Research Project Portfolio

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Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis (PrEliMS-2): A Multiple Single Case Series

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Thesis Portfolio Abstract[1]

Introduction

Multiple Sclerosis (MS) is a neurological, progressive disease, for which there is no known cure. The diagnosis period generates a range of difficult emotional responses. Support around this time is crucial to longer-term coping with the disease, however it is not currently part of national service provision. A recent feasibility randomised controlled trial (PrEliMS-1) investigated how to provide this support using an Acceptance and Commitment Therapy (ACT) informed intervention, delivered by MS Nurse Specialists. No signals of efficacy were found however interview data suggests not all aspects of the intervention could be delivered. Therefore, we aimed to address this issue by having a Trainee Clinical Psychologist (TCP) deliver the intervention. Specifically, we were interested in (a) signals of efficacy of the PrEliMS intervention for improving the psychological impact of MS, (b) understanding possible mechanisms of change, (c) comparing signals of efficacy with PrEliMS-1, and (d) exploring potential improvements.

Method

We used a mixed-methods, multiple single case AB design to investigate the effectiveness of a four-session PrEliMS intervention, delivered as telephone-supported bibliotherapy. The principle primary outcome measure was the Multiple Sclerosis Impact Scale-Psychological Subscale (MSIS-Psy). Additional primary outcomes measures were Generalised Anxiety Disorder (GAD-7), Patient Health Questionnaire (PHQ-9) and the Comprehensive Assessment of Acceptance and Commitment Therapy Processes (CompACT-8). Primary outcome data were gathered weekly during both AB phases. Secondary outcomes were stress, MS-related self-efficacy, Health Related Quality of Life (HRQoL) and fatigue , and data gathered pre-, 1-week post- and 1-month post- intervention. Visual analysis, and reliable and clinically significant change informed analysis. Comparisons were also made with the original PrEliMS study. Participants were invited to a post-intervention feedback interview, which was analysed using framework analysis.

[1] Under supervision from Dr Nima Moghaddam, Dr Anna Tickle and Prof Roshan das Nair, Bethany Thompson developed and wrote a research protocol, parts of which are now included in the final thesis.

Results

Five participants, recently diagnosed with MS (<1 year), completed the intervention. All experienced improvements in MSIS-Psy and criteria were met to demonstrate systematic change in the psychological impact of MS, as a result of the intervention. A lack of change was observed in psychological flexibility; visual analysis revealed this varied considerably across the sample. Clinically significant levels of distress improved, except for one participant. Change in secondary outcomes was varied, with favourable results for stress and MS-related self-efficacy. Comparisons with PrEliMS-1 indicate promising signs of efficacy for TCP-delivered PrEliMS support. Overall, the intervention was experienced positively, although improvements were recommended to increase flexibility to the needs of people with MS.

Discussion

TCP-delivered PrEliMS is effective at improving the psychological impact of MS. Although the main aim of ACT is not symptom reduction, those presenting with clinical levels of distress are likely to benefit also. The change observed in outcomes, often in the absence of psychological flexibility, is not congruent with the positioning of psychological flexibility as a mediator of positive coping outcomes. Potentially, the measure used lacks sensitivity for people with MS in this context, or this outcome may not be important to the PrEliMS intervention. Our sample was also not representative of diversity and ethnicity within the wider MS population; therefore, findings are limited to pwMS who are white British and on average, 4-months post-diagnosis. Further testing is warranted to understand how we can strengthen effects observed, determine mechanisms of change in PrEliMS and increase representativeness of all demographics within samples.

Statement of Contribution

Dr Nima Moghaddam, Professor Roshan das Nair and Dr Nikos Evangelou helped Bethany Thompson with project design and applying for ethical approval. Dr Nikos Evangelou also supported with recruitment from the MS clinic he works in. Henrie Hall (HH), fellow DClinPsy student, conducted feedback interviews. Bethany Thompson wrote the review of the literature, collected the data, conducted data entry and analysis, and wrote the thesis portfolio, supervised by Dr Nima Moghaddam, Dr Anna Tickle, Dr Nikos Evangelou, and Professor Roshan das Nair.

Small Scale Research Project

"I felt like a person, not a number": Evaluating the utility of a 'Newly Diagnosed' Multiple Sclerosis Clinic[2]

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[2]This service evaluation is intended for submission to the International Journal of MS Care. Instructions for authors can be found at: https://meridian.allenpress.com/ijmsc/pages/Author-Information

Practice Points:

- A specific clinic for newly diagnosed Multiple Sclerosis (MS) patients can aid adjustment to diagnosis, addressing practical and information needs.
- Relational empathy in clinic consultations was identified as valuable by MS patients. Nurse self-ratings of relational empathy were relatively lower compared to patients, however remained high.
- The majority of MS patients considered Clinical Psychology (CP) input likely to be helpful in addressing unmet emotional and adjustment needs, alongside longer-term diagnostic support. In contrast, only a minority of nurses (1 in 4) acknowledged a need for CP input; generally, nurses reported satisfaction in dealing with issues a CP would help with.

Abstract

Background: Current service provision recommends a follow-up appointment within 6-weeks of Multiple Sclerosis (MS) diagnosis. A positive diagnostic experience, typically conceptualised as empathic and person-centred patient-professional interactions, is associated with improved adjustment to diagnosis. However, varying service experiences are reported.

This service evaluation explores the utility of a 'newly diagnosed' MS Clinic in a large regional MS service.

Methods: PwMS attending the clinic were sent an online survey, consisting of the Consultation and Relational Empathy (CARE) measure and a bespoke questionnaire to assess the extent to which their needs were met, and whether there is a role for Clinical Psychology (CP). Nurse facilitators were also sent an adapted CARE measure and bespoke online survey, to assess whether they felt enabled to provide person-centred support and if additional CP support is needed. Mixed-methods analyses consisted of descriptive statistics and framework analysis.

Results: Twenty-two pwMS and four nurses participated. Most pwMS agreed the clinic met practical needs. Fifty-four percent of pwMS rated Nurse relational empathy as 'excellent', with Nurse self-ratings as slightly lower. Various emotional needs were reported by patients with 64% identifying a need for CP, compared to only 25% of the nurses. Framework analysis highlighted the value of information provision and compassionate interaction in the clinic, which also extends to meeting needs of pwMS' support systems.

Conclusions: Although the person-centred clinic has utility, unmet emotional and adjustment needs are still prevalent. Recommendations are made to improve identification and cueing discussion around emotional needs at diagnosis.

Introduction

The uncertain nature of Multiple Sclerosis (MS) diagnosis negatively impacts Quality of Life (QoL), which is compounded by a range of physical, demographic, and social factors (e.g., employment status, fatigue, pain, and social support)[1]. As such, psychological difficulties are common; clinically significant depressive or anxiety symptoms occur in 35% and 34% of People with MS (pwMS), respectively[2] . Collectively, findings highlight the need for early, holistic support, acknowledging the psychological impact of diagnosis.

Evidence shows that early support is a psychological correlate of improved adjustment to MS diagnosis and subsequently QoL[3,4]; as demonstrated in Topcu et al.'s model of psychosocial adjustment to MS[5]. Diagnostic support involves receiving timely information and care from services to aid understanding of MS, mediating negative emotional responses[5]. Both practicalities (e.g., the presence of a significant other, shared decision making, and >20-minute appointments[6]) and positive interaction with a Healthcare Professional (HCP) are important to the diagnostic process. The HCP-pwMS relationship has been highlighted by MS involvement groups as central to accomplishing optimal care[7]. Positive interaction within this context, according to pwMS and HCPs, prioritises clear, empathic communication to address emotional needs and is person-centred (e.g., rapport is developed through listening to, and prioritising, patient preference)[8,9]. Given pwMS report ambivalence towards the timeliness of prognosis information, research highlights person-centred care as paramount to addressing these needs[10].

Recent findings suggest disparity between implementation of evidence-based practice recommendations and pwMS' post-diagnosis experience[11]. Qualitative investigation revealed experiences of HCP 'abruptness', a lack of response to emotional struggles, and pwMS receiving little opportunity to discuss personal priorities [7], such as current emotional wellbeing[12]. Neurologists were often viewed as 'diagnosers', whereas MS nurses were perceived as better suited to discussing emotional and practical struggles due to frequent positive communication experiences[12]. Similar findings were reiterated in a recent meta-synthesis, which also showed a lack of support or provision of timely follow-up care is associated with

anger and anxiety, subsequently hindering the diagnostic adjustment process[13]. Overall, findings support authors calling for an improvement to services, particularly prioritising empathic communication with pwMS to support diagnosis[14] and increase the quality of HCP-pwMS interaction[7]. However, the emphasis on qualitative findings limits the establishment of specific changes needed and whether experiences are reflective across services.

One possible explanation for inconsistent experiences of empathic communication may be HCP perspective on their ability to manage discussion around the emotional impact of diagnosis. HCPs frequently report time constraints within MS services[8], which may present a barrier to developing these skills and recognising 'hidden' symptoms[7], such as psychological distress. However, the time-limited nature of services also emphasises the importance of prioritising positive HCP-pwMS interactions. Tintoré et al. surveyed 900 Neurologists and 982 pwMS and found there are 'uncomfortable' topics (e.g., mood difficulties and the psychological impact of symptoms) from both pwMS and HCP perspectives which are often avoided in consultations[15]. Despite this, psychological support is reportedly the second most common health-related need for pwMS, which is unmet for over a third (34.1%) of pwMS[16]. Piccolo et al. identified in the first diagnosis consultation, pwMS are four times more likely to 'cue' emotional difficulties (e.g., verbal, or nonverbal 'hints') rather than explicitly stating emotional concerns[17]. Potentially, these factors contribute to the discrepancy between patient need and service provision.

Currently, research recommends either onward referral to a psychologist to address emotional needs or embedding Clinical Psychology (CP) as part of the multi-disciplinary team within MS Care Units[12,19]. The latter approach is currently being encouraged within primary care to aid identification and provision of mental health support[20]. Arguably, this may address the unmet need of psychological support. However, if diagnostic experience can be improved through positive interactions, identification of emotional needs and adequate HCP facilitation, this may reduce the need for CP.

Context of the Current Evaluation

The presented MS service is part of an outpatient Neurology department in a large United Kingdom (UK) regional MS centre, within the National Health Service (NHS). Provisions within the service have been somewhat coherent with national guidelines and service frameworks[21,22]. However, recommendations of a face-to-face follow-up appointment within 6-weeks of MS diagnosis[23], has been inconsistently implemented by the service. This has also been reflected in patient feedback and internal evaluation by Thomason et al[24]. Findings show pwMS felt isolated and 'left' after diagnosis. Notably, 91% of pwMS surveyed reported emotional difficulties, with all clinicians and over half of patients highlighting a need for CP to address this. Thomason et al.'s service recommendations included a specific follow-up appointment post-diagnosis [24].

Collectively, this led to the establishment of a 'newly diagnosed' clinic, to ensure pwMS are offered a one-off face-to-face follow-up appointment with a specialist MS Nurse, within 6-weeks post-diagnosis. The appointment aims to support adjustment to diagnosis by adopting a patient-led approach. Patients can discuss support needs (including whether an onward CP referral is necessary), and receive information resources about prognosis. However, literature suggests that pwMS prefer ongoing, joined-up care rather than a one-off conversation about prognosis[12,13], suggesting the clinic may still be lacking in adequately meeting early-diagnosis support needs. To date, there has yet to be a service evaluation of this clinic.

Aims

The specific aims were to examine:

1. whether the clinic was supporting patient adjustment to MS diagnosis and addressing patient needs
2. patient and nurse experience of a person-centred approach and relational empathy in their clinic appointment
3. nurses perceived self-efficacy in clinic facilitation and nurse and patient perspectives on a role for Clinical Psychology (CP) in the clinic.

Methods

The evaluation was registered and approved by the relevant NHS Trust's Clinical Effectiveness Team (Reference: 22-141C). Ethical approval was not required as this is a service evaluation.

Participants[3]

Sixty-nine patients were diagnosed with MS since the clinic began in June 2021. Up to May 2022, 66 patients attended their appointment in the newly diagnosed clinic. Within this sampling-frame, ten patients' clinic appointment involved a Consultant Neurologist. As this was not part of usual practice for the newly diagnosed clinic, these participants were excluded.

We consequently targeted 56 patients who attended their clinic appointment and the five nurses facilitating the clinic. We aimed to sample at least >10% of the target population (six patients and one nurse), as the sampling error significantly decreases when sampling more than this fraction, creating narrower confidence intervals thus more accurate estimates of population responses[25].

Materials

We developed patient and nurse surveys on Microsoft Forms (see Appendices A and B). Survey development was informed by those used in the MS service's previous evaluation[24].

Pre- and post-appointment patient surveys were considered however were not included in the final design to minimise the risk of probing clinic appointments (e.g., surveying patients' level of emotional distress may prompt discussion on this topic which would not be a true reflection of the patient-led nature of a typical appointment). Consequently, the survey was only completed retrospectively.

[3]The two participant groups will be referred to as 'patients' and 'nurses' from this point onwards.

Patient Survey

Qualitative items. Eleven items comprised forced-choice and free-response questions. These captured information about practical and emotional needs, and whether patients felt there was a role for CP, both in the clinic and for ongoing diagnostic support.

Consultation and Relational Empathy (CARE) Measure. The CARE contains 10-items pertaining to patient experience of empathy in HCP consultations. Each statement is rated on a 5-point Likert scale ('poor' to 'excellent') or 'does not apply'[26]. The measure was developed for use across clinical settings demonstrating high reliability ($\alpha = 0.93$) and concurrent validity ($r = 0.84 – 0.85$)[26]; MS patients were part of validation samples[27]. This measure was selected as authors determined the items map onto MS patient empathic communication needs identified in the literature.

Nurse Survey[4]

Qualitative items. Nurses were asked five items about a possible role for CP within the clinic, perceived ability in facilitation of the clinic, and current signposting for patients reporting emotional difficulties.

Adapted CARE measure. For comparison purposes, the CARE measure was adapted, as in similar research [28], to elicit what extent *the nurses* felt competent in each item. The purpose was to capture whether nurses felt able to provide suitably sensitive, empathic conversations using a person-centred approach, to address aims two and three.

Procedure

The NHS Trust's Digital Services texted a patient survey link to 56 patients. A nurse survey link was emailed to five nurses. Completion of the survey was considered implied consent to participation; surveys included a participant information sheet. No demographic or personally identifiable information was

[4] Nurses also completed additional measures pertaining to confidence in healthcare communication, which form the focus of a separate service evaluation and report.

obtained, in line with the Trust's service evaluation guidance. Weekly reminders were sent for the six-week recruitment window.

Analysis

Quantitative data were analysed by the first author in IBM Statistics Package 27 to summarize descriptive statistics, addressing all aims. Normative data for the CARE measure were available and at least 25 scores were required for comparative analysis[26].

To address aim one, Framework Analysis (FA) was applied to free-text responses using the following process: familiarisation, identifying a framework, indexing, charting, and mapping and interpretation[29]. FA was chosen over other qualitative methods (e.g., Thematic Analysis or Content Analysis) because this enabled a specific model of adjustment to guide analysis. The framework was developed based on results of a meta-synthesis of psychosocial adjustment to MS[5], meaning a deductive approach was taken. Initial ideas and themes were discussed with all authors to promote trustworthiness and reliability of analysis.

Results

Response rates were 39% of patients (*n* = 22) and 80% of nurses (*n* = 4).

Aim 1: Examine whether the clinic was supporting patient adjustment to MS diagnosis and addressing patient needs.

Quantitative data

Table 1 presents a summary of patient responses to questions about appointment practicalities.

Table 1
Summary of Responses to Questions 1-5

	Response (*n,* %)
1. Did 45-minutes feel sufficient?	Yes (18, 82%) No (4, 18%)
2. Do you feel your knowledge of MS increased because of the appointment?	Yes (18, 82%) No (4, 18%)
3. Did you have a family member or significant other present during the appointment?	Yes (13, 59%) No (9, 41%)[a]
4. Please rate how **helpful** your appointment was **overall**:	Very unhelpful (1, 5%) Fairly unhelpful (1, 5%) Not helpful nor unhelpful (1, 5%) Fairly helpful (2, 10%) Very helpful (17, 77%)[b]
5. Did anything happen during the appointment which might have been **hindering**?	Yes (1, 5%)[c] No (21, 95%)

[a] Covid-19 restrictions were identified by 5 out of 9 (56%) respondents as the reason why they went alone. Significant others mentioned were spouses (*n* = 4), children (*n* = 1) and parents (*n* =1). Seven patients reported the presence/absence of another had "*no impact*" on the appointment and five patients noted their significant other could ask questions they otherwise would not have considered.
[b] When asked what was most helpful to discuss, most common responses were "*treatments*" (*n* = 6; 28%) and "*symptoms*" (*n* =5; 23%).
[c] The presence of a family member meant they "*didn't get as personal as [they] could have*".

Figure C1 and Table C1 (see Appendix C) present a summary of the emotional need's patients identified since receiving an MS diagnosis: anxiety (73%), sadness (55%), and frustration (50%) were most common. Emotional difficulties were reported by 86% (*n* =19) of patients and discussed in 68% (*n* = 13 out of 19) of appointments. For 53% (*n* = 10 out of 19) of patients, these emotional difficulties were not currently being addressed. Seventy percent (*n* = 7 out of 10) of these patients would have liked professional support with the unmet emotional needs identified.

Qualitative data

Four themes and two subthemes were derived using FA. We focused on understanding ways the clinic was or was not experienced as supportive towards patient adjustment and addressing patient needs.

Valuable and compassionate facilitation: "Like talking to a friend"

Fourteen patients acknowledged caring qualities they valued in their interaction with the nurses:

"*I was able to ask questions about my illness that were answered with care and compassion"* (P11).

Additional qualities included: being made to feel "*at ease"* (P9), "*kind, upbeat, helpful and knowledgeable"* (P22), and "*able to ask questions without being rushed"* (P12). Four patients would have liked an hour-long appointment or an additional 30-minute follow-up as they "*needed longer time to discuss everything*" (P1), demonstrating the value of the appointment. Two patients highlighted concerns about a *"stretched"* (P19) and "*under-funded NHS*" (P22), and the impact on availability of an appointment and the wider MS team. For one patient, this impacted the extent to which they experienced person-centred care: "*the nurses are great if not a little overstretched to really know the individual"* (P5). Despite these concerns, six patients highlighted that all their questions were answered, making them feel "*reassured"* (P11). For one patient, the person-centred nature of the appointment was noted as "*strange at first",* in comparison to previous healthcare appointments, but consequently made them feel *"in safe hands"* (P19).

Information provision: "Makes it [diagnosis] easier to deal with"

Nine patients expressed their appointment facilitated learning about treatment options available and the effect of MS on their body (*n* = 7). This provided validation and reassurance for patients:

> "*I learnt that my symptoms are normal and that I'm lucky my episode did not leave me with worse damage. I understand now what is happening to my body and this makes it easier to deal with"* (P7).

Four patients acknowledged they had researched queries prior to the appointment, which were then further confirmed in their discussion with the nurse: "*the MS nurse at the appointment confirmed/reiterated what I had read to be true"* (P19).

Specific informational needs were also addressed for four patients, such as: "*difference between neurological and muscular skeletal pain"* (P16) and "*could I*

carry on with water sports" (P11). Overall, treatments and MS prognosis were identified as most helpful aspects to discuss, with patients commenting this helped them feel "*mentally prepared"* (P7) for the future and obtain advice in how to communicate this information to others. In contrast, two patients reported they did not get any new information and one commented "*I do find it easier to take in information visually"* (P19), highlighting the importance of information accessibility.

Beyond individual sense-making

Eight patients spoke about the benefit of having another person present in their appointment, to support with memory, focus and making sense of information: "*my daughter comes with me as I tend to forget what I have been told"* (P4). Family members were also able to ask their own questions (*n* = 7) that patients "*had not thought of*" (P7), which improved their knowledge and understanding as well as the patients'. Comments noting the improvement to their appointment include:

> "*It made me feel much more comfortable knowing there is someone there to take everything in with me. I didn't feel so alone*". (P20)

> **"***It made it feel less worrying as we are all frightened about the future and the impact that it may have on our lives and how we shall cope"* (P7)

In contrast, three patients were happy to go alone, mainly due to concerns about the impact on others and as a coping strategy: "*I like to be independent about my condition, I don't like people rationalising my condition. I feel like a burden to people"* (P21). Worries about the impact on others was mentioned by three patients and was possibly a barrier to having another present in the appointment, despite recognising the value of this. On one occasion, having a family member present appeared hindering: "*having someone else present, I didn't get as personal as I could have"* (P17).

Unmet, ongoing needs: "It's a life-long condition"

This theme has two sub-themes to capture ongoing life-changes patients continue to experience, and the emotional impact of this.

Adapting to life changes. Patients described "*frustration*" (*n* = 5) at deteriorating cognition and physical abilities: "*failing memory…fatigue*" (P18), "*I can't write properly or use my hands like I used to*" (P11) and "*I fall over a lot…get too tired"* (P20). Two patients (P20, P17) acknowledged compromising or avoiding socialising to cope with these life changes. Proactive coping strategies were also noted: "*I have been extremely careful about what I eat/how much I exercise*" however this was "*affecting my self-esteem*" (P17). Arguably, there is still a need for patients to explore more effective coping strategies for these changes and timeliness of this information appears significant; one patient acknowledged:

> *"I couldn't think of questions at the time, but now I feel I have questions to ask… how to make positive changes to my lifestyle"* (P19).

Two patients identified an ongoing need for strategies "*to improve my memory*" (P4) and "*coping mechanisms… insight into the mood swings, memory loss and fatigue*" (P18). In contrast, two patients demonstrated acceptance of life changes: "*you can still live a full life even though it might be at a slower pace*" (P4) and "*although it is a life-long condition, it won't always stop you having a life*" (P9). Comments suggested a positive attitude was encouraged in their appointment: "*the nurse complemented me on my attitude and agreed go and do what you want to do"* (P3).

Impact on emotion: "A bit of a rollercoaster". Patients described feeling "*suicidal*" (*n* = 1), "*worried*" (*n* = 7), "*lonely"* (*n* = 4), and "*depressed*" (*n* = 2) since diagnosis. Patients continued to experience "*uncertainty*" (*n* = 3) and "*fear of the unknown*" (*n* = 2). Two patients highlighted "*there isn't long term support*" (P22) for the emotional difficulties mentioned:

"*I feel at the moment you are told you have MS you then leave the hospital with little support… being told you have MS greatly affects your mental health and I feel you are not given support for that".* (P13)

One patient suggested "*if the support was standard, it would be much easier for anyone struggling*" (P22). This was highlighted as a reason why patients would access CP; indicating these are needs beyond what can be addressed in one clinic appointment. Despite patients reporting unmet emotional needs, barriers to accessing support appear to be the availability and personal difficulty:

"*People find it difficulty opening up and saying they are struggling emotionally, which a psychologist would be easier to talk about*" (P17).

In contrast, four patients demonstrated positivity towards their future: "*I decided I am not going to let this [MS diagnosis] destroy me*" (P3). This seemed a conscious choice to be a "*positive person*" (P6), possibly to manage the negative emotional impact.

Aim 2: Examine patient and nurse experience of a person-centred approach and relational empathy in their clinic appointment.

Table 2 presents a summary of patient and nurse responses to the CARE measure.

Table 2

Summary of Descriptive Statistics from Patient and Nurse CARE Measures

	Total mean CARE score (*SD*)	Total Score Range	Average Individual Item Score (*M, SD*)	Individual Item Score Range	Highest scoring Items	Lowest Scoring Items
Patient Responses (*n* =22)	45.27 (7.78)	19 – 50[a]	'Very good' (4.53, 0.78)	2 – 5	*"Making you feel at ease"* *"Letting you tell your story"* "*Being positive*"	*"Fully understanding your concerns"* *"Helping you take control"* *"Making a plan of action with you"*
Nurse Responses (*n* = 4)	40.75 (6.08)	32 – 46	'Very good' (4.075, 0.61)	3 – 5	*"Letting patients tell their story"* *"Really listening"*	*"Making you feel at ease"* *"Being interested in them as a whole person"* *"Helping them take control"* *"Making a plan of action with them"*

[a]Twelve patients (54.5%) scored the nurses a maximum score of 50.

Given the required 25 data points were not met, comparison of patient data to normative data was interpreted with caution. Normative CARE data from 162 practitioners were available. Patients mean item scores are marginally lower in comparison to the normative data (*Median* = 4.69), however, patient median item scores are higher (*Median* = 5). See Appendix D for a visual comparison to normative data. Percentile ranks for normative data show a median average item score of 4.89 in the 95th - 100th percentile, suggesting our median CARE item score is above average, relative to normative data.

As we were adapting the CARE measure for nurse-use and only four responses were received, data could not be compared with normative data.

Aim 3: Examine nurse's perceived self-efficacy in facilitating the clinic and perspectives on a role for clinical psychology in the clinic.

Nurses scored their relational empathy qualities on the CARE measure as lower relative to patient's (see Table 2). When asked "*Do you think the issues a CP could help with are dealt with in a satisfactory way through the existing staff?",* three nurses agreed and one disagreed, identifying "*no formal training"* as a barrier. If available, 74% (*n* = 14 out of 19) of patients reporting emotional difficulties would have accessed a CP for support. In the wider context of MS diagnostic support, 82% (*n* = 18) did not identify additional needs requiring CP input. Of those who did (18%; *n* = 4), specific needs included: coping strategies, learning to live with uncertainty, and accessing support for partners/family.

One nurse agreed there would be downsides to having a CP in the team, reporting that patients need time to accept and understand their MS diagnosis first. Nurses would likely refer to Clinical Psychology for "denial of diagnosis" (*n* = 3), anxiety (*n* = 2), depression (*n* = 2), and cognitive difficulties (*n* = 1). Without a CP, Nurses referred patients to Local Mental Health Team (*n* = 2), MS Society (*n* = 2), Crisis Team (*n* = 2), Improving Access to Psychological Therapies Service (*n* = 4), and General Practitioner (*n* = 2).

Discussion

Overall, findings support the utility of the newly diagnosed clinic. Information needs were adequately addressed, within a compassionate and supportive space. Themes derived from the FA are coherent with positive experiences in the early stages of MS diagnosis[6,8,9]; a key factor in positive adjustment to diagnosis[5]. Findings show the clinic meets patient practical needs highlighted in the literature[6], however may benefit from flexibility in longer appointment durations.

Both qualitative and quantitative findings highlighted an underdeveloped area of the MS adjustment model[5]: addressing emotional needs. Patient emotional difficulties were prevalent, with anxiety the most frequent; a finding which was anticipated[30]. Of those reporting emotional needs, a third (32%) did not discuss these in their appointment and over half (53%) reported these as unmet, with 70% of this group in need of professional support; findings which were higher relative to previous research[16]. These unmet needs are likely to contribute to patients feeling isolated after diagnosis; an issue which was reported in the previous evaluation before the clinic began[24] . This suggests there is still a need for ongoing long-term support, in line with previous findings[12,13], which the newly diagnosed clinic has yet to address.

Potentially it is beyond the scope of one clinic appointment to adequately address emotional needs, however the clinic could facilitate initial identification of such difficulties. At present, in line with previous research[15,17], patients may typically 'cue' emotional difficulties rather than express explicit concerns, or nurses and patients may avoid discussion. Patients may be provided with the opportunity however do not feel able to disclose emotional issues, or there is a lack of appropriate elicitation by nurses. This may indicate a training need for nurses however, consistent with previous service recommendations[11], using a structured assessment of mood within the clinic would also aid identification of, and discussion about, emotional needs. This would also provide a threshold for signposting to professional support.

Nurse relational empathy was above average and 'excellent' for over half of patients, suggesting the clinic is addressing research recommendations for improved quality of HCP-pwMS interactions[7]. This finding was anticipated, given previous

research demonstrates positive interaction with MS nurses[12]. In addition, both nurses and patients identified *"Letting you/them tell your/their story*" as the highest scoring item, suggesting a person-centred approach, in line with national guidance[21,22]. A possible ceiling effect may be evident on the CARE however, limiting discrimination between items and scores. Nurse CARE scores were slightly lower relative to patient ratings, potentially indicative of reduced perceived ability in facilitating a person-centred approach, relative to patients. However, only four responded compared to 22 patients and patients rated a single consultation whereas nurses captured clinic facilitation across appointments, limiting the validity of direct comparisons. Nurse CARE scores remained high, however. Future research would benefit from analysing the quantity of appointments nurses have facilitated as arguably this confounds perceived ability in managing empathic communication.

Most nurses reported satisfaction in managing the issues a CP would deal with, also suggestive of confidence in clinic facilitation. There was a discrepancy between nurse and patient perspectives as 64% of patients identified a need for CP in the context of their diagnosis. This may be explained by HCPs prioritising focus on symptomatic treatment compared to pwMS prioritising hidden symptoms (e.g., mental health aspects of MS), a disparity reported by Rieckmann et al.[7]. In contrast, a need for CP was reported by both patients and clinicians in the previous MS service evaluation, conducted before the newly diagnosed clinic began [24]. In the current evaluation, one nurse suggested patients need to "*get to terms*" with their diagnosis before considering CP input, perhaps indicating hesitancy, specific to diagnosis, in immediate additional support. However, the psychosocial model of MS adjustment shows early support is needed to ensure future engagement with services[5]. Therefore, later support, including CP, may not occur because pwMS may have already disengaged with services.

Limitations of the study include the use of retrospective accounts, introducing possible recall bias. Demographic data were not collected, limiting direct comparisons with previous evaluation data, and understanding of contextual factors when interpreting findings. Additionally, the nature of using an online survey limited the depth of responses. Despite this, both qualitative and quantitative methods enabled operationalisation of empathic communication alongside personal accounts

of patient and nurse experience. Inclusion of such quantitative measures addresses a limitation of reliance on qualitative accounts within the literature.

Notably, the response rate was higher than the previous service evaluation[24], potentially indicative of the perceived importance of, or satisfaction with, the clinic. However, 34 out of 56 (61%) did not respond, suggesting they may differ in clinic experience, leading to a selection bias in that response's over-estimate positive patient clinic experiences. Further analyses would benefit from identification of motivations for evaluation participation e.g., disinterest or dissatisfaction in the utility of the clinic or satisfaction with their appointment that did not warrant a response, which would have different implications for interpretation of the data in the wider context.

Overall, the clinic is meeting patient information and practical needs for additional support in the early stages of MS diagnosis. Both patient and nurse perspectives suggest empathic communication is high. However, ongoing emotional and adjustment needs are still evident. The clinic would likely benefit from implementing emotional need identification, alongside training to appropriately cue discussion about, and address, emotional needs.

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Systematic Review

Efficacy of Acceptance and Commitment Therapy for improving quality of life and mood in individuals with Multiple Sclerosis: A systematic review and meta-analysis[5]

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Abstract

Objective: To review the evidence for the effectiveness of acceptance and commitment therapy (ACT) intervention for quality of life and mood, for individuals with a diagnosis of multiple sclerosis (MS).

Method: A systematic search was conducted of PsycINFO, CINAHL, Embase, MEDLINE, Web of Science, Scopus and ContextualScience.org up to 16/07/21. In addition, grey literature was also searched via ProQuest Dissertations and Theses, and Prospero. We included randomised controlled trials and clinical controlled trials, published in English, that examined the efficacy of ACT for people with a diagnosis of MS. We were interested in outcomes of quality of life (QoL), mood (e.g., anxiety, depression, and stress) and ACT-targeted processes. Methodological quality was assessed using the Cochrane Risk of Bias Tool v2. Where available, the extracted data was input into a meta-analysis to determine weighted effect size estimates for the outcomes of interest.

Results: Six studies (191 participants) from 137, met inclusion criteria. Meta-analyses found a moderate, nonsignificant effect on QoL, in favour of control conditions (*SMD* 0.39 [95% CI of -0.08 – 0.85]). Meta-analyses were also indicative of a moderate effect on anxiety, depression, stress and ACT-targeted processes, in favour of ACT. These findings were significant for stress; anxiety and depression was also significant when applying sensitivity analyses. The effect on ACT-targeted processes was nonsignificant. Methodological quality of the studies was variable; all but one study had at least one high risk of bias.

Conclusions: Findings give some indication of a small to moderate effect of ACT on anxiety, depression, stress, and ACT-targeted processes for people with MS. Due to small sample sizes and few studies within this area, generalisability of findings is limited. Recommendations for future research include higher quality, controlled trials of ACT for people with MS.

Key words: multiple sclerosis, acceptance and commitment therapy

Efficacy of Acceptance and Commitment Therapy for improving quality of life and mood in individuals with Multiple Sclerosis: A systematic review and meta-analysis

Introduction

Approximately 2.5 million people worldwide have a diagnosis of Multiple Sclerosis (MS) (MS Trust, 2020). The physical, cognitive and psychological (e.g., anxiety, depression) problems caused by MS negatively impact the Quality of Life (QoL) of those living with the disease (Gil-González et al., 2020). This is further exacerbated by the uncertainty and life changes People with MS (pwMS) face e.g., unable to obtain an accurate prognosis and increased social isolation (Nielsen et al., 2018; Wilkinson & DasNair, 2013). Given these numerous factors impacting on QoL, it is understandable that pwMS experience significantly lower QoL in comparison to the general population (Amtmann et al., 2018).

QoL is defined by the World Health Organisation (WHO) as “an individual’s perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (WHO, 1995). Within MS research and clinical practice, there is increasing emphasis on QoL as a focus for treatment and to evaluate the effectiveness of interventions (Opara et al., 2010). Reduced QoL has been found to have negative implications for psychiatric comorbidities within the MS population; most commonly dysfunction in mood, e.g., anxiety and depression (Hauer et al., 2020). Prevalence rates for depression and anxiety for pwMS vary from above 20% for anxiety and depression diagnoses and over 34% for symptoms (Hauer et al., 2020; Marrie et al., 2015; Boeschoten et al., 2017).

Psychological interventions for pwMS

Within the MS population, psychological interventions are used to: treat depression and anxiety, aid coping with an MS diagnosis, support management of MS symptoms (e.g., pain and fatigue), and improve QoL (Thomas et al., 2006). A recent meta-analysis found psychological interventions had a significant effect on

reducing depression and anxiety, and increasing QoL in pwMS, [*d* = 0.271-0.398], which was sustained at follow-up (>1-month post-intervention end) [*d*= 0.212-0.0.308] (Sesel et al., 2018).

Whilst current service provision recommendations for pwMS do not specify the use of psychological interventions (National Institute for Health and Care Excellence [NICE], 2019), Cognitive Behavioural Therapy (CBT) is recommended for treating depression in neurological conditions (NICE, 2009). In line with this, CBT is predominantly used for pwMS (Thomas et al., 2006). A recent meta-analysis showed small to moderate effects of CBT on QoL and moderate effects on depression, in pwMS (Fiest et al., 2016). CBT is also reportedly effective at decreasing symptoms of anxiety and stress within the MS population (Graziano et al., 2014; Van Kessel et al., 2008). However, the evidence-base for CBT is varied.

Sesel et al. (2018) found CBT to be less efficacious in comparison to other psychological interventions (e.g., progressive muscle relaxation and mindfulness). This could be explained by the small sample sizes within CBT studies for pwMS, which meant the meta-analysis was likely underpowered to detect an effect. However, Sesel et al. (2018) also suggested CBT is potentially unsuitable for the MS population due to the emphasis on learning strategies and completing homework, which can be challenging given cognitive impairment is common in MS. Further, CBT's focus on challenging negative thoughts has been criticised as invalidating, given these thoughts are likely to be realistic and logical within chronic, unpredictable conditions, such as MS (Meek et al., 2021).

Acceptance and Commitment Therapy

Acceptance and Commitment Therapy (ACT) is a psychological intervention with a growing evidence base; since 1986 there have been 794 Randomised Control Trials (RCTs) of ACT (Hayes, 2021). ACT targets an individual's relationship to psychological events, rather than seeking to change or challenge such events, by increasing 'psychological flexibility' (Hayes et al., 2012). This is an important distinction between ACT and CBT. Whilst the focus of ACT is not on reduction of signs of distress, researchers have included symptom reduction outcomes within

RCTs on ACT (Ost, 2014). It is also important to recognise these outcomes are often most concerning to individuals presenting to psychological services.

The approach has demonstrated efficacy for both mental (anxiety and depression) and physical health (pain and substance use) (Gloster et al., 2020). Efficacy is sustained in comparison to control conditions (waitlist/treatment as usual/psychological placebo), however, findings are varied in comparison to established psychological interventions (e.g., CBT) (A-Tjak et al., 2014; Harrison et al., 2017; Ruiz, 2012). Potentially, this can be explained by the difficulties in drawing direct comparisons between other psychological interventions, as ACT is unique in not prioritising symptom reduction (Harris, 2006).

ACT and MS

Given thoughts and beliefs about chronic illness and symptoms are accurate, arguably ACT is a more appropriate psychological intervention for pwMS (Dennison et al., 2011). ACT has an emerging evidence base for use with pwMS, with recent acknowledgement in British Psychological Society (BPS) guidance for psychological interventions for pwMS (BPS, 2021). A pilot study of a half-day ACT-workshop for pwMS reported a large effect on reduction in depressive symptoms and improved QoL (Sheppard et al., 2010). Similarly, a pilot study of an ACT-based training programme for pwMS also reported significant improvements for depression, stress, 3 ACT-targeted processes (defusion, values and, acceptance) and both physical and mental health components of QoL (Pakenham et al., 2018). Whilst these initial findings are encouraging, sample sizes are often small, therefore limiting the potential detection of an effect.

Regarding systematic reviews in this context, the efficacy of ACT for chronic disease and long-term conditions has been shown for outcomes including QoL and reduction in distress (Graham et al., 2016). However, studies were found to be generally of low quality, with few RCTs and small sample sizes. A recent systematic review of mindfulness (a focus of ACT) based intervention in pwMS showed improvements in anxiety, depression, fatigue and health-related QoL which remained significant at six-month follow-up (Simpson et al., 2014). However, only three

studies were included in the review, highlighting the lack of research on interventions for pwMS.

Purpose of this review

To date, there has not been a systematic review to evaluate the effectiveness of ACT-based psychological interventions in the MS population. Therefore, the aim of this review is to synthesis the research to-date to (i) understand the cumulative effect of ACT on QoL and mood, (ii) examine the quality of the evidence and (iii) provide guidance for future research and offer clinical recommendations based on the extant evidence.

Method

Protocol and registration

The review protocol was registered on PROSPERO (CRD42021269541)[6] and at the University of Lincoln (project ID: 7106).

Eligibility Criteria

Inclusion criteria:

1. Peer reviewed, published in English;
2. Quantitative studies examining the effectiveness of ACT for pwMS;
3. Adults (≥18 years) with a clinically confirmed diagnosis of MS;
4. All sub-types of MS;
5. All types of delivery modes (i.e., online, telephone, face-to-face), format (i.e., individual or in a group), length/number of sessions and facilitating clinician (e.g., psychologist, nurse, occupational therapist etc);
6. RCTs or Clinical Control Trials (CCTs);
7. One or more measure of QoL and/or mood;

Studies were excluded if:

1. They were articles from conference papers and books

[6] This can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=269541

2. Outcome data from studies investigating a group of chronic disease or long-term neurological conditions did not have MS-related data available separately.
3. Outcome data from studies investigating “psychological interventions” generally, did not have ACT-related data available separately.

We did not set a date restriction on studies to remain inclusive.

Searching

The following online databases were searched: PsycINFO, CINAHL, Embase, MEDLINE, Web of Science and Scopus. A review by Bramer et al. (2017) concluded for optimal systematic review searches, a combination of Embase, MEDLINE, Web of Science and Google Scholar is recommended, with PsycINFO and CINAHL for specialised reviews in healthcare settings. Contextualscience.org list of RCTs in ACT was also searched using the keyword “multiple sclerosis”.

We accessed grey literature by searching ProQuest Dissertations and Theses, and Prospero; this is because its inclusion can help minimise this risk of publication bias within a review (Hopewell et al., 2007). Grey literature refers to documents not controlled by commercial publishing organisations, often representing research at its initial development (Adams et al., 2016; Pappas & Williams, 2011). If studies were identified through both grey literature and peer-reviewed publications, the peer-reviewed publication was used.

We used the following search terms: multiple sclerosis, acceptance and commitment therapy, with truncations for a broader search of the literature. The search strategy was developed in consultation with the authors and a subject specialist librarian. See Appendix E for an example search strategy used in PsycINFO. Where appropriate, medical subject headings (MeSH) or subject descriptors (DE) were used for these terms and equivalent searches were conducted across all databases for consistency. QoL and mood were not included as search terms because these were not primary outcomes in some articles. Of the full-text

articles screened, the reference lists were screened by title to identify any additional articles. The last search was conducted on 16/07/2021.

Study Selection

The PRISMA flow diagram in Figure 1 outlines the searching and selection process. Studies from database searches were imported into RefWorks and duplicates removed. The first author (BT) applied the eligibility criteria to titles and abstracts. The remaining full-text articles were then reviewed against the eligibility criteria to obtain the selected papers for the review. Reasons for exclusion are summarised in Figure 1. Any uncertainties were resolved in consultation with one other author.

The primary outcomes of interest were QoL and mood. For the purpose of this review, ‘mood’ refers to key elements of emotional distress (anxiety, depression, and stress). In accordance with the development of the Depression Anxiety and Stress Scale (DASS-21; Lovibond & Lovibond, 1995), anxiety, depression and stress are key, related components of psychological distress. This scale has clinical utility and is widely used as both a general measure of distress and for the specific subscales (Henry & Crawford, 2005; Sinclair et al., 2012) and has been used in research on ACT for pwMS (Pakenham et al., 2018). We were also interested in process measures of ACT.

Data Extraction

The first author (BT) extracted data from each eligible study and input into Microsoft Excel. A predesigned form was used for data extraction, agreed between the authors (see Appendix F). Table 3 outlines the relevant data extracted from each study. Studies were assigned a number (1-6) for clarity within the results section.

Table 3

Summary of the Extracted Data

Study number, author(s), date, location	Methods	Participants	Intervention	QoL, mood-related or ACT-process outcomes	Effect sizes[c], summary and key findings
1.Giovannetti et al. (2020), Italy	Pilot single blind RCT	**Total:** *n*=39 ACT intervention: *n*=20 Control: *n*=19 **Age (years)[a]:** *M*=45.7; *SD*=9.1; Range=NR **Gender[a]:** Women *n*=22 (59%) **Ethnicity/race:** NR **Type of MS[a]:** RR *n*=30 (81%); SP *n*=6 (16%); PP *n*=1 (3%)	**Mode of delivery:** group **Number, length, and frequency of sessions:** 7; 2.5hrs weekly sessions and 1 booster-session 5-weeks later, **Facilitator:** CP **Comparator:** 7 weekly 1-hour RT with a 1-hour booster session 5-weeks later. **Fidelity:** Assessed. **Adverse events:** NR	**Measures (with subscales)[b]:** **QoL:** MSQoL-54 (physical health, mental health) **Mood:** HADS (anxiety, depression) PSS (positive, negative) **ACT:** CompACT (OE, BA, VA) MAAS VLQ **AAQ-II** DDS **Timepoints:** Baseline (pre-randomisation) Post-intervention: 7 weeks post-randomisation Longer-term follow-up: 12- and 24-weeks post-randomisation	**MSQoL MHC.** *SMD* = 0.69, favouring control. **HADS Anxiety.** *SMD* = -0.54, favouring ACT. **HADS Depression.** *SMD* = -0.73, favouring ACT. **PSS.** *SMD* = -0.43, favouring ACT. **AAQ-II.** *SMD* = -0.30, favouring ACT. **CompACT.** *SMD* = 0.46, favouring control. No statistically significant differences, at baseline, were found between ACT and RT apart from higher MSQoL-54 MHC in the ACT arm. The majority of participants reported significant improvements at the three month follow-up. Differences between control and ACT intervention increased at each time-point,

Table 3

Summary of the Extracted Data

Study number, author(s), date, location	Methods	Participants	Intervention	QoL, mood-related or ACT-process outcomes	Effect sizes[c], summary and key findings
					suggesting a "promising longitudinal trend" (p. 20). However, findings did not show ACT to be more efficacious that the control (RT) in showing significant improvements on all outcomes.
2.Khalifeh-Soltani & Borhani (2019), Iran	Experimental pre- post-test	**Total:** *n*=60 ACT intervention*: n=30* Control: *n=30* **Age (years):** ACT Intervention: *M*=54.17; *SD*=11.02; Range=49-58. Control: *M*=52.63; *SD*=10.18; Range=48=58. **Gender:** NR **Ethnicity/race:** NR **Type of MS:** NR	**Mode of delivery:** NR **Number, length, and frequency of sessions:** NR **Facilitator:** NR **Comparator:** Control **Fidelity:** NR **Adverse Events:** NR	**Measures (with subscales):** **Mood:** PSS (positive, negative) **Timepoints:** Baseline (immediately pre-intervention) Post-intervention: Reported but timeframe not specified. Longer-term follow-up: Reported but timeframe not specified.	**PSS.** *SMD* = 0.52, favouring ACT. There was a positive effect of ACT on perceived stress in comparison to the control group. Scores in the control group decreased however this was not significant. Time limitations meant no follow-up examination was completed.
3.Meek et al. (2021), UK	Feasibility RCT	**Total:** *n*=14 ACT intervention*: n=7* Control*: n=7* **Age (years):**	**Mode of delivery:** Telephone with 1st session face-to-face; individual	**Measures (with subscales):** **QoL**: EQ-5D-5L **Mood:** HADS (anxiety, depression)	**EQ-5D-5L.** *SMD* = 0.20, favouring control. **HADS Anxiety.** *SMD* = -0.67, favouring ACT.

