Conceptualization, Funding acquisition, Investigation, Methodology, Writing – review; DO: Investigation, Methodology, Writing – review; AW: Conceptualization, Funding acquisition, Writing – review; SB: Funding acquisition, Methodology, Writing – review; SN: Funding acquisition, Formal analysis, Writing – review; JLH: Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – review & editing

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Supplementary Files

Multimedia Appendixes

Supplementary Material.
URL: http://asset.jmir.pub/assets/1778e441a6d9bd209ed3c225b9a9fcff.docx