Table 3

Summary of the Extracted Data

Study number, author(s), date, location	Methods	Participants	Intervention	QoL, mood-related or ACT-process outcomes	Effect sizes[c], summary and key findings
		ACT Intervention: *M*=54.40; *SD*=6.58; Range=NR. Control: *M*=51.60; *SD*=8.39; Range=NR. **Gender:** Women ACT intervention: *n*=5 Control: *n*=5 **Ethnicity/race[a]:** White British *n*=14 **Type of MS[a]:** SP *n*=14	**Number, length, and frequency of sessions:** 6; 30-minute weekly sessions **Facilitator:** Trainee CP **Comparator**: TAU **Fidelity**: Assessed **Adverse events:** None to report	**ACT:** CompACT (OE, BA, VA) **Timepoints:** Baseline (pre-randomisation) Post-intervention: 8 weeks post-randomisation Longer-term follow-up: 12-weeks post-randomisation	**HADS Depression.** *SMD* = -0.32, favouring ACT. **CompACT.** *SMD* = 0.07, favouring control. No significant effect were found between or within groups. The study was underpowered; a sample of 121 in each arm would provide sufficient power to detect an effect size of *d* = 0.362 at 8-weeks.
4.Mojtabaie & Khoshcheshm (2014), Iran	Quasi-experimental pre-post-test	**Total:** *n*=30 ACT intervention*: n=15* Control*: n=15* **Age (years)[a]:** *M*=NR; *SD*=NR; Range=20-45. **Gender:** NR **Ethnicity/race:** NR **Type of MS:** NR	**Mode of delivery:** Face-to-face; group **Number, length, and frequency of sessions:** 8; 45–60-minute workshops. Frequency: NR. Frequency: NR **Facilitator:** NR **Comparator**: No intervention **Fidelity**: Assessed. **Adverse events:** NR	**Measures (with subscales):** **Mood:** BDI-II **Timepoints:** Baseline (immediately pre-intervention) Post-intervention: timepoint not specified. Longer-term follow-up: NR.	**BDI-II.** *SMD* = -3.51, favouring ACT. The effect of ACT on depression was significant. Difference between depression scores post-intervention was also significant, in favour of ACT intervention.

Table 3

Summary of the Extracted Data

Study number, author(s), date, location	Methods	Participants	Intervention	QoL, mood-related or ACT-process outcomes	Effect sizes[c], summary and key findings
5.Nordin & Rorsman (2012), Sweden	Pilot RCT	**Total:** *n*=21 ACT intervention*: n=11* Control*: n=10* **Age (years):** ACT Intervention: *M*=43; *IQR*=36-45. Control: *M*=48.5; *IQR*=38-55. **Gender*:** Women *n*=16 **Ethnicity/race:** NR **Type of MS[a]:** SP *n*=5 RR *n*=16	**Mode of delivery:** Face-to-face; group **Number, length, and frequency of sessions:** 4; weekly sessions. 1 booster session 3-months later **Facilitator:** CPs **Comparator:** RT; 3 face-to-face weekly group sessions and the 4th session over the phone, individually. 1 booster session 3-months later. **Fidelity:** NR **Adverse events:** NR	**Measures (with subscales):** **Mood: HADS** (anxiety, depression) BDI **ACT**: **AAQ-II** **Timepoints:** Baseline (pre-randomisation) Post-intervention: 14 weeks post-randomisation Longer-term follow-up: 26-weeks post-randomisation	**HADS Depression.** *SMD* = -0.20, favouring ACT. **HADS Anxiety.** *SMD* = 0.40, favouring control. **AAQ-II.** *SMD* = 0.03, favouring control. Between group comparisons did not show ACT to be more efficacious over the control (RT) on any outcome. Within group comparisons showed ACT had a positive effect on AAQ-II; this was maintained at 3-month follow-up. Further, analysis also showed the control experienced a larger decline in depressive symptoms compared to ACT.
6.Proctor et al. (2018), UK	Pilot RCT	**Total:** *n*=27 ACT intervention: *n*=14 Control: *n*=13 **Age (years):**	**Mode of delivery:** Telephone; individual **Number, length, and frequency of sessions:** 8; weekly sessions.	**Measures (with subscales):** **QoL:** EQ-5D-5L **Mood:** GAD-7 PHQ-9	**EQ-5D-5L.** *SMD* = 0.05, favouring control. **GAD-7.** *SMD* = -0.81, favouring ACT.

Table 3

Summary of the Extracted Data

Study number, author(s), date, location	Methods	Participants	Intervention	QoL, mood-related or ACT-process outcomes	Effect sizes[c], summary and key findings
		ACT Intervention *M*=46; *SD*=12.4, Range=NR. Control: *M*=45.8; *SD*=8.8, Range=NR. **Gender:** Women *ACT* Intervention: *n*=3, Control: *n*=0 **Ethnicity/race:** NR **Type of MS:** ACT Intervention: RR *n*=9; PP *n*=2; SP *n*=3 Control: RR *n*=10; PP *n*=2; SP *n*=1	Average length *M*=14 mins; *SD*=6 **Facilitator:** Trainee CP **Comparator:** TAU **Fidelity:** NR **Adverse events:** NR	**ACT: AAQ-II** **Timepoints:** Baseline (pre-randomisation) Post-intervention: 12-weeks post-randomisation Longer-term follow-up: NR	**PHQ-9.** *SMD* = -0.17, favouring ACT. **AAQ-II.** *SMD* = -0.19, favouring ACT. A large significant effect was found in favour of ACT, for GAD-7 at follow-up. Within the sample, there were higher levels of anxiety than depression, so it was hypothesized participants likely used the intervention to manage their primary presenting problem. A lack of power and high attrition rate limit the confidence in the results.

Note. NR = Not reported. AAQ-II; Acceptance and Action Questionnaire, BA; Behavioural Awareness, BDI-II; Beck's Depression Inventory, CompACT; Comprehensive Assessment of Acceptance and Commitment Therapy Processes, CP; Clinical Psychologist, DDS; Drexel Defusion Scale, EQ-5D-5L; Euro Quality of Life measure, GAD-7; Generalised Anxiety Disorder-7 item, HADS; Hospital Anxiety and Depression Scale, MAAS; Mindful Awareness Attention Scale, MHC; Mental Health Composite, MSQoL-54; Multiple Sclerosis Quality of Life-54 item, OE; Openness to Experience, PHQ-9; Patient Health Questionnaire-9 item, PP; Primary Progressive, PSS; Perceived Stress Scale, RR; Relapsing Remitting, RT; Relaxation Training, SEIQoL-DW; Schedule for the Evaluation of Individual Quality of Life-Direct Weighting, SP; Secondary Progressive, TAU; Treatment as Usual, VA; Valued Action, VLQ; Valued Living Questionnaire.

Table 3

Summary of the Extracted Data

Study number, author(s), date, location	Methods	Participants	Intervention	QoL, mood-related or ACT-process outcomes	Effect sizes[c], summary and key findings

[a]of total sample size.

[b]not included SEIQoL-DW as qualitative interview-based instrument.

[c]*SMD* not reported in paper but calculated in RevMan; all post-intervention.

Quality Appraisal

The first author assessed the selected studies for methodological quality using the Cochrane Risk of Bias Tool version 2 (RoB2), which is recommended for use in reviews synthesising RCTs (Higgins et al., 2019). This tool assesses five main areas of bias: randomisation, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Risk of bias was judged as “low”, “some concerns” or “high”, based on responses to signalling questions.

Data synthesis

Meta-analyses were conducted on the two outcomes of interest, QoL[7] and mood; we also conducted meta-analyses on ACT process measures. Data for these outcomes were continuous. Extracted means, standard deviations and sample sizes were input into the Cochrane Review Manager software (RevMan), version 5.4 (The Cochrane Collaboration, 2020). We included Intention to Treat (ITT) analysis to limit attrition bias. Where studies had not given a mean, standard deviation or effect size, the median was taken as the mean value and interquartile ranges were used to estimate standard deviations using the following formula: $SD=IQR/1.35$. Where the mean and standard error were reported, standard deviations were calculated using the following formula: $SD=SE \times \sqrt{N}$.

We used a random effects model for each meta-analysis due to the variability between studies e.g., variable outcome measures. The inverse variance method was used to calculate a weighted average and Standardised Mean Difference (*SMD*) was the summary statistic (Higgins & Thomas, 2021). Forest plots were generated for comparisons and heterogeneity of studies was assessed using the I^2 statistic. Variability between studies was anticipated due to clinical and methodological diversity; Higgins & Thomas (2021) was used as a guide to interpret the I^2 statistic (i.e., 30-60% moderate, 50-90% substantial, 75-100% considerable heterogeneity).

[7] Where studies had reported physical health and mental health composites (MHC) for QoL, the MHC was included in the meta-analysis as this was deemed most appropriate to the aims of this review.

Where a study used multiple measures of a single outcome of interest, the measure most used across studies was preferentially selected (as indicated in bold in Table 3); this maximised between-study homogeneity and cross-comparability for each outcome. Where studies had multiple data collection timepoints, those most similar across studies were selected. Any remaining timepoints were extracted and described narratively.

Further to overall pooled analyses, separate analyses were planned (for each outcome) to compare effects of ACT against active (e.g., alternative treatment) vs. passive (e.g., Treatment as Usual [TAU]) control conditions. Where this was not possible due to the limited number of studies (less than two), results were described narratively.

Sensitivity analyses were also conducted on the basis of methodological quality of studies by removing the lowest scoring study on quality from the meta-analysis to examine the impact on the *SMD*. If there was no lowest scoring from the quality analysis, then sensitivity analysis was based on methodological similarity.

We intended to assess publication bias by funnel plot asymmetry analysis if there were at least 10 studies, as specified in the Cochrane Handbook (Page et al., 2021).

Results

Study Characteristics

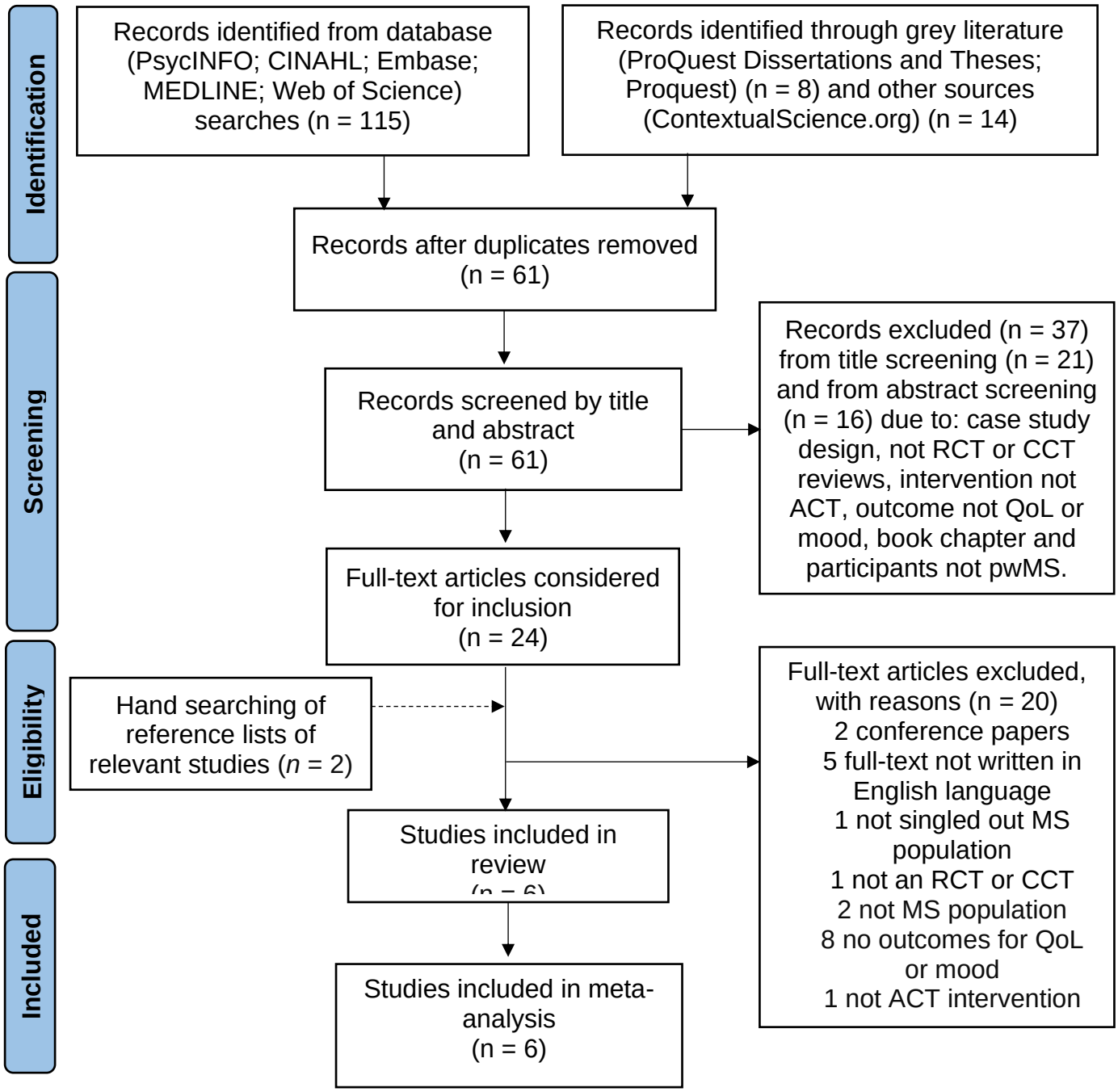
Initial searches retrieved 137 studies, 24 full-text articles were considered for inclusion, and six articles met inclusion criteria (with 191 participants in total). In addition, searches on Prospero identified seven “ongoing” articles; these were not included, and it was unclear when they are going to be completed.

The eligible studies were published from 2012-2021 and conducted in Italy, Iran, the United Kingdom, and Sweden. Three studies examined QoL (1, 3, 6), four examined anxiety (1, 3, 5, 6), five examined depression (1, 3, 4, 5, 6) and two examined stress (1, 2). Four studies (1, 3, 5, 6) also included one or more ACT process measures. Three studies (3, 4, 6) compared ACT to Treatment as Usual (TAU), two studies (1, 5) compared ACT to Relaxation Training (RT) and one (2) did not specify the nature of the control.

The following measures were used to assess QoL: Multiple Sclerosis Quality of Life-54 (MSQoL-54) and Euro Quality of Life measure (EQ-5D-5L). Measures for anxiety were Hospital Anxiety and Depression Scale (HADS) and Generalised Anxiety Disorder measure (GAD-7). Measures for depression were Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire (PHQ-9) and Beck's Depression Inventory (BDI/BDI-II). Perceived Stress Sale (PSS) was used to measure stress. For ACT-targeted processes, studies used: Comprehensive Assessment of ACT Processes (CompACT), Mindful Awareness Attention Scale (MAAS), Valued Living Questionnaire (VLQ), Acceptance and Action Questionnaire (AAQ-II), and Drexel Defusion Scale (DDS). Subscales of these measures are noted in Table 3.

Only one study reported on adverse events (3).

Figure 1
PRISMA Flow Diagram of Study Selection



Quality Appraisal

There was variability in the quality of studies, as detailed in Table 4 and summarised in Figure 2. Four of the six studies scored low risk of bias for

randomisation as they used an independent researcher or computer-generated randomisation (1, 3, 5, 6). The remaining studies scored “some concerns” due to not outlining the randomisation process in detail.

Regarding deviations from the intended intervention, three studies (1, 2, 4) did not report whether the intervention was delivered in accordance with protocol interventions, despite one of those publishing a protocol (1). The remaining three scored “low risk” as deviations from the trial protocol occurred and were reported (i.e., number of support-calls differed, or session homework completion was variable).

All studies were judged “low risk” for missing outcome data. Five studies reported outcome data for nearly (>95%) or all participants (1, 2, 3, 4, 5). The remaining study reported attrition, however had controlled for missing outcome data bias through intent-to-treat analyses (6).

Only one study (5) used blinding in scoring and analyses; all other studies either did not provide information on blinding or blinding did not occur which introduces a risk that intervention knowledge could influence assessment outcome. Two studies (1, 3) were judged as low risk of bias for selection of the reported result as this occurred in accordance with a plan specified in a trial protocol. One study (6) had published a trial protocol however an analysis plan was not specified which met criteria for “some concerns”. The remaining three studies were also judged as “some concerns” due to no information on conducting analyses in line with a pre-specified plan.

An overall risk of bias judgment was calculated by the RoB v2 algorithm (Higgins et al., 2019) and showed all except one study (5) to be “high” risk of bias.

Table 4

Risk of Bias Judgements in Selected Studies

Study	Randomisation Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of Outcome	Selection of the Reported Result
1.Giovannetti et al. (2020)	Low risk; "Randomization was provided by an independent randomization service at the Neuroepidemiology Unit, using computer-based stratified randomization" (p. 5).	Some concerns; Trial protocol[a] published but no information on whether deviations occurred.	Low risk; Outcome data available for nearly all participants. "Two participants (ACT) withdrew before beginning the intervention due to unexpected work commitments" (p. 8).	High risk; Knowledge of intervention received likely to influence assessment of the outcome.	Low risk; Results were analysed in accordance with a published trial protocol, published before unblinded outcome data was available.
2.Khalifeh-Soltani & Borhani (2019)	Some concerns; Unclear description provided. "experimental and control groups were matched using a simple random method" (p. 37).	Some concerns; No information on availability of a trial protocol or adherence/deviations to a protocol.	Low risk; Outcome data available for all participants.	High risk; No information on blinding.	Some concerns; No information on adherence/deviations from the analysis plan outlined in a trial protocol.
3.Meek et al. (2021)	Low risk; "randomisation was completed by the Lead Researcher using an online randomisation service and randomly sized	Low risk; Deviations from the trial protocol[b] reported but are consistent with what would occur outside of the trial context. "30 support calls, four were rearranged" (p. 164).	Low risk; Outcome data available for nearly all participants. "all HADS, MSIS and EQ-5D-5L questionnaires completed (100%), and	High risk; Knowledge of intervention received likely to influence assessment of the outcome.	Low risk; Results were analysed in accordance with a published trial protocol, published before unblinded

Table 4

Risk of Bias Judgements in Selected Studies

Study	Randomisation Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of Outcome	Selection of the Reported Result
	permeated blocks to each arm (ratio: 1:1)" (p. 161).	"the average length of time a participant took to complete the six-week intervention was 6.65 weeks (range = 5.29–8.14 weeks) (SD = 0.96 weeks)" (p. 164).	41 of 42 (98%) CompACT questionnaires completed (one pack returned unfilled). The MSSE was frequently completed incorrectly, due to an unclear layout, and 31 of 42 (74%) were interpretable" (p. 164).	"No blinding was used as participants were aware if they were receiving psychological therapy input, as this was not part of treatment as usual." (p. 161).	outcome data was available.
4.Mojtabie & Khoschcheshm (2014)	Some concerns; Unclear description provided. "participants were randomly distributed in control and experiment groups" (p. 871).	Some concerns; No information on availability of a trial protocol or adherence/deviations to a protocol.	Low risk; Outcome data available for all participants.	High risk; No information on blinding.	Some concerns; No information on adherence/deviations from the analysis plan outlined in a trial protocol.
5.Nordin & Rosman (2012)	Low risk; "Patients were randomly assigned by an independent co-worker to one of two treatment groups following pairwise matching based on EDSS,	Low risk; Deviations reported but are consistent with what would occur outside of the trial context. "One patient (RT group) had a MS relapse with complete recovery during treatment" (p. 89).	Low risk; Outcome data available for nearly all participants. "Discontinued intervention (withdrew at own request after first session) (n = 1)" (p. 88).	Low risk; "Scoring and data analyses were conducted blindly" (p. 88).	Some concerns; No information on adherence/deviations from the analysis plan outlined in a trial protocol[c].

Table 4

Risk of Bias Judgements in Selected Studies

Study	Randomisation Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of Outcome	Selection of the Reported Result
	anxiety, and depression scores" (p. 88).				
6.Proctor et al. (2018)	Low risk; "The randomisation sequence was computer-generated by one researcher (NM), concealed from other researchers, and entered into a standalone web-based system" (p. 5).	Low risk; Deviations from the trial protocol reported but are consistent with what would occur outside of the trial context. "three received the eight, scheduled support-calls, and completed the book within the expected seven weeks. Two received an extra phone-call, due to not completing chapters within the allotted time-period" (p. 8).	Low risk; Evidence the result was not biased by missing outcome data. "Overall, 9 of 27 (33%) participants dropped out of the study… RCT analysis used an intention-to-treat approach… This method provides unbiased estimates in the presence of missing data" (p. 8).	High risk; No information on blinding.	Some concerns; Analysis plan not specified on the published protocol; no information on adherence/deviations from an analysis plan.

Note. Table shows risk of bias judgements using the Cochrane RoB Tool version 2.

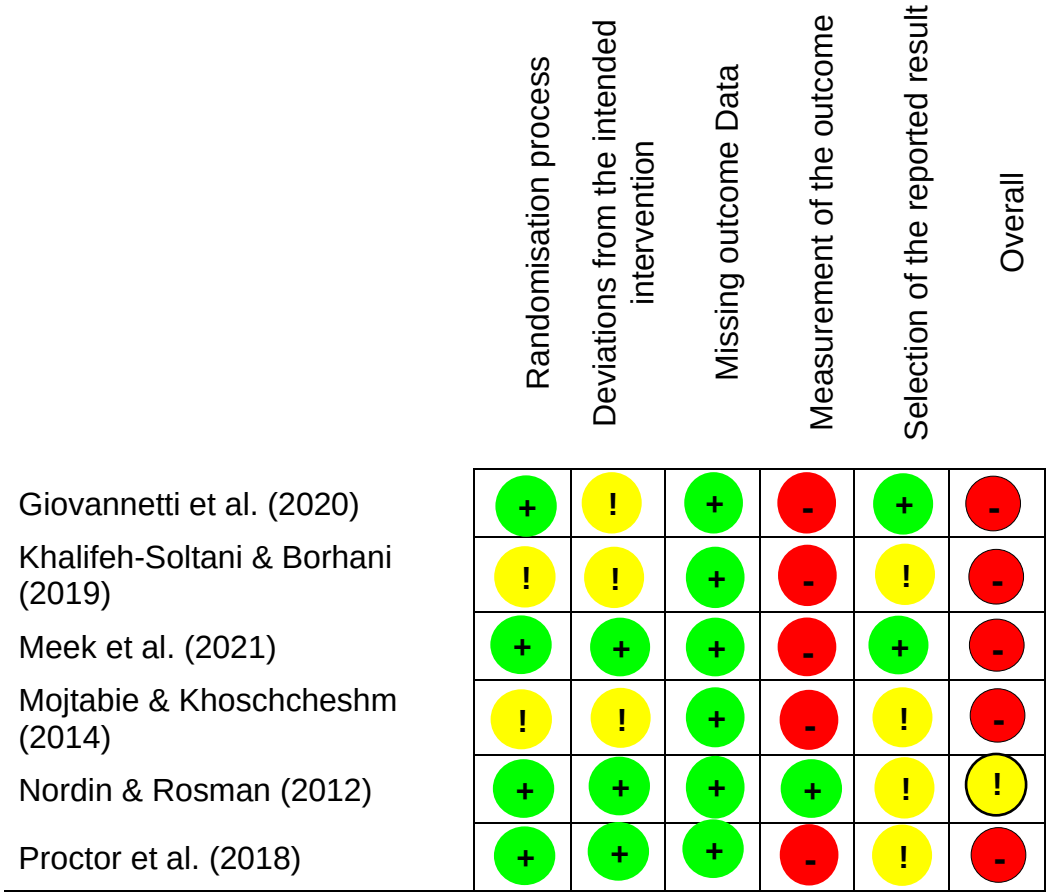
[a]Protocols.io; doi: dx.doi.org/10.17504/protocols.io.bcqjivun

[b]Clinicaltrails.gov; ID: NCT04239664

[c]trial protocol was available on request but unavailable in English.

[d]ClinicalTrials.gov; ID: NCT02596633

Figure 2
Risk of Bias Judgements; Output from RoB Tool v2



Note. Positive signs indicate “low risk” judgement, exclamation marks indicate “some concerns” judgement and negative signs indicate “high risk judgements”

Meta-Analysis

All meta-analyses were conducted on outcomes post-intervention, which ranged from 7 weeks post-randomisation to 14 weeks post-randomisation.

Quality of Life

Three studies (74 participants) measured QoL when comparing ACT against a control (1, 3, 6). Figure 3 shows the RevMan output for the meta-analysis. A medium, nonsignificant effect on QoL, favouring the control group, was found (*SMD* 0.39 [95% CI of -0.08 – 0.85]). Statistical heterogeneity was 0%, assessed using I^2.

Separate analyses on active vs passive control conditions, by removing the active control (Relaxation Training [RT]) study (1), showed statistical heterogeneity as I^2 = 0% and a nonsignificant small effect, favouring control (*SMD* 0.10 [95% CI of

-0.54 – 0.75]). This also formed the sensitivity analysis. For active control, a medium, significant effect on QoL was found, in favour of the RT control (*SMD* 0.69 [95% CI of 0.02 – 1.35]).

Mood

Anxiety. Four studies (97 participants) measured anxiety when comparing ACT against a control (1, 3, 5, 6). Figure 4 shows the RevMan output for the meta-analysis. A medium, nonsignificant effect on anxiety was found, favouring ACT (*SMD* -0.41 [95% CI of -0.93 – 0.11]). Statistical heterogeneity was moderate, I^2 = 35%.

A large, significant effect on anxiety was found for the two studies using passive controls (3, 6), favouring ACT (*SMD* -0.76 [95% CI of -1.41 – -0.10], *p* = 0.02), with I^2 = 0% heterogeneity. For the two studies using active controls of RT (1, 5), a nonsignificant small effect was found, favouring ACT (*SMD* -0.12 [95% CI of -1.04 – 0.80]), with substantial heterogeneity (I^2 = 65%).

Depression. Five studies (127 participants) examined depression when comparing ACT against a control (1, 3, 4, 5, 6). Figure 5 shows the RevMan output for the meta-analysis. A large, nonsignificant effect size was found, favouring ACT (*SMD* -0.92 [95% CI of -1.91 – 0.06]). The I^2 statistic showed substantial heterogeneity (I^2 = 84%). For the sensitivity analysis, one study (4) was removed on the basis of scoring lowest on the quality analysis and no overlap of the confidence intervals of the other studies. A medium, significant effect on depression was found, favouring ACT (*SMD* -0.40 [95% CI of -0.81 – -0.00]).

Three studies used passive controls (3, 4, 6) and showed a large, nonsignificant effect on depression, favouring ACT (*SMD* -1.30 [95% CI of -3.25 – 0.66]), with considerable heterogeneity (I^2 = 91%). For studies using active controls of RT (1, 5), a medium, significant effect on depression, in favour of ACT, was found (*SMD* -0.53 [95% CI of -1.06 – -0.00], *p* = 0.05), with no heterogeneity.

Stress. Two studies (97 participants) measured stress (1, 2); Figure 6 shows the RevMan meta-analysis output. A medium, significant effect on stress was found, in favour of ACT (*SMD* -0.49 [95% CI of -0.89 – -0.08]), with no heterogeneity.

One study (1) used an active control of RT. A moderate, nonsignificant effect, favouring ACT, was found (*SMD*-0.43 [95% CI of -1.08 – 0.22]). The other (2) used a passive control. A moderate, significant effect was found, in favour of ACT (*SMD* -0.52 [-1.04 – -0.01], $p = 0.05$).

ACT-targeted Processes

The most frequent measure was the AAQ-II. This was used by three studies (1, 5, 6) (82 participants) and Figure 7 shows the RevMan output for the meta-analysis. A small, nonsignificant effect on AAQ-II scores was found, in favour of ACT (*SMD* -0.18 [95% CI of -0.62 – 0.25]) with no heterogeneity.

Two studies used active controls of RT (1,5) and showed a small, nonsignificant effect, favouring ACT (*SMD* -0.18 [95% CI of -0.70 – 0.34]), with no heterogeneity. For passive control conditions of TAU (6), a small, nonsignificant effect, in favour of ACT, was found (*SMD* -0.19 [95% CI of -0.99 – 0.62]).

Regarding additional measures, two studies (1, 3) used the CompACT; with one (1) also measuring mindfulness, defusion and valued living. Both studies reported the ACT intervention was not more efficacious that the control in showing significant improvements on these outcomes.

Figure 3

Forest Plot for ACT vs Control; QoL at Post-Intervention

	ACT			Control				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Giovannetti 2020	70.7	17.82	18	58.2	17.87	19	48.5%	0.69 [0.02, 1.35]
Meek 2021	41.43	19.73	7	36.43	26.41	7	19.4%	0.20 [-0.85, 1.25]
Proctor 2018	0.45	0.22	12	0.44	0.2	11	32.1%	0.05 [-0.77, 0.86]
Total (95% CI)			**37**			**37**	**100.0%**	**0.39 [-0.08, 0.85]**

Heterogeneity: Tau² = 0.00; Chi² = 1.56, df = 2 (P = 0.46); I² = 0%

Test for overall effect: Z = 1.63 (P = 0.10)

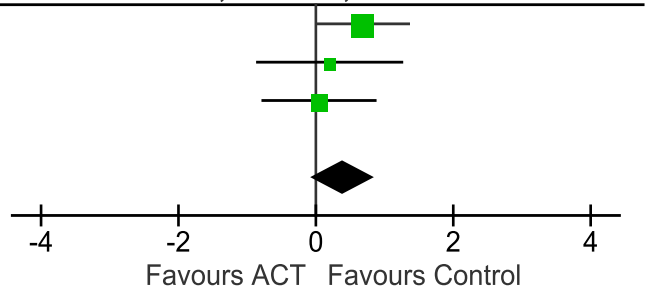


Figure 4

Forest Plot ACT vs Control; Anxiety at Post-Intervention

	ACT			Control				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Giovannetti 2020	5.9	3.82	18	8.05	3.92	19	33.3%	-0.54 [-1.20, 0.11]
Meek 2021	8.57	4.69	7	12.29	5.65	7	17.3%	-0.67 [-1.76, 0.42]
Nordin & Rosman 2012	10	6.67	11	7.5	5.19	10	23.9%	0.40 [-0.47, 1.27]
Proctor 2018	12.7	5.2	13	16.8	4.6	12	25.6%	-0.81 [-1.63, 0.02]
Total (95% CI)			**49**			**48**	**100.0%**	**-0.41 [-0.93, 0.11]**

Heterogeneity: Tau² = 0.10; Chi² = 4.61, df = 3 (P = 0.20); I² = 35%

Test for overall effect: Z = 1.54 (P = 0.12)

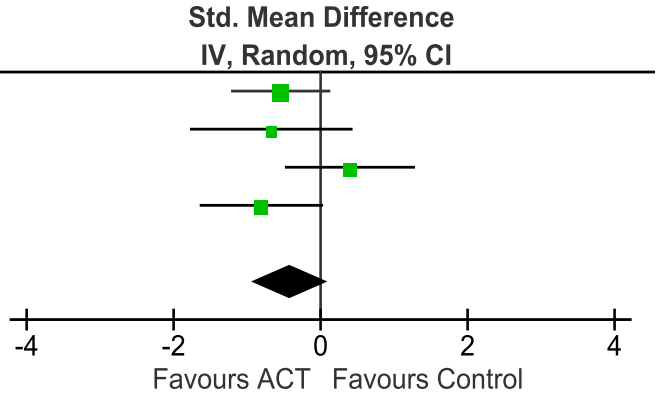


Figure 5
Forest Plot ACT vs Control; Depression at Post-Intervention

	ACT			Control				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Giovannetti 2020	3.6	3.82	18	6.5	3.92	19	21.8%	-0.73 [-1.40, -0.06]	
Meek 2021	8.86	3.8	7	10.29	4.46	7	18.9%	-0.32 [-1.38, 0.73]	
Mojtabaie & Khoshcheshm 2014	13.2	2.11	15	22.8	3.12	15	17.9%	-3.51 [-4.70, -2.32]	
Nordin & Rosman 2012	3	5.93	11	4	2.96	10	20.4%	-0.20 [-1.06, 0.66]	
Proctor 2018	18.4	7.5	13	19.6	6.3	12	21.0%	-0.17 [-0.95, 0.62]	
Total (95% CI)			**64**			**63**	**100.0%**	**-0.92 [-1.91, 0.06]**	

Heterogeneity: Tau² = 1.04; Chi² = 24.87, df = 4 (P < 0.0001); I² = 84%
Test for overall effect: Z = 1.84 (P = 0.07)

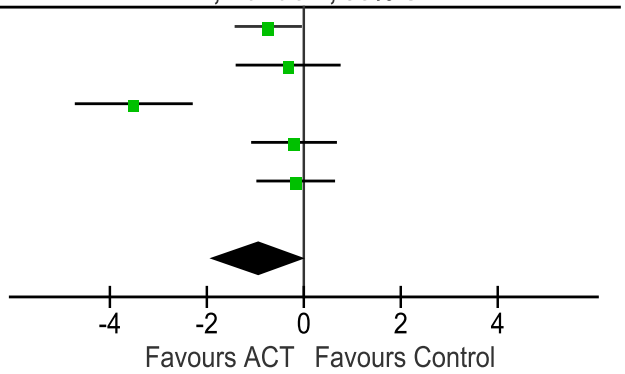


Figure 6
Forest Plot ACT vs Control; Stress at Post-Intervention

	ACT			Control				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Giovannetti 2020	15.5	7.21	18	18.6	6.97	19	38.4%	-0.43 [-1.08, 0.22]	
Khalifeh-Soltani & Borhani 2019	37.6	4.61	30	40.5	6.23	30	61.6%	-0.52 [-1.04, -0.01]	
Total (95% CI)			**48**			**49**	**100.0%**	**-0.49 [-0.89, -0.08]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.82); I² = 0%
Test for overall effect: Z = 2.36 (P = 0.02)

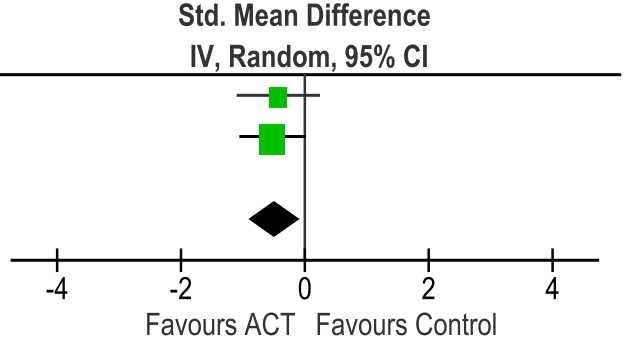


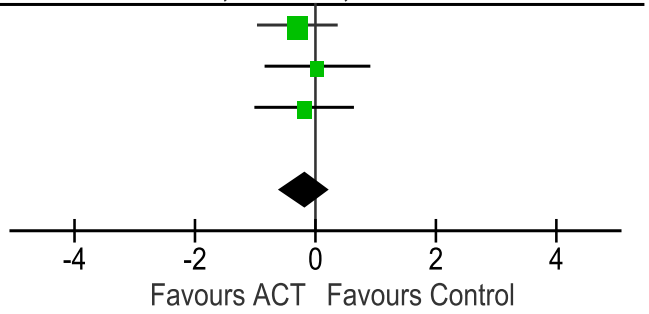
Figure 7

Forest Plot ACT vs Control; ACT Processes at Post-Intervention

	ACT			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Giovannetti 2020	31.5	10.18	18	34.6	10.02	19	45.0%	-0.30 [-0.95, 0.35]
Nordin & Rosman 2012	49	8.89	11	48.5	18.52	10	25.8%	0.03 [-0.82, 0.89]
Proctor 2018	20.9	13.2	13	23.4	12.5	11	29.2%	-0.19 [-0.99, 0.62]
Total (95% CI)			**42**			**40**	**100.0%**	**-0.18 [-0.62, 0.25]**

Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 2 (P = 0.83); I² = 0%

Test for overall effect: Z = 0.82 (P = 0.41)



Longer-term follow-up timepoints

Three studies (74 participants) included longer-term follow-up timepoints (1, 3, 5). Two studies (3, 5) measured 12-weeks post-randomisation and 26-weeks post-randomisation, respectively. One study included two longer-term follow-up points of 12 and 24-weeks post randomisation (1).

Khalifeh-Soltani & Borhani (2019) reported means and SDs for a follow-up timepoint (timeframe was not specified) however noted "*time limitations that did not allow for a follow-up examination on the study results*" (p. 39). There was no reference to a follow-up assessment within the methodology, therefore these results were not included in the review.

Where follow-up data were available, initial gains were sustained at each follow-up point following the ACT intervention for QoL, mood and ACT-targeted processes (1). Conversely, Meek et al. (2021) reported no significant effect, which was also demonstrated at 12-week follow-up.

Nordin and Rorsman (2012) reported an effect on AAQ-II within the ACT arm, which was maintained at longer-term follow-up. Initially the effect on depressive symptoms favoured the control (RT) however this was not maintained at longer-term follow-up. The control condition also favoured an effect on anxiety, which followed the same trend at follow-up; no effect was seen in the ACT intervention condition.

Publication bias

This was not conducted as we had fewer than 10 studies.

Discussion

This review examined the effectiveness of ACT for QoL and mood, in pwMS. Six studies were eligible for the review and meta-analysis. Overall, our findings indicate a small to medium effect of ACT on anxiety, depression, stress. The effect on stress was significant, likewise, we found a significant large effect on anxiety in comparison to passive control conditions (TAU). When applying a sensitivity

analysis, we also found a significant medium effect on depression over active (RT) control conditions. There was some indication of a small effect on ACT-targeted processes (AAQ-II); however, this was non-significant. We also found a nonsignificant, moderate effect on QoL, which was favourable of control conditions.

Our findings are in line with previous research exploring ACT for pwMS and psychological interventions for pwMS; demonstrating an improvement in depression, stress and the ACT-targeted process of acceptance (Pakenham et al., 2018; Sesel et al., 2018; Sheppard et al., 2010). Further, findings are also comparable to the wider ACT literature (Gloster et al., 2020), which also showed ACT to be efficacious for anxiety and depression and sustained in comparison to passive control conditions (e.g., TAU) but variable in comparison to active control conditions (e.g., CBT).

The meta-analysis did not find a significant effect of ACT on QoL, relative to control. In comparison to previous research (Pakenham et al., 2018; Sesel et al., 2018; Sheppard et al., 2010), this result was surprising. The most frequent measure of QoL was the ED-5D-5L, which includes mobility, usual activities, and pain/discomfort. A potential explanation for these results is given the variable nature of MS, these factors may not change or can worsen, even over the short timescale of an RCT or CCT. This may confound both the outcome and ability to engage with the intervention, questioning the validity and reliability of the results. In addition, Giovannetti et al. (2020) reported significantly higher MHC of QoL within the ACT intervention group at baseline, suggesting a potential ceiling effect, which also questions the validity of these findings.

Regarding ACT-targeted processes, the meta-analysis was indicative of a small, nonsignificant effect, favouring ACT. Four of the six studies had explored ACT-targeted processes: three using the AAQ-II and one using the CompACT. As the goal of ACT is not symptom reduction (Harris, 2006), but on acceptance and living a meaningful life, it is of theoretical importance to include specific ACT process measures. Potentially, detecting a larger, significant effect was limited due to the small sample size and reduced number of studies including ACT process measures.

Strengths and limitations of included studies

Overall, the majority of studies indicated high risk of bias so findings should be interpreted with caution. A large, contributing factor to this judgement was the measurement of the outcome. Only one study reported blinding participants (Nordin & Rosman, 2012). The challenge of blinding is consistent with conducting psychological intervention trials and introduces response bias and expectations of a positive outcome from participants' perspective (Juul et al., 2021). Four studies did complete baseline measures pre-randomisation; a strength that reduced potential risk of bias.

Across studies, there were small sample sizes; an issue which is commonly reported within psychological intervention studies on this population (Thomas et al., 2006). Only one study acknowledged potential adverse events, which is required when adhering to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Schulz et al., 2010). Further, only three studies assessed intervention fidelity.

The nature of the intervention was variable across studies. The number of sessions ranged from five to eight, with two studies including one-off "booster" sessions up to three months post-intervention completion. In addition, frequency of daily practice was difficult to control; Nordin & Rorsman (2012) reported a higher frequency of daily practice in the RT control group, potentially increasing consolidation of skills over the ACT intervention. Three studies used a group intervention format and two administered the intervention individually, either over the phone or face-to-face. Of those reporting the facilitator, two used a Trainee CP and two used qualified CPs. Future research may warrant sub-group analyses to determine what format of intervention is best for pwMS. Notably, Khalifeh-Soltani & Borhani (2019) did not report on the details of intervention delivery, which was a significant limitation as this prevents replicability and is also not in line with reporting standards (Schulz et al., 2010).

The inclusion of follow-up timepoints was also variable. Of those that included longer-term follow-up timepoints, this enabled longer-term effects of the intervention

to be examined, for example Giovannetti et al. (2020) reported a trend of increasing difference between the ACT vs control group. Future studies would need to consider longer timescales to demonstrate whether efficacy is sustained.

Strengths and limitations of the review

Inclusion of grey literature increased study inclusion however, included studies were all peer-reviewed, introducing potential publication bias towards positive results. Hand searching of reference lists broadened the search strategy, which was developed and tested with a subject-specialist librarian.

We recognise that specifying outcomes of “QoL” and “mood” within the eligibility criteria somewhat limited the searches. These are common outcomes of interest when examining efficacy of psychological interventions, making direct comparisons more coherent. For pwMS, it is important to acknowledge there are additional outcomes of interest from psychological interventions and ACT research, such as pain and fatigue (Davoodi et al., 2019). Inclusion of these factors would broaden searches further and strengthen the applicability of findings for pwMS.

Only one author (BT) reviewed titles, abstracts, and full texts for inclusion. A strength of this review is that, to reduce potential bias and increase reliability, a second author supported with uncertainty about inclusion and conducting the meta-analyses. Quality appraisal analysis was also completed by one author (BT). Despite a standardised tool being used, the subjective nature of the task introduces potential bias. To minimise this, at least two or more authors should consult for a quality appraisal. Further, given the difficulties of blinding within psychological intervention trials, the review could be strengthened by applying the RoB v2 tool with adaptations, as suggested by Munder & Barth (2018).

Generalisability of findings is limited due to the small number of studies and the variability across the studies: number of participants varied (*n* = 14 to 60), different comparators (TAU or RT) and outcome measures. The heterogeneity within the MS population (e.g., severity, length of illness) should also be acknowledged when generalising findings. The limited number of studies and variable quality within

the existing literature, is representative of the state of the current evidence available, which can be addressed by further, fully-powered empirical RCT's.

Implications

Given the review has shown some indication towards ACT being an effective psychological intervention for this population, there is a rationale for future research to address the methodological limitations highlighted in this review. For example, prioritising RCT designs, with longer-term follow-up points, including ACT process measures and ensuring an appropriate randomisation method is used and reported. Whilst current research has used RT as an active control, comparators should also include other psychological interventions, such as CBT, to explore direct comparisons. A cost-effectiveness analysis would also provide a more in-depth understanding as to effectiveness, particularly from a commissioner and service perspective for pwMS.

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Declaration of conflicting interests

Bethany Thompson reports no conflicts of interest and completes this work as partial fulfilment of the requirements for a Doctorate in Clinical Psychology at the University of Nottingham and University of Lincoln.

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Journal Paper

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TITLE PAGE

Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis (PrEliMS-2): A Multiple Single Case Series

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Abstract

Objectives

Support during Multiple Sclerosis (MS) diagnosis is salient to future coping, and adjustment to the disease. Acceptance and Commitment Therapy (ACT) has demonstrated promising results in improving adjustment-related outcomes. A recent feasibility randomised controlled trial (PrEliMS-1) investigating ACT-based support, did not find a signal of efficacy. However, interview data with the MS nurse specialists delivering the intervention suggested difficulties in aspects of delivery and

[8] See Appendix G for full author guidelines

facilitation. We aimed to address issues raised by having a Trainee Clinical Psychologist (TCP) deliver the intervention, to explore signals of efficacy, and understand possible mechanisms of change.

Design

A mixed-methods, multiple single-case AB design with five participants.

Methods

Our principle primary outcome was the psychological impact of MS. We were also interested in psychological flexibility, anxiety, and depression. Data were gathered weekly, during both AB phases. Secondary outcomes were gathered pre-, 1-week post- and 1-month post- intervention. Analyses comprised visual analysis, reliable and clinically significant change, comparison with PrEliMS-1 and framework analysis on post-intervention feedback.

Results

An effect on improving the psychological impact of MS was demonstrated. Participants with clinical levels of distress also benefitted from the intervention. Significant change in psychological flexibility was minimal. Secondary outcome results were more variable. Overall, the intervention was positively received with some improvements recommended.

Conclusions

We found promising support for TCP-delivered PrEliMS intervention. Findings are limited to pwMS who are white-British, and on average, 4-months post-diagnosis. Individual-level change observed was favourable compared to PrEliMS-1. Findings suggest psychological flexibility may not mediate positive adjustment-related outcomes. Future research is warranted to understand the target outcomes of PrEliMS and replicate findings in samples with improved demographic representation.

Keywords: *Psychological Distress, Multiple Sclerosis, Acceptance and Commitment Therapy, Emotional Support*

Conflict of Interest

Professor Roshan das Nair (RdN), Dr Nima Moghaddam and Dr Nikos Evangelou (NE) contributed to the development and write-up of the first PrEliMS study. NE has received lecture fees from Biogen and participated in paid advisory board for Biogen, Roche, and Merck in MS, and RdN has received funding to prepare and deliver lectures (speakers bureau) on cognitive rehabilitation and MS and mental health from Novartis, Merck, and Biogen.

No conflicts of interest were reported by Bethany Thompson or Dr Anna Tickle.

Data Availability Statement

The authors do not intend to make study data publicly available, in line with ethical approval obtained.

Acknowledgements

We would like to thank Jacqui Mhizha-Murira for the provision of the original PrEliMS data for data analysis purposes. We would also like to thank Alexandra Frost for her support with recruitment.

This study was part funded by Health Education East Midlands. Bethany Thompson completed the work as partial fulfilment of the requirement of a Doctorate in Clinical Psychology at the University of Nottingham and University of Lincoln.

STATEMENT OF CONTRIBUTION PAGE

Statement of Contribution

What is already known on this subject?

- Emotional distress is common around Multiple Sclerosis (MS) diagnosis, which can affect later service use.
- Acceptance and commitment therapy is a promising approach for improving adjustment and coping-related outcomes.
- A feasibility trial failed to find signals of efficacy, however practicality and delivery issues limited findings.

What does this study add?

- Psychologist-delivered acceptance-based support generated change across a range of coping-related outcomes.
- Individual-level change observed was favourable compared to previous trials of this intervention.
- Suggested improvements would further promote accessibility and be flexible to MS patient needs.

MAIN TEXT FILE[9]

Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis (PrEliMS-2): A multiple single case series

[Acknowledgements here]

[Abstract here]

Key words: *Psychological Distress, Multiple Sclerosis, Acceptance and Commitment Therapy, Emotional Support*

Introduction

Multiple sclerosis (MS) is a chronic, neurological disease, causing inflammation and degeneration of the central nervous system, resulting in a range of symptoms: pain, fatigue, muscle weakness, and cognitive impairments (Calabresi, 2004). In England, on average, 4,950 new cases of MS are diagnosed annually (Public Health England, 2020). Disease symptomology and progression vary greatly between individuals and providing an accurate prediction of prognosis is difficult (Dennison et al., 2016). Consequently, both being diagnosed and living with MS generates considerable uncertainty for the individual, which results in poor psychological health (Wilkinson & das Nair, 2013).

Obtaining an MS diagnosis is typically a lengthy process over several months, due to increased waiting times, investigation, and sometimes disbelief of symptoms from medical professionals (Goldenberg, 2012; Strickland et al., 2017). This has been conceptualised as a 'rollercoaster effect' of varied and fluctuating emotional responses (including relief, fear, uncertainty, sadness, and anger) (Topcu et al., 2022). Empirical findings highlight clinically significant levels of anxiety and depression following MS diagnosis, which also persist into the future (Conradsson et al., 2018; Giordano et al., 2011).

Currently, the diagnostic support nationally recommended for People with MS (pwMS[10]) (National Institute for Health and Care Excellence [NICE], 2022) is not responsive to patient need. MS Information booklets have been found to have no impact on anxiety (Solari, 2014) and local support groups, as recommended, can

[9] For double anonymous peer review BJHP requires all information identifying authors to be removed from main text file.
[10] This is an abbreviation accepted within the MS community and used by MS charities (Multiple Sclerosis: News Today., 2018).

evoke fear of witnessing decline in others, hence pwMS can be hesitant to attend (Dennison, 2011). Equally, pwMS often avoid discussion about diagnosis to avoid associated experiences of uncertainty and fear for the future. These findings support the drive towards patient-centred care approaches within healthcare for long-term neurological conditions (Department of Health, 2005). However, pwMS continue to lack individually-tailored psychological support around diagnosis; a need which is often ignored (Borreani et al., 2014; Desborough et al., 2020; Topcu et al., 2022). Together, findings suggest support needs to be: (I) flexible, (ii) sensitive to individual needs, (iii) available on an individual basis, and (iv) targeted towards unhelpful avoidance of their diagnosis. This reflects recommendations to improve engagement in psychological support for neurological conditions, suggested in a recent systematic review (Pinto et al., 2022).

The lack of current guidance on individual psychological support around diagnosis is possibly explained by the lack of research in to how best to provide this. Cognitive Behavioural Therapy (CBT) is the most tested and empirically supported form of psychological support for pwMS (Sesel et al., 2018; Thomas et al., 2006). However, findings vary for use in pwMS. In some research, CBT has demonstrated efficacy in improving quality of life and reducing depressive symptoms in pwMS, alongside reported improvements in maladaptive beliefs about, and acceptance of, illness (Fiest et al., 2016; Kiropoulos et al., 2016; Moss-Morris et al., 2013). However, a review by Sesel et al. (2018), did not find CBT to be effective for distress in pwMS when tested in isolation, and less efficacious in comparison to alternative interventions such as mindfulness. Equally, the use of CBT within this context has received criticism for invalidation, through challenging realistic and logical fears about deterioration associated with MS (Meek et al., 2021).

Whilst CBT may reduce symptoms of distress for pwMS, there are additional determinants of successful adjustment to MS. A key element is the period around diagnosis (Topcu et al., 2020); a factor which had yet to be considered by alternative models of adjustment in the context of MS (Dennison, 2011; Soundy et al., 2016; Wilkinson & das Nair, 2013). Specifically, positive experiences during this critical period will strengthen the positive association between adaptive coping and MS adjustment. Regarding *how* interventions can promote this, the ‘Y-shaped’ process

model of adjustment outlines a staged approach (Gracey et al., 2009). Most salient, is acknowledgment and resolution of 'discrepancies' such as fear of stigma and perceived difference between current self and hoped-for-self. This can be achieved through safe therapeutic spaces and engaging in behavioural change to consolidate pre-injury/illness values. This model supports additional findings that associate expression and acceptance of emotion, self-management, and reprioritisation of what is important in life, to successful adjustment to MS (Austenfeld & Stanton, 2004; de Ridder et al., 2008). Consequently, psychological support during this period should be promoting quality of life and reduced avoidance of emotional distress.

A psychological therapy that offers an alternative is Acceptance and Commitment Therapy (ACT); a third-wave, transdiagnostic behavioural therapy that focuses increasing an individual's 'psychological flexibility', which captures acceptance, mindfulness, and values-based action (Harris, 2019). Psychological distress is understood to arise because of experiential avoidance of unwanted thoughts, memories, and bodily sensations. Further, pain and suffering are viewed as inevitable parts of life, rather than located within the individual as problematic (Hayes et al., 2012). Negative thoughts and beliefs are likely to be realistic within chronic long-term conditions like MS, thus ACT arguably provides an effective, acceptable intervention in opening opportunity to accept these experiences and increase valued behaviours (Graham et al., 2016).

The emerging evidence-base for ACT has demonstrated promising results for both positive mental and physical health outcomes, particularly within chronic, long-term physical health conditions (Gloster et al., 2020; Graham et al., 2016; Veehof et al., 2016). Within MS practice and research, recognition of the value of ACT is growing (British Psychological Society, 2021; Nordin & Rorsman, 2012; Pakenham et al., 2018; Proctor et al., 2018). Preliminary findings suggest ACT can generate significant improvements in stress for pwMS (*SMD* = -0.49) (Thompson et al., 2022), with signals of efficacy for improving psychological flexibility, anxiety, depression, and quality of life (Zarotti et al., 2023). However, further research is required to replicate effects and consolidate findings.

Currently, most of the research in this field explores the use of ACT across the trajectory of MS, often targeting reduction in already high levels of distress.

However, given the outcome of interest is improving psychological flexibility, there is utility in using ACT as a preventative source of support around the point of diagnosis. Empirical findings demonstrate psychological flexibility to have a mediating role between life stressors and outcomes (including wellbeing), thus is arguably a crucial public health target (Gloster et al., 2017). Greater psychological flexibility is associated with better coping outcomes in MS (i.e., lower distress, higher quality of life) (Meek et al., 2022). Further, promoting acceptance-focused coping styles around the point of diagnosis is a key factor in positive psychosocial adjustment to MS, and the consequent trajectory of future coping (Topcu et al., 2020).

A recent feasibility Randomised Control Trial (fRCT) of emotional support around the point of MS diagnosis (PrEliMS-1) used a newly designed, ACT-based "PrEliMS intervention" (das Nair et al., 2023). This 3-arm RCT compared a (I) nurse-supported intervention with (ii) a nurse plus peer-supported intervention, with (iii) usual care. The interventions involved completion of an MS-specific, ACT-based, workbook, alongside support sessions with an MS Nurse Specialist (and/or peer support [ii]). The format of bibliotherapy and teletherapy was used. Research demonstrates this is helpful in promoting accessibility and flexibility of intervention in this context (Pinto et al., 2022), and is a format which has demonstrated some efficacy in reducing anxiety for pwMS (Proctor et al., 2018).

Despite positive qualitative feedback from PrEliMS-1 participants – identifying that the intervention enabled coping strategies and functioned as a "lifeline" – there was no signal of efficacy in aggregated quantitative analyses (das Nair et al., 2023). Similar issues were highlighted when using the same workbook, supplemented by teletherapy, in adjusting to secondary progressive MS diagnosis (Meek, 2021). Additionally, in PrEliMS-1, nurses had reduced capacity to attend intervention training and some participants noted concerns that not enough time was spent discussing psychological issues within sessions. Subsequently, recommendations were made to have the intervention facilitated by a practitioner in psychology; a suggestion corroborated by Borreani et al. (2014).

As the PrEliMS pathway (Tindall et al., 2023) and ACT-based workbook were developed directly in response to needs raised by pwMS, with aspects already identified as helpful, further testing is warranted. To address the practicality and

delivery issues highlighted, the current study aimed to test the intervention on a small scale, facilitated by a Trainee Clinical Psychologist (TCP); specifically, to:

1. *examine* the efficacy of the PrEliMS intervention for improving the psychological impact of MS, in newly diagnosed pwMS when administered by a TCP (PrEliMS-2).
2. *explore* whether the PrEliMS-2 intervention has a positive impact on health-related quality of life, perceived stress, MS-related self-efficacy, and fatigue.
3. *compare* the efficacy of the PrEliMS-1 intervention with PrEliMS-2.
4. *explore* experience of the PrEliMS-2 intervention and potential improvements.

Materials and Methods

Ethical approval was obtained from Berkshire-B research ethics committee (ref: 22/SC/0034)[11]. The study protocol was registered on ClinicalTrials.gov (ID: NCT05225012).

Design

We used a mixed-methods, non-concurrent Multiple Single Case Experimental Design (MSCED)[12]. This can be described as an AB design whereby a baseline is established ('A') followed by an intervention ('B') (Barker et al., 2016). This was used across participants, resulting in a series of AB replications.

Recruitment

Participants were recruited through an MS outpatient clinic at a UK National Health Service (NHS) trust. Participants were aged ≥18 and had received a diagnosis of MS within the last twelve months[13], confirmed by a Consultant Neurologist. Informed consent was obtained. Participants were screened using the Psychological Subscale of the Multiple Sclerosis Impact Scale (MSIS-Psy)[14] and eligible if they scored ≥18. Participants were excluded if they were unable to speak and read English, unable to use/did not have access to a phone or computer with

[11] See Extended Methods 2.1 for further detail on ethical approval.
[12] See Extended Methods 2.2 for further detail on the design and rationale.
[13] Ethical amendment: This was changed from 6-months to 12-months post-diagnosis based on feedback from potential participants and the clinicians approaching potential participants. See Extended Methods 2.3.2.
[14] Ethical amendment: This was changed from ≥8 on the GAD-7 and/or ≥10 on the PHQ-9 to ≥18 on the MSIS-Psych. See Extended Methods 2.3.2 for the rationale.

internet connection or were receiving other psychological therapy. We aimed to recruit between three and seven participants. In an MSCED, a minimum of three participants is recommended to demonstrate an effect (Smith, 2012)[15].

Measures[16]

Principal primary outcome

The psychological impact of MS was captured by the psychological subscale of the Multiple Sclerosis Impact Scale (MSIS-Psy; Hobart et al., 2001; Ramp et al., 2009); a quality-of-life (QoL) measure concerning the health impact of MS. This has good internal consistency ($\alpha = 0.91$) and convergent and discriminant validity with extant QoL measures (Hobart et al., 2001).

Primary outcomes

We used the Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001) and Generalised Anxiety Disorder-7 (GAD-7; Spitzer et al., 2006) to measure distress (anxiety and depression). The PHQ-9 has acceptable internal consistency in the MS population (Patrick & Connick, 2019) and high sensitivity (Marrie et al., 2018). The GAD-7 also has good internal consistency and convergent validity within the MS population (Terrill et al., 2015).

Three visual analogue scales were also used to capture: the extent to which current distress relates to receiving an MS diagnosis, and how confident participants feel in managing both the physical and psychological impact of MS[17].

Process Measure

The abbreviated version of the Comprehensive Assessment of Acceptance and Commitment Therapy processes (CompACT-8; Dawson & Golijani-Moghaddam, 2020; Morris et al., 2019) was used to capture potential changes in participants' psychological flexibility. The CompACT-8 demonstrates high internal consistency $\alpha = 0.734$ (Morris et al., 2019) and validity (Francis et al., 2016).

[15] See Extended Methods 2.4 for further details about sample size and sampling methods.
[16] See Extended Methods 2.5 for tabulated information about all measures, further details, and rationale.
[17] See Extended Methods 2.5.3 for the visual analogue scales.

Secondary Outcomes

Secondary outcomes were the EQ-5D-5L (Herdman et al., 2011) to assess Health-related Quality of Life (HRQoL), the Perceived Stress Scale (PSS-10; Cohen et al., 1983), the Multiple Sclerosis Self Efficacy Scale (MSSES; Rigby et al., 2003) and the Modified Impact Fatigue Scale (MFIS-5; Fischer et al., 1999; Fisk et al., 1994)[18].

Procedure[19]

Potential participants were informed about the study by their neurologist or MS nurse specialist and were contacted within a week by the lead researcher (BT) to complete screening[20]. If eligible, participants were sent an information sheet[21] and consent form[22] and demographic data were collected[23]. Those not eligible were signposted, if needed, to their General Practitioner and/or MS team[24].

For phase 'A', the primary and process measures were administered weekly, for three weeks, to establish a baseline. Questionnaires were administered using Qualtrics. If participants showed variability during baseline, this was extended by two weeks, meaning baseline periods consisted of four to six data points. Secondary outcome measures were also administered in the first week of baseline.

Primary and process measures continued to be repeated weekly throughout intervention delivery (four data points). All measures were repeated at two further time points post-intervention: one-week after the final session and one-month later[25].

Intervention

For phase 'B', the PrEliMS-2 intervention was introduced. Table 5 provides a brief outline. This consisted of one-to-one ACT-based support sessions, alongside independent completion of a 52-page workbook: "Better Living with a diagnosis of MS". The workbook was originally developed for PrEliMS-1 (das Nair et al., 2023)

[18] See Extended Methods 2.5.5 for further details and rationale for the secondary outcome measures.
[19] See Extended Methods 2.3.1 for a diagram showing the flow of participants through the study.
[20] See Extended Methods 2.6 for further details about the study procedure.
[21] See Appendix H for participant information sheet.
[22] See Appendix I for consent form.
[23] See Appendix J for demographic data form.
[24] See Extended Methods 2.8.1.1 for further details.
[25] See Extended Methods 2.5 for further information on the measures used and timepoints.

and uses ACT-based exercises, drawn from previously designed guided self-help ACT resources (Brassington et al., 2016; Ford, 2017; Hayes & Smith, 2005)[26].

The accompanying sessions aimed to support participants in applying ACT principles and techniques into their everyday lives, thus, increasing psychological flexibility and acceptance. Sessions were delivered by a trainee clinical psychologist (BT), under the supervision of two qualified clinical psychologists practicing ACT (NM and AT). Sessions occurred by video call (Microsoft Teams) and were recorded.

Table 5

PrEliMS-2 Intervention Description

Facilitator	Trainee clinical psychologist with two years' experience in (a) delivering ACT within NHS mental-health settings, and (b) working with pwMS.
Format	Four, weekly online video call sessions. Initial session was an hour long and the remaining three sessions ranged between 30-45 minutes.
Materials	A hard copy of a 52-page ACT-based workbook consisting of three sections: (1) Introduction, (2.1) Dealing with unhelpful thoughts, feelings and physical sensations, (2.2) Mindfulness, and (3) Doing what matters. These sections map on to overarching areas of the ACT Hexaflex: 'open up', 'be aware', and 'do what matters'. Sections included metaphors, practical exercises, and homework tasks.
Session Content	Both the facilitator and participant had a hard copy of the workbook to work through together during sessions. Pacing was based on individual need. Completion of the workbook was not an expectation. Sessions were collaborative in deciding homework tasks and reviewing workbook content, based on participant progress. In the final session, discussion centred on aspects the participant wished to take forward, beyond the intervention.

Feedback interview

One week after the final session, we invited participants to complete a 30-minute semi-structured feedback interview[27] to explore their experience of using the workbook[28] (adapted from Elliott et al., 2001). Interviews were one-to-one with a researcher independent to the intervention (HH), via Microsoft Teams and recorded[29].

[26] See Extended Methods 2.6.3 for further details on the intervention.
[27] See Appendix K for interview consent form.
[28] See Appendix L for interview schedule.
[29] See Extended Methods 2.5.6 for further details on the feedback interviews.

Analysis

Individual Analysis[30]

Within-participant analyses took two approaches. Firstly, data relating to the primary (MSIS-Psy, GAD-7, PHQ-9) and process outcomes (CompACT-8) were plotted on a graph and visual analysis was used to identify phase-related change. This was supplemented by Fisher's dual criteria method (Fisher et al., 2003; Krasny-Pacini & Evans, 2018). An adjusted baseline trend and mean was projected into the intervention period and the number of data points above or below this trend was used to aid interpretation of an intervention effect. Secondly, reliable, and clinically significant change indices (RCI; CSC) were used to examine whether any change holds practical and reliable significance (Jacobson & Truax, 1991). This analysis was also applied to secondary outcomes (PSS, MSSES, EQ-5L-5D, MFIS-5).

Sample comparisons (PrEliMS-1 vs PrEliMS-2)[31]

Findings were compared to PrEliMS-1 data to examine:

1. the proportion of individuals achieving reliable and clinically significant change (CSC).
2. the primary principal outcome (MSIS-Psy) change on a single case compared to the PrEliMS-1 sample, using the Bayesian Standardised Difference Test (BSDT; Crawford & Garthwaite, 2007).

Feedback Interviews

Framework analysis was used to analyse the interview qualitative data using the procedure outlined by Gale et al. (2013). Deductive coding was prioritised, in line with the study aims, however open coding was also used so data were not missed.

Intervention Fidelity

A sample of five (25%) session recordings were assessed by two clinical psychologists (NM and AT) against a published ACT Fidelity Measure (ACT-FM; O'Neill et al., 2019)[32]. They have several years' experience in ACT and co-developed (NM) the PrEliMS-1 intervention.

[30] See Extended Methods 2.7.2 for further details on individual analysis.
[31] See Extended Methods 2.7.3 for further details on sample comparisons analytic methods used.
[32] See Appendix M for a description and scoring of the ACT-FM

Results

Between May 2022 and December 2022, ten individuals were referred by the neurology clinic[33]. Nine individuals consented to screening and met the eligibility criteria. One participant withdrew during phase 'A'. A baseline was obtained for eight participants. Three withdrew following completion of one session, providing one data point within their 'B' phase[34]. The remaining five participants completed the study in its entirety.

For the journal paper, the five complete data sets will be reported. Additional, incomplete data sets are reported and commented on within an extended paper[35]. Baseline demographic details are in Table 6.

Table 6
Demographic Information[†]

	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5
Age	59	44	18	32	39
Gender	Man	Woman	Woman	Woman	Man
Employment status	Unable to work due to MS	Freelance	Employed part-time	Education full-time	Employed full-time
MS Diagnosis duration	3 months	8 months	4 months	3 months	6 months
Type of MS	Relapsing-remitting	Relapsing-remitting	Relapsing-remitting	Relapsing-remitting	Not known
Duration to obtain MS diagnosis	3 months	8 months	12 months	11 months	7 months

Note: All participants were of White British ethnicity.
[†]Correct at time of screening

Initial sessions ranged from 50 to 63 minutes (*M* = 58.42; *SD* = 4.79), and follow-up sessions ranged from 33 to 45 minutes (*M* = 38.6; *SD* = 3.52). There were no missed sessions, and all outcome measures were completed. Participant 1 completed a further two data points within the baseline period, due to variability

[33] See Extended Results 3.1 for further information on recruited participants.
[34] See Extended Discussion 4.6.1 for further thought on recruitment and attrition.
[35] See Extended Results 3.2 and 3.3 for demographic details and quantitative data of participants who withdrew.

within scores. Fidelity checking found a consistent level of therapist adherence to ACT-congruent therapeutic style and content, demonstrated by scores on the ACT-FM.

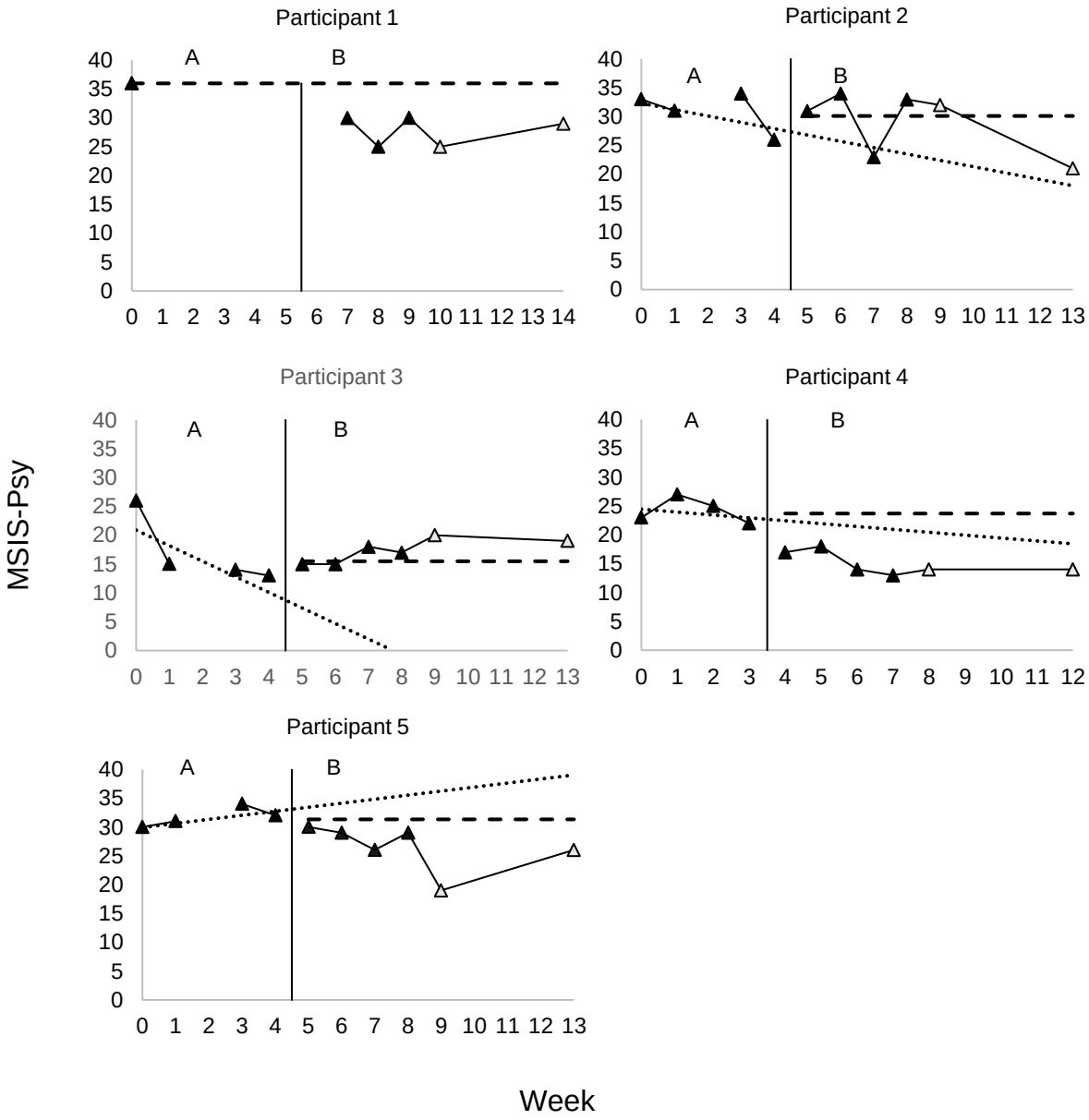
Visual and Clinically Significant Analysis of Change

MSIS-Psy

Changes in the psychological impact of MS can be seen in Figure 8.

Figure 8

Psychological Impact Scores for Each Participant During Baseline and Intervention



Note. ·····Projected baseline trend minus .25 SD; – – –Mean baseline score minus .25 SD; —▲— Total Scores; —△— Follow-up point; 'A' denotes baseline phase; 'B' denotes intervention phase including 1-week and 1-month follow-up points; Greater scores indicate greater psychological impact of MS; Participant 1 only completed one data point in baseline as this occurred before primary outcome amendment [36]

Overall, the psychological impact of MS appeared to reduce across phases for four participants (P1, P2, P4, P5). Applying the dual criterion method, systematic change can be implied for three (P1, P4, P5) out of five participants, as all data

[36] See Extended Methods 2.3.2 for more detail on study amendment.

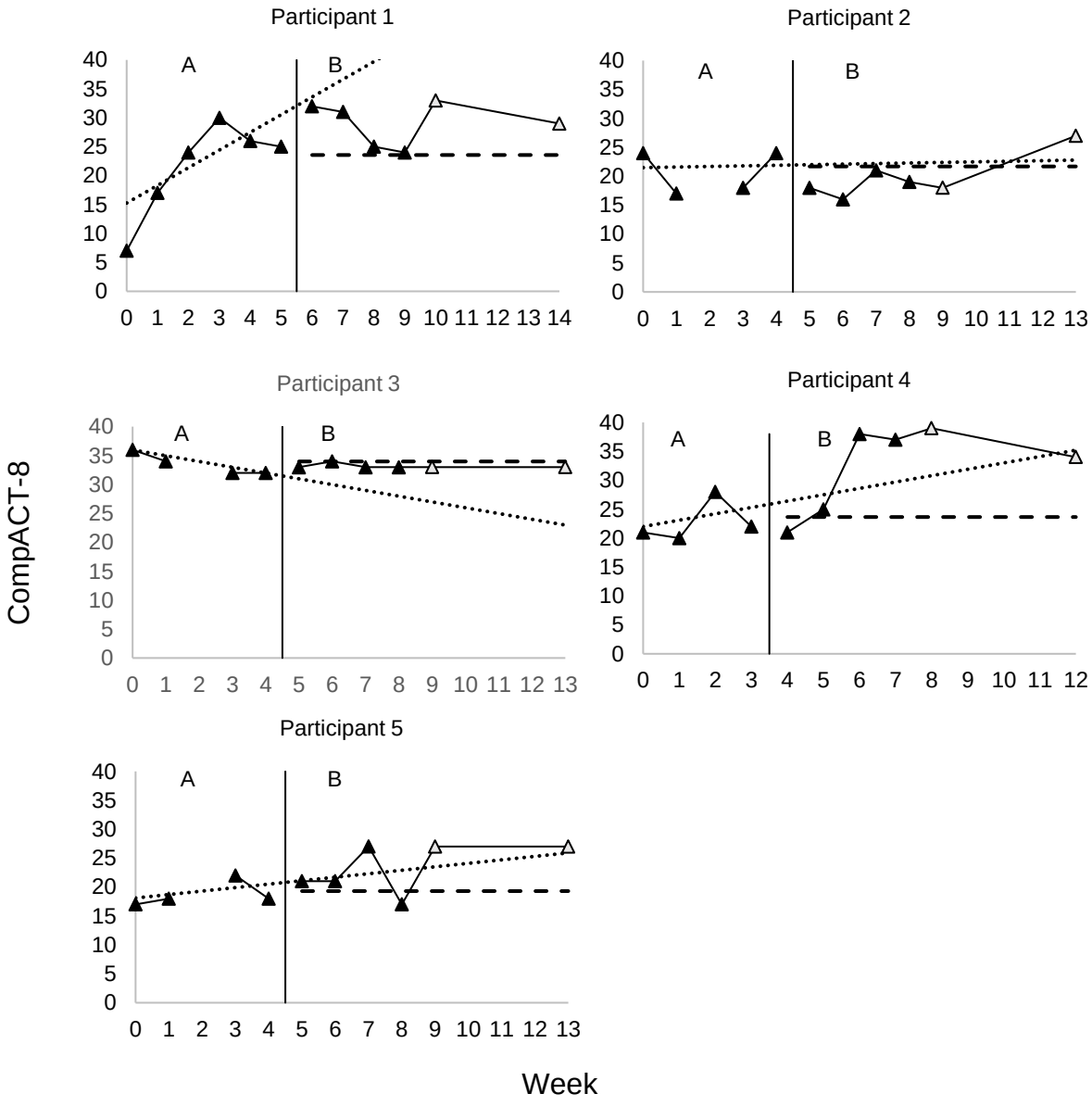
points were below the mean and trend lines during the intervention phase; criterion is applied with caution for Participant 1 as only one data point is representative of the baseline phase. Data for Participant 3 suggested an increase from baseline to intervention, as scores were above the projected mean and trend. Equally, Participant 2 showed high variability in scores across both phases, with four out of six data points above the projected mean and trend. From baseline to post-intervention, reliable change was observed for all participants, however this was not clinically significant.

CompACT-8 (Psychological Flexibility)

Changes in psychological flexibility can be seen in Figure 9.

Figure 9

Psychological Flexibility Scores for Each Participant During Baseline and Intervention



Note. ····· Projected baseline trend plus .25 SD; – – · Mean baseline score plus .25 SD; —▲— Total Scores; —△— Follow-up point; 'A' denotes baseline phase; 'B' denotes intervention phase including 1-week and 1-month follow-up points; Greater scores indicate greater psychological flexibility.

Across all participants, systematic change in psychological flexibility did not occur, according to the dual method. Three participants (P1, P4, P5) demonstrated an upward projected trend, suggesting an improvement in psychological flexibility

during baseline. During intervention, this trend either sustained (P4, P5) or stabilised (P1). Participant 3 demonstrated a declining trend during baseline which stabilised during intervention. All but one data point within the intervention phase for Participant 2 were below the projected trend and mean. This is suggestive of a gradual decline in psychological flexibility; however, the final data point is an exception to this. Reliable change was observed in two participants (P1 and P4) at both post-intervention timepoints. For participant 4, this was a clinically significant at 1-week post-intervention.

Emotional Distress (GAD-7 and PHQ-9)

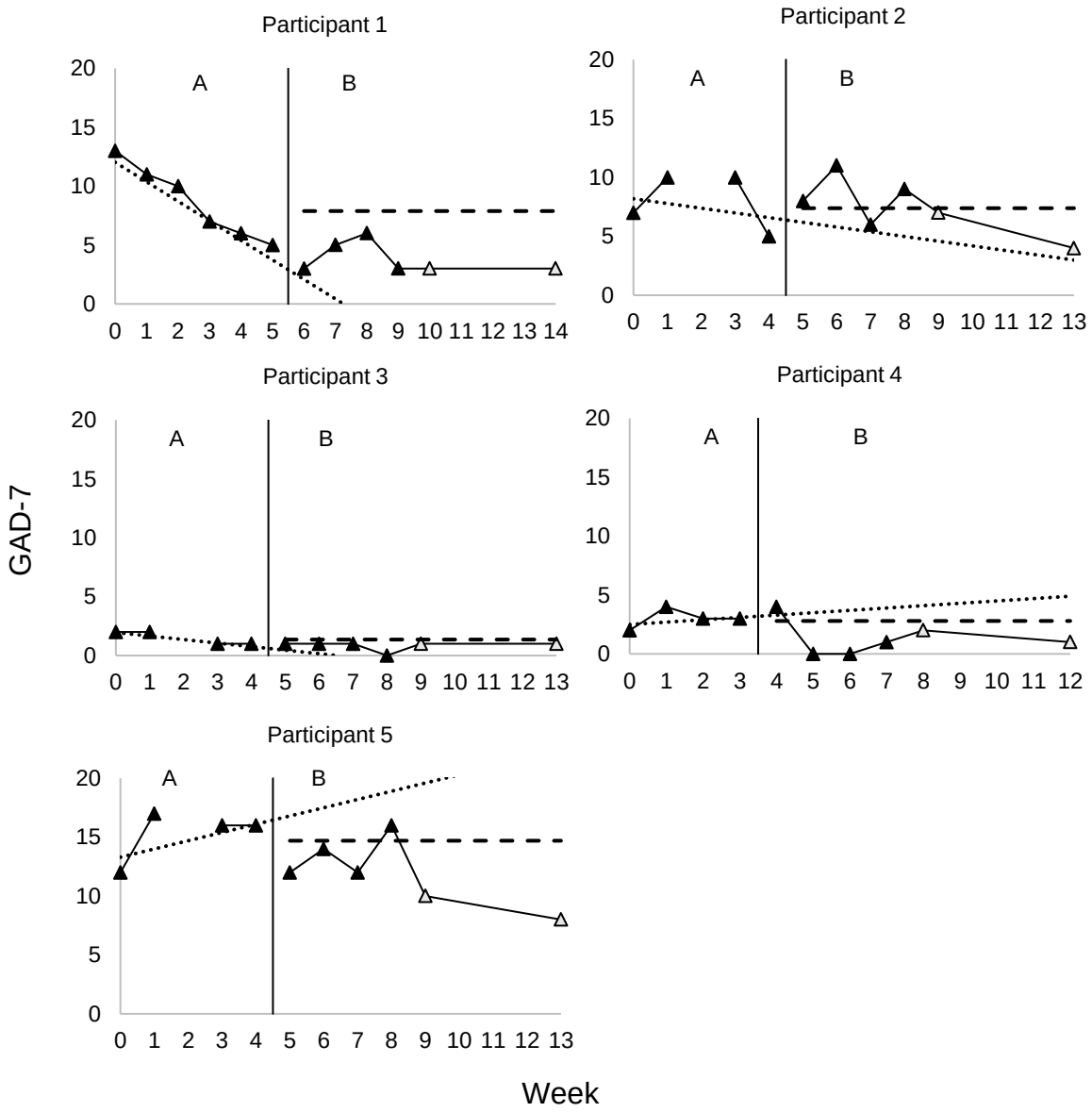
Changes in emotional distress are seen in Figures 10 and 11.

Weekly observations of distress attributed to MS varied[37]. Applying the dual criterion method, only Participant 3 showed a systematic change, in the direction of deterioration. Two participants (P1, P2) showed a stabilisation in trend during the intervention phase. This was also observed for Participant 5, however individual scores were more variable. Participant 4 demonstrated a clear downwards trend during baseline. The trend within the intervention was more variable, however improvement was sustained.

[37] See Extended Results 3.7.1 and 3.7.2 for graph plots of measures relating to distress and confidence in managing MS.

Figure 10

GAD-7 Scores for Each Participant During Baseline and Intervention



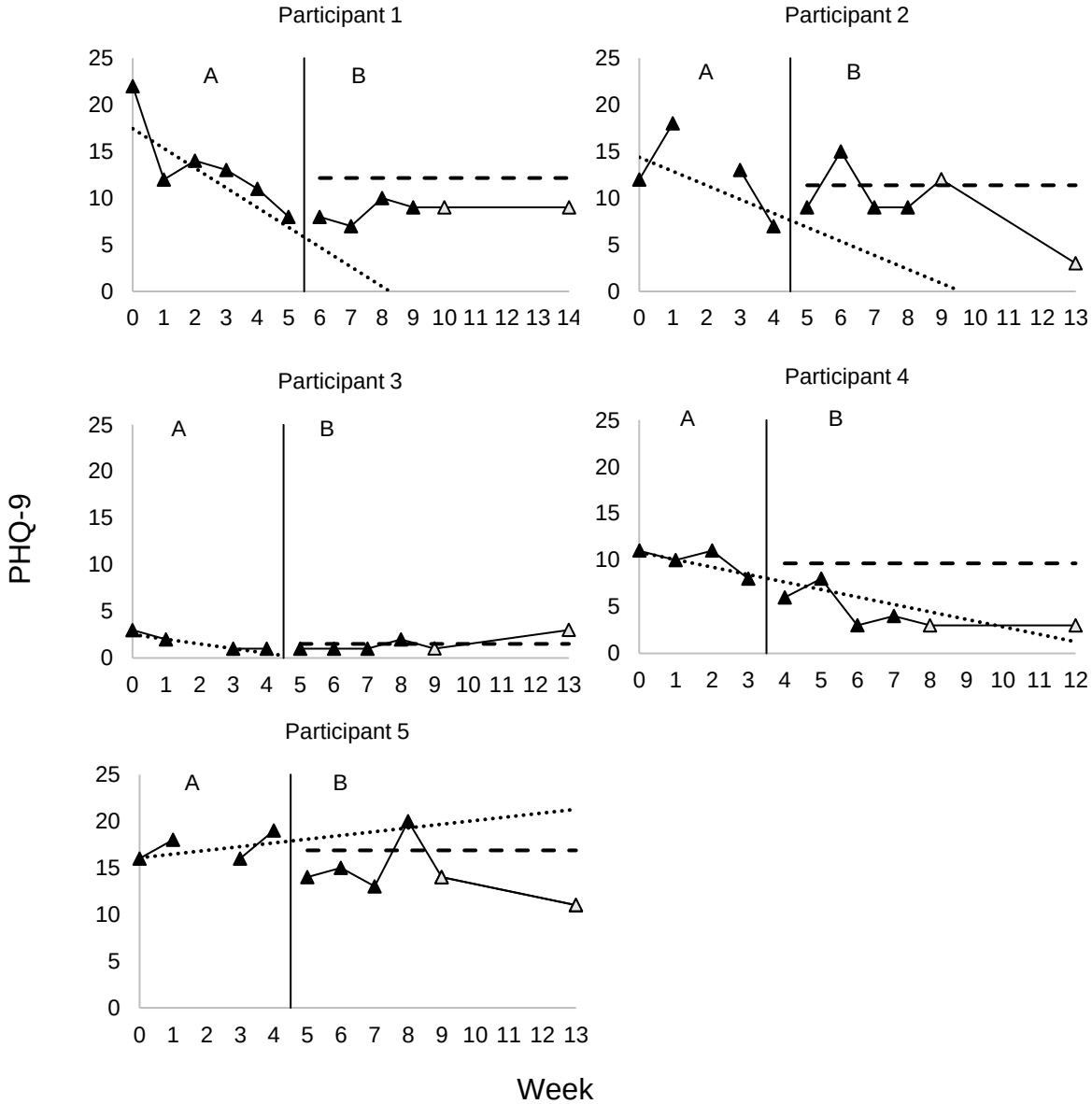
Note. ····· Projected baseline trend minus .25 SD; – – · Mean baseline score minus .25 SD; —▲— Total Scores; —△— Follow-up point; 'A' denotes baseline phase; 'B' denotes intervention phase including 1-week and 1-month follow-up points; Greater scores indicate greater presence of anxiety symptoms.

No participants reached sufficient data points below the projected mean and trend to indicate systematic change. Two participants (P4, P5) were one data point below the required amount to demonstrate change in the direction of improvement. Notably, Participant 1 demonstrated an improving trend during baseline and anxiety symptoms appeared to stabilise across the intervention phase. Participants 2 and 3 showed no change; scores were already below clinical cut-off pre-intervention.

Participant 3 demonstrated low levels of anxiety symptoms across phases, below clinical cut-off. Only Participant 1 demonstrated reliable and clinically significant change at both timepoints post-intervention.

Figure 11

PHQ-9 Scores for Each Participant During Baseline and Intervention



Note. ·····Projected baseline trend minus .25 SD;– – · Mean baseline score minus .25 SD; —▲— Total Scores; —△— Follow-up point; 'A' denotes baseline phase; 'B' denotes intervention phase including 1-week and 1-month follow-up points; Greater scores indicate greater presence of depression symptoms

Overall, four out of five (P1, P2, P4, P5) participants demonstrated an improving trend during baseline. Participant 3 scored below clinical level throughout phases. When assessing with dual criterion methodology, the intervention was not

effective at reducing symptoms of depression. Participant 5 was one point below the required amount to show a systematic change. Only one participant (P5) showed a worsening trend in symptoms of depression during baseline. Reliable and clinically significant change was observed at both post-intervention timepoints, in two participants (P1, P4). Participant 2 also demonstrated reliable and clinically significant change 1-month post-intervention.

Secondary Outcomes

Stress

Reliable and clinically significant change was observed for two participants (P1 and P4) and sustained at 1-month follow-up. Participant 5 also demonstrated reliable change at 1-month follow-up, however this was not clinically significant. Participant 3 demonstrated reliable and clinically significant deterioration at both post-intervention time-points.

Self-efficacy[38]

Participants 4 and 5 demonstrated reliable and clinically significant improvement at 1-month follow-up. Equally, participant 2 showed reliable and clinically significant improvement at 1-week post-intervention. Participant 3 showed a reliable deterioration at 1-week post-intervention which was sustained at 1-month follow-up, and within the clinical range at this time-point. Scores were above cut-off at each time-point for participant 1; change observed was not reliable.

Health-Related Quality of Life[39]

No reliable or clinically significant change was observed in any participants. Scores improved for two participants (P4 and P5) and either decreased (P2 and P3) or stayed the same (P1) for the remaining participants.

Fatigue

Only one participant (P4) showed reliable improvement, however this was not clinically significant. Remaining participants showed a slight increase in scores (P1, P2, P3), which were not sustained for participant three. A decrease in scores was observed for participant five.

[38] See Extended Results 3.6.2 for additional weekly measures relating to confidence in managing MS.
[39] Additional EQ-5D-5L profiles are commented upon within the Extended Results section 3.8.

A summary of all pre-, 1-week post- and 1-month post- intervention scores can be seen in Table 7, with reliable and clinically significant change criteria.

Table 7

Outcome Scores at Pre- Post- 1-month Follow-up and Reliable and Clinically Significant Change Criteria

Participant and measure	MSIS-Psy	CompACT-8	GAD-7	PHQ-9	PSS	MSSES	EQ-5D-5L	MFIS-5
RC min	5.17 (↓)	12.31 (↑)	4.33 (↓)	5.6 (↓)	6.65 (↓)	7.13 (↑)	25.08 (↑)	6.84 (↓)
Cut-off	<12.2†	>36.44†	≥8‡	≥10‡	<17.62§	>35.8†	>78.43§	<5.91§
1								
Pre-Intervention	36	7	13	22	25	39	40	13
Post-Intervention	25 R+	33 R+	3 R+ CS+	9 R+ CS+	14 R+ CS+	42	40	15
1-month Follow-up	29 R+	29 R+	3 R+ CS+	9 R+ CS+	17 R+ CS+	43	40	15
2								
Pre-Intervention	33	24	7	12	27	27	53	6
Post-Intervention	32	18	7	12	28	37 R+ CS+	50	7
1-month Follow-up	21 R+	27	4	3 R+ CS+	21	35 R+	50	10
3								
Pre-Intervention	26	36	2	3	6	49	70	9
Post-Intervention	20 R+	33	1	1	19 R- CS-	39 R-	65	12
1-month Follow-up	19 R+	33	1	3	21 R- CS-	34 R- CS-	65	6
4								
Pre-Intervention	23	21	2	11	24	56	67	17
Post-Intervention	14 R+	39 R+ CS+	2	3 R+ CS+	10 R+ CS+	62	85	7 R+
1-month Follow-up	14 R+	34 R+	1	3 R+ CS+	8 R+ CS+	67 R+ CS+	90	8 R+
5								
Pre-Intervention	30	17	12	16	30	30	30	18
Post-Intervention	19 R+	27	10	14	29	35	45	14
1-month Follow-up	26	27	8	11	23 R+	39 R+ CS+	34	17

Note. RC Min; Minimum change-score required to demonstrate a reliable change at 95% confidence. ↑ ↓ = direction of clinical gain. R+ = reliable improvement in relation to first available score. R- = reliable deterioration in relation to first available score. C+ = clinically significant improvement in relation to first available score. C- = clinically significant deterioration in relation to first available score.

†according to clinically significant change criterion A established cut-off.

‡according to published clinical cut-off criteria for pwMS.

§according to clinically significant change criterion C established cut-off.

Comparison with PrEliMS-1 (das Nair et al., 2023)

Data were available to compare percentage of RCI and CSC in five outcomes: psychological impact of MS, anxiety, depression, stress, and self-efficacy. In PrEliMS-2, a higher percentage of reliable and clinically significant improvement, in comparison to PrEliMS-1, was observed across all outcomes[40]. In PrEliMS-1, CSC improvement was observed in two outcomes (depression, 8%; stress, 21%), whereas the current study observed this in four out of five variables (anxiety, 20%; depression, 60%; stress, 60%; and self-efficacy, 60%).

BSDT[41] analyses for the MSIS-Psy revealed one participant (P2) demonstrated change at 3.7 months post-baseline, that was significantly larger compared to the PrEliMS-1 3-month post-baseline sample. Further, when comparing 2.5 months post-baseline, with 3-months post-baseline in PrEliMS-1, two participants (P1, P5) in PrEliMS-2 experienced significantly larger change in the MSIS-Psy. Results are presented in Table 8.

Table 8
BSDT for MSIS-Psy

	Baseline vs 2.5 months† post-baseline		**Baseline vs 3.7 months† post-baseline**	
	D	***p*‡**	***D***	***p*†**
Participant 1	11	0.02*	7	0.1
Participant 2	1	0.56	12	0.02*
Participant 3	6	0.27	7	0.2
Participant 4	9	0.14	9§	0.14
Participant 5	11	0.04*	4	0.33

Note. MSIS-Psy = Multiple Sclerosis Impact Scale Psychological subscale. *r* = Correlation coefficient. D^{XY} = raw difference between X and Y. D^{XZ} = raw difference between X and Z.
* = significant $p < 0.05$
†Average time at follow-up points, post-baseline across participants
‡Probability that the standardized difference for a participant in the control group would be greater than the individual case
§Same score from 1-week post-intervention, obtained at 1-month post-intervention

[40] See Extended Results 3.9.1 for the percentages of RCI and CSC in each outcome, across both studies.
[41] See Extended Results 3.9.2 for additional BSDT results for the MSSES.

Qualitative Feedback

Four participants consented to interview[42]. Table 9 presents the themes from the framework analysis of the feedback interviews[43].

Table 9
Themes from Feedback Interviews

Utility of ACT processes and techniques	
Value of Sessions	
Making use of the workbook	
Suggestions for improvements	
Meeting support needs around MS diagnosis	Getting the timing right
	Remaining support needs

All participants discussed the importance of acceptance; avoidance was typically a previous coping strategy and opening up awareness had provided an alternative. However, one participant felt this was challenging, despite acknowledging it was necessary. Three spoke of the direction that identifying values had provided; one participant has continued to use exercises of scheduling in value-driven behaviours. Regarding ACT-specific techniques, one participant experienced the analogies as dismissing and patronising. Others found these memorable, and complementing of cognitive defusion, present moment awareness and acceptance.

In sessions, participants felt listened to. This appeared salient given comments about diagnosis feeling lonely, overwhelming, and not well understood by others. Equally, the sessions amplified learning and application of the workbook content. Use of the workbook was overall a positive experience and having a tangible record of the broad range of techniques eased cognitive load for two participants.

Recommended improvements included placing the values techniques earlier in the intervention; it was felt this would have increased engagement with other sections. More frequent sessions were recommended. Two participants felt four sessions should be a minimum; six appeared more desirable. Equally, longer

[42] See Extended Results 3.10 for an extended table of quotations and themes
[43] See Appendix N for supplementary material to the journal paper; a table of themes and example quotations

sessions to were suggested by all participants. It was recommended the length would need to be flexible to participants' needs, recognising the variable nature of mood within MS.

Views on *when* the intervention should occur varied from straight after diagnosis, to allowing time to come to terms with physical symptoms, return to work, and emotional responses. Concerns were also raised about remaining needs. Two participants felt uncertain about where to get support after the intervention. One participant suggested a group setting may meet these ongoing support needs, with another identifying his family and podcasting.

Discussion

This study aimed to provide further testing of the PrEliMS intervention when administered by a TCP. We were interested in (a) the efficacy of the PrEliMS intervention for improving the psychological impact of MS, (b) whether the intervention had a positive impact on stress, self-efficacy, HRQoL and fatigue, (c) comparing signals of efficacy with PrEliMS-1, and (d) exploring potential improvements to the PrEliMS-2 intervention. Overall, the intervention was effective in improving MSIS-Psy scores. We also observed some improvements for emotional distress, psychological flexibility, stress, and MS-specific self-efficacy. Comparison with PrEliMS-1 provides some promising results in favour of PrEliMS-2. Participants experienced PrEliMS-2 as positive, with a number of improvements recommended to increase sensitivity to the needs of pwMS.

Improving the psychological impact of MS

We hypothesised the principal primary outcome of the psychological impact of living with MS diagnosis, would improve as a result of the intervention. Visual analysis of MSIS-Psy scores revealed systematic change occurred in three participants. This comfortably meets specified criteria to infer a causal relation in a sample of five participants (Kratochwill et al., 2010; Lanovaz & Turgeon, 2020). This contributes to support for ACT-based interventions to be effective in improving mental-health quality of life (Pakenham et al., 2018). Furthermore, reliable improvements were also observed in all participants. These were not of clinical

significance however, which is consistent with previous findings in a similar intervention for pwMS, which report a non-significant medium effect of on MSIS-Psy (*d* = 0.46) (Proctor et al., 2018). Arguably, the lack of a clinical cut-off for the MSIS-Psy means significance may be more challenging to demonstrate.

The intervention also demonstrated reliable and significant improvements for participants presenting with clinical levels of distress (i.e., above cut-off scores), despite an absence of systematic change. Notably, one participant was an exception whereby scores remained above clinical cut-off, even with improvements. Significant change observed was sustained at 1-month follow-up, suggesting improvements in distress were maintained. These findings are in support of ACT-based interventions improving distress in the MS population (Pakenham & Landi, 2023; Zarotti et al., 2023), as well as other chronic, long-term physical health problems (Graham et al., 2016). Given that we observed improvements in the psychological impact of MS, and symptoms of distress, a possible clinical implication may be to include screening measures of emotional wellbeing during MS diagnosis. This may help with triaging patients in busy MS clinics to receive appropriate type and level of care; a need identified within initial PrEliMS development (Tindall et al., 2023).

In relation to the broader literature around psychological interventions for pwMS, our findings are in line with evidence for psychosocial interventions (e.g., mindfulness, motivational interviewing, and progressive-muscle relaxation) improving mental health-related quality of life (Sesel et al., 2018). Equally, improvements observed in distress-related outcomes of anxiety and depression are akin to evidence for alternative therapeutic modalities like CBT (Kiropoulos et al., 2016). This supports more recent findings of ACT lacking signals of efficacy in comparison to other approaches (Zarotti et al., 2023), which may question the need for this alternative. However, a salient difference in an ACT-based intervention is arguably the alignment to relevant models of adjustment (Gracey et al., 2009; Topcu et al., 2020) in promoting acceptance, behavioural change, and alignment with post-illness values. Further, our findings support trials of ACT-based programmes for pwMS (Pakenham et al., 2018; 2023) and demonstrate signals of efficacy beyond previously tested ACT-based programmes (Meek et al., 2021; Proctor et al., 2018). Given the dearth of literature exploring psychological interventions for pwMS, further

larger scaled trials are warranted to compare ACT to alternative approaches (Thompson et al., 2022).

Psychological Flexibility

Levels of psychological flexibility varied considerably during baseline and intervention. Two participants demonstrated reliable improvements, with only one being significant. Equally, visual analyses suggest systematic change over phases did not occur in any cases. The observation of change in other outcomes, in the absence of change in psychological flexibility is surprising. Psychological flexibility is suggested to mediate positive coping-related outcomes in pwMS i.e., reduced distress and improved QoL (Meek et al., 2022). Further, similar interventions have demonstrated signals of efficacy in improving psychological flexibility for pwMS (Zarotti et al., 2023). Potentially, our findings might be explained by reduced sensitivity of the process measure (CompACT-8). In support of this explanation, qualitative accounts did suggest changes in aspects of psychological flexibility such as willingness to open-up and accept difficult emotions and increasing values-directed behaviour.

Secondary outcomes

With respect to secondary outcomes, we observed some indications of an effect, but these are less consistent. We found significant improvements for stress (*n* = 2) and self-efficacy (*n* = 3); although one participant deteriorated. Promotion of self-efficacy has key implications for improved adjustment, as demonstrated within both the MS-diagnosis specific and the 'Y-shaped' adjustment models (Gracey et al., 2009; Topcu et al., 2020). Potentially, findings are consistent with Topcu et al.'s (2020) adjustment model, in support around the diagnosis period moderating the relationship between adjustment and personal attributes, like self-efficacy. Equally, findings for improvements in stress are consistent with the wider ACT literature (Gloster et al., 2020; Pakenham & Landi, 2023; Thompson et al., 2022), suggesting ACT to be effective in improving stress for pwMS.

Only one out of five participants had a reliable improvement in fatigue, akin to similar findings for the impact of ACT on fatigue within MS (Sheppard et al., 2010). No improvements were observed for HRQoL as measured by the EQ-5D-5L. Whilst this supports findings from similar bibliotherapy interventions for pwMS (Proctor et

al., 2018), some studies have demonstrated clinically significant improvements in physical health QoL (Pakenham et al., 2018; Pakenham & Landi, 2023). The latter used MS-specific measures (MS QoL Instrument-54; Vickrey et al., 1995), which are likely more sensitive to specific physical challenges pwMS face. This is an important consideration for future testing of the PrEliMS intervention and is also in line with research recommendations for using MS-specific measures (Thomas et al., 2006).

Comparison to PrEliMS-1

Individual-level difference testing of the psychological impact of MS demonstrated only one participant showed significantly greater change than the PrEliMS-2 group at 3-months post-baseline. Despite this, the percentage of reliable and significant improvements observed across all variables, favours TCP-delivered PrEliMS intervention in generating greater positive outcomes. Findings should be interpreted with caution however, given the difference in sample sizes across the two studies.

Suggested Improvements to PrEliMS-2

Our final aim was to explore participant experience of PrEliMS-2 and whether any improvements are necessary. In line with previous trials of this kind of intervention (Meek et al., 2021), an overall positive experience was reported. Participants suggested improvements to ACT-specific content and format; specifically, introducing values-related work sooner. Participants felt either longer or more sessions were needed; six appeared to be the consensus recommendation. Flexibility in timing the intervention post-diagnosis was also salient, in line with previous recommendations within the literature (Pinto et al., 2022). Suggested timings (3- to 8-months post-diagnosis), varied. Overall participants recommended pwMS should be made aware of available emotional support at diagnosis, to then engage with at their discretion.

Strengths and Limitations

The nature of the methodology facilitated understanding of how outcomes of interest may change over time. This is often not captured within experimental or RCT designs. Given the unpredictability and variability within MS, this was important insight to obtain. Although, this variability also hindered achievement of stable

baselines for participants, which is typically desired within a SCED design to infer an effect (Smith, 2012). Extension of the baseline by two-weeks was introduced to account for significant variability in scores. However, the design could have been further strengthened by adding a predetermined stability criteria i.e., datapoints remained within ±3. Despite this, a triangulation of methods to support inferences about effectiveness was a strength, in conjunction with framework analysis to enable further contextualisation of the data. Initial development of the framework was generated collaboratively (BT, AT) and later categorisation reviewed by further members of the research team (NM, NE), thus minimising the potential for bias in interpretation. Equally, having an independent researcher conduct semi-structured interviews also minimised social desirability bias in participant responses.

Despite a successful recruitment strategy, a limitation was high attrition during the baseline phase, with just under half of recruited participants dropping out. The high participation demands of completing multiple and repeated measures as part of a SCED design may have contributed to this. To further strengthen the study design and ethical considerations, the MS Patient and Public Involvement (PPI) group could have been consulted on selection of measures used, their repeated use, and the feasibility of achieving stability in the psychological impact of MS during baseline. This may have precluded attrition issues therefore future research would benefit from MS PPI group input.

The attrition also raises an important clinical implication relating to the timing of the intervention. Pinto et al. (2022) found that uptake of psychological support was higher if individuals experienced higher problems related to their condition, particularly in early stages. Equally, PrEliMS-1 found that participation was somewhat dependant on whether MS diagnosis was anticipated; often the intervention was “too soon” if diagnosis was unexpected (das Nair et al., 2023). As suggested, consultation with an MS PPI group on appropriate timing and approaching of potential participants may have helped inform recruitment strategy. Notably, qualitative feedback from the current study suggests optimal intervention timing is idiosyncratic, however *knowing* an intervention is an option when diagnosed may support and empower patient decision-making about treatment needs, in line with the national framework (DoH, 2005).

Another limitation is determining the effect of therapeutic factors (e.g., speaking with a “human being”, who is non-judgemental and “not afraid to listen”) from intervention factors, in understanding change. From an ACT perspective, therapeutic factors largely encompass modelling and empowering the six dimensions of psychological flexibility in contact with individuals (Pierson & Hayes, 2007). This was highlighted in qualitative data as salient to engagement with sessions and workbook content. Thus, potentially, this may play a role in mediating positive outcomes. However, given this is a complex intervention, with many interacting components, this is challenging to distinguish.

Directions for future research

As findings indicate signals of efficacy, a larger trial exploring the role of psychology in the provision of this intervention is warranted. This would include the suggested improvements to the workbook and intervention format. Such improvements would likely increase the specificity of this intervention to the MS population, which has been missing from previous bibliotherapy and teletherapy research in this field (Proctor et al., 2018).

Given all participants in the sample were of the same ethnicity, there is limitations in reflecting demographic characteristics of the wider MS population, i.e., pwMS from diverse ethnic backgrounds. To aid accurate demographic representation of pwMS in future research, service population data could also be collected. Additionally, removing a specific level of psychological distress from eligibility criteria may overcome recruitment and generalisability limitations.

Based on the emphasis of therapeutic factors in our qualitative data, future research may also benefit from comparing ACT with other approaches that emphasise similar factors. Furthermore, testing the same intervention across a range of therapists, including peer support, may also help minimise bias, as the current study only used one therapist.

Conclusion

Results suggest the PrEliMS-2 intervention is effective at improving the psychological impact of MS around the point of MS diagnosis, providing important contributions towards the piloting of PrEliMS. Further, promising signs of efficacy

were also indicated for improvements in a range of clinically relevant outcomes, important to pwMS at the point of diagnosis. Arguably, facilitation by a TCP plays an important role in emphasising focus on psychological need, as predicted in prior trials of the intervention (das Nair et al., 2023). Further testing is vital to determine the active components of PrEliMS, particularly in light of the relatively limited effects observed on psychological flexibility. This would promote further understanding of the target outcomes of PrEliMS, to refine the intervention further. Given the small sample within this study, a larger trial would also help determine how this can be implemented within clinical practice to meet a crucial, yet currently unmet need, for pwMS.

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Extended Paper

1 Extended Introduction

In the extended introduction, the nature and diagnosis process of MS are discussed. The impact of the diagnostic process is considered, alongside an overview of relevant adjustment models and coping styles in the context of MS diagnosis. Psychological therapy within MS is reviewed, drawing focus on the Acceptance and Commitment Therapy (ACT) evidence-base within the MS population and specifically bibliotherapy. Finally, an overview of the PrEliMS-1 study will be presented, followed by the epistemological position for the current study (henceforth referred to as PrEliMS-2).

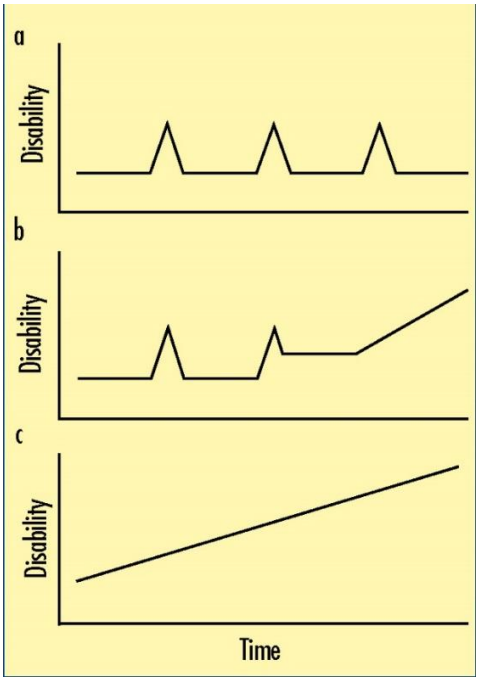
1.1 What is Multiple Sclerosis (MS)

Specifically, MS is an autoimmune disease which attacks and destroys the myelin that protects axons in the central nervous system, disrupting transmission of chemical signals (Calabresi, 2004). This can cause a range of cognitive, physiological, and psychological symptoms; examples are provided in the short paper. Additional symptoms include balance difficulties, bladder dysfunction, muscle weakness, tremors and numbness, mood changes (e.g., emotional lability), vertigo and, temperature sensitivity (Compston & Coles, 2008). The underlying cause of MS remains unknown. Whilst there are treatments to help control some aspects of MS (such as Disease Modifying Therapies [DMTs] and symptomatic treatments), there is currently no known cure. In the United Kingdom, MS cases are typically (60% of 1713 cases) diagnosed between the ages of 30 and 49 years, with a mean age of 42 years (Jick et al., 2015).

Initially, when MS is suspected, patients are classified with a Clinically Isolated Syndrome (CIS). Patients may then experience further neurological events (relapses) with periods of recovery and stability (remissions) (Goldenberg, 2012) and MS is likely to be diagnosed according to the McDonald et al. (2001) criteria. This is typically diagnosed as Relapsing-Remitting MS (RRMS), the most common subtype, affecting about 85% of patients. This may then worsen to relapses without remission, classified as Secondary-Progressive MS (SPMS). In some cases, remission may not occur from disease onset, resulting in a gradual worsening of symptoms from the

beginning, classified as Primary-Progressive MS (PPMS). Figure 12 demonstrates the disease course of the three subtypes of MS (Hassan-Smith & Douglas, 2011).

Figure 12
Clinical Course for Multiple Sclerosis a. RRMS. B. SPMS. C. PPMS



1.2 Diagnosis of MS

1.2.1 Diagnostic process

MS symptoms can be 'invisible' to others, which can lead to experiences of invalidation from healthcare professionals, or not feeling believed or understood by others (L. S. Parker et al., 2021). Subsequently this can lead to delays in seeking support as patients may doubt the legitimacy of their experience. Once they do access support, patients can experience several contacts with healthcare professionals, before symptoms start to be linked together and a diagnosis of MS considered (Edwards et al., 2008). As there are other conditions which can mimic presenting symptoms of MS (e.g., Parkinsons, functional neurological disorder, motor neurone disease and fibromyalgia), these needs to be ruled out first (Dobson & Giovannoni, 2019). In addition, patients typically undergo invasive, extensive scans and examinations (e.g., magnetic resonance imaging (MRI) and examination of cerebrospinal fluid through a lumbar puncture), sometimes over a period of a few

months to determine whether distinct episodes occur (Goldenberg, 2012). As such, the process is often experienced as lengthy with delays due to long waiting times for the investigative tests (Edwards et al., 2008).

1.2.2 Emotional impact of MS diagnosis

The short paper outlines some experiences of the emotional impact of receiving an MS diagnosis. A systemic review by Topcu et al. (2022) provides a comprehensive account of the variability in emotional responses following diagnosis. In some cases, relief at receiving a diagnosis was reported, as patients had a name for their symptoms and learnt their diagnosis was not terminal. A finding which is supported by Desborough et al. (2020), where participants reported validation and relief at finally having an explanation for their symptoms. In contrast, Topcu et al. (2022) also found fear, anxiety, and worry were the most common emotional reactions. These emotional responses are understood in the context of an uncertainty about potential future MS progression, the impact diagnosis may have on relationships and threatened goals for the future. Denial, sadness, and anger were also common reactions, associated with a perceived lack of control and helplessness. Equally, these findings are frequently supported within the literature; individuals report devastation, uncertainty for the future, and struggling alone, either from denial or wanting to protect others (Edwards et al., 2008; Strickland et al., 2017).

A meta-review found emotional distress to be consistently reported by individuals in the context of MS diagnosis. Some individuals still recalled the diagnostic period as distressing many years later (Solari, 2014). Such qualitative accounts are also reflected in empirical data. Giordano et al. (2011) reported clinically significant anxiety from the start of the diagnosis process which remained 6 months post-diagnosis. The prevalence of clinically significant depression in MS is reportedly 30.5% and 22.1% for anxiety (Boeschoten et al., 2017). Further, Conradsson et al. (2018) reported persistent depression symptoms in individuals with moderate/severe MS across a 10-year period (29% at baseline, 22% at 2 years, and 25% at 10 years, $p>0.167$), highlighting the sustained nature of psychological difficulties for individuals with MS.

1.2.3 Current service provision for supporting MS diagnosis

Clinical guidance for adults with MS, published by the National Institute for Health and Care Excellence (NICE), recommend that newly diagnosed patients receive information about the disease, symptom management, legal requirements, and support groups (NICE, 2022). A face-to-face follow-up appointment should also take place within 6-weeks of diagnosis. However, there is no specific psychological intervention or emotional support recommended at this time (NICE, 2022). Guidance does note that *ongoing* care should use a multidisciplinary approach, including access to psychologists. Additional recent recommendations also include “stress management and wellbeing approaches such as mindfulness and cognitive behavioural techniques*”* although this is in the specific context of ongoing fatigue management.

In addition, in 2005 the National Service Framework for Long Term Conditions (NSF for LTC) was launched (Department of Health, 2005). This framework recommends 11 quality requirements, from the point of diagnosis and aims to promote person-centred care within healthcare for long-term conditions. The importance of ‘prompt’ diagnosis is recognised, alongside identification of emotional difficulties relating to diagnosis and recommendations for “specialist emotional support” in progressive conditions. Despite this, service user perspectives have highlighted concerns with healthcare professionals not acknowledging mental health, and delays in diagnosis which led to deteriorations in their mental well-being (Sixsmith et al., 2014).

1.3 Psychological therapy in MS

NICE guidelines do not recommend a specific psychological therapy for pwMS (NICE, 2022). At the time of Thomas et al.'s (2006) systematic review of psychological interventions for MS, the evidence-base consisted of small trials therefore limiting conclusions about the most effective psychological intervention for pwMS. However, CBT was identified as an effective approach in the treatment of depression in pwMS, which is supported in a more recent review (Hind et al., 2014) and RCT’s in pwMS newly diagnosed (within 5 and 10 years of diagnosis, respectively; Kiropoulos et al., 2016; Moss-Morris et al., 2013). CBT is typically the most common psychological intervention tested, as demonstrated in a review of

thirteen randomised controlled trials by Sesel et al. (2018), in addition to mindfulness-based interventions and motivational interviewing. However, studies are limited in number and the dosage of CBT sessions was much lower compared to non-CBT studies (e.g., mindfulness and progressive muscle relaxation). The short paper also provides critique as to why CBT may not be the most appropriate psychological therapy in the context of MS.

Overall, psychosocial interventions (e.g., progressive-muscle relaxation, mindfulness, motivational interviewing, CBT, and coping skills training) have been found to be effective at reducing depression, anxiety, fatigue and increasing mental-health related quality of life and overall quality of life (d = 0.212 – 0.444), which remained evident at follow-up (Sesel et al., 2018). These findings are also reflective of group-based psychological interventions for pwMS (Firth, 2014). However, there is still no one standard psychological therapeutic approach recommended (British Psychological Society, 2021). Importantly, recommendations for psychological interventions in neurodegenerative diseases include personalisation of interventions, accessibility (i.e., intervention materials, session durations, homework tasks and mode of delivery), flexibility in when support is accessed, and exploration of acceptability (Pinto et al., 2022). This systematic review captures adaptations needed to improvement engagement, based on the nuances of this clinical population.

1.4 Adjustment and coping styles

Within the chronic illness literature, ‘adjustment’ is frequently cited as salient to maintaining psychosocial wellbeing and functioning. This has been defined as a ‘healthy rebalancing by patients to their new circumstances’ (de Ridder et al., 2008) Further, in the context of MS, these ‘rebalancing acts’ are ongoing and can apply to possible future states, as well as current states (Dennison, 2011).

In understanding adjustment further, Lazarus and Folkman's (1984) Stress and Coping Model explains there is a transaction between the environment and the individual (e.g., appraisal of the illness-related event as threatening and reduced belief in their ability to cope) which results in a stress response. The model has been applied to understanding adjustment in MS (P. L. Fisher et al., 2020; Pakenham, 1999) and suggests interventions supporting adjustment should focus on cognitive

appraisal and coping resources. However, recently the utility of the model in the context of MS has been challenged as reappraisals within MS are not always possible, given the progressive and uncertain nature of the prognosis (Topcu et al., 2020).

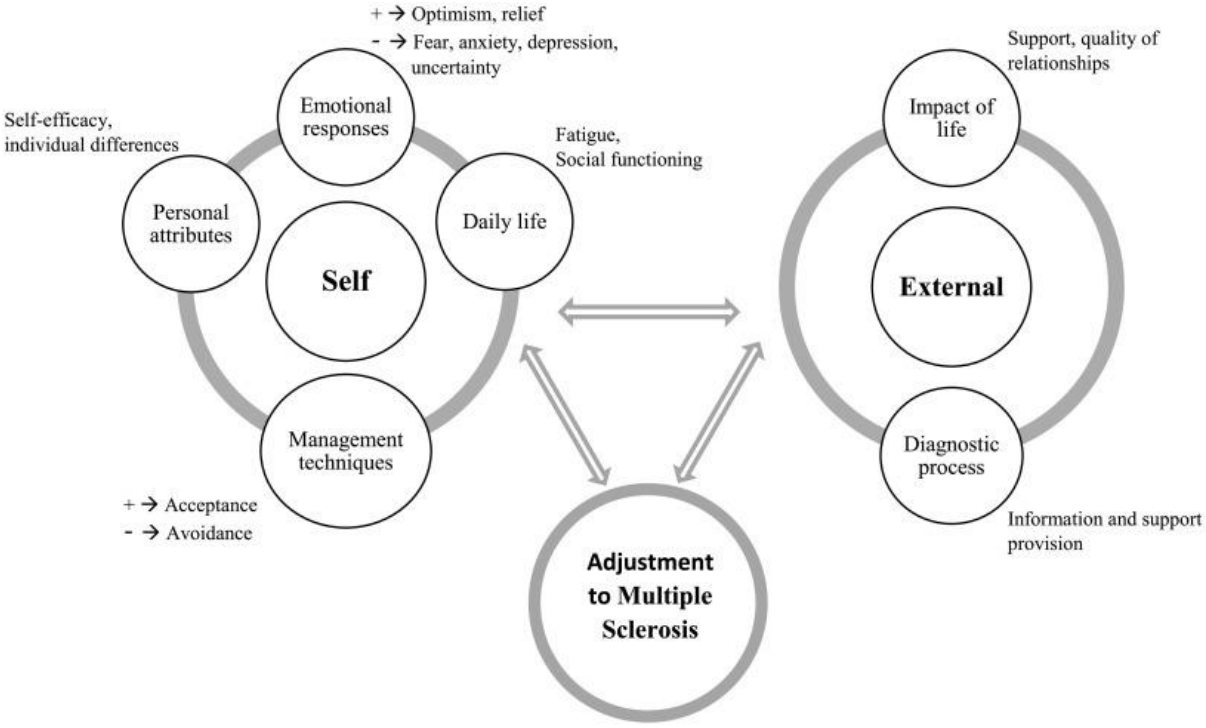
As such, a number of adjustment models specific to MS have emerged through qualitative reviews and research (Dennison, 2011; Soundy et al., 2016; Wilkinson & das Nair, 2013). Overall, the proposed models emphasise the cognitive, behavioural, and emotional impact associated with adjustment. Common coping techniques recognised by these models were behavioural withdrawal or isolation, 'wishful thinking' (e.g., wishing for a miracle cure) and escape-avoidance or denial/rejection (e.g., trying to forget or ignore the MS and/or unpleasant emotional response), all of which relate to poorer adjustment or hindered ability to cope. In contrast, hope, positive embracement, and acceptance of illness (Dennison, 2011; Wilkinson & das Nair, 2013) are factors relating to successful adjustment. In line with these findings, acceptance-focused coping styles, where individuals are willing to accept unpleasant emotions, predicted lower levels of anxiety and depression, in contrast to emotionally avoidant coping styles predicting higher emotional distress (P. L. Fisher et al., 2020; Pakenham, 2007). Collectively, findings promote the need for support for pwMS which acknowledges these positive adjustment related factors. However, findings are based upon the experience of *living with* an MS diagnosis, rather than the process of being *diagnosed with* MS and the subsequent aftermath. As outlined in section 1.2.1, this critical period presents additional challenges.

A meta-review of 30 systematic reviews aimed to address this limitation and subsequently proposed a model of adjustment to MS, which includes consideration of the 'diagnostic process', as shown in Figure 13 (Topcu et al., 2020). Arguably, this is most relevant for the current study. Aspects of the diagnostic period such as timely support, access to healthcare professionals, and information provision, relate to improved adjustment. Conversely, worse adjustment is associated with lengthy diagnostic investigations, a lack of information and difficulty accessing support services. The latter was also found to directly link to experience of fear, anxiety, and distress in response to diagnosis. Overall, the model highlights the importance of positive experiences of the diagnostic period to strengthen the relationship between adjustment and internal processes (e.g., emotional response, coping strategies, and

daily functioning). Positive adjustment has implications of increased acceptance of MS diagnosis, engagement in psychological interventions and support from healthcare professionals (Topcu et al., 2020).

Figure 13

Conceptual Map from Topcu et al. (2020) of Psychosocial Factors Relating to Adjustment to MS Diagnosis



Whilst the framework coherently conceptualises the relationship between positive adjustment factors, there is still ambivalence about *how* interventions may promote these. Gracey et al. (2009) proposes a staged model of social adaptation. Although this was generated in the context of brain injury, the model is arguably applicable to chronic illness in that both require a biopsychosocial approach to clinical intervention and rehabilitation. The model centres on addressing three types of 'discrepancies': social (e.g., withdrawal due to fear of stigma), interpersonal (e.g., clients holding differing views to their families/friends about illness-perception), and personal (e.g., current self vs hoped-for-self). The paper provides an overview of how this may inform intervention activities which address social, emotional, and cognitive factors. Many of these can be linked to Topcu et al.'s (2020) MS adjustment model, such as: management techniques of acceptance like mindfulness meditation, exploring personal views on illness perception, information provision as an alternative narrative for what are viewed as problems and promoting self-efficacy

through behavioural change in line with new-meanings post-illness (i.e., identifying pre-illness values that may not have been threatened by the illness).

1.5 Acceptance and Commitment Therapy (ACT)

The following section provides an overview of the theory underpinning ACT, the model, and a rationale for the appropriateness of ACT in this population.

Acceptance and Commitment Therapy (ACT) is a 'third-wave' behavioural therapy, which is distinct from other 'first' and 'second' wave approaches (i.e., Cognitive Behavioural Therapy) due to the emphasis on acceptance and mindfulness. The aim of ACT is to expand the potential for an individual to live a rich and meaningful life. This is achieved through increasing an individual's 'psychological flexibility', which encompasses the ability for mindful, values-guided action (Harris, 2019).

1.5.1 ACT Theory

The theory underpinning ACT has been referred to as the 'house of ACT' (Harris, 2019). ACT is at the top floor, with Relational Frame Theory (RFT) the next floor down, Applied Behavioural Analysis (ABA) on the ground floor, and functional contextualism forming the foundations. Explaining RFT, ABA and functional contextualism in depth is beyond the scope of this paper, however they have been briefly summarised in this section.

Functional contextualism is the philosophy underpinning the theories behind ACT. This philosophical stance understands the *function* of behaviour, or the effect it has, within different *contexts.* Context refers to anything that may influence a behaviour, including both internal and external events or processes e.g., emotions, thoughts, physical health, developmental learning history or genetic factors. In this view, emotions, thoughts, and memories are not seen as problematic or 'maladaptive', rather dependant on context. This contrasts commonly used mechanistic psychological models, typical of second-wave approaches, where emotions, thoughts, and memories are viewed as 'faulty' or 'dysfunctional', therefore need to be challenged, repaired, or replaced (Harris, 2019). Removing 'problematic' behaviours from the contexts of events, is seen to undermine the nature of the problem (S. C. Hayes, 2004). As such, functional contextualism uses Applied

Behavioural Analysis (ABA) to explore the purpose of a behaviour, or how this may be serving an individual, to further understand “prediction and influence” (S. C. Hayes, 2004). This involves identification of an antecedent, the behaviour, and the resulting consequence.

Relational Frame Theory (RFT) is an extension of ABA and is the dominant theory supporting ACT. Whilst ABA understands the core learning principles of behaviour, RFT aims to address the additional complex role of language and cognition in understanding behaviour. RFT posits that ‘relational framing’ is at the core of human language and cognition. This refers to the ability to spontaneously relate events or stimuli. This relational learning can also be transferred to events which are not necessarily formally related through direct experience, yet are related based on arbitrary contextual cues, deriving new relations. For example: considering “James is taller than Pete and Pete is taller than Mike”, we also derive new relations of “James is taller than Mike” and “Mike is smaller than James”. Within relational framing, there are many different cues e.g., “is taller than”, “is the opposite of”, or “is the same as”; (see McHugh et al., 2019) creating multiple types of relations frames. Equally, the function, meaning the effect of a behaviour, can also be transferred (for example, visiting the dentist may bring about thoughts of an unpleasant hospital appointment, through a “similar to” relational frame, resulting in anxious feelings towards the dentist). Overall, vast relational networks are formed, enabling new thoughts and learning, without needing direct experience of events. This has clinical implications in that the bidirectionality in relational framing means past, unpleasant experiences and events can be related to the future, resulting in unpleasant thoughts and feelings. Equally, pleasant past experiences can be framed with positive thoughts and feelings about the future.

1.5.2 ACT Model

Psychological flexibility consists of six inter-relating concepts: ‘experiential acceptance’ of unwanted thoughts, feelings and physical sensations, ‘defusion’ (i.e., distancing oneself from unhelpful thoughts), ‘present moment awareness’ (through mindfulness exercises), ‘noticing self’ (i.e., the distinction between the self and the avoided psychological content), ‘values’ (i.e., deeply held views on what matters most to the individual), and ‘committed action’ (i.e., specific behavioural components

of ACT designed to promote actions based on values) (S. C. Hayes et al., 2012). All six processes are related to one another and are equally components of psychological flexibility (Harris, 2019). These six core processes are typically presented in a ‘hexaflex’, or within a ‘triflex’ to demonstrates the three ‘pillars of ACT’: Open Up, Be Present, and Do What Matters. Both are presented in Figures 14 and 15 below.

Figure 14
ACT 'Hexaflex'; (Harris, 2019)

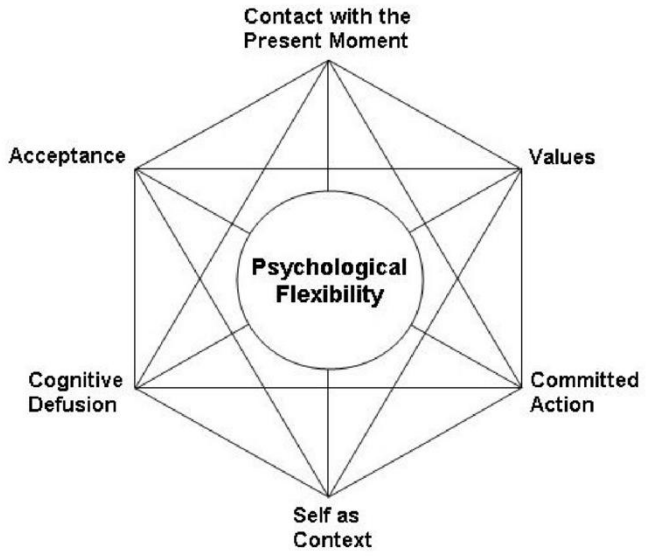
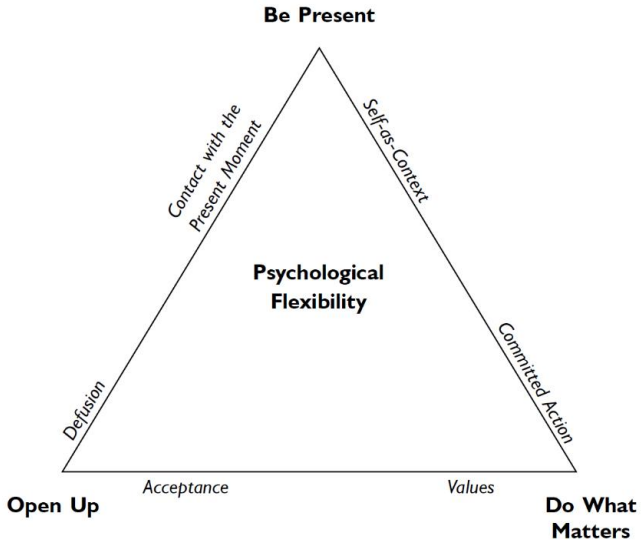


Figure 15
ACT 'Triflex'; (Harris, 2019)



1.5.3 ACT evidence-base

The first study on ACT (Zettle & Hayes, 1986) and initial published texts outlining the approach (S. Hayes et al., 2002; S. C. Hayes et al., 1999) are relatively recent. Thus, the evidence-base for ACT is still emerging through trials in a range of target conditions within both physical and mental health.

ACT has commonly been used in the treatment of chronic pain. An RCT demonstrated a significant reduction in pain-related anxiety and pain interference with life, however an effect was not observed for physical or mental health-related quality of life (Wetherell et al., 2011). Interestingly, increased perceived control over pain, as opposed to the goal of increasing acceptance of pain, was found to be driving reductions in pain interference. It was suggested the use of behavioural strategies may influence perceived control, though more research is recommended on the underlying mechanisms of change. Variability in findings has also been reflected in a wider review. Veehof et al. (2016) found a small effect for pain intensity [SMD = .24] and a moderate effect for pain interference with everyday life [SMD = 0.62] and anxiety [SMD = .51]. Small effects were also found for depression, disability, and quality of life. Overall, the intended effect on chronic pain is small given its nature; this limitation is likely also applicable to other physical health conditions.

The literature for chronic and long-term physical health problems is even more sparse. A review of 18 studies revealed promising evidence for ACT to be effective in improving distress [*d* = 0.75 – 1.86], disease self-management [*d* = 0.20 – 0.68], quality of life [*d* = 0.24 – 1.59] and psychological flexibility [*d* = 057 – 0.72] (Graham, Gouick, Krahe, et al., 2016). However, most studies were found to be of low quality and there remains a need to continue establishing ACT for use in long-term health conditions.

In terms of mental health related outcomes, ACT has been found to generate signals of efficacy in improving anxiety, fatigue, and depression (A-Tjak et al., 2014; Fledderus et al., 2011; Hacker et al., 2016; Ruiz, 2012). However, in comparison to active controls (i.e., CBT), there is still insufficient evidence to conclude ACT to be effective over alternative psychological interventions.

To summarise the available evidence, a recent review of 20 meta-analyses found ACT to be efficacious for a range of mental (anxiety, depression) and physical (substance use, pain) needs (Gloster et al., 2017). Specifically, an overall mean small effect size for improving depression, anxiety, and chronic pain. Despite the focus of ACT to be on improving functioning and wellbeing, only 6 of the 20 meta-analyses had quality of life as an outcome; the mean effect size was small. Equally, only three meta-analyses examined psychological flexibility and the overall mean effect was also small. Gloster et al. (2020) stipulates that targets of ACT ought to be studied simultaneously to encourage more rigorous testing of ACT. In addition, studying trajectories of change was another recommendation, given the methodological quality of the current evidence-base is variable.

1.5.4 Rationale for ACT in MS

As discussed, a significant predictor of coping in MS is acceptance-focused coping styles, a factor in psychological flexibility, thus a target of ACT. Furthermore, empirical investigation has found psychological flexibility to have a buffering role between the impact of life stressors and health and wellbeing outcomes within the general population, hence can be a protective factor for wellbeing (Gloster et al., 2017). Within the MS literature, increased psychological flexibility has been linked to coping outcomes of lower distress and higher quality of life (Meek et al., 2022). Furthermore, ACT has demonstrated meaningful, positive outcomes in anxiety, life satisfaction, pain-intensity, and pain-interference with life, in muscle disorders and chronic pain (Graham, Gouick, Ferreira, et al., 2016; Veehof et al., 2016); two physical conditions which share similar symptoms to MS. Given the nature of progressive conditions, and the transdiagnostic approach of ACT, this offers greater scope to improve outcomes, above teaching individuals to change beliefs or control distress (Brassington et al., 2016; Graham, Gouick, Ferreira, et al., 2016).

1.5.5 ACT in MS evidence-base

The British Psychological Society (BPS) have recently recognised ACT as an approach for working with pwMS (BPS, 2021) due to the growing evidence base. A recent review of ACT RCTs in this population, by Thompson et al. (2022), found the methodological quality of studies to be inconsistent, with frequent high risk of bias. A small significant effect was found for improvement in stress for pwMS, however

remaining outcomes of interest (anxiety, depression, psychological flexibility, and quality of life) showed no significant effect. Potentially due to the inclusion of lower methodological quality studies, these findings are not consistent with the wider literature of ACT for pwMS.

A study using a pre- post- group intervention design reported significant improvements for resilience [*g* = .47], physical health QoL [*g* = -.76], mental health QoL [*g* = -.46], depression [*g* = .38], stress [*g* = .33], and the three 3 processes of psychological flexibility: defusion [*g* = -.54], values [*g* = .38], and acceptance [*g* = .39]. The intervention format was eight group sessions with minimal drop-out rates and positive feedback (Pakenham et al., 2018). Similar findings were also reported following a half-day ACT workshop for pwMS (Sheppard et al., 2010). Scores for depression and the effect of pain on behaviour and mood, significantly decreased post-intervention, along with the tendency to suppress thoughts. Quality of life increased, however mindfulness and fatigue showed no improvements. This study holds importance in being the first to test ACT for pwMS, however this was a small sample size and was not tested against any controls.

A recent review of third-wave approaches for pwMS, included nine studies using ACT, five of which were RCTs (Zarotti et al., 2023). Overall, preliminary empirical findings indicated improvements in anxiety, depression, stress and QoL, however, these findings were not replicated across all studies. As such, Zarotti et al. (2023) concluded that larger samples are needed within the evidence-base to further determine the effectiveness within this population.

1.5.6 ACT bibliotherapy and teletherapy in MS

Given the nature of MS, there is a need for practical, ongoing disease management which is flexible and accessible. Further, given services are under increasing pressures, with limited capacity, time and resources, access to face-to-face psychological therapy is often limited. Bibliotherapy (self-help literature) offers a mode of therapy which can empower individuals to manage their own care and has been recommended for use in neurological conditions such as MS, to reduce healthcare costs and improve access (Rae-Grant et al., 2011).

Web-based ACT interventions have demonstrated efficacy in managing depression in the general population (Brown et al., 2016), as well as improving

positive coping outcomes in chronic pain (Trindade et al., 2021). Similar findings have been replicated within the MS population. Pakenham and Landi (2023) trialled an online ACT intervention for pwMS in a pilot RCT, addressing literature limitations in the lack of controlled trials. The intervention was compared to a wait-list control group, with the intervention group reporting greater improvement in anxiety (*d* = 0.56) and stress (*d* = 0.62). However, due to the small sample the study was underpowered to detect an effect at 95% confidence interval (CI), therefore an adjustment to 90% CI was made. Overall, usability of the intervention was positive however adhering to progression guidelines was satisfactory. A review of ACT self-help interventions by French et al. (2017) suggested that clinician guidance can improve outcomes, likely because this can support adherence to the intervention protocol.

Bibliotherapy combined with remote therapy ('teletherapy') has an emerging evidence-base in pwMS, as an approach which may further improve outcomes. Initial evaluation through a case-series (*n* = 7) suggests significant improvements in targeted-outcomes (pain interference and severity) (Harrison et al., 2017). However, outcomes were mixed for those deemed to have more complex presenting difficulties (i.e., a range of baseline scores within clinical significance), suggesting a need for more tailored support. For all participants, contact with a therapist was valued highly. A trial of telephone-supported bibliotherapy in pwMS reported a large significant effect on anxiety at follow-up (*d* = 0.84), and a moderate effect on the psychological impact of MS (d = 0.46) although this was not significant (Proctor et al., 2018). Overall, attrition was high, limiting power to detect significant changes. Notably the telephone component of the intervention was positive, however the literature used was deemed to have some flaws. Participants found the content too generic and therefore challenging to relate to their MS.

In line with these recommendations, Meek et al. (2021) tested a telephone-supported ACT bibliotherapy using a workbook specific to SPMS. Despite the intervention being deemed acceptable, no clear signals of efficacy were demonstrated. Challenges with recruitment were potentially a significant factor in not detecting an effect. Qualitative data revealed the value participants placed upon having the intervention, describing this as a "lifeline" and experiencing positive changes in coping and mindset. Overall, preliminary evidence for combining

bibliotherapy and teletherapy for pwMS is mixed and warrants further testing. In the context of offering ACT-based interventions as part of newly diagnosed MS service provision, the combination offers an accessible format, which draws upon benefits of both self-help and clinician-guided remote therapy.

1.6 Initial PrEliMS Study (das Nair et al., 2023)[44]

The PrEliMS study proposed two interventions, which are complex (in that there are several interacting components) and developed in line with Medical Research Council (MRC) guidelines (O'Cathain et al., 2019). The first proposed intervention was standardised support provided by MS Nurse Specialists alongside completion of an ACT-based, 52-page workbook, called "Better Living with a Diagnosis of MS" (Brassington et al., 2016; Ford, 2017; S. C. Hayes & Smith, 2005). The support with MS Nurse Specialists was a 1:1 session (face-to-face, videoconference or telephone), within two weeks of diagnosis, with subsequent sessions if required. This support answered questions about MS, and covered a range of strategies and techniques, including acceptance and commitment therapy, psychoeducation, and supportive listening. The second intervention was this *plus* peer support from someone with lived experience of MS. These two groups were compared to a control group of usual care, as per NICE guidance (NICE, 2022).

The interventions were developed following two key systematic reviews (Topcu et al., 2020, 2022) exploring experiences pertaining to MS diagnosis and a conceptualisation of the adjustment process. Within the proposed adjustment framework, information provision and coping resources were suggested to facilitate the adjustment process through reducing negative emotional responses and promoting management techniques. Development also involved direct consultation with members of a local MS Public and Patient Involvement (PPI) group and relevant stakeholders, to enquire as to how a new PrEliMS pathway would map onto the needs identified (Tindall et al., 2023). Requirements for this support included provision by a healthcare professional knowledgeable in MS, possible triaging for ongoing emotional support and primarily to be individual-based. Possible barriers

[44] Henceforth to be referred to as PrEliMS-1

identified included an increase in staff workloads, resulting in concerns about reduced time for tailored support.

The following outcome measures were used to explore signals of efficacy: Perceived Stress Scale-4 item (PSS-4), Hospital Anxiety and Depression Scale (HADS), MS Impact Scale Psychological Subscale (MSIS-Psy), MS Self-Efficacy Scale (MSSES) and EQ-5D-5L to assess Health-Related Quality of Life (HRQoL). Data were obtained at baseline, and at 3-months and 6-months post-intervention. Qualitative data were also obtained through semi-structured feedback interviews.

Forty participants were recruited to the feasibility RCT. Interim analyses highlighted some participants found parts of the workbook and intervention helpful. The content of MS Nurse Specialist sessions was typically signposting, information provision and symptom management with 55% of time spent discussing the intervention content (referring to the workbook, discussing onward referral needs). Whilst nurses were viewed as trust-worthy for information, participants indicated preference for less focus on medications and symptoms, and more time discussing the workbook content and emotional needs. From the MS Nurse Specialist perspective, the intervention was feasible to deliver, however more training on psychological concepts (e.g., ACT techniques) and adjustment to diagnosis were identified as future needs.

Regarding signals of efficacy, no significant differences between groups at any time-points were observed, in any measure. The most observed effect sizes were up to small magnitude (0.005 – 0.041) and the effect on HRQoL was moderate at 6-months follow-up (0.086). On an individual level, findings were mixed. Significant change was observed for depression and stress at 3-months follow-up, and anxiety at 6-months follow-up for a small number of participants (*n* = 1-3; 8%-23% participants). This is potentially suggestive of some signals of efficacy and utility of the intervention for this population. This is supported by qualitative findings that the intervention is acceptable and was positively received. Salient findings also suggested that MS Nurse Specialists found it difficult to take time off for training to deliver the support and equally some felt that dealing with adjustment/mood problems was not within their remit (R. das Nair, personal communication, November 4, 2020). Subsequently, suggestions were made for another workforce to deliver the

intervention such as Assistant Psychologists. Similarly, Borreani et al. (2014) found pwMS felt a psychologist was best placed to address the emotional aspects relating to the time of diagnosis. Thus, potentially facilitation from a Psychology Practitioner, independent from the usual care team, may address some of the practicality and delivery issues highlighted in PrEliMS-1. Notably, the intervention was delivered by a Trainee Clinical Psychologist within Meek et al. (2021) and deemed acceptable and suitable.

1.7 Epistemological position

The current study has been completed from a pragmatist position, meaning there was a focus on the practical benefits and utility of findings, and emphasis on using the methodology to maximize the potential for answering the research question (Barker et al., 2016; Feilzer, 2010). Pragmatism upholds that there are singular and multiple realities which can be empirically investigated; research should focus on being *useful* in providing an accurate account of what is being investigated, rather than striving to represent reality in the most accurate way (Feilzer, 2010). Pragmatism opens the option of using a mixed methods approach which has been frequently observed within literature. This approach arguably provides a more coherent representation and avoids biases associated with using a single method (Denscombe, 2008).

Another term for pragmatism is contextualism. This provides a good foundation for investigating ACT-based interventions as ACT is based on a form of contextualism termed ‘functional contextualism’ (S. C. Hayes et al., 2012). In this sense, the entity of interest is the ‘act/event in context’ and whether this results in the accomplishment of a predetermined goal (S. C. Hayes et al., 2012; McHugh et al., 2019). There is also reduced interest in what is “true”, for example if individuals struggle to determine if their thoughts are “true”, there is instead a focus on what impact that struggle is having and whether this is successfully working or not (S. C. Hayes et al., 2012). In this vein, ACT is interested in ‘workability’ as truth criterion. Further, functional contextualism posits that analysis is true if it meets the goal of prediction and influence over behaviour (McHugh et al., 2019). Implications for research include specification of variables which precede and follow the behaviour of interest, and meeting the criteria of precision, scope (e.g., explanation applies wide

ranging) and depth (e.g., coherence across multiple levels of analysis: psychological, sociological, neurophysiological etc.). Section 1.5.1 provides further information on functional contextualism.

2 Extended Method

The extended methods provide further detail on ethical approval, the rationale for the study design, and aspects of participant recruitment. Then, discussion is presented as to the measures used in the current study and a rationale for this, followed by the study procedure and detail pertaining to the PrEliMS-2 intervention. The analysis will then be explained for quantitative and qualitative data.

2.1 Ethical approval

To recruit through the outpatient NHS neurology clinic, ethical approval was granted by the NHS Berkshire B Research Ethics Committee (REC) (ref: 22/SC/0034) and Nottingham University Research and Development Department (Appendices O - R).

2.1.1 Informed consent

Obtaining informed consent was in accordance with the REC guidance and Good Clinical Practice (GCP) guidelines. The decision to participate was entirely voluntary and participants were made aware that consent may be withdrawn at any time, without this affecting the quality or quantity of their current or future medical care. The study intervention did not take place until informed consent had been obtained.

After the initial approach by a member of potential participants usual MS care team (Neurologist or MS Nurse Specialist), verbal consent was obtained to pass on contact details to the lead researcher (BT). When first contacted by them, they provided further information pertaining to the study, a participant information sheet, and responded to queries, to ensure consenting to the study was fully informed.

2.1.2 Confidentiality and Data Protection

Each participant was assigned a study identity code number for use on Study Forms (SFs) and the electronic database, for example “X01”. In the case of completing study questionnaires in Qualtrics, participants were prompted to input

their study identity code number to enable questionnaire identification and serve as a validation step in the software. The lead researcher (BT) made a separate password-protected, confidential record of participants names, date of birth, contact details, and identify code number, to permit identification of all participants enrolled in the study, in accordance with regulatory requirements and for follow-up. These details were restricted to be accessed only by the lead researcher and personnel approved by the Chief or local Principal Investigator (PI).

The license for Qualtrics was provided by the University of Lincoln which uses an 'EU Data Silo' option whereby all data are processed in Europe. Participant personal details were not required to access the system. Qualtrics is a GDPR compliant platform. Access to the data was individually controlled (by the lead researcher). Data was downloaded (in .csv format) and stored separately on the University of Nottingham-secured system. Once the study closed, we ensured the data are downloaded and backed-up on to a University of Nottingham account, held securely and password protected, and erased from the Qualtrics servers. All data was gathered using the online platforms; therefore, the storage of any paper forms was not required.

Information about the study in the participant's medical records / hospital notes was treated confidentially in the same way as all other confidential medical information.

2.1.3 Safeguarding

No safeguarding issues were anticipated as a result of participating in the study. However, talking about difficulties experienced in the early diagnosis of MS may generate distress for participants. The PIS signposted participants to additional support (e.g., MS Society). The lead researcher (BT) is a trainee clinical psychologist and has >3 years' experience of dealing with such situations in an empathic manner, and signposting to additional support where necessary. Where participants were identified as having clinically significant distress (the PHQ-9 [>20] or GAD-7 [>15]), we recommended they contact their GP and/or MS team to discuss further. In the event participants disclosed information which suggested themselves, or others, were at risk of harm (e.g., reporting suicidal ideation or thoughts of self-harm), the

lead research passed this on to the PI, as the clinical team responsible for the patients care.

2.2 Single Case Design and Rationale

Within healthcare research, large group designs such as Randomised Controlled Trials (RCTs) have taken precedence, however the emphasis on the average outcomes of these large samples and stringent eligibility criteria, mean inferences about individual behaviour and experience, and therapeutic process are significantly limited. Singe Case Designs (SCDs) offer an alternative, particularly in the development and evaluation of treatment within clinical settings (Morley, 2018).

SCDs within research are employed to test an intervention on one individual or a small sample. SCDs use repeated measurements of the dependant variable/s over several phases of an intervention. These are an established baseline period ('A'), the introduction of the intervention ('B' period), and after the intervention (follow-up; FU). This is commonly referred to as an AB design. The participant acts as their own control and repeat measurement enables change to be closely monitored (Barker et al., 2016). This enables control of many confounding variables, such as gender, age, and socioeconomic level (Lobo et al., 2017), and of particular saliency to the heterogeneity within the MS population. What Works Clearinghouse standards include specification of a minimum of three attempts to show an intervention effect, at three separate time points, with an 'attempt' qualifying as a minimum of three data points in a phase (Kratochwill et al., 2010). Within this design, the number of repeated measures informs the power, rather than the number of participants (Krasny-Pacini & Evans, 2018). A drawback of using SCDs is weakness in establishing causality of the intervention as change may be attributable to an uncontrolled variable (Anderson & Kim, 2005; Barker et al., 2016).

To overcome this limitation, by replicating treatment effect, further variations of the AB design have been developed. These include reversal designs or 'ABAB', and multiple baseline designs (Lobo et al., 2017). Within an ABAB design, the AB is extended to intervention withdrawal following stable outcomes, followed by re-introduction the intervention (Krasny-Pacini & Evans, 2018). The design permits replication and verification of a causal relationship (Anderson & Kim, 2005). However, within the current study, it was deemed unethical to withdraw the

intervention and ‘carry-over’ effects from the earlier intervention would be unavoidable given this is a psychological therapeutic intervention (Lobo et al., 2017).

Where withdrawal of the intervention is not possible, Multiple Baseline Designs (MBDs) can be used. In an MBD the introduction of the intervention is staggered over time, across several participants. This means data can be compared between participants, and causality inferred when comparing those who have begun the intervention with those still within baseline (Anderson & Kim, 2005). Given the need to return to baseline is withdrawn, this design has been deemed well suited for evaluating interventions with long-lasting effects, for example within rehabilitation (Krasny-Pacini & Evans, 2018), or psychological therapy. However, a disadvantage of this design is withholding the intervention for a period of time to enable varying starting points. Given the current study recruited individuals recently diagnosed with MS, likely experiencing significant psychological distress, this design presents ethical concerns and was deemed unsuitable.

We used a Multiple Single Case Experimental Design (MSCED) for the current study. This involves a series of AB replications across a small sample of participants. The introduction of the intervention is nonconcurrent, meaning it is introduced at different time points across participants (J. D. Smith, 2012), as opposed to staggering baseline periods as in an MBD. This was deemed the most appropriate design for the study given the smaller sample size, heterogenous sample in regard to the nature of MS and ethical considerations towards the potential emotional distress of participants and limiting the withholding of a therapeutic intervention. The nature of the design is also well suited to contributing towards the piloting phase, and refining the application of, PrEliMS-1 to this population (Krasny-Pacini & Evans, 2018).

2.3 Recruitment

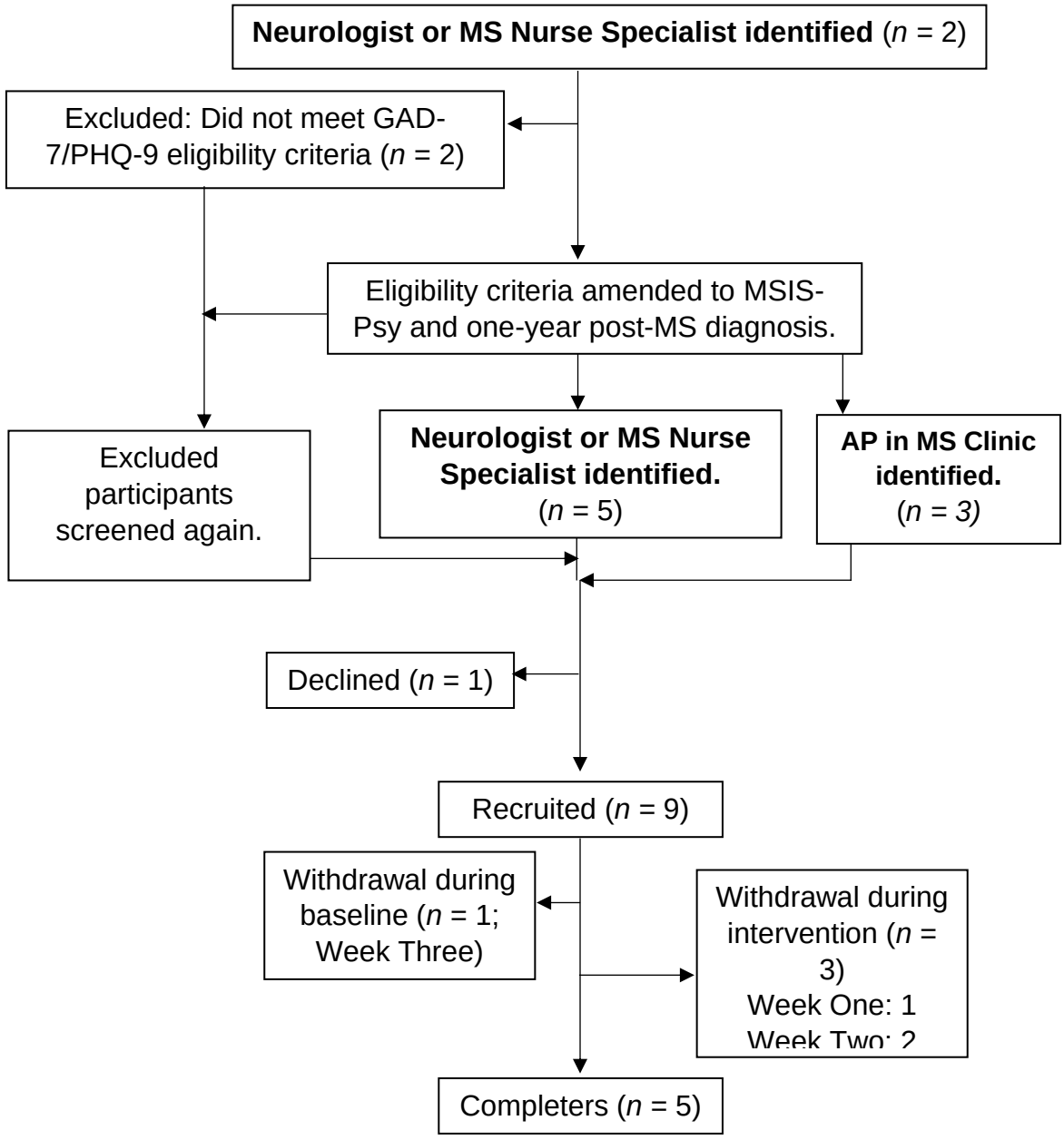
2.3.1 MS Clinic

Participants were recruited from an MS Outpatient Clinic in a Neurology Department at a local UK National Health Service (NHS) trust. The lead researcher (BT) had shadowed the MS Clinic prior to recruitment and attended the weekly MDT meeting to present the study. Potential participants were seen in clinic as part of routine care. The clinician (Neurologist or MS Nurse Specialist) mentioned the study

where it was felt they would benefit from additional emotional support in light of their recent diagnosis. An Assistant Psychologist (AP) within the team also identified potential participants through recruitment for a different study. If participants were not eligible for that study, the AP provided details about PrEliMS-2.

Across both recruitment routes, if they appeared interested in the study, verbal consent was obtained by the clinician to pass on their contact details (name, telephone number and/or email address) to the lead researcher (BT). They then made contact via telephone or email (depending on participant preference) to provide more information about the study and obtain consent to send a participant information sheet via email. Potential participants were then contacted again, after 48 hours, to confirm their interest and consent to taking part. They were then sent a Qualtrics link to sign an informed consent form and complete the screening questionnaires. After 1-week, potential participants were contacted via telephone, to discuss their eligibility based on the screening questionnaires. If eligible, participants were invited to complete measures for secondary outcomes, and repeat baseline measures for the next 3 weeks. If not eligible, participants were signposted to support either through their General Practitioner, or the MS Team (see section 2.8.1.1 for further details). Figure 16 provides further details on the routes of recruitment and how the reported sample number was reached.

Figure 16
Recruitment Flow-Chart



In the event that participants scored at a clinically significant level on screening measures (PHQ-9 [>20] or GAD-7 [>15]), we recommended they contact their GP to discuss this further and obtained consent to inform their MS Team (by contacting the PI [Consultant Neurologist in the MS Clinic]).

2.3.2 Inclusion criteria

We aimed to recruit up to 6-months post-MS diagnosis as research shows psychological distress is still clinically significant 6-months post-diagnosis (Giordano

et al., 2011). In July 2022, this was extended to 12 months post-diagnosis (as shown in Figure 16)[45]. This decision was made as the MS Team identified that potential participants were more frequently reporting emotional distress *after* the 6-month post-diagnostic period. Expanding the eligibility criteria also enabled our sampling strategy to be more inclusive. Although specific to secondary-progressive MS, this also reflected similar actions taken by (Meek et al., 2021) in expanding recruitment from six to 12-months after receiving a secondary-progressive diagnosis. Notably, PrEliMS-1 recruited participants within 2 years post-MS diagnosis (das Nair et al., 2023). However, the average time since diagnosis for the forty participants before starting the intervention was 37 days, including three outliers (56 days [2 months]; 730 days [roughly 2 years]; 112 days [roughly 3.5 months]). For the current study, within 12-months of a diagnosis was still deemed most appropriate given the feedback received from the MS Team.

Initially eligibility was based upon scoring ≥8 on the GAD-7 and/or ≥10 on the PHQ-9. Within the literature, cut-off points vary, however for the MS population a pragmatic approach suggested ≥10 on the PHQ-9 provides the best balance between specificity and sensitivity with pwMS (Patrick & Connick, 2019). Similarly, a cut-off score of ≥8 on the GAD-7 has been used within the MS population as optimal for identifying GAD (Litster et al., 2016; Terrill et al., 2015). In October 2022 this was changed to ≥18 on the MSIS-Psy based on feedback from participants who were initially excluded due to not meeting the minimum score on the GAD-7 or PHQ-9 (as shown in Figure 16)[46]. These participants acknowledged utility of the intervention as described in the PIS, despite not being eligible. In addition, the nature of the emotional support intervention is to be offered regardless of the level of clinical distress patients present with (das Nair et al., 2023). In a similar study providing ACT-based support, Meek et al. (2021) also experienced difficulties with recruitment rate due to inclusion criteria of meeting a minimum threshold on a measure of psychological distress (Hospital Anxiety and Depression Scale). Consequently, Meek et al. (2021) recommended removing this requirement altogether, particularly given ACT-targeted interventions are not aimed at reducing distress and arguably also benefit those not experiencing clinical levels of depression and/or anxiety. Given this

[45] See Appendix S for non-substantial amendment ethical approval.
[46] See Appendices T and U for substantial amendment ethical approval.

study is a SCED, setting a threshold was still deemed important for the eligibility criteria to be able to demonstrate an effect. As a result, to make the study more inclusive, the MSIS-Psy replaced the GAD-7 and PHQ-9 as a screening measure as this captured diagnosis-adjustment related items, conducive to quality of life, which is arguably more in line with the focus of ACT in learning to live a richer, more meaningful life. Participants previously excluded were provided opportunity to complete screening measures again based on the amended eligibility criteria (Figure 16).

Participants were required to be aged 18 and/or over which was met by all participants.

2.3.3 Exclusion criteria

Potential participants were excluded if they were unable to speak and read English. This is because all measures used have been standardised and validated in English. In addition, the workbook, which is required to be used independently by participants, is only available in English. Equally, participants were excluded if they were unable to use/did not have access to a telephone or a computer with an internet connection as this was required to access the support calls.

We also specified that eligible participants were not to be receiving psychological therapy (i.e., being delivered by a trained therapist or mental health professional) at the time of the study. This was to ensure that any change cannot be attributed to another intervention.

2.4 Rationale of sample size

A systematic review of standards of published SCED studies, suggested to demonstrate an effect in a case series, a minimum of three participants is recommended (J. D. Smith, 2012), with four or more suggested as more desirable and statistically advantageous (Kratochwill et al., 2010). Therefore, we aimed to recruit between three and seven participants, providing some allowance for attrition. This was deemed appropriate for the timescale for the study based on data from the PrEliMS-1 study (das Nair et al., 2023). Over 18-months, 60 referrals were received, and 40 participants recruited, showing recruitment rate was approximately two participants per month (J. Mhizha-Murira, personal communication, February 15, 2021).

Recruitment remained open until a minimum of six individuals had started intervention. Smith (2012) recommend recruiting six participants to protect against attrition. Equally, within ACT self-help interventions, a meta-analysis found an average of 80.1% (range: 50% - 94.3%) of participants completed ACT intervention which was predominantly self-help (French et al., 2017). Therefore, given the time frame available for the current study, this recruitment strategy was deemed appropriate.

2.4.1 Sampling

A purposive sampling strategy was used as potential participants were eligible based on specific criteria relating to the research question (Barker et al., 2016). Opportunity sampling was used for recruitment to feedback interviews following completion of the intervention. This was deemed the most appropriate sampling method given the small number of participants.

2.5 Measures

Where appropriate, the same measures as the PrEliMS-1 study were prioritised for use to allow for direct comparison in the analysis (das Nair et al., 2023).

Short form versions were prioritised to minimise participant burden. Table 10 outlines the frequency of data collection for each measure. Table 11 outlines the characteristics of the primary measures, which were used on a weekly basis.

The reflective period of questionnaires was altered to a week, or four weeks, where appropriate, to avoid overlap.

2.5.1 Demographic Measures

Demographic information was collected for all participants: age, gender, ethnicity, employment status, time since received an MS diagnosis, type of MS and length of time it took to obtain an MS diagnosis.

2.5.2 Principal Primary Outcome Measure

The psychological subscale of the Multiple Sclerosis Impact Scale (MSIS-Psy; Hobart et al., 2001; Ramp et al., 2009) consists of 9 items which are rated on a likert scale from 1 (‘not at all’) to 5 (‘extremely’). Total scores range from 9-45, and higher

scores indicate greater perceived psychological impact of MS. The measure has good internal consistency (α = 0.91) and convergent and discriminant validity (Hobart et al., 2001). This is part of a broader 29-item measure, with excellent internal consistency α= 0.97 (K. H. Jones et al., 2013), which has been used in MS populations recruited from the same NHS Trust exploring an ACT intervention (Meek et al., 2021; Proctor et al., 2018). Further, specifically the psychological subscale was used in PrEliMS-1 (das Nair et al., 2023).

Along with the October 2022 amendment to include the MSIS-Psy in the eligibility criteria (see Extended Methods 2.4.2), the MSIS-Psy was made the principal primary outcome as a critical indicator of change, given the increased emphasis on the use of the measure. The measure captures views about the daily psychological impact of MS and was also deemed to have diagnosis adjustment related items i.e., “how much have you been bothered by… worries related to your MS? …lack of confidence?”. Notably, most of the items are similar to distress related outcomes in the GAD-7/PHQ-9, pertaining to worry, feeling depressed and trouble sleeping. However, the MSIS was generated in the context of a lack of validated MS-specific QoL measures. Existing measures had not been developed through a standard psychometric approach and/or did not consult patient perspective (Hobart et al., 2001), thus the MSIS aimed to address these pitfalls. Overall, the measure is positioned as a QoL measure, specifically capturing the health impact of MS on a physical and psychological level (MSIS-Psy). Correlation between these subscales suggest they are related but distinct constructs (0.62). When testing construct validity, the MSIS-Psy correlated most with mental health and thinking/fatigue scales of other standardised QoL measures; correlations with more physical-health related items i.e., pain, self-care, mobility, were also present (Hobart et al., 2001).

As discussed in section 2.3.2, using a QoL measure is more congruent to the focus of ACT on living well in the context of MS. Equally, the MSIS-Psy items map better to focus on emotional adjustment to MS diagnosis. Thomas et al. (2006) recommends the use of MS specific measures (e.g., are of direct relevance to people with MS) where possible as these are likely more able to pick up changes in outcomes like QoL, in comparison to more generic measures. The measure typically asks individuals about the impact of MS “during the past two weeks” however this was altered to one-week for the current study, to avoid crossing over reflective

periods. This reflective period has previously been used within a case-series study (Martínez-Lemos et al., 2020).

2.5.3 Primary Outcome Measures

Emotional distress, as a factor in the psychological impact of MS, was captured by the Patient Health Questionnaire 9 (PHQ-9), Generalised Anxiety Disorder 7 (GAD-7), and Visual Analogue Scales. In PrEliMS-1, the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) was used as a measure of emotional distress and was considered for use in this study. The HADS has two subscales: anxiety and depression and has been validated for use in the MS population (Watson et al., 2014). However, the HADS is not publicly available for use and alternative measures have demonstrated higher reliability and sensitivity within the MS population (Marrie et al., 2018); potentially this is a drawback of using one measure with anxiety and depression subscales, rather than separate measures. Both anxiety and depression are prevalent within the MS population, as indicators of emotional and psychological distress, particularly within the context of MS diagnosis (Boeschoten et al., 2017; Giordano et al., 2011; Solari, 2014), and is therefore important to capture sensitively. As a result, the GAD-7 and PHQ-9 were prioritised.

PHQ-9. The PHQ-9 (Kroenke et al., 2001) was chosen to assess psychological distress, specifically signs of depression. The measure has nine items, which are rated on a frequency likert scale from 0 (‘not at all’) to 3 (‘nearly every day’). Total scores range from 0 to 27, with higher scores indicating greater symptoms of depression. The PHQ-9 has acceptable internal consistency and convergent validity in the MS population (Amtmann et al., 2014; Patrick & Connick, 2019) and has the highest sensitivity (84%) in comparison to similar measures of depression used in the MS population (Marrie et al., 2018). Further, the PHQ-9 has been used within ACT-intervention research in an MS population (Proctor et al., 2018).

GAD-7. The GAD-7 (Spitzer et al., 2006) was also selected to measure psychological distress, to capture symptoms of anxiety. Seven items are rated on a likert scale from 0 (‘not at all’) to 3 (‘nearly every day’). Higher scores indicate greater symptoms of anxiety. Excellent internal consistency ($\alpha = 0.92$) and convergent validity within the MS population has been demonstrated (Marrie et al., 2018; Terrill

et al., 2015). As with the PHQ-9, the GAD-7 has also been used within ACT-intervention research in an MS population from the same NHS Trust (Proctor et al., 2018).

Visual analogue scales[47]. Three additional questions were used to measure the extent to which current distress related to receiving an MS diagnosis, and how confident participants feel in managing the physical and psychological impact of MS. Each item was rated on a scale from 0 ('not at all') to 10 ('all of my current distress' / 'very confident'). The following text was used:

> *"How much of your current psychological distress is related to receiving a diagnosis of MS?"*
> *"How confident do you feel in managing the physical impact of MS day-to-day?"*
> *"How confident do you feel in managing the psychological impact of MS day-to-day?"*

The purpose of including the VASs was to control a possible confounding variable of their presenting distress being unrelated to MS. Further, PrEliMS-1 reported that participants experienced difficulty in completion of the Multiple Sclerosis Self-Efficacy Scale (MSSES) (das Nair et al., 2023), demonstrated through a number of missing items. Therefore, the inclusion of specific VAS pertaining to confidence over managing aspects of MS, were to pre-empt such issues repeating.

2.5.4 Process Measure

The brief version of the Comprehensive Assessment of Acceptance and Commitment Therapy processes (CompACT-8; Dawson & Golijani-Moghaddam, 2020; Morris et al., 2019) was used as a process measure, to track any changes in participants' psychological flexibility. The shorter version was prioritised to reduce participant burden in completing weekly measures. The following subscales compute to a total CompACT score of psychological flexibility: 'openness to experience', 'behavioural awareness' and 'valued action'. The short-form version comprises eight items, rated on a likert scale from 0 ('strongly disagree') to 6 ('strongly agree'). Within the short-form the subscales are not well standardised, therefore we just focused on

[47] See Appendix V for the visual analogue scales

the total score. Total scores range from 0 to 48, with higher scores indicating greater psychological flexibility. Items two, three, four, six and seven are revered scored.

Although this was not used in PrEliMS-1, the emphasis on the intervention within this study being on ACT principles meant it was important to include a measure of the mechanism of change within ACT. The Acceptance and Action Questionnaire (AAQ-II; Bond et al., 2011) was considered as a measure of psychological flexibility, as used by Proctor et al. (2018). However, the measure has been criticised for conflating ACT processes with distress-related outcome variables, making it challenging to gauge whether AAQ-II scores reflect psychological inflexibility, or levels of experienced emotions and worries (Francis et al., 2016; Gámez et al., 2014; Wolgast, 2014). Further, the AAQ was primarily developed to measure experiential avoidance; only one process of psychological flexibility (Gámez et al., 2014). Conversely, measures of multiple dimensions of psychological flexibility have produced more clinically meaningful and nuanced patterns, such as the CompACT (Rogge et al., 2019). The CompACT-8 demonstrates high internal consistency $\alpha = 0.734$ (Morris et al., 2019) and validity (Francis et al., 2016), with excellent discriminant validity compared to the AAQ-II (Ong et al., 2020). Further, the CompACT has been used with an MS population in demonstrating greater psychological flexibility is associated with lower distress and higher quality of life within pwMS (Meek et al., 2021, 2022). On that basis, it was selected for this study.

2.5.5 Secondary outcomes

Health-related quality of life. The EQ-5D-5L (Herdman et al., 2011) was selected, in line with PrEliMS-1. This measure explores health related quality of life in five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), with good reliability and validity in the MS population (Kuspinar & Mayo, 2014). Responses are rated 1 to 5 and collated into a 5-digit number to be converted into an index score; higher index scores indicate greater health related quality of life.

Perceived levels of stress. The Perceived Stress Scale (PSS-10; Cohen et al., 1983) is comprised of 10 items, rated on a likert scale from 0 (‘never’) to 4 (‘very often’). Total scores range from 0 to 40, with higher scores indicating greater perceived level of stress. Items four, five, seven and eight are revere scored. This

scale was selected as it has been validated for use within the MS population, demonstrating good internal consistency (α = 0.91) and validity (Wu & Amtmann, 2013). Notably, PrEliMS-1 used the 4-item version, however given we were interested in possible mechanisms of change, it was important to capture more sensitivity and specificity, therefore the 10-item version was prioritised for PrEliMS-2.

Self-efficacy in the context of MS. The Multiple Sclerosis Self Efficacy Scale (MSSES; Rigby et al., 2003) assesses how much individuals feel in control of their MS. The measure has 14 items, rated on a scale from 0 ('strongly disagree') to 6 ('strongly agree'). Scores range from 0-84, with higher scores indicated greater level of self-efficacy. Items three, four, nine, ten, twelve and fourteen are reverse scored. Recently, the first PrEliMS study reported difficulty in participants completing the MSSES due to a number of missing items, possibility indicative this measure was not appropriate (das Nair et al., 2023). This was perhaps unexpected given the MSSES was developed through collaboration with individuals with MS, demonstrating high face validity. Good internal consistency and test-re-test reliability have also been demonstrated (Rigby et al., 2003). The MSSES was still included in this study as the measure was deemed to have appropriate adjustment-related items. We have also included the VASs, pertaining to confident over managing aspects of MS, to mitigate if similar difficulties were to arise in this study.

Levels of fatigue. The Modified Impact Fatigue Scale (MFIS-5; Fischer et al., 1999; Fisk et al., 1994) was used to assess the perceived impact of fatigue on daily activities. Although this measure was not used in PrEliMS-1, it was deemed important to include as higher scores on measures of psychological distress (i.e., anxiety and depression) and worse adjustment to MS diagnosis, are associated with higher levels of fatigue (Marrie et al., 2018; Topcu et al., 2020). Further, a systematic review reported that levels of fatigue in pwMS appeared to benefit from psychological intervention (Pagnini et al., 2014). On the MFIS-5, five items are rated on a likert scale from 0 ('never') to 4 ('almost always'); total scores range from 0-20 with higher scores indicating greater impact of fatigue on activities. The measure has good internal consistency (α = 0.90) and validity has been demonstrated (Fisk et al., 1994; Meca-Lallana et al., 2019). The MFIS-5 forms part of the MS Quality of Life Inventory which has been shown to have high construct validity and generated specifically for the MS population (Fischer et al., 1999; Vickrey et al., 1995).

2.5.6 Feedback Interview

A week after completion of the intervention, participants were invited to a feedback interview. This was completed with a trainee clinical psychologist who was independent from the intervention, to minimise bias in obtaining feedback. The interview schedule drew on aspects of Elliott et al.'s (2001) change interview protocol, in terms of what was helpful and unhelpful during the intervention. In line with the study aims, questions were also added to explore whether any improvements could be made to the intervention, alongside more explorative questions around their general experience of the intervention. Further, a specific optional question was added to explore whether any dips/peaks in psychological impact of MS had occurred during the intervention. This was to promote contextualisation of quantitative findings. The interview was semi-structured, and the schedule used flexibly by the facilitator to enable prompts and follow-up questions to be used[48].

[48] See Appendix L for the interview schedule.

Table 10

Evaluation Time Point(s) of Outcome Measures

Outcome Measure	Measure Time Point(s)									
	Screening/ Pre-Intervention	Baseline (A period)		Intervention (B period)					Post-Intervention	1 Month Follow-Up
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	
MSIS-Psy	X	X	X	X	X	X	X	X	X	X
PHQ-9	X	X	X	X	X	X	X	X	X	X
GAD-7	X	X	X	X	X	X	X	X	X	X
VAS	X	X	X	X	X	X	X	X	X	X
CompACT-8	X	X	X	X	X	X	X	X	X	X
PSS-10		X							X	X
MSSES		X							X	X
EQ-5D-5L		X							X	X
MFIS-5		X							X	X
Qualitative Feedback Interview									Optional	

Note: MSIS-Psy: Psychological Subscale of Multiple Sclerosis Impact Scale, PHQ-9: Patient Health Questionnaire, GAD-7: Generalized Anxiety Disorder, VAS: Visual Analogue Scales, CompACT-8: Comprehensive Assessment of Acceptance and Commitment Therapy Processes, PSS-10: Perceived Stress Scale, MSSES: Multiple Sclerosis Self-Efficacy Scale, EQ-5Q-5L: EuroQoL Health Related Quality of Life, MFIS-5: Modified Fatigue Impact Scale – abbreviated version.

Table 11

Primary Outcome Measures, Psychometric Properties and Scoring

Name and author	Purpose	No. of items, reference period and example item	Reliability	Validity	Scoring and scale direction
Multiple Sclerosis Impact Scale – Psychological Subscale (MSIS-Psy; Hobart et al., 2001; Ramp et al., 2009).	To assess the perceived psychological impact of MS.	9 (psychological subscale), the past two weeks "How much have you been bothered by… worries related to your MS? 1 Not at all 2 A little 3 Moderately 4 Quite a bit 5 Extremely".	Internal consistency: $\alpha \leq 0.91$ (Hobart et al., 2001).	Both subscales of the measure (physical and psychological) correlate higher with measures of a similar nature showing both convergent and discriminant validity (Hobart et al., 2001). Rasch analysis by Ramp et al. (2009) showed support for the psychometric properties of the MSIS-29 psychological subscale.	Total scores range from 9-45, with higher scores indicating greater perceived psychological impact of MS.
Patient Health Questionnaire – 9 (Kroenke et al., 2001)	To assess signs of depressive symptoms, as one indicator of psychological distress	9, the past week "How often have you been bothered by… feeling down, depressed or hopeless? 0 Not at all 1 Several days More than half the days 3 Nearly every day	The PHQ-9 has good internal consistency and has the highest sensitivity (84%) in comparison to similar measures of depression used in the MS population (Marrie et al., 2018).	Acceptable convergent validity in the MS population (Amtmann et al., 2014; Patrick & Connick, 2019). Used within ACT-intervention research in an MS population (Proctor et al., 2018).	Total score ranges from 0-27, with higher scores indicating greater symptoms of depression

Table 11

Primary Outcome Measures, Psychometric Properties and Scoring

Name and author	Purpose	No. of items, reference period and example item	Reliability	Validity	Scoring and scale direction
Generalised Anxiety Disorder – 7 (Spitzer et al., 2006)	To assess signs of anxiety symptoms, as one indicator of psychological distress	7, the past week "How often have you been bothered by… not being able to stop or control worrying? 0 Not at all 1 Several days 2 More than half the days 3 Nearly every day	Internal consistency (α = 0.92) (Marrie et al., 2018).	Excellent convergent validity has been demonstrated within the MS population (Marrie et al., 2018; Terrill et al., 2015)	Total score ranges from 0-21, with higher scores indicating greater symptoms of anxiety
Comprehensive assessment of Acceptance and Commitment Therapy processes (CompACT-8; Dawson & Golijani-Moghaddam, 2020; Morris et al., 2019)	To assess change processes of the ACT-based intervention.	8, at the present time "I act in ways that are consistent with how I wish to live my life: 0 Strongly disagree 1 Moderately disagree 2 Slightly disagree 3 Neither agree nor disagree 4 Slightly agree 5 Moderately agree 6 Strongly agree".	Internal consistency of 8-item version: α = 0.734 (Morris, 2019) Test-retest reliability shown over a two-week period (Bayliss, 2018).	Demonstrated good convergent and discriminant validity with measures of wellbeing, distress, and experiential avoidance (Francis et al., 2016). Used within an MS population (Meek et al., 2021, 2022)	Total score ranges from 0-48, with higher scores indicating greater psychological flexibility.

2.6 Procedure

2.6.1 Contact with potential participants.

Following initial telephone contact between the Lead Researcher (LR) and potential participants, an email using the following structure, was sent:

"Hi X,

Thanks for chatting with me over the phone this afternoon. As discussed, please find an information sheet attached to this email. This talks you through what the study involves and provides additional contact details.

If this sounds like something you'd be interested in, please complete the questionnaires below. There are three to complete.

***Your participant identifier is: X0n.** You'll need this when completing the surveys.*

Consenting to the study:
https://unioflincoln.eu.qualtrics.com/jfe/form/SV_23IMlVJuy76m6vY

Demographic information:
https://unioflincoln.eu.qualtrics.com/jfe/form/SV_eRGzFeJgTClGVOC

Mood questionnaires:
https://unioflincoln.eu.qualtrics.com/jfe/form/SV_b9mniSI6xFGABca

I'll give you a call, or get in touch via email, in a week or so to discuss the results of the questionnaire and whether you are eligible to take part. Any questions at all, please don't hesitate to drop me an email.

Take care

With best wishes,

Beth"

If eligible, the following proforma of the minimal dataset for medical case note entries was used for Nurses to input a clinical note onto the participants clinical record within the neurology clinic:

Document the introduction and discussion of the study by the usual care team

Document the name of study and the patient ID number

Document whether patient gave verbal consent for their contact details to be passed on to the primary researcher to discuss the study further

Document deviations to the protocol

Document details of any safety issues reported (SAE/SADE/ASADE/USADE)

Sign and date the entry

To be completed by Primary Researcher/Trainee Clinical Psychologist	**To be documented by the team**
Assess eligibility on first contact with potential participants	Document whether eligibility criteria are fulfilled
Completed MSIS-Psy, GAD-7 and PHQ-9 with potential participant as part of assessing eligibility	Document the MSIS-Psy, GAD-7 and PHQ-9 scores
Complete informed consent procedure, including going through the participant information sheet, signing and dating the informed consent form	Document the informed consent procedure, sign and date Add an alert to the patient's record as per SOP-RES-016 if the patient has consented to participate in research or has explicitly refused to take part

2.6.1.1 Non-eligible participants

Following completion of screening measures, the lead researcher (BT) spoke with potential participants over the phone to discuss eligibility. If a participant was not eligible, the following script was flexibly used:

"We are recruiting people with a certain degree of mood problem and based on the results from these questionnaires, we've found you are not at that level for participation in the study. Based on our understanding of how this therapy works, we don't feel you would benefit from this intervention, as it's pitched at a level for individuals scoring higher".

"This does not mean that you are not finding things tough/difficult at the moment, and I fully appreciate this is frustrating. If things feel really emotionally tough at the moment, please speak to (Neurologist, MS Nurse, MS Trust, MS Society, IAPT, your GP)".

"You may not be eligible for this study, but would you like me to pass on your details to our MS PPI group; they send out newsletters every quarter with new studies".

2.6.2 Baseline Phase

The primary (MSIS-Psy, GAD-7, PHQ-9) and process (CompACT-8) measures were administered weekly for three weeks to establish baseline. Participants received a weekly email reminder from the lead researcher (BT) to support with adherence to the case series timeline and improve response rates. There is long-standing dispute over the ideal number of data points within the baseline phase of SCED research. Suggestions within the literature range from three to 12 data points (Center et al., 1985; Huitema, 1985; Jones et al., 1977; Sharpley, 1987). A review of SCED standards by Smith (2012) concluded that whilst longer baseline periods can reduce bias and increase validity, a minimum of three is necessary. Further, What Works Clearinghouse propose that more than three data points is preferred (Kratochwill et al., 2010).

Given we were recruiting from a population often presenting with a significant level of distress following diagnosis (Giordano et al., 2011), the minimum recommended number of three data points within the baseline phase was deemed most appropriate. This was to minimise the withholding of psychological intervention for an extended period. Completing measures bi-weekly was also considered, to increase the number of data points within baseline, however reducing participant burden was also a priority. Given we have four baseline measures for participants to complete, completion more than one week was deemed too much for participants.

Stability (i.e., limited variability in scores) within the baseline phase is also preferred for inferring an effect (Smith, 2012). If participants showed significant variability in the baseline, (determined through visual analysis of the baseline trend i.e., large variability in scores across a four-week period), then the baseline period was extended by a maximum of two weeks. However, variability was not a determinant of eligibility for the study. This was due to pragmatic reasons such as

the ethical issues of withholding an intervention in a population known to experience variability in emotional distress (Morley, 2018; Topcu et al., 2022). Overall, in addition to screening data, participant's baselines consisted of between four and six data points, in adherence with SCED recommendations.

2.6.3 Intervention Phase

Primary and process measures continued to be repeated weekly throughout the 4-week intervention delivery. Weekly email reminders were sent to participants to improve measure response rates.

The PrEliMS-2 intervention consists of a 52-page workbook, titled "Better Living with a Diagnosis of MS", alongside weekly sessions to provide emotional and psychological support based upon the ACT model, and respond to queries about the workbook exercises. The workbook was posted out to participants in the final week of baseline, which they kept during and after the study.

2.6.3.1 Workbook

The workbook was used in the PrEliMS-1 study and developed based on findings from two systematic reviews (Topcu et al., 2020, 2022). Development was also informed by consultations with an MS Patient and Public Involvement group, clinical expertise, and stakeholders. The workbook uses exercises based on previously designed guided self-help materials for ACT and in the context of long-term health conditions (Brassington et al., 2016; Ford, 2017; S. C. Hayes & Smith, 2005). The exercises and content map onto the six processes of the 'Hexaflex' (Harris, 2006). The workbook is split into three sections, which are summarised in Table 12[49]. Pacing through the workbook was based on individual needs of participants however typically consisted of one section per session; denoting section two as two separate sessions based on the sub-section format. Homework was set between sessions based on the progress made through the workbook and recommended exercises from the workbook to practise[50]. Table 13 presents a TIDieR checklist (Hoffmann et al., 2014).

[49] See Appendix W for examples of pages from the workbook.
[50] See Appendix X for examples of exercises from the workbook.

Table 12

Summary of PrEliMS Intervention Workbook

Section	Content	Underlying ACT process†
1.Introduction	Exploring how MS diagnosis has impacted on your life. Considering treatments and strategies tried so far. MS related distress and how we respond to it. Moving forward with MS: "Sailing our boat" analogy. Introduction to the workbook. Exercise: Identify ways to live better alongside MS.	Acceptance: opening up to difficult thoughts and feelings.
2.1 Dealing with unhelpful thoughts, feelings, and physical sensations. 2.2 Mindfulness	Revisit sailing boat analogy. Acceptance: Allowing for difficult experiences. Exercise: 'Observe, breathe, expand, allow'. De-powering unwanted thoughts and feelings. Mindfulness: Staying Present. Exercise: 'Simply noticing'. Exercise: '5 senses of mindfulness'. Exercise: 'Conveyor belt'. Exercise: 'Mindfulness of your body'. Exercise: 'Mindful moments'.	Acceptance: opening up to difficult thoughts and feelings. Being Present: attending to the here-and-now. Defusion: viewing thoughts as ongoing events separate from the individual. Noticing Self: taking a perspective of an observer that's separate from thinking.
3.Doing what matters.	Exercise: 'Clarifying values'. Practice: 'Acting on values'. Exercise: 'Remembering what's important'. Exercise: 'Strategies to help us act on our values'. Moving forward.	Values: understanding and developing what is personally valuable. Committed Action: acting in accordance with one's values.

†Graham et al. (2016); Hayes et al. (2012)

Table 13

TIDieR Checklist for the PrEliMS-2 Intervention

Checklist Item	Description of Intervention
Brief Name	ACT based emotional support
Why	The intervention is based on one arm of the PrEliMS-1 intervention, and both the workbook and emotional support sessions have been used in a similar format in progression to secondary progressive MS (Meek et al., 2021). ACT aims to increase psychological flexibility and quality of life.
Materials	52-page ACT-based workbook adapted from previously designed self-help ACT resources. The workbook is the same as used in the PrEliMS-1 study and is available in an online pdf format or hard copy. There are three sections in total which map on to the three overarching areas of the ACT hexaflex: 'open up', 'be aware', and 'do what matters'. All participants elected to have a hard-copy of the workbook.
Procedures	Participants were posted the workbook in the week before the intervention started and kept this during and after the study. The facilitator also had a hard-copy of the workbook and during sessions they worked through it together. Pacing was based on individual need and completion of the workbook was not an expectation. The participant and facilitator collaborated on setting homework tasks each week, based on workbook progress, and this was then reviewed in the following session. In the final session, discussion centered on aspects the participant wishes to takes forwards, beyond the intervention.
Who	A third-year trainee clinical psychologist (female, 26) delivered the support sessions. They had two years' experience in delivering ACT within NHS mental health settings and also two years' experience in working with individuals with a diagnosis of MS. They were also the Lead Researcher.
How	Online video calls via Microsoft Teams.
Where	Participants will be at home.
When	Four online video sessions. The initial session was an hour long with the remaining three sessions ranging between 30 – 45 minutes. Sessions occurred weekly over four weeks.
Tailoring	In the support sessions, participants and the facilitator worked through the ACT exercises in the workbook. The exercises focused on were workbook-based and selected based on individual need and preference.

Table 13

TIDieR Checklist for the PrEliMS-2 Intervention

Checklist Item	Description of Intervention
Modifications	Where appropriate, additional ACT metaphors were introduced by the facilitator. These were the 'beachball' analogy during discussion of section one and the 'sky and the weather' analogy during section 2.2.
Fidelity	Fidelity was assessed by two clinical psychologists (NM and AT) with several years' experience in delivering ACT. A 25% sample of session recordings were assessed against published criteria (ACT-FM: O'Neill et al., 2019). Of the five participants who completed the intervention, all sessions were completed and adhered to the weekly timeframe.

Note. ACT: Acceptance and Commitment Therapy, ACT-FM: Acceptance and Commitment Therapy Fidelity Measure

2.6.3.2 Session format

The first session lasted around an hour whereby participants were familiarised with the workbook, goals for the support were discussed and section one was started. The subsequent three sessions were each between 30 and 45 minutes long. Support sessions involved psychological support theoretically orientated to the ACT model, through discussion about the exercises in the workbook which had been completed. We adapted the pace of working through the workbook to each participant's needs. This approach was used in the PrEliMS-1 study, thus has informed decision making around format and length of sessions. Compliance with the intervention was assessed based on completion of measures and attendance of sessions. For all five participants, no sessions were missed.

2.6.4 Follow-up

The follow-up phase consisted of two time points: one-week after intervention completion and again at one-month after. On both occasions, this consisted of completion of primary, process and secondary measures. This enabled measurement of whether any changes that had occurred, were sustained over time. Equally, to explore whether there had been any additional effects of the intervention. Notably, the PrEliMS-1 study had longer follow-up phases of three- and six-month follow-up, however due to the timescale of the current study, this was not feasible.

In addition, all participants were invited to complete a feedback interview one week after completion of the intervention. This was to gather qualitative feedback pertaining to their experience of the PrEliMS-2 intervention and specifically whether any improvements could be made[51].

2.6.5 Comparison of methodology between PrEliMS-1 and -2

Table 14 provides a summary of the differences in methodology between PrEliMS-1 and PrEliMS-2, as referred to within the extended introduction and methods sections.

Table 14

Differences and Similarities Between the Methods Within PrEliMS-1 and PrEliMS-2

	PrELiMS-1 (das Nair et al., 2023)	PrEliMS-2
Design	Three-arm randomized controlled trial	Multiple single case experimental design
Eligibility	Aged ≥18 Within two years of MS diagnosis *or* undergoing diagnosis process. Able to communicate in English and provide consent.	Aged ≥18 Within one year of MS diagnosis. Scored ≥18 on MSIS-Psy Able to communicate in English and provide consent.
	Excluded if: had severe co-morbid psychiatric condition, were receiving, or had received psychological interventions in the past 3 months.	Excluded if: unable to use/did not have access to phone/computer with internet connection, receiving other psychological therapy.
Measures	Demographics MSIS-Psy HADS PSS-4 MSSES EQ-5D-5L Bespoke service use questionnaire	Demographics MSIS-Psy GAD-7/PHQ-9 CompACT-8 VAS PSS-10 MSSES EQ-5D-5L MFIS-5

[51] See Extended Methods 2.6.5 for further details about the feedback interview.

Table 14

Differences and Similarities Between the Methods Within PrEliMS-1 and PrEliMS-2

	PrELiMS-1 (das Nair et al., 2023)	PrEliMS-2
Timepoints	All measures at baseline, 3- and 6-months follow-up (post-baseline) Semi-structured interview between two follow-up points.	Primary/process outcomes weekly throughout intervention and 1-week and 1-month after intervention has ended. Secondary outcomes pre-, post- and 1-month after intervention. Semi-structured interview between two follow-up points.
Intervention	(1) Nurse supported bibliotherapy. (2) Plus, peer-supported intervention (3) Usual care [control group]	TCP supported bibliotherapy
Facilitation/ delivery	[Intervention one only] One-to-one video/telephone session with an MS Nurse-specialist within two weeks of diagnosis. Sessions lasted up to 90 minutes. Workbook provided. Additional support sessions were optional.	Workbook provided. Four, weekly, one-to-one sessions with a TCP. Sessions intended to last between 30 – 60 minutes.

Note. MSIS-Psy = Multiple Sclerosis Impact Scale Psychological Subscale; HADS = Hospital Anxiety and depression Scale; PSS-4/10 = Perceived Stress Scale; MSSES = Multiple Sclerosis Self-Efficacy Scale; EQ-5D-5L = Health Related Quality of Life measure; GAD-7 = Generalised Anxiety Disorder scale; PHQ-9 = Patient Health Questionnaire; VAS = Visual Analogue scales; CompACT-8 = Comprehensive Assessment of Acceptance and Commitment Therapy Processes; MFIS-5 = Modified Impact Fatigue Scale; TCP = Trainee Clinical Psychologist.

2.7 Analysis

2.7.1 Descriptives

Demographic information was analysed using descriptive statistics (*M*, range, *SD,* percentages). Demographic characteristics were also compared to the PrEliMS-1 study to promote contextualisation of the sample.

2.7.2 Individual level change

A triangulation of analysis methods was used within the current study, which includes reliable and clinically significant change (Jacobson & Truax, 1991), visual analysis (Kratochwill et al., 2010) and the conservative dual criterion method (Fisher et al., 2003). Each one is outlined in the following section.

2.7.2.1 Reliable and clinically significant change

To analyse whether change observed in individuals is meaningful or not, Jacobson and Truax (1991) proposed two methods for operationalising this: 1) reliable change index and 2) clinically significant change.

2.7.2.1.1 *Reliable Change Index (RCI)*

The RCI is used to infer whether individual change is a reliable change, based on confidence intervals set at ±1.96 (equivalent to 95% confidence interval around the baseline score) (Jacobson & Truax, 1991; Morley, 2018). To calculate the RCI, the difference between the individual's pre-treatment score and post-treatment score, is divided by the standard error of difference between the two test scores, as shown in the formula below:

$$RCI = \frac{(pre\ treatment\ score - post\ treatment\ score)}{SEdiff}$$

The standard error of the difference describes the spread of the distribution of change scores which would be expected if there were no change. This can be calculated using the formula below:

$$SEdiff = \sqrt{2 \times SEM^2}$$

The standard error of measurement (SEM) is calculated using the standard deviation (SD) of the individuals scores and the reliability coefficient (r):

$$SEM = SD\sqrt{(1 - r)}$$

An RC value larger than 1.96 would be unlikely to occur due to chance (p < .05) i.e., the change is reflecting more than the typical fluctuations of the psychometric. Overall, the RC value is suggesting the amount of change required between scores for this to be reliable. The estimate of RC is typically made from a

data set within a comparable clinical sample using the reliability coefficient (typically Cronbach's alpha [α], or less common, test-retest reliability), mean and standard deviation. In the current study, this was used to compare pre- and post- (1-week and 1-month intervals) intervention scores for primary, process and secondary outcomes. Reference data is presented in the extended results section 3.6.

2.7.2.1.2 *Clinically Significant Change (CSC)*

If a change is deemed to be reliable, the second question Jacobson and Truax (1991) propose is whether this is a large enough change for it to be clinically meaningful i.e., a return towards normative functioning (a non-clinical group). Some psychometric measures hold an established clinical cut-off score, which should be used in the first instance, if available. If not, there are three (A, B and C) criteria to determine clinically significant change:

A) Participant's post-treatment score falls outside the clinical range, defined as more than two standard deviations beyond the clinical mean, in the direction of the non-clinical population. *This is used when reference data for a normative functioning group are unavailable.*
B) Participant's post-treatment score falls within the range of the non-clinical group, the range being within two standards deviations from the mean of the non-clinical group. *This is used when the data for clinical and non-clinical groups are available, and these scores do not overlap.*
C) Participant's post-treatment score is closer to the mean of the non-clinical group than to the mean of the clinical group. *This is used when the data for clinical and non-clinical groups are available, and these scores do overlap.*

Reference data used for assessing clinically significant change in the current study are presented in the extended results section.

2.7.2.2 Visual analysis

Visual Analysis (VA) is commonly used in SCED research to support implication of whether there is evidence of a relation between an independent variable and an outcome, alongside the *strength* of that relation. Specifically, visual analysis holds six features: level, trend, variability, immediacy of effect across

phases, overlap and consistency of data patterns across similar phases (Kratochwill et al., 2010). To enable visual analysis, graphs for the weekly observations of primary and process outcomes were prepared in line with guidance recommended by Morley (2018).

Despite VA having long-standing, historical origins in SCED research, it has come under criticism for subjectivity within the analysis. Specifically, the risk of bias within idiosyncratic interpretation and lack of standardised criteria to support judgements about change (DeProspero & Cohen, 1979; Furlong & Wampold, 1982). As such, researchers have more recently proposed strategies to address these limitations (Morgan & Morgan, 2009). The Split-Middle (SM) method involves superimposing a trendline into the treatment phase to aid interpretation of whether the pattern, or trend, was continuous (Bailey, 1984). The was expanded upon to consider the number of data points above/below this projected trendline and then calculate the probability of this occurring by chance (Kazdin, 2011). However, due to serial dependence, whereby the observation at one time-point is influenced by/relates to an observation at another time-point, it was suggested there are difficulties with validity within SCED research.

Subsequently, Fisher et al. (2003) proposed a refinement of the SM method, termed the Conservative Dual Criterion (CDC) method, which has demonstrated improved control over type 1 error rates, with higher power to detect treatment effects. This involves projecting the mean and trend from baseline, into the second phase and observing how many points are above/below these projections, to draw conclusions about whether a change has occurred. To further improve the reliability and validity of these judgements, an adjusted mean and trend was suggested whereby the mean is adjusted by 0.25 of the Standard Deviation (SD) as well as the intercept value of the baseline trend line. The adjustment depends on the direction of change (i.e., when the treatment is expected to reduce scores, the adjusted mean and trend is the observed baseline M minus 0.25 of SD, and in the case of an anticipated increase in scores, this is added instead) (Fisher et al., 2003; Morley, 2018). In application to the current study, criteria for six data points within the treatment phase, is six observed data points above/below both criterion lines to imply a systematic change.

Such conservative methods have been recognised as reducing the probability of a type one error i.e., ineffective treatments interpreted as effective; a false positive, and improving objectivity within visual analysis (Scruggs et al., 2006). An alternative considered was Tau-U (R. I. Parker et al., 2011) which assesses trends in data sets and can calculate an effect size for the intervention phase. However, this approach is relatively new to SCD research and has been criticised within the What Works Clearing house guidance (Kratochwill et al., 2010) in the use of effect sizes. Overall, there is a lack of consensus as to quantifying the size of an effect, and the method to do so. Subsequently, there remains a preference for visual analysis within the literature.

FDC method can be further supplemented by the Percentage of Non-overlapping Data (PND; Scruggs & Mastropieri, 1998). This considers the percentage of data points which are above/below the highest or lowest (depending on the direction of clinical gain) baseline score and was considered for the current study. However, the analysis of percentage values on the small number of data points within the intervention phase of this study (six), was deemed inappropriate. Equally, the approach has been criticised for the use of only a single score on the baseline to determine PND, as well as having no associated statistical tests for PND (Morley, 2018).

2.7.3 Sample comparisons

Comparison of change between the current study and the PrEliMS-1 findings will be explored in two ways:

1) The proportion of individuals from each study achieving reliable and clinically significant change. As part of this, the outcomes on which change was achieved will also be compared, to assess whether there are similarities or differences across the two studies.
2) Comparing change in a single case from the current study, with the differences observed in the PrEliMS-1 as a control sample, using the method and programme by Crawford and Garthwaite (2007). This tests for a difference between an individual cases scores on two tasks, or two time-points (i.e., pre-, and post- intervention), by comparing the difference observed with that of a control sample. In this case, the PrEliMS-1 sample is

our control. An interval estimate of the effect size is obtained through Bayesian methods. The Bayesian Standardised Difference Test (BSDT) was selected, as the two time-points differ in their M and SDs. This test standardises the scores on each time-point using the control data. The BSDT estimates the percentage of the control population that will have a larger difference than the individual participant, provides an interval estimate of this quantity and provides a significance test.

2.7.4 Framework Analysis

Qualitative data from the feedback interviews was analysed using Framework Analysis (FA); a structured, systematic approach to analysing qualitative data (Galeet al., 2013; Hackett & Strickland, 2018). The approach sits within the broader category of thematic analysis and holds some similarities to content analysis (Barker et al., 2016). The main feature of FA is the use of a coding framework matrix, whereby rows represent participants, columns are defined by codes and the cells are summarised data. This enables analysis both *across* and *within* participant cases, within a structured framework (Gale et al., 2013).

Given the approach is useful when working deductively to explore similar key issues, it was selected for the current study. Analysis commenced with transcribing the audio recordings of interviews. Notably, familiarisation and initial coding was completed on one transcript at a time. In line with the study aims and interview schedule, a deductive coding framework was prioritised[52] which was later added to through additional open coding of each transcript. Once the final framework was generated, this was applied to each transcript. This was then arranged into a matrix of categories and codes, for each participant row.

3 Extended Results

This section provides additional information about recruiting, and results obtained for non-completers of the study. Following this, fidelity results will be presented, with further detail as to quantitative analyses of change. Visual analysis of additional

[52] See Extended Results 3.8 for more detail.

variables is also provided, followed by comparative analyses with the PrEliMS-1 study, and additional framework analysis results. Lastly, a synthesis of results is presented, followed by a summary per participant.

3.1 Recruited Participants

Figure 17 provides a graph representation of all participants' (completers and non-completers) progression through the study. Of the ten individuals who were approached about the study by a member of the MS Team, nine consented to screening. The individual who did not consent (X10) was waiting for surgery and therefore did not feel they could prioritise the intervention.

Of the nine individuals who consented to screening and met eligibility criteria, one withdrew following two weeks of the baseline 'A' phase (X01). They had just received a diagnosis of another chronic long term health condition (diabetes) and therefore felt completion of the study would have been too much. They kept the workbook and were signposted to additional sources of support and the MS Team notified.

Eight participants completed the baseline 'A' phase and progressed to starting the intervention. After receiving the workbook, one participant (X07) asked to withdraw during the first session, citing that they did not wish to access emotional support due to fears this may "uncover unwanted feelings". In line with the protocol, they were signposted to additional sources of support and the MS Team notified. Following session one, two further participants withdrew due to difficulties committing to sessions (X04; their working hours as a nurse were variable) and not feeling the intervention was relevant for them (X02). As shown in Figure 17, participant X04 completed outcome measures for week two of the intervention, before then withdrawing.

The remaining five participants completed the intervention 'B' phase, and both 1-week and 1-month follow-up points.

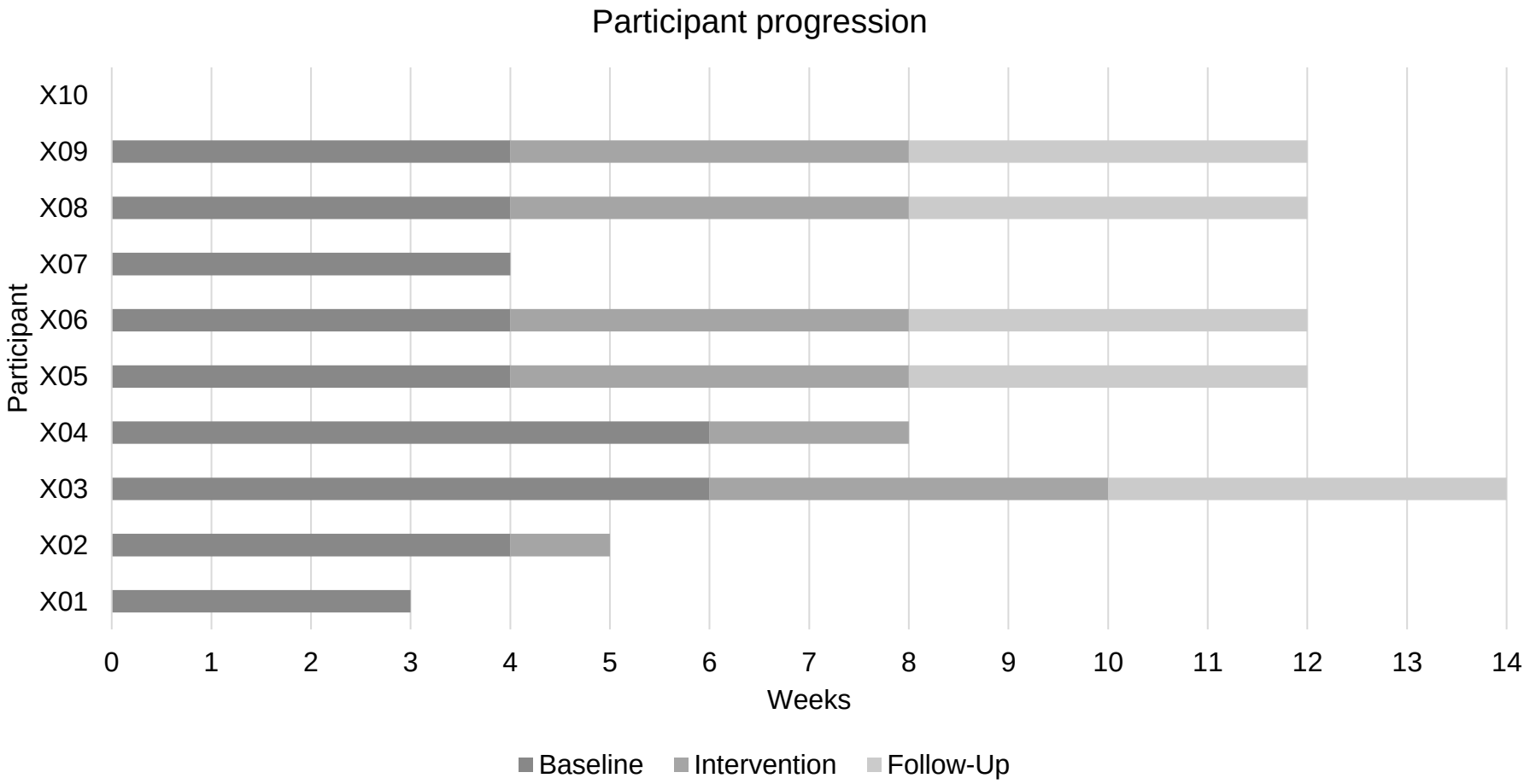
3.1.1 Non-eligible participants

Due to the study being advertised on clinicaltrials.gov, the Lead Researcher (BT) was contacted via email by three individuals (one male, one female and one mother enquiring on behalf of her son) asking to take part. All were not receiving

their MS care as part of the recruiting NHS Trust and therefore were not eligible to take part. All were signposted to the MS Society website and agreed for their email address to be securely stored in the event recruitment would be expanding. Given the required number of participants was achieved, recruitment was not expanded.

Being approached through study advertisement online was not an anticipated recruitment channel. Given the study uses a bibliotherapy format, potentially this could have been made more accessible. However, due to the small sample size required and needing direct contact with their clinical team, the use of one NHS site felt appropriate for the study design and safeguarding considerations.

Figure 17
Progress of All Participants During the Study



3.2 Demographic details

Table 15 below presents the demographic details of the participants (*n* = 4) who withdrew from the study ("non-completers"). Demographic details of the remaining five participants are presented in the short paper and summarised in Table 16.

When considering all nine individuals who were recruited into the study, seven (77.77%) were female. The mean age was 40.56 years (SD = 11.81; range 18-59 years). The average length of time they had been diagnosed with MS at the point of recruitment was 4.44 months (SD = 2.13; range 2-8 months). Three (33.33%) had been diagnosed with MS for 6-months at the point of recruitment to the study. Eight (88.88%) had a diagnosis of relapsing-remitting MS, and one did not know their type of MS. The time to obtain a diagnosis of MS ranged from 1 – 30 months (*M* = 10.67; SD = 8.31). All participants were White British. Five (55.55%) were in full-time employment, however one lost their job part-way through the study due to their MS; 'dismissal due to ill health'. Two participants (22.22%) were in part-time employment. One participant was unable to work due to his MS, one was employed freelance, and one was in full-time education completing a PhD.

Table 15
Demographic Information†

ID	Age (years)	Gender	Ethnicity	Employment	MS Diagnosis duration (months)	Type of MS	Duration to obtain MS diagnosis (months)
X01	44	Female	White (British)	Employed full-time	6	RR	12
X02	38	Female	White (British)	Employed full-time	6	RR	12
X04	38	Female	White (British)	Employed full-time	2	RR	1
X07	53	Female	White (British)	Employed part-time	2	RR	28

Note. ID = Identifier; RR = Relapsing-remitting
†Correct at time of screening

3.2.1 Demographic and clinical characteristic sample comparisons

Table 16 presents a summary of demographic and clinical characteristics across the PrEliMS-1 sample, and completers and non-completers from the current

study sample. The samples are similar in the average age of participants, the weighting of female representation and employment status. The PrEliMS-1 sample has more variation in ethnicity, however shares similarities in that the majority of participants are white. Participants in PrEliMS-1 had notably fewer months diagnosed with MS in comparison, however this difference likely reflects the change in eligibility criteria in the current study. Across samples the most common type of MS is relapsing-remitting, with a few cases of primary-progressive diagnosed in the PrEliMS-1 sample. The time taken to obtain an MS diagnosis was fairly similar across samples, with fewer months observed in the completer sample of the current study.

Importantly, these demographics are somewhat reflective of the wider MS community. MS is more common in females than males, age at diagnosis is most commonly between 36 and 45 years and is relapsing-remitting MS (MS Register, 2023).

Table 16

Comparisons of Demographic and Clinical Characteristics of Samples[†]

Sample	n	Age; years (M [SD])	Gender *n* (%)	Ethnicity; *n* (%)	Employment; *n* (%)	MS Diagnosis duration; months	Type of MS; *n* (%)	Duration to obtain MS diagnosis; months (M [SD])
PrEliMS-1 (das Nair et al., 2023)	40	39.77 [12.2]	Male 12 (30) Female 28 (70)	White 37 (92.5) Black 2 (5) Mixed ethnicity 1 (2.5)	Employed 30 (75) Not employed 8 (20) Voluntary 1 (2.5) Education 1 (2.5)	1.25[†] (M 37 days [18.9][‡])	RR 32 (80) PP 8 (20)	12.6 [13.2][§]
Non-completers	4	43.25 [7.09]	Male 0 Female 4 (100)	White 4 (100)	Employed full-time 3 (75) Employed part-time 1 (25)	4 [2.31]	RR 4 (100)	13.75 [12.01]
Completers	5	38.4 [15.11]	Male 2 (40) Female 3 (60)	White 5 (100)	Unable to work due to MS 1 (20) Employed part-time 1 (20) Employed full-time 1 (20) Education full-time 1 (20) Freelance 1 (20)	4.8 [2.17]	RR 4 (80) Not known 1 (20)	8.2 [3.56]

Note. ID = Identifier; RR = Relapsing-remitting; PP = Primary Progressive

[†]*n* = 39

[‡]study recorded in days. Three outliers or 56, 112 and 730 days.

[§]*n* = 37

3.3 Quantitative data for non-completers

All non-completers provided scores for primary and secondary measures at initial screening. These scores have been used as part of the clinical reference data for analyses on the completed data set[53], and therefore have been presented below in Table 17.

Table 17
Baseline Scores for Primary and Secondary Outcomes

Participant identifier	X01	X02	X04	X07	Mean (SD)
MSIS-Psy	16	20	22	36	23.5 (8.69)
CompACT-8	19	20	25	13	19.25 (4.92)
GAD-7	1	3	11	18	8.25 (7.8)
PHQ-9	7	8	7	8	7.5 (0.58)
PSS-10	12	22	14	26	18.5 (6.61)
MSSES	55	48	62	39	51 (9.83)
EQ-5D-5L	100	80	80	72	83 (11.94)
MFIS-5	10	7	4	8	7.25 (2.5)
Distress attributed to MS diagnosis	7	7	10	10	8.5 (1.73)

Note. MSIS-Psy = Multiple Sclerosis Impact Scale Psychological Subscale; CompACT-8 = Comprehensive Assessment of Acceptance and Commitment Therapy Processes; GAD-7 = Generalised Anxiety Disorder scale; PHQ-9 = Patient Health Questionnaire; PSS-10 = Perceived Stress Scale; MSSES = Multiple Sclerosis Self-Efficacy Scale; EQ-5D-5L = Health Related Quality of Life measure; MFIS-5 = Modified Impact Fatigue Scale

Baselines were completed for four non-completers. In general, when projected into the intervention phase, baseline trends were either stable or improving for all primary measures. This is perhaps in line with reasons for withdrawing from the study. Potentially, people were being referred to the study who did not require support. Notably, for two participants, scores for the PHQ-9 and GAD-7 were on an upward trend, indicating a potential decline in mood. Arguably, this can be understood in the context of their reasons for withdrawal (received another diagnosis of a chronic health condition and another did not want to discuss unwanted feelings). Overall, these differences in trends are in line with trends observed for study completers.

[53] See Extended Results 3.6 for more details on the reference data used.

3.4 Fidelity Checks[54]

A sample of intervention recordings were assessed for therapist adherence to ACT. The measure captures four key areas of ACT consistency: therapist stance, open response style, aware response style, and engaged response style. Five (25%) recordings were selected, representative of all session time-points and all participants, across the intervention delivery. Results on the ACT-FM reveal an average ACT consistency score of 28.6 out of 36, with a median item rating of 3, indicating “therapist consistently enacts ACT-congruent behaviours”.

3.5 Means and standard deviations of measures.

Table 18 provides the means and standard deviations for each primary, process, and secondary outcome measures for the five completers of the study.

Table 18
Descriptive Statistics for Each Outcome Measure (n = 5)

Measure	Mean (SD)			Min	Max	Direction of clinical gain
	Pre-	1-week Post-	1-month Post-			
MSIS-Psy	29.6 (5.22)	22 (6.82)	21.8 (5.89)	9	45	↓
Comp-ACT-8	21 (10.56)	30 (7.94)	30 (3.32)	0	48	↑
GAD-7	7.2 (5.26)	4.6 (3.78)	3.4 (2.88)	0	21	↓
PHQ-9	12.8 (6.98)	7.8 (5.63)	5.8 (3.9)	0	27	↓
PSS-10	22.4 (9.45)	20 (8.4)	18 (6)	0	40	↓
MSSES	40.2 (12.32)	43 (13.56)	43.6 (13.56)	0	84	↑
EQ-5D-5L	52 (17.16)	57 (18.23)	55.8 (22.43)	0	100	↑
MFIS	12.6 (5.13)	11 (3.81)	11.2 (4.66)	0	20	↓
Distress attributed to MS diagnosis	7.4 (2.07)	6 (3.16)	6.4 (3.65)	0	10	↓

Note. MSIS-Psy = Multiple Sclerosis Impact Scale Psychological Subscale; CompACT-8 = Comprehensive Assessment of Acceptance and Commitment Therapy Processes; GAD-7 = Generalised Anxiety Disorder scale; PHQ-9 = Patient Health Questionnaire; PSS-10 = Perceived Stress Scale; MSSES = Multiple Sclerosis Self-Efficacy Scale; EQ-5D-5L = Health Related Quality of Life measure; MFIS-5 = Modified Impact Fatigue Scale

[54] See Appendix M for ACT-FM description and scoring

3.6 Reliable (RCI) and Clinically Significant Change (CSC) calculations

As outlined in the Extended Method, reliable and clinically significant change were calculated on each outcome measure. These were analysed at both 1-week post intervention and 1-month post-intervention, relative to baseline scores. Table 19 provides the clinical and non-clinical data used for these calculations.

Due to the small sample size within this study, use of clinical norms from the MS literature were prioritised where possible. Homogeneity between the RCI reference data used and the current study was prioritised by ensuring baseline scores were within ±2 SD of the clinical population means, and the sample shared similar demographic/clinical characteristics with the current data set. The criterion used for CSC calculation are presented in Table 20. Where clinical cut-offs were used (GAD-7; PHQ-9), these were obtained from MS populations given mean psychological distress values tend to be higher compared to normative functioning in the general population. Where normative data was obtained for CSC calculations, it was checked whether clinical *M*±SD overlaps with normative *M*±SD; if so, criterion C was used, and if not, criterion B. If normative data were not available, criterion A was used (post-intervention score is more than 2SDs from the clinical mean).

3.6.1 MSIS-Psy

Due to a reliability coefficient not being reported within the RCI reference data (Lincoln et al., 2020), this was sourced from a clinical population which shared a similar mean and SD (McGuigan & Hutchinson, 2004). Given the former study had a wider participant sample and recruited pwMS newly diagnosed, this was prioritised for reference data.

3.6.2 CompACT-8

Given the short-form of the CompACT has not yet been used within this clinical population, reference data from the current study were used. Equally, the reliability coefficient taken from the development of the measure (Morris et al., 2019) for the same reason.

3.6.3 PHQ-9 and GAD-7

Initially, data from Proctor et al. (2018) were considered given this study used the same local recruitment channels (MS patients from Nottingham University NHS

Hospitals Trust Neurology Outpatient Clinic) and was completed recently. However, the mean and SD differed compared to this sample (*n* =27; PHQ-9 *M* 21.65 SD 6.52; GAD-7 *M* 17.55 SD 4.9). Therefore, alternative reference data was obtained. This data was from much wider samples of people with MS, predominantly female, as with the current sample, with over half having a diagnosis of relapsing-remitting, with an average age of 51.4 (SD 10.9) years (Terrill et al., 2015) for GAD-7 reference data, and 50.7 (SD 11.6) for PHQ-9 reference data (Amtmann et al., 2012).

3.6.4 PSS-10

Reference data from the PrEliMS-1 would have been preferred however this used the 4-item version rather than the 10-item. As such, reference data similar to the observed mean and SD of the current study were sourced. As this measure is not specific to MS, normative data from a UK population were also obtained, with a similar age range to the current sample and women were represented more within the sample compared to men (Denovan et al., 2017), akin to the current study.

3.6.5 MSSES

Reference data from the PrEliMS-1 study was used given reference data is sparse within the literature. This population was deemed suitably similar to the current study given participants were recruited from the same local service. The mean and SD from the three arms in the trial was combined to produce the reference data used. As the reliability coefficient from the PrEliMS-1 was unavailable, this was sourced from an alternative study (Rigby et al., 2003).

3.6.6 EQ-5D-5L

Data from the CRAMMS (Cognitive Rehabilitation for Attention and Memory in pwMS; Lincoln et al., 2020) trial and the PrEliMS-1 study were both considered. Overall, the CRAMMS trial sample was deemed more representative of the current study as the mean and SD were closer compared to the PrEliMS-1 (*n* = 37; *M* = 68.72; SD 21.87) study. Given a reliability coefficient was not reported, this was obtained from another study for pwMS (Fisk et al., 2005), and was the intra-class correlation coefficient for test re-test reliability as Cronbach's alpha has yet to be explored in the literature. Normative data from a large UK sample (*n* = 5046) with no chronic health conditions were also obtained for CSC analyses (Spronk et al., 2021).

3.6.7 MFIS-5

Despite reference data being taken from a US sample of pwMS (J. Smith et al., 2018), the proposed RCI value from the study was also observed in the current study. Equally, the sample was predominantly female, reporting RR MS and shared a similar average age to the current study. Given this is a short version of the larger scale, normative data is not yet available. Normative data was derived from a US sample (Strober et al., 2020). This used the full MFIS, therefore the M and SD were prorated (divide the original M/SD by 21 [to get item-level mean/SD] then multiplied this by 5 [to get the MFIS-5 equivalent]). Within Strober et al., (2020), the prorated M of the MS sample was comparable to that observed in the current study, therefore prorating the mean was deemed appropriate to obtain non-clinical reference data.

Table 19

Reference Data for RCI and CSC Analyses

Measure	Sample	Population	N	Mean (SD)	Reliability (α)	Clinical cut-off (if available)
MSIS-Psy	Clinical (Lincoln et al., 2020)	MS patients accessing National Health Service Hospitals, MS Register and MS Society, diagnosed within 3 months; UK	430	24 (5.9)		
	Clinical (McGuigan & Hutchinson, 2004)	Community-based sample of adults with MS diagnosis; Republic of Ireland	172	[28.7 (21.3)]	0.90	
CompACT	Clinical (current study)	Participant recruited to current study; UK	9	20.22 (8.11)		
	Non-clinical (Morris et al., 2019)	Non-clinical opportunity sample of adults; UK	377		0.70	
GAD-7	Clinical (Terrill et al., 2015)	MS patients recruited from the National MS society; United States.	513	5.99 (3.12)	0.75	≥8
PHQ-9	Clinical (Amtmann et al., 2012)	MS patients recruited from the National MS Society; United States.	1271	8.3 (6.1)		≥10
	Clinical (Beswick et al., 2022)	MS patients recruited through advertisements, referrals from local Neurology clinics and the MS register; UK.	103		0.89	
PSS-10	Clinical (Wu & Amtmann, 2013)	Participant with self-reported MS recruited through the MS Society; United States	446	14.90 (8.00)	0.91	

Table 19

Reference Data for RCI and CSC Analyses

Measure	Sample	Population	N	Mean (SD)	Reliability (α)	Clinical cut-off (if available)
	Non-clinical (Denovan et al., 2017)	University students in UK	524	19.79 (6.37)		
MSSES	Clinical (das Nair et al., 2023)	MS patients from Nottingham University Hospitals NHS Trust Neurology Outpatient Clinic; UK	37	50.16 (13.39)		
	Clinical (Rigby et al., 2003)	MS patients with a confirmed diagnosis for a minimum of 6 months; UK	142		0.81	
EQ-5D-5L	Clinical (Lincoln et al., 2020)	MS patients accessing National Health Service Hospitals, MS Register and MS Society, diagnosed within 3 months; UK	448	59.75 (20.76)		
	Clinical (Fisk et al., 2005)	Registered MS patients from two healthcare sites; Canada	187		0.81	
	Non-clinical (Spronk et al., 2021)	Adults from the UK general public, invited to complete a web-based survey.	5046	81 (15.7)		
MFIS-5	Clinical (baseline data; Smith et al., 2018)	MS patients participating in a larger study (Bruce et al., 2016), confirmed MS diagnosis by a Neurologist; United States	168	9.91 (5.04)	0.76	

Table 19

Reference Data for RCI and CSC Analyses

Measure	Sample	Population	N	Mean (SD)	Reliability (α)	Clinical cut-off (if available)
	Non-clinical (Strober et al., 2020)	Adults from the United States general population, as part of a wider survey research study.	675	3.64 (2.85)		

Note. MSIS-Psy = Multiple Sclerosis Impact Scale Psychological Subscale; CompACT-8 = Comprehensive Assessment of Acceptance and Commitment Therapy Processes; GAD-7 = Generalised Anxiety Disorder scale; PHQ-9 = Patient Health Questionnaire; PSS-10 = Perceived Stress Scale; MSES = Multiple Sclerosis Self-Efficacy Scale; EQ-5D-5L = Health Related Quality of Life measure; MFIS = Modified Fatigue Impact Scale 5 item version

Table 20

A Summary of the Criterion Used to Inform CSC Calculations

Measure	CSC Criterion used
MSIS-Psy	A
Comp-ACT-8	A
GAD-7	MS population clinical cut-off
PHQ-9	MS population clinical cut-off
PSS-10	C
MSSES	A
EQ-5D-5L	C
MFIS	C

Note. MSIS-Psy = Multiple Sclerosis Impact Scale Psychological Subscale; CompACT-8 = Comprehensive Assessment of Acceptance and Commitment Therapy Processes; GAD-7 = Generalised Anxiety Disorder scale; PHQ-9 = Patient Health Questionnaire; PSS-10 = Perceived Stress Scale; MSES = Multiple Sclerosis Self-Efficacy Scale; EQ-5D-5L = Health Related Quality of Life measure; MFIS = Modified Fatigue Impact Scale 5 item version

3.6.8 Baseline score characteristics

An important contextual factor is whether participants started the current study within a range where change will not necessarily be observed, for example participant three scored close to the specified cut-off score, and maximum score, at baseline. The average baseline score for the GAD-7 was below the clinical cut-off for pwMS (*M* 7.2; SD 5.26). Specifically, three out of five participants scored below clinical cut-off at pre-, 1-week post- and 1-month post- intervention. For two of these participants (P3, P4), scores remained below cut-off for the duration of the study. This was also true of the PHQ-9 and PSS-10 for participant three.

Similarly, considering the suggested cut-off for the MSSES, three (P1, P3, P4) out of five participants were outside of the clinical range at baseline, which was sustained for two participants throughout the duration of the study (P1, P4).

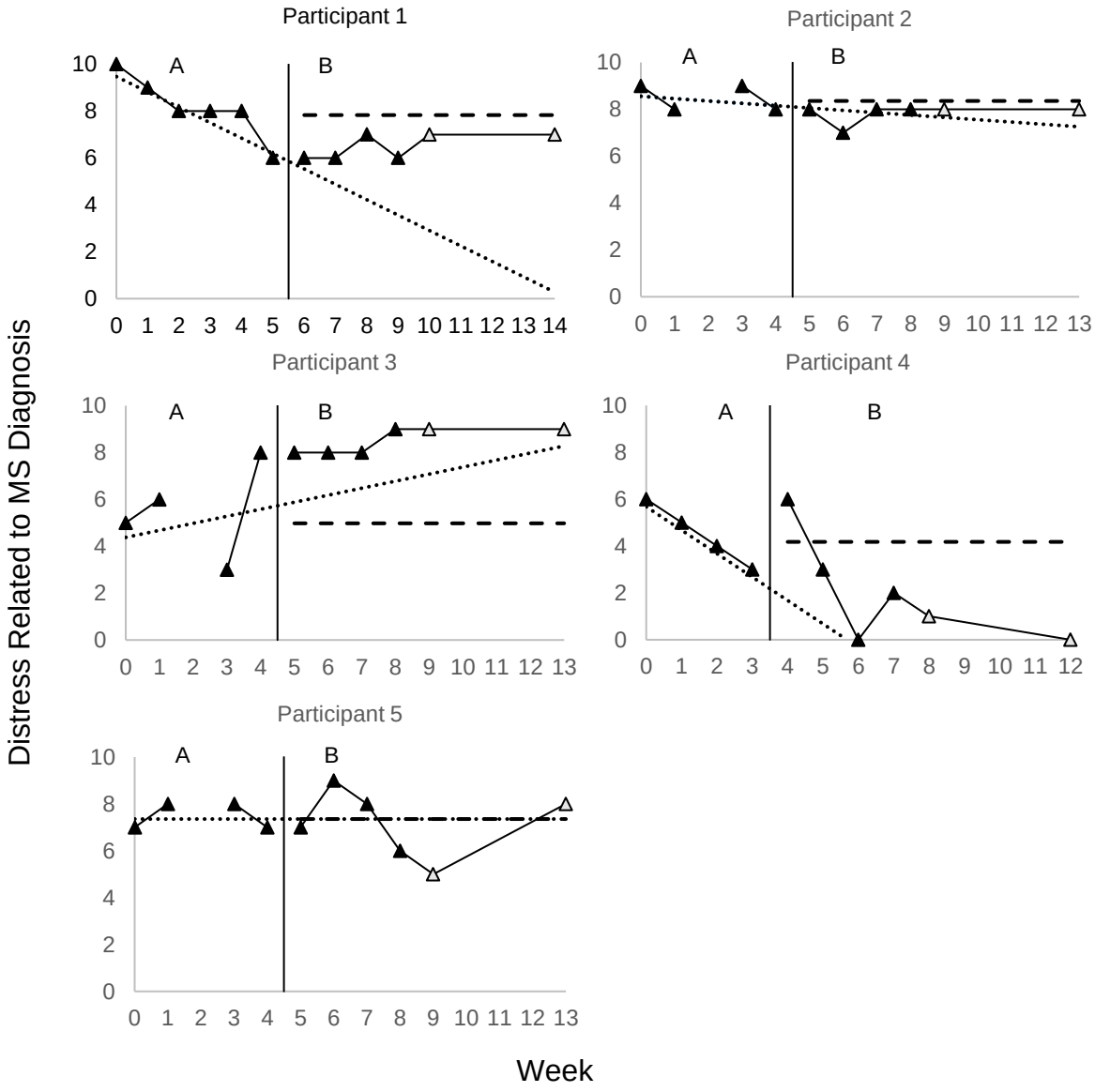
3.7 Visual Analysis

Participant 1 extended baseline due to variability within scores. The journal paper presents the graph plots for the primary and process measures. Graphical representations of additional outcomes (i.e., amount of current distress related to MS) are presented below and commented upon within the journal paper.

3.7.1 Additional distress results

Figure 18

Distress Related to MS for Each Participant During Baseline and Intervention



Note. ·····Projected baseline trend minus .25 SD; – – · Mean baseline score minus .25 SD; —▲— Total Scores; —△— Follow-up point; 'A' denotes baseline phase; 'B' denotes intervention phase including 1-week and 1-month follow-up points; Greater scores indicate greater distress related to MS diagnosis

3.7.2 Additional confidence results

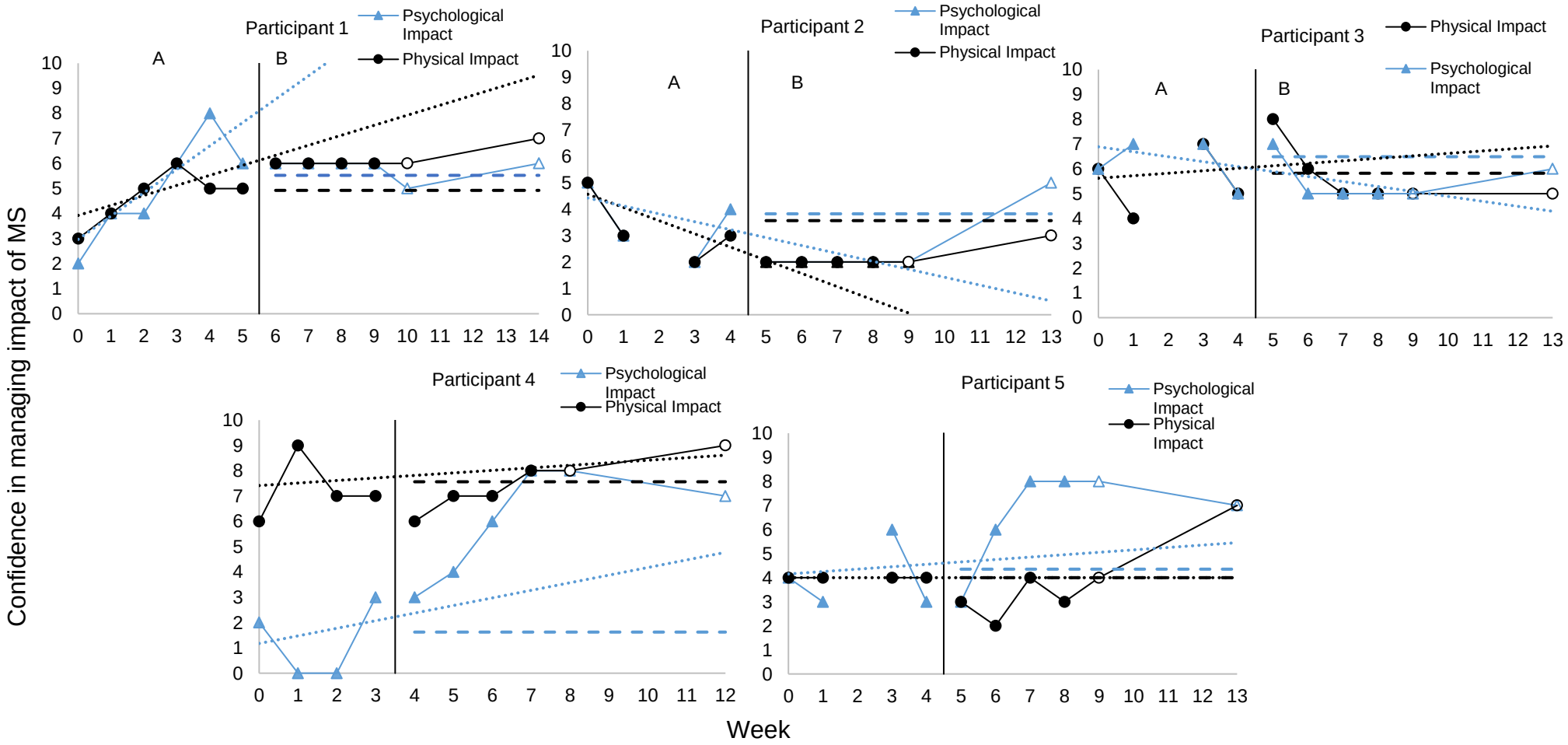
Weekly observations of scores relating to confidence in managing the psychological and physical impact of MS are seen in Figure 19. In applying the dual criterion method, participant four and participant one met the sufficient number of data points above/below the projected mean and trend for psychological impact and physical impact, respectively. Three participants (P2, P3, P5) did not experience a change in either variable according to dual criterion method. Trends were variable across all participants.

Three out of five participants (P1, P3, P4) showed an improving trend through baseline, for confidence in managing the physical impact of MS, which was sustained for two participants (P1, P4). Participant 3 showed an initial worsening trend in the intervention phase which then stabilised; this was also true of their confidence in managing the psychological impact.

Overall, two out of five (P4, P5) participants showed a general increase in confidence in managing the psychological impact of MS. Participant five was one data point below the required to demonstrate a systematic change. Participant 1 had an improving trend within the baseline phase which then stabilised during intervention. For participants 2 and 3, trends were gradually declining during the baseline phase and observed scores in the intervention phase following this trend, before stabilising to a consistent level. Notably, observed follow-up points for participant two generated an upward (improving) trend, which was also reflected by another three (P1, P4, P5) participants for ‘physical impact’ and two (P1, P3) participants for ‘psychological impact’.

Figure 19

Confidence in Managing Physical and Psychological Impact of MS for Each Participant During Baseline and Intervention



Note. ····· Projected psychological impact baseline trend minus .25 SD; ····· Projected physical impact baseline trend minus .25 SD; – – Psychological impact mean baseline score minus .25 SD; – – Physical impact mean baseline score minus .25 SD;

Psychological impact 1-week and 1-month follow-up points **;** —○— Physical impact 1-week and 1-month follow-up points; ‘A’ denotes baseline phase; ‘B’ denotes intervention phase including 1-week and 1-month follow-up points; Greater scores indicate greater confidence in managing the impact of MS

3.8 Additional EQ-5D-5L profiles

Table 21 presents the EQ-5D-5L profiles for each participant. This was administered pre-, 1-week post- and 1-month post- intervention. Profiles are derived from the five subscales: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Participants also completed the Health-Related Quality of Life (HRQoL) Visual Analogue Scale (VAS); the results for which are presented and analysed in Extended Results section 3.5 and the journal results section.

Overall, profiles showed minimal change across the study duration. Mobility and usual activities were the highest scoring subscales, suggesting increased prevalence of difficulties in this area, across the sample. Self-care was the lowest scoring item overall; this relates to the impact physical functioning on self-care.

Table 21
EQ-5D-5L Profiles per Participant

Participant	Time-point	M	SC	UA	PD	AD	HRQoL VAS
1	Pre-	4	3	4	3	3	40
	1 week post-	4	3	4	4	3	40
	1 month post-	3	2	2	3	2	40
2	Pre-	3	1	2	1	3	53
	1 week post-	3	1	3	2	3	50
	1 month post-	3	1	3	1	3	50
3	Pre-	3	2	3	1	1	70
	1 week post-	3	2	3	2	2	65
	1 month post-	3	2	2	1	1	65
4	Pre-	2	1	3	2	2	67
	1 week post-	1	1	2	1	1	85
	1 month post-	1	1	2	1	1	90
5	Pre-	4	3	4	4	3	30
	1 week post-	4	2	3	4	2	45
	1 month post-	4	2	3	3	4	34
Mean (SD)	Pre-	3.2 (0.84)	2 (1)	3.2 (0.85)	2.2 (1.3)	2.4 (0.89)	52 (17.16)

Table 21
EQ-5D-5L Profiles per Participant

Participant	Time-point	M	SC	UA	PD	AD	HRQoL VAS
	1 week post-	3 (1.22)	1.8 (0.85)	3 (0.71)	2.6 (1.34)	2.2 (0.84)	57 (18.23)
	1 month post-	2.8 (1.1)	1.6 (0.55)	2.4 (0.55)	1.8 (1.1)	1.8 (0.84)	55.8 (22.43)

Note. Range of 5-subscales (M = mobility, SC = self-care, UA = usual activities, PD= pain/discomfort, AD = anxiety/depression) is 1 to 5; 1 indicates no difficulties and 5 is the highest level of difficulties present. HRQoL; Health Related Quality of Life. Range of HRQoL is 0 – 100; 0 being the worst health and 100 being the best health.

3.9 Comparison with PrEliMS-1

3.9.1 Percentage achieving RCI and CSC

The journal paper provides a brief summary of the percentage of change observed across the current study and PrEliMS-1 (das Nair et al., 2023). Table 22 presents direct comparison of the changes observed. Notably, three variables differed in the outcome measure used. Where this was the case, the percentage of change observed is presented alongside the outcome measure of the same variable within the comparison study.

Table 22
Comparison of PrEliMS-1 (das Nair et al., 2023) % Achieving RCI/CSC with Current Study

Variable	Study	Outcome Measure	n (%)		
			No change	Improved	Deteriorated
Psychological impact of MS	A	MSIS-Psy	0	5 (100)	0
	B	MSIS-Psy	11 (92)	1 (8)	0
Anxiety	A	GAD-7	4 (80)	1 (1*) (20)	0
	B	HADS anxiety	13 (100)	0	0
Depression	A	PHQ-9	2 (40)	3 (3*) (60)	0
	B	HADS depression	8 (67)	1 (1*) (8)	3 (25)
Stress	A	PSS-10	1 (20)	3 (2*) (60)	1 (1*) (20)

Table 22

Comparison of PrEliMS-1 (das Nair et al., 2023) % Achieving RCI/CSC with Current Study

Variable	Study	Outcome Measure	n (%)		
			No change	Improved	Deteriorated
	B	PSS-4	9 (64)	3 (3*) (21)	2 (14)
Self-efficacy	A	MSSES	1 (20)	3 (3*) (60)	1 (1*) (20)
	B	MSSES	0	5 (42)	7 (58)

Note. Reliable change at $p<0.05$; *Clinically significant change; Study A = current study; Study B = PrEliMS-1 (intervention group 1; MS Nurse Support)

*3.9.2 **Bayesian Standardised Difference Test*** (Crawford & Garthwaite, 2007)

Unlike the outcomes above, the Bayesian calculations can only be computed where outcome measures are the same across the current study and the PrEliMS-1. The principal primary outcome (MSIS-Psy) is the priority for this study and reported within the journal paper. Within this extended section, exploration of the MSSES was also conducted.

The “control group” used was the Intervention 1 (MS Nurse Support) group from the PrEliMS-1 study (n = 13), at baseline and 3-months post-baseline. The latter was the closest time-point to compare 1-week and 1-month post-intervention points of the current study; an average of 2.5-months and 3.7-months post-baseline, respectively.

The results for the MSIS-Psy are presented in Table 23 below. The control sample (n = 13) data used for baseline was M = 21.54 (SD = 5.27), and for 3-months post-baseline was M =20.23 (SD = 7.03), with a correlation between the two of r = 0.719.

Table 24 presents additional comparison results for the MSSES. The control sample (n = 14) data used for baseline was M = 53.86 (SD = 14.22), and for 3-months post-baseline was M = 49.54 (SD = 14.31), with a correlation between the two of r = 0.739. Notably average scores within the control sample had decreased, indicating deterioration in self-efficacy post-intervention.

Table 23
BSDT for MSIS-Psy

	Baseline vs 2.5 months† post-baseline			Baseline vs 3.7 months† post-baseline		
	D	*p*‡	Bayesian point estimate [95% CI]§	*D*	*p*‡	Bayesian point estimate [95% CI]§
Participant 1	11	0.02*	1.22% [0.001% - 83.7%]	7	0.1	4.85% [0.03% - 25.22%]
Participant 2	1	0.56	27.92% [3.12% - 68.14%]	12	0.02*	0.986% [0.001% - 6.616%]
Participant 3	6	0.27	13.16% [2.55% - 32.08%]	7	0.2	9.83% [1.44% - 26.72%]
Participant 4	9	0.14	7.25% [0.75% - 2.11%]	9¶	0.14	7.25% [0.75% - 2.11%]
Participant 5	11	0.04*	1.79% [0.02% - 9.47%]	4	0.33	16.71% [2.19% - 43.65%]

Note. MSIS-Psy = Multiple Sclerosis Impact Scale Psychological subscale. *r* = Correlation coefficient. *D* = raw difference between the two time-points. * = significant $p < 0.05$
†Average time at follow-up points, post-baseline across participants
‡Probability that the standardized difference for a participant in the control group would be greater than the individual case
§percentage of the control population having a more extreme difference, in the same direction
¶same score from 1-week post-intervention, obtained at 1-month post-intervention

Table 24
BSDT for MSSES

	Baseline vs 2.5 months† post-baseline			Baseline vs 3.7 months† post-baseline		
	D	*p*‡	Bayesian point estimate [95% CI]§	*D*	*p*‡	Bayesian point estimate [95% CI]§
Participant 1	3	0.49	24.64% [7.39% - 48.79%]	4	0.44	21.835% [6.06% - 45.08%]
Participant 2	10	0.21	10.27% [0.68% - 33.27%]	8	0.27	13.7% [.19% - 40.33%]
Participant 3	10	0.6	29.78% [11.84% - 52.5%]	15	0.33	16.33% [3.54% - 7.56%]
Participant 4	6	0.34	16.97% [4.3% - 37.24%]	11	0.17	8.32% [0.9% - 4.94%]
Participant 5	5	0.4	19.95% [3.07% - 48.93%]	9	0.23	11.59% [1.11% - 34.21%]

Note. MSSES = Multiple Sclerosis Self-Efficacy Scale. *r* = Correlation coefficient. *D* = raw difference between the two time-points.
* = significant $p < 0.05$
†Average time at follow-up points, post-baseline across participants
‡Probability that the standardized difference for a participant in the control group would be greater than the individual case
§percentage of the control population having a more extreme difference, in the same direction

The short paper provides a summary of the results observed for the MSIS-Psy. For the MSSES, no statistically significant differences were observed when comparing change from baseline to 2.5-months post-baseline, or 3.7-months post-baseline.

3.10 Framework Analysis

Stages one and two of the analysis were fulfilled through transcription of, and listening back to, the audio recordings of the interviews. In stage three of coding, the Lead Researcher (BT), used predominantly deductive coding, in line with the study aims of exploring how the intervention could be improved. This was also supplemented by open coding, to ensure relevant and important aspects of qualitative accounts were not missed, in line with Gale et al. (2013). Coding was reviewed by a research supervisor (AT), and any discrepancies discussed, to promote reliability. Both researchers (BT and AT) also collaborated to develop the categories and codes in the initial analytical framework (stage four; see Table 25). During this process, the research team reflected on ensuring a balance between the frequency of codes vs the importance across the data, through deductive and inductive coding. To organise the data, the following categories were identified: ACT Theory (psychological flexibility and techniques used; Harris, 2019), extra therapeutic factors informed by those acknowledged within Elliott et al. (2002) single case therapy research, aspects specific to the nature of bibliotherapy, and factors relating specifically to experience of MS diagnosis using application of Topcu et al. (2020) adjustment model. This was then reviewed by the research team (Lead researcher, research supervisors and field supervisor), before being applied to the data in stage five. A category of ‘other’ was included to ensure data was not missed. Through this, aspects of ‘future support’ and ‘barriers’ to bibliotherapy were coded and subsequently included in the refined analytical framework.

In stage six, the data was charted into an excel file matrix, by category, for each participant. References to quotes from the data were included and balanced with reducing the data further, to the codes in Table 26. In line with stage seven, the data were interpreted resulting in the themes presented in the short paper. Table 27 presents an extended table of themes and related quotations

Table 25

First Draft of Stage Four Analytical Framework

CODE		DESCRIPTION
Abbrev.	ACT THEORY: Psychological Flexibility (Harris, 2019)	
EA	Experiential acceptance	*Non-judgemental awareness, opening-up to internal and external events, letting go of the struggle*
CD	Cognitive defusion	*Noticing thoughts rather than getting caught up in the content*
PM	Present moment	*Noticing sensory experiences in the present moment*
SaC	Self as context	*Noticing the 'observing self'*
Va	Values	*Defining what's most important, connecting with what matters*
CA	Committed action	*Taking steps towards values, behavioural changes*
	ACT THEORY: ACT techniques (Harris, 2019) (metaphors and exercises; in the book and additional from therapist)	
WE/M	Workbook exercises/metaphors	*Salient metaphors/exercises from the workbook*
AE/M	Additional exercises/metaphors	*Those added by the therapist*
	Extra therapeutic factors (Elliott et al., 2002)	
RF	Relational factors	*Client improved to please therapist, factors relating to therapeutic relationship*
EF	Expectancy factors	*Client's expectation have led to a change*
SC	Self-correction	*Improvement is caused by self-help*
LE	Life events	*Additional events which may have interacted with therapy*
PF	Psychobiological factors	*Changes in medication, changes in illness state, starting new treatment*
RE	Reactive effects	*Of participating in research*
	Bibliotherapy format (mode of delivery)	
UWbk	Using the self-help workbook	*Improvement to be made, helpful aspects, hindering aspects*
POse	Participating in online sessions	*Improvement to be made, helpful aspects, hindering aspects*
	Relationship to MS (adjustment model; Topcu et al. 2020)	
MS ER	Emotional responses	*Negative and positive responses to MS*
MS DP	Diagnostic process	*Impact of the process of obtaining a diagnosis*
MS DL	Daily life	*How MS affects day-to-day life, fatigue, social functioning, cognitive difficulties*
MS PA	Personal attributes	*Individual differences, confidence in managing MS*
MS MT	Management techniques	*Ways of coping with MS*

MS IL	Impact of life	*Quality of relationships and support*
	'OTHER'†	
Oth	Future support / Barriers	*Needs for ongoing support, what would like future support to look like, external events impacting therapy.*

†Added throughout initial application of codes.

Table 26

Stages of Applying the Analytical Framework Using Gale et al. (2013)

Stage 4 Developing the Analytical Framework		Stage 5-6 Applying and Charting the Framework†	Stage 7 Interpreting the Data (Themes)
Categories	Codes		
ACT Theory: Psychological Flexibility (Harris, 2019)	Experiential acceptance Cognitive defusion Present moment Self-as-context Values Committed action	Opened awareness (1) Acceptance (1) MS doesn't define me (1) Mindfulness (1) Values (1) New ways of coping (1) Memorable metaphors (1) Relevance of metaphors (1) Useful exercises (1) Impact of therapist (2) Language improvements (4) Timing of sessions (4) Using the workbook (3) Cognitive difficulties (3) Online sessions (2) Timing after diagnosis (5) Ongoing support needs (5) Emotional labor (5) Social support (5) Lonely (2) Listened to (2) Sharing with others (2)	(1) **Utility of ACT for MS diagnosis** (2) **Value of sessions** (3) **Making use of the workbook** (4) **Suggestions for improvements** (5) **Meeting support needs for MS diagnosis.** Timing; Remaining needs.
ACT Theory: Techniques (Harris 2019)	Workbook exercises/metaphors Additional exercises/metaphors		
Extra therapeutic factors (Elliott, 2002)	Relational factors Expectancy factors Self-correction Life events		
Bibliotherapy format	Using the workbook Online sessions Barriers to intervention		
Relationship to MS (Topcu et al., 2020)	Emotional responses Diagnostic process Daily life Personal attributes Management techniques Impact of life Ongoing support		

†Numbers (1-5) relate to themes in final column

Table 27

Participant Quotes from Feedback Interviews

Theme	Participant 1	Participant 2	Participant 4	Participant 5
Utility of ACT processes and techniques	"It's opened my awareness" (6) "I'm sort of starting to see a pattern on a weekly basis…about the way I'm feeling" (98) "I think the one I always refer back to is the conveyor belt bit [cognitive defusion exercise]…by using that it sort of lessens the effect of those feelings" (88-94)	"squashing things down [emotions] constantly is quite exhausting" (40-41) "it's picked at a scab and it's kind of left it a little bit open…" (14-16) "bits in there that really resonated with me and found useful, so things like thinking about my values, thinking about what's important" (5-7) "the analogies like the ship [sailing boat metaphor] I found that a little bit patronizing" (9-10) "I think the analogies were not helpful for me"(67)	"the conveyor belt was… a much more active way of dealing with it" (14-18) "you know what your values are and how you can kind of live towards them… and then incorporate them in spite of MS issues" (111-113) "I found myself thinking about the sailing boat quite a lot" (158) "talking about that [acceptance] was the bit where the penny dropped" (168-169) "I could give names to what was important. And like [therapist/BT] picked up on, like, humor is just like the cornerstone of my life". (178-180)	"the idea of the water going onto the boat, um that very much struck a chord… there's all sorts going on in my head but I'm pushing them all to one side… but actually that's making me feel worse" (12-14) "like a beachball being held underwater… if you hold this stuff down, its gonna come out and smack you in the face" (25-27) "the breathing exercises… take a minute to just breathe and just be calm" (65-66) "the conveyor belt… it seemed a bit too intricate for my possible thought processes" (114-116)
Value of sessions	"it was good to have someone to talk to that	"it's nice to see a human being and kind of talk	"I don't now anyone else with MS" (27)	"[therapist/BT] is incredibly

Table 27

Participant Quotes from Feedback Interviews

Theme	Participant 1	Participant 2	Participant 4	Participant 5
	understands where you're at and what it's like… it makes you feel like you just not er- there's somebody there who knows and understands it and it makes it easier to talk about" (48-50) "before I took this on I felt quite alone… it's surprising how many people don't really know what MS is" (143-147) "the biggest thing for me is having someone totally independent you can really off load to (275)	about what you've just unpacked" (171) "she [therapist/BT] did add extra bits and obviously would be able to talk about different things as well" (178-179)	"the very first session was quite emotionally fraught" (41) "Time to talk to someone who knows about the condition but who isn't family" (205-206) "it's nice to talk to someone and kind of bounce some ideas around" (85) "non-judgmental supportive structure was so important" (209)	knowledgeable… it's the calm attitude and not afraid to listen. If we start going off topic, that didn't matter" (82-83)
Making use of the workbook	"because you know you're going to be talking to somebody about it… you focus more on the workbook" (24-25) "there was nothing about it I didn't really like. The workbook was easy to follow, very clear, it wasn't complicated in any way" (73-74)	"a good breadth of things in there [workbook] to kind of tailor how you wanted to use it as well" (209-210) "I think if you had just given me the booklet I might have been really sad and quite lonely" (174)	"had I just been handed the workbook is quite easy to kind of maybe get lost or feel unsupported…. I think having to do the two in tandem is is the only way that it's gonna work" (260-262) "we kind of cherry-picked a little bit having	"if you'd have just sent the workbook… it would never have come out of the packed… talking to someone alongside it brought everything together" (91-93) "It very much was a case of when things are being read to me,

Table 27

Participant Quotes from Feedback Interviews

Theme	Participant 1	Participant 2	Participant 4	Participant 5
			a read through it, but I think that went quite well" (99-100) "having everything sort of strategy-wise written down, so I could do it in my own time rather than just talking about it, that was really helpful" (146-147)	you could see exactly what was going on in the book, it was very easy to follow the flow of the book and everything else, perfect" (139-140)
Suggestions for improvements	"I suppose that I could talk to [therapist/BT] longer, then yeah, go longer" (34) "I can't think of anything that cries out that you would need to change" (109)	"a little more time would be beneficial, maybe a couple of weeks [in between sessions]" (22-25) "that [values exercise] might have been easier to do earlier on" (90) "it felt too young... like it was almost written for a child… I can imagine reading that as part of a bed time story" (246 – 254) "sometimes the sessions would overrun… we needed more time" (218)	"we arrived at the values section, I think week three… I think doing it at session two might have been a more logical way" (101-102) "none of that [exercises, layout, readability] needs to change" (201) "four [sessions] seems quite a small number… would you do six? Actually it might not work quite well with the workbook… the number of [workbook] sections	"there were two analogies [sky and the weather; beachball] that [therapist/BT] used that weren't in the book, but… I think they probably should be" (21-22) "four [sessions] is probably minimum… maybe five or six would have been about right" (152-154)

Table 27

Participant Quotes from Feedback Interviews

Theme		Participant 1	Participant 2	Participant 4	Participant 5
				is still quite good" (218-219)	
Meeting support needs around MS diagnosis	Getting the timing right	"it came at the right time… gave me the opportunity for, in that gap, before talking with [therapist/BT], an understanding of what I was now dealing with" (297-298) "I would say about three or four weeks [after diagnosis]" (308)	"where it's come for me has been good… when I was first diagnosed I was offered different things of support and I know of feel like those bits have come to an end" (147-148)	"it came at a great time because I'd been able to kind of look after myself, get back to work… then you're just left with the emotional side" (72-73) "If I had known when I came to hospital that it was there, I would have parked it and then gone back to it when I was ready" (74-75)	"sooner would have absolutely been more helpful… me personally, probably pretty much straight away [after diagnosis]" (51-54)
	Remaining support needs	---	"I've let it out [emotion] and it's kind of hard to put the lid back on" (17) "there's a lot of unpacking that you start to do… it feels like it's laid out. It needs to be folded up a little bit, maybe stack neatly" (24-25)	"ongoing support or top-up of sessions or monthly sessions might be a helpful offering, because I think that's the thing now like it's a bit of an unknown, where do we go from here" (223-224) "I feel like a group might be the way forward… having that kind of	"I've got a decent network of friends… . I've got a podcast that I do where I will just sit and talk and get things out, and OK I'm not talking to anyone in particular, but I'm talking" (174-176) "I've been having real issues with regards to work… considering

Table 27

Participant Quotes from Feedback Interviews

Theme	Participant 1	Participant 2	Participant 4	Participant 5
			space and then learning from other people feels like the kind of next step speaking to other people on what they do and how they deal with it would be really helpful" (233-238)	dismissal due to ill health" (239-240)

Note. Dashes indicate no appropriate quotation.

3.11 Overall Synthesis

Taking into consideration the results collectively, a synthesis of the findings can be suggested. All participants experienced reliable improvement in the primary outcome of the psychological impact of MS, however none of this change was of clinical significance. In comparison to the PrEliMS-1 study, difference across baseline to 3-months post-baseline was statistically significant for one participant (P2). Equally, three participants demonstrated systematic change, in the direction of improvement, according to dual criterion method, suggesting an effect on MSIS-Psy scores. Regarding the remaining two primary outcomes, only one participant demonstrated clinical improvement in anxiety. Notably, three (P2, P3, P4) participants entered the study below clinical cut-off. Depression improved for three participants (P1, P2, P4) which achieved clinical significance. The remaining two participants either did not start at a clinical level (P3), or scores did not decrease enough to below cut-off (P5).

Where improvements on depression were observed, this corroborated with improvements in psychological flexibility (P1, P4). Equally, improvements were also seen in perceived stress for these participants, except for one other change in stress, which was a deterioration (P3). This observed deterioration was seen in self-efficacy for the same participant, suggestive of a relation between these outcomes. Self-efficacy did improve for three participants (P2, P4, P5), which also related to observed improvements in weekly measures of confidence in managing the psychological and physical impact of MS. In comparison to the PrEliMS-1 study, the change observed on the MSSES was not significantly different, however PrEliMS-1 observed a deterioration rather than improvements.

Distress related to MS varied largely between participants and visual analysis demonstrated this fluctuated significantly. Where baseline scores relating to distress where high, as was scores on this variable. Only two out of five participants experienced a large decrease in scores at the end of the intervention phase. Interestingly, these two participants experienced the most changes across all outcomes (P1; five changes, P4; six changes).

Qualitative feedback revealed two participants would have liked ongoing support. One of these participants demonstrated change on six outcomes, whereas other had

change on only two outcomes. Equally, both participants had significant improvements in self-efficacy related to MS. Collectively, this suggests ongoing support needs may not be relative level of current difficulties or self-efficacy.

Regarding the intervention, the wording and use of metaphors in the workbook was seen as a hindering factor by one participant, however another identified the metaphors (capturing defusion, acceptance and self-as-context) as a significant driver of change. Recommendations included moving the values section to sooner in the intervention, as this was identified by the majority of participants to be one of the most significant parts of the intervention, alongside 1:1 support with someone who understands MS.

3.12 Summary results for each participant

3.12.1 Participant one

Participant One (P1) demonstrated reliable improvement in the psychological impact of MS, psychological flexibility, anxiety, depression, and perceived stress. Further, three of these outcomes reached change which was of clinical significance: anxiety, depression, and perceived stress. Equally, visual analysis demonstrated change was systematic for the psychological impact of MS. At 1-week post-intervention, this was significantly different compared to the PrEliMS-1 group at 3-months post-baseline. Notably, both depression and anxiety outcomes were also improving during baseline (i.e., on a downward trend) and appeared to stabilise during the intervention phase, at a level below cut-off.

Psychological flexibility was also improving during the baseline phase. This was more variable during intervention, with a dip during the final two weeks of the intervention. This then returned closer to the average score in the final two data points, post-intervention suggesting change was sustained up to a month after finishing the intervention. Qualitative data demonstrated that P1 had found the intervention helpful in increasing his awareness of the impact of MS. Equally, participant one also found value in the therapeutic relationship formed through the intervention. During the feedback interview, P1 also discussed joining an MS support group during the intervention phase which had a positive impact on feeling less alone in his experience of MS.

During week three, P1 did experience an increase in anxiety and depression scores; exploration within the qualitative interview revealed that P1 had attributed this to an increase in fatigue due to the MS. This was also demonstrated in an increase in scores that week of how much distress is related to MS. There was no reliable change observed for Health-Related Quality of Life (HRQoL), fatigue or self-efficacy in relation to MS. Notably, weekly scores relating to confidence in managing the physical and psychological impact of MS were on an increasing trend during the baseline phase. These stabilised during the intervention and increased slightly post-intervention. HRQoL subscales were highest for 'mobility' and 'usual activities'; the latter decreased slightly at 1-month post-intervention.

3.12.2 Participant Two

Reliable change was observed in three outcomes for Participant Two (P2); psychological impact of MS, depression and self-efficacy relating to MS. The latter two were also of clinical significance. Further, the difference observed in the MSIS-Psy was significant compared to the PrEliMS-1 group. Weekly scores of confidences in managing MS were on a declining trend during baseline, however stabilised during intervention and then increased 1-month post intervention, which may relate to self-efficacy. Anxiety and depression scores did increase during week two; this corresponded with P2 telling her workplace about her MS and her children returning back to school after an enjoyable half-term holiday. Notably, anxiety remained below clinical cut-off pre- and post-intervention, and only went above cut-off at two points during baseline and one point during intervention.

Visual analysis revealed that the psychological impact of MS was decreasing during the baseline phase. Scores during the intervention phase were more variable, with week three and 1-month post intervention, demonstrating change beyond the projected trend and mean. Psychological flexibility remained relatively stable through the baseline and intervention phases, however increased 1-month post-intervention. A similar pattern was also observed in anxiety and depression scores. Potentially, this alludes to something salient within the 1-month follow-up period e.g., withdrawal of the intervention, and/or more time to consolidate learning. Interestingly, distress related to MS remained at the same level post-intervention. Given other outcomes relating to distress had decreased, this may suggest that whilst the level of distress

was the same, P2 had developed skills in coping with the distress, to lessen its impact. No change was observed in HRQoL or fatigue; subscales pertaining to HRQoL were highest for ‘mobility’ and ‘anxiety/depression’.

Qualitative feedback obtained revealed that P2 struggled with the wording of the workbook as “patronising”. Also, she described the intervention as opening up her experience of MS, which she acknowledged needed to happen, however had left her feeling as though this needed to be “packed away” again. Subsequently, they were referred to local psychological support services (e.g., Improving Access to Psychological Therapies [IAPT]).

3.12.3 Participant Three

Reliable change was observed in only one of the primary outcomes: psychological impact of MS. The process measure of psychological flexibility remained high through the duration of the study, and above the adjusted baseline trend during intervention. Both anxiety and depression scores remained below clinical cut-off for the duration of the study. Collectively, these findings suggest the level of change anticipated would be low, given Participant Three (P3) entered the study within the well-functioning ranges on three out of four primary outcomes.

Regarding secondary outcomes, P3 experienced reliable and clinically significant deterioration in two secondary outcomes: perceived stress and self-efficacy relating to MS. This was also reflected in weekly scores of confidences pertaining to the management of psychological and physical impact of MS; scores decreased and stabilised at a level below the projected trends, during intervention phase. Also, distress related to MS increased the week before starting intervention and then remained at this level during the intervention phase. No change was observed in HRQoL or fatigue; ‘mobility’ was the highest scoring subscale for factors of HRQoL. Qualitative feedback was not obtained from P3 as they declined to take part in an interview.

3.12.4 Participant Four

Participant Four (P4) demonstrated reliable change in psychological impact of MS and depression, with the latter a clinically significant change. Equally, change was also observed in psychological flexibility, which was of clinical significance and

sustained at 1-month follow-up. At screening, anxiety was below clinical cut-off and remained at this level for the duration of the study, limiting the observed level of change for clinical gain.

For secondary outcomes, perceived stress and self-efficacy related to MS were reliable and clinically significant improvements. Notably, visual analysis of scores relating to confidence in managing MS showed an increase during the intervention; confidence pertaining to physical impact increased further at 1-month follow-up however psychological-impact scores decreased slightly at this time-point. Distress relating to MS had decreased to the lowest level at 1-month post-intervention. Levels of fatigue also demonstrated reliable improvement. No change was observed for HRQoL. Ability to do 'usual activities' was the highest scoring subscale of HRQoL.

Qualitative feedback revealed that P4 particularly found the implementation of value-guided behaviour important in the intervention and would have preferred this earlier on. Despite the changes observed, P4 revealed that she felt ongoing support was needed and post-intervention felt "an unknown"; it was considered this could either be further 1:1 support, but a preference for an MS group to then learn from others.

3.12.5 Participant Five

Participant Five (P5) demonstrated reliable change in the psychological impact of MS. This difference from baseline was significant in comparison to the PrEliMS-1 sample when looking at 1-week post-intervention. The remining primary outcomes of anxiety and depression decreased slightly but this was not a reliable change, and both remained within the clinical range at 1-month post-intervention. Regarding the process measure, psychological flexibility did increase, although not to a reliable level. Visual analysis revealed this was a gradual change; equally with anxiety and depression. Notably, scores appeared anomalous in week three of the intervention. Qualitative findings revealed this was due to losing his job because of MS.

In terms of secondary outcomes, there was a reliable change in stress at 1-month post-intervention, as with self-efficacy which was also clinically significant. Corroborating with those findings, confidence in managing MS also increased over

the course of the intervention. Distress relating to MS decreased during the intervention, however returned to baseline level at 1-month post intervention. No change in HRQoL or fatigue was observed. Subscales of HRQoL revealed areas of difficulty to be ‘mobility’, and ‘usual activities’.

Qualitative feedback identified additional positive factors of a close support network. Mindfulness and defusion techniques were identified as most useful from the sessions, as well as the combination of sessions with the workbook. A preference for six rather than four session was shared.

4 Extended Discussion and Reflection

The extended discussion will elaborate further on contextualisation of findings in the journal paper, and comment on theoretical and clinical implications. Additional strengths and limitations will be presented, followed by recommendations for future research. At the end of this section is a critical reflection on some of the scientific, ethical, and theoretical issues raised during the research process.

4.1 Improving the psychological impact of MS

Collectively, replications of an effect in three cases, reliable improvements across all participants and qualitative feedback, suggest the psychological impact of MS improved as a result of the intervention. Replicating demonstrations of an effect in three participants supports external validity and is sufficient, at acceptable power levels (80%), to infer a relationship whilst minimising the false positive rate ($p < .05$) (Lanovaz & Turgeon, 2020). The level of psychological distress participants attributed to their MS was a more unclear. Overall, this appeared to stabilise during the intervention period, but at varying levels. From an ACT perspective, we may anticipate this outcome to decline in line with the MSIS-Psy, as participants develop skills in managing distress that shows up. Although, distress attributed to MS may conversely increase as participants open-up to, and accept, emotional responses to MS diagnosis.

Although ACT does not target symptom reduction, symptoms can reduce as they are viewed from an alternative perspective (Bennett & Oliver, 2019). Equally, markers of psychological distress, such as symptoms of anxiety and depression, are

frequently experienced around the point of MS diagnosis (Conradsson et al., 2018). Thus, inclusion of distress-related outcomes was important. This study observed some clinically significant improvements in anxiety and depression, although systematic change in visual analyses was absent for both anxiety and depression. Similar interventions also have mixed findings for improvements in anxiety (Pakenham & Landi, 2023; Proctor et al., 2018) and depression (Giovannetti et al., 2020; Zarotti et al., 2023), with other studies reporting minimal changes (Meek et al., 2021). Improvements observed were those presenting within clinical levels pre-intervention, apart from one who remained at this level, despite improvements in scores. It could be suggested that this intervention is effective for those presenting with high psychological distress. This supports previous research in that acceptance-focused coping styles predict lower levels of anxiety and depression (Pakenham, 2007).

It is important to note that two participants (40%) presented with clinically significant anxiety symptoms at baseline, and four (80%) relative to depression symptoms. This differed from recent literature investigating an ACT intervention for pwMS (Pakenham & Landi, 2023), noting only a quarter (23.64%) of participants were above clinical cut-off for anxiety, depression and/or stress. Subsequently, the small sample size within this study may have reduced generalisability. Furthermore, an important consideration here is the role of help-seeking in those with high levels of psychological distress and whether this impacts on engagement. It could be implied those not accessing the intervention felt adequately resourced and not in need of support. As such, clinical implications may include consideration of the framing of ACT-based intervention, to target those who would also benefit, however are not highly distressed. However, looking at data for non-completers, this hypothesis falls short as two out of four potential participants were above clinical cut-off for anxiety yet declined the intervention. Potentially, the offering of support would benefit from targeting avoidance of presenting distress, as well as an intervention to support ‘living well with MS’.

4.1.1 Process Outcome: Psychological Flexibility

ACT primarily targets psychological flexibility; therefore, this was included as a process measure. We hypothesised psychological flexibility would increase, thus also improving the psychological impact of MS, as the literature suggests this

mediates impact on psychological distress-related outcomes (e.g., anxiety, depression, and stress; Pakenham 2018). Further, psychological flexibility has been proposed to buffer the impact of life stressors (Gloster et al., 2017). Although improvements were observed, this was lower than expected and is arguably inconsistent with these hypotheses. Notably, similar findings have been demonstrated, where only small, nonsignificant effect on psychological flexibility was found in ACT interventions for pwMS (Thompson et al., 2022). Conversely, when looking at the evidence base for chronic, long-term conditions, small-to-moderate (*d* = 0.57-0.72) effect sizes on psychological flexibility have been reported (Graham, Gouick, Ferreira, et al., 2016). These findings have also been replicated within the wider general population (Gloster et al., 2017). The inconsistencies of our findings with the wider evidence-base for ACT, yet not for ACT with pwMS, suggests there may be additional interacting factors in pwMS effecting change in psychological flexibility. For example, baseline levels of psychological flexibility in individuals newly diagnosed with MS (e.g., higher rates of avoidant coping styles) may differ from the general population who do not have MS. A lack of normative data for the CompACT-8 means comparative conclusions are difficult to draw, however. This also potentially hindered RCI and CSC analyses as reference data from our own sample of nine was used, as opposed to comparing with another clinical or non-clinical population.

Further theoretical implications of these findings are discussed in the extended discussion section 4.4.

4.2 Additional secondary outcome findings

PrEliMS-1 findings suggested the MSSES was not appropriate for future testing (das Nair et al., 2023), however we observed no missing data for this measure and changes in self-efficacy as a result of the intervention were evident. To mitigate any anticipated difficulties, confidence in managing the physical and psychological impact of MS was also captured weekly, through VAS. Systematic change was minimal, which may reflect the variable nature of MS symptom management day-to-day. Where systematic change was observed for confidence in managing the psychological impact, significant improvement was also seen in the MSSES, supporting the utility of the VAS in capturing the trajectory.

The lack of change observed on the EQ-5D-5L contrasted previous findings of a moderate effect observed in within-group analyses PrEliMS-1 (das Nair et al., 2023). Notably, confidence intervals within PrEliMS-1 were wide ranging and we also had stringent criteria within the RCI and CSC analyses (RC min change: 25.08, CSC cut-off: >78.43). The average HRQoL scores within the non-clinical sample (Spronk et al., 2021) are higher than the MS sample used (Lincoln et al., 2020), indicating the MS population likely experience lower HRQoL at baseline. Subsequently, the level of change anticipated as a result of a four-session intervention is questionable; particularly given the progressive and debilitating nature of many physical symptoms of MS. The EQ-5D-5L was selected to replicate the HRQoL measure in PrEliMS-1. However, four out of the five items (mobility, self-care, usual activities, pain/discomfort), are arguably not sensitive to an ACT-based intervention; minimal change was observed on an individual item level. Similar interventions have also observed minimal change where the EQ-5D-5L was used (das Nair et al., 2023; Meek et al., 2021; Proctor et al., 2018). ACT is targeting *acceptance* of physical health, rather than physical symptom change which may explain why minimal change was observed in our findings. This is an important implication for research in proposing a move away from exploring physical health QoL measures as a mechanism for change in ACT interventions.

4.3 Additional comparisons with PrEliMS-1

Direct comparison with the original PrEliMS is limited given the difference in sample size however applying the BSDT in analyses aimed to mitigate such differences. This test compares on an individual case level, where the same outcome measures were used. Results for the MSIS-Psy and MSSES suggest minimal difference was observed relative to PrEliMS-1. However, when considering percentage of improvements, findings indicate PrEliMS-2 generated more positive outcomes, across all variables, compared to PrEliMS-1. One hypothesis for this difference may be that a TCP-facilitator places reduced emphasis on medication within interventions, which was an issue raised in nurse-led support in PrEliMS-1 (das Nair et al., 2023). Further, having a therapist independent from usual MS care, where emotional difficulties could be discussed, was valued by participants in qualitative feedback. Potentially these findings support national recommendations for access to psychologists within the MDT, as part of ongoing diagnostic care for pwMS

(NICE, 2022). However, this implication for clinical practice is tentative given there were a number of differences between PrEliMS 1 and 2, beyond a change in facilitator, including variations in outcome measures, format of sessions, and eligibility criteria.

Another large difference was the increase in sessions offered with the facilitator in PrEliMS-2. Similar bibliotherapy and teletherapy research has emphasised contact with a therapist as important for maintaining motivation, equally a higher level of clinician guidance has been demonstrated to improve distress-related outcomes (French et al., 2017; Harrison et al., 2017). This may explain why comparative results are in favour of PrEliMS-2, and equally support a clinical implication of longer and/or more frequent sessions, as discussed in section 4.5.

4.4 Theoretical Implications

Psychological flexibility has consistently been positioned as a mediator of positive intervention outcomes (e.g., improvements in resilience, anxiety, depression, stress and HRQoL) (Giovannetti et al., 2020; Pakenham et al., 2018). Where positive change was observed in the psychological impact of MS, depression symptoms and stress, improvements were also observed in psychological flexibility. This provides some support for this notion; however, generalisability is limited due to the small sample. Equally, improvements were also seen in outcomes, in the absence of psychological flexibility, presenting some incongruence with the theoretical underpinnings of ACT mechanisms of change. Thus, this warrants further consideration of specifically, (i) how well was psychological flexibility measured and (ii) was this targeted by the intervention.

For the former, the journal paper suggests reduced sensitivity in the outcome measure used: CompACT-8. Notably, where similar interventions have demonstrated efficacy in improving psychological flexibility in pwMS, alternative measures of psychological flexibility have been used, such as the AAQ-II or the Multidimensional Psychological Flexibility Inventory (Nordin & Rorsman, 2012; Pakenham et al., 2018; Pakenham & Landi, 2023). Potentially this highlights the CompACT may warrant further testing in the applicability to the MS population as Meek et al., (2021) also reported minimal change on the full-item version.

The latter question raised about the target of the intervention is more challenging to discern as our findings are based on a small sample, and PrEliMS-1 did not use a psychological flexibility outcome measure. One explanation may be that the intervention served as a vehicle for common therapeutic factors (e.g., therapeutic alliance, managing expectations and goals and specific factors like expressing difficult emotions; Wampold, 2015), which may have mediated positive outcomes. In support of this explanation, qualitative feedback highlighted the value of engaging with a “human being” and the emphasis on a psychological focus. Although, separation of factors responsible for change is challenging due to the complexity of interacting factors in therapy (Tschacher et al., 2014).

Furthermore, this was a short-term intervention of only four sessions that took a person-centred focus (i.e., time spent on modules was based predominantly on participant preference). Pakenham and Landi (2023) found psychological flexibility increased as the length of time engaging with the intervention increased. Thus, it is plausible to suggest longer may be needed to consolidate learning and apply strategies day-to-day, as well as ensuring adequate targeting of all six psychological flexibility processes. The same reflection was also suggested by Meek et al. (2021) within testing of a six-week bibliotherapy ACT intervention for pwMS.

Another important finding is the change observed in self-efficacy. Clinically significant improvement was observed in three out of five participants. This outcome was captured within the PrEliMS studies as relevant adjustment models highlight the importance of promoting self-efficacy to improvement adjustment to illness (Gracey et al., 2009; Topcu et al., 2020). Specifically, Gracey et al. (2009) postulates this can be improved through identification of pre-illness/injury values and engaging in behavioural change (i.e., behavioural experiments to develop and consolidate new meanings). This is in line with the behavioural underpinnings of ACT and provides support for the utility of ACT within the context of adjusting to MS diagnosis. Potentially an increase in value-driven behaviours promotes an increase in the perceived control and/or confidence in managing the impact of MS diagnosis. It is also important to consider PrEliMS may be targeting improvement in adjustment related factors, rather than psychological flexibility. However, in theory many of these factors (e.g., anxiety, perceived ability to cope) are mediated by psychological flexibility, so we would expect to see an increase in psychological flexibility also.

Previous findings within chronic pain found ACT intervention increased perceived control over pain, which drove reduction in the impact of pain, rather than acceptance (Wetherell et al., 2011). Interestingly, similar may be observed in our study, as behavioural changes may have influenced perceived control over MS, potentially driving reduction in the psychological impact, rather than increase psychological flexibility.

4.5 Implications for Clinical Practice

Our findings provide preliminary support for the use of ACT-based interventions around the point of MS diagnosis, in improving the psychological impact of MS. To further strengthen this, our study has highlighted several implications for clinical practice. These relate to components of the intervention which participants deemed important for future refinement and delivery.

A common finding within the qualitative data was the use of the workbook in minimising cognitive load i.e., this prompted memory of what was discussed and could be referred back to. Other participants also felt the therapist was enough within the intervention. This arguably reflects the heterogeneity within the MS population and highlights an important clinical implication of flexibility in the type of support offered, to meet varying needs. This supports findings from Pinto et al. (2022) in recommends of tailoring support content and format to individual preferences, in light of physical and cognitive symptoms. As such, it may be that a bibliotherapy format is offered, along with options for telephone support calls and/or peer support (as in PrEliMS-1). A group setting was also recommended by one participant, as provision of ‘top-up’ sessions following the PrEliMS-2 intervention. This is a noteworthy implication for clinical care as peer support for pwMS has been positively received (das Nair et al., 2023) and multiple patients could access support at one time, somewhat alleviating service pressures. This is in line with needs identified directly with stakeholders in the initial consultation process of developing PrEliMS (Tindall et al., 2023).

Qualitative feedback also revealed a preference for longer and/or more sessions. This appeared to relate specifically to needing more time at the beginning of the intervention within the ACT pillar of ‘opening-up’ to difficult emotional reactions. This was anticipated given avoidance of discussing diagnosis is a

commonly identified coping strategy within the literature (Dennison et al., 2011). Conversely, participants suggested that values-based discussion felt most logical to occur at the start of the intervention, potentially indicating this was better tolerated than the process of opening-up. On a theoretical level, values represent verbal relational networks which can alter whether consequences of behaviour are reinforcing or punishing. This arguably generates a broader sense of self which is less focused on current processes and can respond flexibly (McHugh et al., 2019). Values are one aspect of the six factors in psychological flexibility and within the literature are typically presented towards the end of ACT-model descriptions e.g., are the last pillar of ACT. Nevertheless, these six factors are not targeted in a linear way (Harris, 2019), nor was PrEliMS designed as such.

Within clinical practice and future PrEliMS testing, introducing values sooner may serve to initially ground individuals in what is meaningful for them. This compliments the 'Y-model' of adjustment in addressing personal discrepancies between current self and hoped-for-self, by putting individuals in contact with pre-illness values (Gracey et al., 2009). This may promote acceptability of the therapeutic model, and support individuals with understanding of why experiential avoidance and cognitive fusion strategies may be needed i.e., are currently obstacles in the way of committed value-based action.

4.6 Extended strengths

The design of this study enabled repeated measurement of outcomes, during both a baseline and intervention period. Given the methodological quality of the current evidence-base for ACT interventions, Gloster et al. (2020) recommends studying trajectories of change over time, alongside capturing mechanisms of change in parallel; both of which have been met by this study.

Of the participants who completed the study, we observed no attrition, missing data or missed sessions. All phases were completed within the anticipated time-frames suggested in the protocol, with the exception of a 1-week break in baseline for two participants, due to the lead researcher being absent. This suggests the MSCED was a feasible design, with appropriate timepoints for completion of outcome measures. This also meant that criteria of a minimum of three data points within a phase, to qualify as an attempt to demonstrate an effect, was adequately

met (Kratochwill et al., 2010). Potentially, providing the option to complete questionnaires online was important in maintaining 100% response rates. The lead researcher also sent weekly email reminders to participants, in between sessions, which could also be attributed to this strength. Further, as discussed in the journal paper, building therapeutic relationships with participants may have contributed to high retention rates. Qualitative data highlighted the importance of contact with someone outside of their usual MS care, and who provided a non-judgemental supportive stance. As such, high retention rates may infer the importance of this kind of supportive for people newly diagnosed with MS.

Secondly, the current study included a measure of psychological flexibility which is the primary target within ACT approaches; a measure which was lacking in PrEliMS-1. Although change observed in psychological flexibility was not as high as expected, this raised important questions about whether PrEliMS is targeting psychological flexibility, or whether the measure used (CompACT-8) is sensitive to capturing systematic change in psychological flexibility for pwMS.

Additional strengths include assessment of fidelity to an ACT therapeutic stance, using a standardised measure (ACT-FM). This also included access to regular supervision by two psychologists experienced in using ACT. To improve credibility of ACT interventions within the MS literature, this is in line with previous research recommendations (Thompson et al., 2022). In addition, gaining qualitative feedback was another strength as this allowed a more in-depth understanding of external factors (e.g., employment dismissal due to ill-health) which may impact on the intervention and be reflected in quantitative data. Equally, we were able to obtain specific details as to how the intervention could be improved; data which would have otherwise not been captured by quantitative measures alone. This can be used in future trials of the PrEliMS intervention, to refine this further based on direct feedback from pwMS. Finally, the provision of the intervention within the format intended for clinical use, i.e., realistic to how emotional support is offered within services, provides ecological validity.

4.7 Extended Limitations

As outlined previously (section 2.6.5), there are multiple aspects of the current study which differ from PrEliMS-1, including intervention facilitation, a more

structured intervention approach, online delivery and selection and measurement of outcomes. It is important to note that each difference identified could be contributing to the results observed when comparing to PrEliMS-1, making it challenging to determine what change led to the difference. Equally, we cannot discriminate between effect generated by online sessions and the workbook content, as these collectively form a complex intervention of a range of interacting factors. Although beyond the possibility of an MSCED, recommendations for testing these factors in isolation is made in directions for future research.

Within the sample, participants were referred based on reports of psychological distress, and therefore may not be fully representative of the wider MS population. This limits generalisability of findings, particularly given this is a small sample. Notably, demographic characteristics of the sample are also limited in reflecting demographics of the wider MS community. There is an absence of Black, Asian, and Minority Ethnic (BAME) participants in the study, yet MS is reportedly more common in this group, with an increase in risk factors for MS also (Dobson et al., 2020; Koffman et al., 2013). Access to service data to compare sample characteristics to the service population may have supported contextualisation. However, given the small recruitment target within MSCEDs, this limitation is potentially challenging to overcome.

Another limitation is the reference data used to determine reliable and clinically significant change. To increase validity of results, we used data which was deemed as close to the current study sample as possible. However, given the current lack of research targeting pwMS at the point of diagnosis, this was challenging as reference data obtained often used samples of pwMS who are further down the journey of their diagnosis. Equally, normative data (i.e., taken from a sample of the population who do not have MS) used for CSC calculations may differ from ‘normative functioning’ within the MS population. Potentially, more stringent criteria may have helped overcome this, for example specifying difference between a ‘clinical MS’ population vs ‘non-clinical MS’ population or ‘non-clinical’ general population and ensuring this is consistent across analyses.

Finally, several participants entered the study outside of clinical range. This potentially contradicts typical MSED research and may limit how much change is

demonstrated. However, this is in line with the focus of ACT for improving wellbeing rather than symptom reduction, as the intervention emphasises adjustment to diagnosis and personal development.

4.7.1 Reflections on attrition and recruitment

As discussed in the journal paper, attrition during recruitment was a main limitation of the study. On reflection, we experienced challenges in engaging the clinicians at the recruitment site to providing referrals. Despite the site recently implementing a 'newly diagnosed' MS care pathway (where those with a new diagnosis are seen within 6-weeks by an MS Nurse Specialist), we experienced hesitancy to offer the study to potential participants due to concerns about this seeming "too soon" for them. Interestingly, those recruited via an assistant psychologist working on another study, appeared more motivated and engaged, potentially as they had already demonstrated their willingness to take part in research. Notably, these two participants also demonstrated more changes in outcomes, above other participants. This suggests inclination or readiness for therapy would have been important to capture, potentially through feedback interviews or during initial screening conversations.

The four participants who withdrew during baseline all cited this was not the "right time" for them. An exit interview was offered, to explore what may have increased feasibility to participate, however this was not taken up. Being prepared to have a more in-depth discussion when withdrawal did occur may have helped remedy this. This provides further support for the importance of timing of support in newly diagnosed pwMS. Qualitative feedback recommended for pwMS to be made aware of support options, to then engage with when they are 'ready'. However, avoidance of diagnosis discussion is a well-documented coping strategy within the literature (Dennison, 2011), which may limit uptake of support. Subsequently, future provision of this support may benefit from factors to mitigate this avoidance e.g., early, frequent discussion about support options available.

4.8 Directions for future research

The main recommendation is for a larger experimental trial of the PrEliMS intervention delivered by a TCP. Signals of efficacy were indicated by the current study, alongside qualitative feedback highlighting the value of emotion-focused

discussion with a healthcare professional knowledgeable in MS, independent from usual care. Whilst this meets requirements identified in the initial PrEliMS stakeholder study (Tindall et al., 2023), a larger trial may provide further understanding as to the mechanisms of change operating in the PrEliMS intervention, particularly the unresolved question around the limited effect on psychological flexibility.

As noted in the journal paper, it would be important for the intervention to be delivered by a range of therapists, to mitigate potential therapist-effects. Particularly as only one therapist delivered the intervention in the current study. Another inclusion for a larger trial could also be for longer follow-up points. This was potentially a drawback of the current study, as follow-up only captured up to 3.5-months post-baseline, in comparison to 6-months post-baseline in PrEliMS-1. As well as enabling more direct comparisons, this would generate understanding as to sustained and longer-term improvements to then consider whether additional 'top-up' support sessions may be needed as alluded to in qualitative feedback. Equally, future access to services could also be captured, as reduced access is a common implication of poorer adjustment to MS diagnosis.

Secondly, future research may also benefit from operationalising the target of the PrEliMS intervention by developing an adjustment measure. A model of adjustment to MS diagnosis was a key factor in ensuring the PrEliMS intervention met the needs of pwMS at diagnosis (Topcu et al., 2020). However, there remains a lack of outcome measures for adjustment to MS diagnosis. Potentially, this would support evidencing of the utility of PrEliMS for pwMS and provide an outcome measure which is arguably more in line with the focus of ACT, in promoting adjustment to live well with MS.

Finally, replicating the current study across a range of contexts, i.e., longer sessions, more sessions, workbook only vs support only, is another potential avenue for research. This would support further refinement of how this intervention could be provided within MS care, ensuring it is responsive to the needs of pwMS.

4.9 Critical Reflective Section

This section provides my critical reflections on the research process, specifically the most salient scientific, ethical, and theoretical issues that arose. The

six aspects of the ACT ‘hexaflex’ model of psychological flexibility have been drawn upon to structure critical reflections.

4.9.1 Scientific reflections

Deciding to research emotional support for people newly diagnosed with MS was largely influenced by my previous experience as an assistant neuropsychologist, completing cognitive assessments for people with the diagnosis. I was interested in how psychology could support coming to terms with a new diagnosis, particularly when the prognosis was likely to be deterioration. Within neuropsychology, case studies are a common design given 1) baseline cognitive performance for individuals are often used as their own control for tracking change and 2) there is much heterogeneity within neurological conditions and brain injuries. Looking back, it is likely this is what drew me to using a SCD. Despite RCTs being viewed as the ‘gold standard’, I felt a SCD closely aligned with my approach to clinical work. It captures nuances of individual experience, otherwise not depicted by group experimental designs and RCTs, and enables a more detailed exploration in response to our research aims. I feel this is also in line with my epistemological position of pragmatism (Feilzer, 2010), as focus remained on providing a *useful* account of participant experience.

At the beginning of the research process, I noticed my passion for the area was potentially tipping into over-ambition. Feedback on my initial protocol for two phases of an MSCED, recommended this was too much for the timescale given. On reflection, I was fused with thoughts of needing to evidence the importance of emotional support for pwMS, as I had seen first-hand how vital this is. Equally, feelings of worry arose that I would not meet this need. To cope, I certainly pushed these feelings down and worked harder to compensate. However, during supervision when I was encouraged to notice my thoughts and feelings in response to my protocol feedback, this helped me gain some distance between myself and my thoughts. I feel I also moved towards acceptance of the potential emotional investment I had in this research, rather than engaging in the struggle of pushing this down. Subsequently, I progressed with just the one phase in this study, which felt more manageable, whilst still adhering to our research aims.

Another challenge arose during the delivery of the therapy; specifically managing the dual role of therapist and researcher. Situations arose where I felt it necessary to bring in alternative ACT metaphors to the workbook, often because the participant was struggling to understand concepts. Keeping within my role as a scientist-practitioner, and balancing research needs (i.e., promoting validity) with therapist needs (e.g., figuring out what works for the client), I kept a record of additional metaphors used so this could be consistent to promote reliability. To further balance this dual-role, within the literature self-awareness, referred to as 'reflexivity', is identified as vital in separating off processes involved in each role (Fleet et al., 2016). As such, I found it helpful to maintain contact with the present moment, particularly within sessions. This involved noticing whether thoughts show up pertaining to this conflict between therapist and researcher, and acknowledging in the moment whether these are helpful or can just be noticed.

On reflection, this development of 'self-as-context' i.e., the observing self, also helped manage difficulties of delivering therapy for four participants in parallel. For the first participant, I was just delivering their sessions, so when I needed to manage four at once this came as a challenge. Holding in mind personalised goals and specific examples across all the sessions generated worry about getting mixed up or impacting the validity of the therapy delivered. Equally, one participant had very limited responses to questions and required a lot of prompting and provision of examples, above and beyond what typically occurred in other sessions. Looking back, I often filled in the gaps and would be suggestive of values. Within the fidelity assessment this is something that was suggest as ACT-inconsistent, given therapists need for foster curiosity rather than impose value on clients (O'Neill et al., 2019). To help acknowledge these different roles I was encompassing, I drew on a metaphor from Bennett and Oliver (2019). There is a dark room ('self-as-context') filled with a range of objects ('self-as-content'). In this case, therapist 'objects' of delivering ACT-based support, progressing through workbook exercises, and holding a non-judgemental stance. Alongside this, researcher 'objects' of recruiting, collecting and analysing data, and writing-up. In the room, I can have control over where my focus can be i.e., 'self-as-process', where the light is shined. It is this understanding that I feel helped somewhat mitigate potential bias that could be introduced by having multiple roles, and also maintaining an observer stance where

needed. This is also something I intend to continue to use in future practice and research, to continue developing this dual role stance.

4.9.2 Ethical reflections

During the recruitment phase, I had conversations with potential participants about them not feeling “ready” to engage in a psychological therapy. This was particularly evident when participants received the workbook through the post, prior to sessions, and subsequently withdrew. Further discussion revealed that they had noticed negative emotional responses since their diagnosis of MS, however, were concerned about what may happen if they “brought everything up” during the intervention. Ethically, I was aware I needed to respect participant right to withdraw. However, therapeutically, I was interested this could be experiential avoidance playing out, which the ACT-based intervention could target. Therefore, they may experience benefits from the intervention, which I found difficult to discount. In line with ethical practice, withdrawals from the study were accepted without need for question or explanation. I was able to contain my urge to persuade participants to take part, within supervision. It was helpful to reflect on the ACT concept of ‘workability’ (Harris, 2019), i.e., avoidance was potentially working well for them, in that moment, thus change may not be necessary. This is arguably also in line with the epistemological stance of contextualism (S. C. Hayes et al., 2012), whereby we are interested in an act or event within a context, as to whether it achieved a goal. I feel this raises an important question about whether clinicians have a role in promoting readiness for therapeutic interventions, or holding in mind that within the context, coping strategies like avoidance may be working well. Looking back, I also now consider that the research process is likely to differ to clinical practice in terms of motivation for therapeutic engagement. Participants were willingly volunteering their time, as opposed to being directly referred, although the right to withdraw applies in both contexts.

My clinical response of wanting to provide more was also evident within sessions; potentially, I had become fused with these thoughts again. I often found myself wanting to formulate and understand difficulties in more depth than was required, making it challenging to stick to the workbook. On reflection, within my clinical practice there is usually some scope to do this. I think this experience also

meant I held a view that formulating and exploring issues further would be beneficial for participants, however, this may not have been true. Additionally, from a research perspective, this would have moved away from the protocol, potentially risking reliability, and validity of findings. I particularly found this difficult where one participant qualitatively reported a decline after the intervention. They described thinking “what now?” and as though they’d been “left” to manage all of their emotion we had opened-up to. I recall noticing thoughts of letting the participant down, and frustration at the limits of a four-session, research intervention. Within clinical practice, there would be capacity to offer further support, and I certainly noticed the pull to do so. However, in maintaining the research and therapy balance, I signposted to sources of support and used supervision to notice and accept the urges showing up. Equally, having direct contact with the clinical team meant I could advise directly on the support needed. I think this also helped maintain that boundary of being an impartial researcher and an empathic, compassionate clinician.

4.9.3 Theoretical reflections

The research process has greatly benefited my learning about ACT and associated theoretical underpinnings. Understanding behaviour as conducive to the context in which it occurs has felt somewhat refreshing compared to alternative second-wave CBT approaches, that would consider this “maladaptive” or “problematic”. This has felt useful in my therapeutic work in validating how individuals cope with distress, particularly when the source of distress cannot be changed i.e., chronic physical health problems or injuries. Holding in mind the three pillars of ACT, I have felt more confident in modelling acceptance of difficult experiences and have learnt about the importance of bringing this back to what is important. I hope to take this learning forward in future clinical work, as well as working within wider teams and systems.

Throughout this thesis I have also benefitted from applying my ACT learning to myself. In supporting participants to consider the difference between values and goals, and reflect on what matters most to them, this prompted my own reflections. My goal or ‘destination’ throughout this research has been to produce a thesis. However, I have also come to identify what I hold important during this process, that is *how* I want to achieve that goal; what the journey may look like. For me, curiosity,

self-care, and gratitude are at the forefront of my own values. At the beginning of this research, I held hope the intervention would benefit every participant. Remaining curious helped ‘unhook’ from unhelpful thoughts like “I’ve failed”, when a change was not observed, or equally, deterioration occurred. As I have been writing this thesis, considering ‘towards moves’ like this has helped keep me connected to what is important. Often, this has prompted helpful breaks to the gym, or setting boundaries on time spent working, in line with self-care. Finally, in coming to the end of my thesis, I remind myself to be grateful for the opportunity to a) contribute to a research area I am passionate about, b) expand my clinical and research skills and c) play a role in the MS diagnosis journey of inspiring individuals. Now my goal has been achieved, I look to the next one, holding in mind what matters most to inform *how* I get there.

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Appendices

Appendix A
Patient Survey for Small Scale Research Project

The Multiple Sclerosis (MS) Clinic has recently set up a "newly diagnosed MS clinic". We hope that patients are offered a consultation appointment with an MS Nurse within 6 weeks after patients receive a diagnosis from their consultant.

We wish to find out whether this pathway is meeting your needs as a patient. We are particularly interested in knowing whether you feel your emotional, psychological, and mental health needs are being met, and what your priorities were for this first appointment, with an MS Nurse, after you received an MS diagnosis.

We hope that by sharing your experiences with us, this may help us to improve standards of care in the future.

Please could you offer 15 minutes of your time to complete the following survey?

Your feedback would be greatly appreciated. Any information that you provide will be treated in the strictest of confidence. The survey is anonymous so you will not be able to be identified. However, should you wish to be informed of the results of this survey you will need to provide your name and contact details.

By filling out this survey your treatment will not be affected in any way. Similarly, you do not have to complete this survey should you so choose.

> If this survey raises any questions or concerns that you would like answered, then please do not hesitate to contact a member of staff.

Please create a participant ID code (the first three digits of your postcode, followed by the last four digits of your phone number, for example "NG1 1234") for confidential identification of your data. Make a note for your records should you wish to withdraw your data in the future:

_____

Please rate the following statements about your first appointment with an MS Nurse, after receiving your diagnosis: (tick the response that best applies to each statement)

How good was the MS Nurse at…	Poor	Fair	Good	Very Good	Excellent	Does not apply
Making you feel at ease (Introducing themself, explaining their position, being friendly and warm towards you, treating you with respect; not cold or abrupt)						
Letting you tell your "story" (Giving you time to fully describe your condition in your own words; not interrupting, rushing or diverting you)						
Really listening (Paying close attention to what you were saying; not looking at the notes or computer as you were talking)						
Being interested in you as a whole person (Asking/knowing relevant details about your life, your situation; not treating you as "just a number")						
Fully understanding your concerns (Communicating that they had accurately understood your concerns and anxieties; not overlooking or dismissing anything)						
Showing care and compassion (Seeming genuinely concerned, connecting with you on a human level; not being indifferent or "detached")						
Being positive (Having a positive approach and a positive attitude; being honest but not negative about your problems)						
Explaining things clearly (Fully answering your questions; explaining clearly, giving you adequate information; not being vague)						

Helping you to take control (Exploring with you what you can do to improve your health yourself; encouraging rather than “lecturing” you)						
Making a plan of action with you (Discussing the options, involving you in decisions as much as you want to be involved: not ignoring your views)						

Comments: If you would like to add further comments on your appointment, please do so below

……
……
……
……
……
……

1. The newly diagnosed MS clinic currently offer 45-minute appointments. Did this feel sufficient?

☐	Yes	☐	No

If no, please tell us what you feel would be sufficient and why:

……
……
……

2. Do you feel that your knowledge about MS increased as a result of the appointment?

☐	Yes	☐	No

If yes, please describe what you learnt about MS:

……
……
……
……
……

……
……
……

3. Did you have a family member or significant other present during the appointment?

☐	Yes	☐	No

(Yes or No) Please explain your reason/s why:

……
……
……
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……
……
……
……

(Yes or No) Please explain the impact this had on the appointment:

……
……
……
……
……
……
……
……

4. Please rate how **helpful** your appointment was **overall**:

Very unhelpful	Fairly unhelpful	Neither helpful nor unhelpful	Fairly helpful	Very helpful
1	2	3	4	5

Please explain your response:

……
……
……
……
……

……
……
……

5. In your appointment, what was **most helpful** to discuss for you personally?

……
……
……
……

6. Did anything happen during the appointment which might have been **hindering**?

YES NO

If yes, please describe below:
……
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……

7. *Since MS diagnosis*, have you experienced any of the following emotions that have significantly affected your daily life? (Tick all that apply)

☐	Anger	☐	Helplessness	☐	Hopelessness	☐	Anxiety/Worry
☐	Denial	☐	Shame	☐	Low self-confidence	☐	Depression
☐	Fear	☐	Sadness	☐	Low self-esteem	☐	Frustration
☐	Grief	☐	Guilt	☐	Loneliness	☐	Suicidal thoughts
☐	Other, please specify…… ……			☐	None of the above		

7a. If you have ticked any of the above, please describe **how** this/these have affected your daily life?

Not at all	Slightly	Moderately	To a large extent	Completely
1	2	3	4	5

Please state in the space below how this has affected your daily life:	**Was this discussed at your appointment?**	**Using the scale above, to what extent is this emotional difficulty currently being addressed?**	**Would you want professional support with this emotional difficulty?**
(1) …….. …… ……	**Y ☐ N ☐**	**1 2 3 4 5**	**Y ☐ N ☐**
(2) …….. …… ……	**Y ☐ N ☐**	**1 2 3 4 5**	**Y ☐ N ☐**
(3) …….. …… ……	**Y ☐ N ☐**	**1 2 3 4 5**	**Y ☐ N ☐**
(4) …….. …… ……	**Y ☐ N ☐**	**1 2 3 4 5**	**Y ☐ N ☐**
(5) …….. …… ……	**Y ☐ N ☐**	**1 2 3 4 5**	**Y ☐ N ☐**

7b. If available, would you have wanted to see a Clinical Psychologist about any of these emotional difficulties? (See definition of a Clinical Psychologist below)

☐	Yes	☐	No

If no, please explain why:

……
……
……
……
……
……
……

NB: What is a Clinical Psychologist?
A Clinical Psychologist helps people to understand their emotional and/or mental health difficulties, alleviate distress, and improve wellbeing.
A Clinical Psychologist can help people to find ways to minimise the impact MS has on their lives, and help them to respond (think, feel and/or behave) in ways that allows them to live their best lives in spite of MS. They can help with issues such as coming to terms with the MS diagnosis, and issues related to relationships, work or education, and cognitive problems.
Clinical Psychologists can offer:

- An initial assessment to discuss your current difficulties.
- A cognitive assessment to assess any changes in cognitive abilities such as memory, attention and concentration, planning, or information-processing.
- A formulation (a psychological way of understanding the development and maintenance of your current difficulties).
- Therapies such as Cognitive Behavioural Therapy (CBT), Acceptance and Commitment Therapy (ACT), or Compassion-Focused Therapy (CFT).
- Referral on to other Services if these better suit your needs.

8. *In the context of MS diagnosis*, do you think there is anything else with which you may need and want the support of a Clinical Psychologist?

☐	Yes	☐	No

If yes, please specify:

……
……
……
……
……
……
……

9. What difference, if any, do you think it would make to have a Clinical Psychologist within the newly diagnosed MS clinic? Please specify:

……
……
……
……
……
……
……

Thank you very much for taking the time to complete this survey.

Appendix B
Nurses' Survey for Small Scale Research Project

As part of evaluating the newly diagnosed clinic, we would like to explore nurses' experience of facilitating the consultation appointments after MS diagnosis. We are also particularly interested in finding out whether people feel there is a need for a Clinical Psychology provision within the MS clinic.

Please could you offer 10 minutes of your time to complete the following survey?

Your feedback would be greatly appreciated. The information that you provide will be treated in the strictest of confidence. The survey is anonymous so you will not be able to be identified. The results of this survey will be presented at a Wednesday morning East Midlands MS MDT meeting.

If this survey raises any questions or concerns that you would like answered then please do not hesitate to contact the service evaluation team using the contact details available at the end of the survey.

During these appointments, to what extent do you feel you are good at… (tick the response that best applies to each statement)

	Poor	Fair	Good	Very Good	Excellent	Does not apply
Making the patient feel at ease (Introducing yourself, explaining your position, being friendly and warm towards them, treating them with respect; not cold or abrupt)						
Letting the patient tell their "story" (Giving them time to fully describe their condition in their own words; not interrupting, rushing or diverting them)						
Really listening (Paying close attention to what they are saying, not looking at the notes or computer as they are talking)						
Being interested in the patient as a whole person (Asking/knowing relevant details about their life, their						

situation; not treating them as "just a number")						
Fully understanding the patients' concerns (Communicating that you have accurately understood their concerns and anxieties; not overlooking or dismissing anything)						
Showing care and compassion (Seeming genuinely concerned, connecting with them on a human level; not being indifferent or "detached")						
Being positive (Having a positive approach and a positive attitude; being honest but not negative about their problems)						
Explaining things clearly (Fully answering their questions; explaining clearly, giving them adequate information; not being vague)						
Helping the patient to take control (Exploring with them what they can do to improve their health themself; encouraging rather than "lecturing" them)						
Making a plan of action with the patient (Discussing the options, involving them in decisions as much as they want to be involved: not ignoring their views)						

Comments: If you would like to add further comments, please do so below

……
……
……
……
……
……

NB: What is a Clinical Psychologist?
A Clinical Psychologist helps people to understand their emotional and/or mental health difficulties, alleviate distress, and improve wellbeing.
A Clinical Psychologist can help people to find ways to minimise the impact MS has on their lives, and help them to respond (think, feel and/or behave) in ways that allows them to live their best lives in spite of MS. They can help with issues such as coming to terms with the MS diagnosis, and issues related to relationships, work or education, and cognitive problems.

Clinical Psychologists can offer:

- An initial assessment to discuss clients' current difficulties.
- A cognitive assessment to assess any changes in cognitive abilities such as memory, attention and concentration, planning, or information-processing.
- A formulation (a psychological way of understanding the development and maintenance of current difficulties).
- Therapies such as Cognitive Behavioural Therapy (CBT), Acceptance and Commitment Therapy (ACT), or Compassion-Focused Therapy (CFT).
- Referral on to other Services if these better suit clients' needs.

1. **Do you think the issues a Clinical Psychologist could help with are dealt with in a satisfactory way through the existing staff?**

☐	Yes	☐	No

Please explain your response:

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2. **Do you feel there would be any downsides/challenges to having a Clinical Psychologist within the newly diagnosed MS clinic?**

☐	Yes	☐	No

If yes, please specify:

……
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……

3. **What sorts of presentations, difficulties, and/or patients would you likely refer to the Clinical Psychologist? Please specify:**

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4. **What would you hope referral to a Clinical Psychologist would achieve? Please specify:**

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……
……

5. At present, without Clinical Psychology, where do you tend to refer/signpost patients if they need additional emotional and/or mental health support?

	No onward referral		MS Nurse
	General Practitioner (GP)		IAPT talking therapies (e.g. Let's Talk Wellbeing)
	NHS 111		Samaritans
	(Adult) Local Mental Health Team		(Older Adult) Community Mental Health Team
	Crisis Team		999 or A&E (emergency services)
	MS Society		Other, please specify…… ……

Thank you very much for taking the time to complete this survey.

Appendix C
Summary of Emotional Needs Identified Since Receiving an MS Diagnosis

Figure C1

Prevalence of Emotional Difficulties Experienced by Patients Since MS Diagnosis

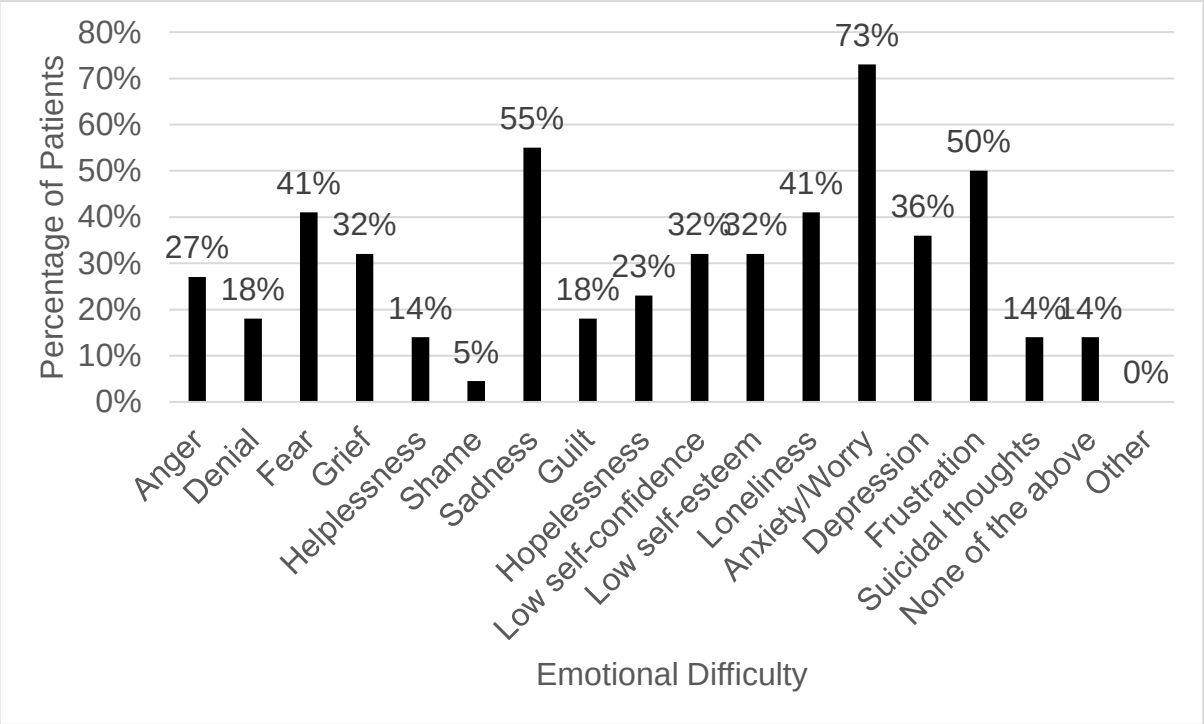
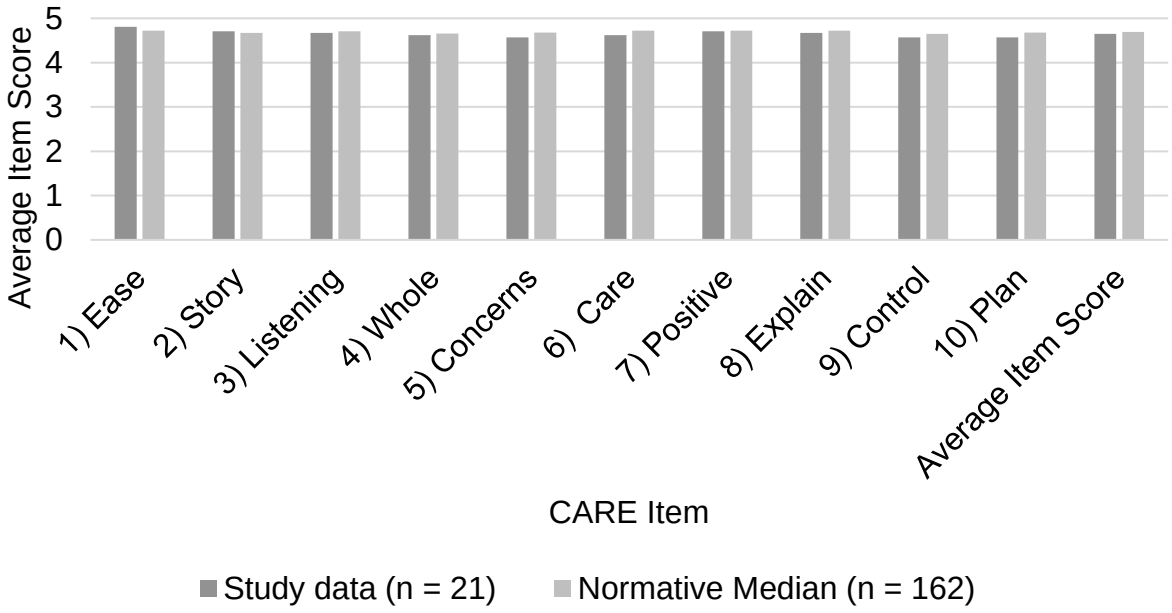


Table C1

Summary of Responses to Questions 7.

	Quantitative Response (*n,* %)
Were these emotional difficulties discussed at your appointment?	Yes (13, 59%) No (6, 27%) Not applicable (3, 14%)
To what extent is this emotional difficulty currently being addressed?	Not at all (10, 45%) Slightly (1, 5%) Moderately (2, 9%) To A Large Extent (4, 18%) Completely (0) Not applicable (5, 23%)
Would you want professional support with this emotional difficulty?	Yes (14, 64%) No (8, 36%)

Appendix D
Comparison to CARE Normative Data Sample



Appendix E
Example Search Strategy in PsycINFO

1. DE “Multiple Sclerosis”
2. Multiple sclerosis
3. S1 OR S2
4. DE “Acceptance and Commitment Therapy”
5. Acceptance and commitment*
6. Acceptance based therap*
7. Acceptance based behavio*
8. S4 OR S5 OR S6 OR S7
9. S3 AND S8

Appendix F
Data Extraction Form Headings

Study identification: Authors, title, date, country

Methodology: Design, recruitment, inclusion, and exclusion criteria

Sample demographics: Total sample size, age, gender, race/ethnicity, type of MS, attrition

Intervention: Delivery mode, setting, number and length of sessions, administrator, comparison, compliance, fidelity assessment

Outcomes: Measures/subscales used, timepoints, adverse events

Results: Statistical methods used, number of missing participants, between group differences, effect sizes, post- intervention change from baseline

Key findings and additional comments

Appendix G
British Journal of Health Psychology: Guidelines for Authors

Written for publication in British Journal of Health Psychology (6000-word limit)

Journal Paper Wordcount: 5809 (*footnotes referencing extended paper: 426)*

Style: APA Style (7th Edition)

Guidelines for Authors:
https://bpspsychub.onlinelibrary.wiley.com/hub/journal/20448287/homepage/forauthors.html

Appendix H
Participant Information Sheet

Participant Information Sheet

(Final version 2.2: 09.09.2022)

IRAS Project ID: 302587

Title of Study: **Providing Emotional Support at the Point of Multiple Sclerosis Diagnosis: PrEliMS 2**

Researcher(s): **Bethany Thompson, Prof Roshan das Nair, Dr Nima Moghaddam & Dr Nikos Evangelou**

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear.

What is this study about?

My name is Bethany Thompson and I am a Trainee Clinical Psychologist at the University of Nottingham and at Nottinghamshire Healthcare NHS Foundation Trust.

By conducting this research, we are interested to find out whether emotional support offered in sessions with a Trainee Clinical Psychologist, alongside completing an MS-diagnosis specific workbook, is helpful for individuals who have recently received an MS diagnosis. Currently there is no referral pathway or guidelines for individual support regarding MS diagnosis so this research will provide crucial information, and broaden our understanding, in how best to provide this much needed support.

Why have I been invited?

You are being invited to take part because you have received a diagnosis of MS within the last 12-months. We are inviting up to 14 participants like you to take part.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights or your usual care.

What will happen to me if I take part?

1. You will be contacted by the Primary Researcher who will answer any further questions about taking part and establish what format you would like to

complete the sessions (e.g., video or over the phone) and the best way for you to complete some questionnaires (e.g., online or via post). These questionnaires will be asking about your mood over the past week and you will be prompted to complete them once a week for the next 9 weeks (the length of time you are anticipated to take part in the study).

2. You will then be sent a workbook, called “Better Living with a Diagnosis of MS”, to explore your feelings around your diagnosis. This will be introduced in your first session with a Trainee Clinical Psychologist, lasting around an hour. The first session will be an hour long, focusing on familiarisation with the workbook, goal setting and for the Trainee Clinical Psychologist to answer any questions. You will also be invited to complete some additional questionnaires which focus on specific MS-related factors, like your fatigue levels and quality of life. These questionnaires will be completed before you start the workbook/sessions and after you finish the workbook/sessions.
3. As you work through the workbook at your own pace, you will continue to meet with the Trainee Clinical Psychologist for another three sessions, each around half an hour. The sessions will be an opportunity to access emotional support, answer any questions and discuss and/or revisit exercises from the workbook. Including the introduction session, you will have a total of four sessions with the Trainee Clinical Psychologist.
4. After these four sessions, you will then be prompted to complete some additional questionnaires (as mentioned above), with another prompt a month after completion also.
5. Finally, you will also be invited to an interview with another Trainee Clinical Psychologist, who will ask some questions to explore your experience of using the workbook.

In total, your participation in the study is anticipated to last around 14 weeks. The research study will last around a year.

Expenses
Participants are not required to travel anywhere so expenses are not necessary.

What are the possible disadvantages and risks of taking part?
Taking part in this research will require giving up your time to complete the questionnaires, read through the workbook, and attend sessions with a Trainee Clinical Psychologist. Some of the questionnaires and/or workbook may evoke some difficult feelings about MS diagnosis. You do not have to discuss anything you do not want to in the sessions; both the sessions and questionnaires aim to be sensitive to your feelings. In the unlikely event you experience a high level of distress we will be able to advise you on seeking further support.

What are the possible benefits of taking part?
We cannot promise the study will help you but the information we get from this study may help inform our understanding of how best to support individuals with MS around the time of diagnosis.

What if there is a problem?
If you have a concern about any aspect of this study, you can ask to speak to the researchers who will do their best to answer your questions. The researchers' contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this either by writing to **NUH NHS Trust, c/o PALS, Freepost, NEA 14614, Nottingham, NG7 1BR**, emailing PALS@nuh.nhs.uk or calling **0800 183 0204**.

The University of Nottingham as research Sponsor indemnifies its staff with both public liability insurance and clinical trials insurance in respect of claims made by research subjects. In the event that something does go wrong, and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensations against the University of Nottingham but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, we will use information collected from you and your medical records during the course of the research. This information will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database at the University of Nottingham. Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study (named above) is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights we will use the minimum personally – identifiable information possible.

You can find out more about how we use your information and to read our privacy notice at:
https://www.nottingham.ac.uk/utilities/privacy.aspx.

The data collected for the study will be looked at and stored by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people from regulatory organisations to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty. Support sessions and interviews will be audio recorded for transcription and fidelity purposes. Either the primary researcher or a professional transcriber will listen to the recordings and type up the conversations we had. These transcripts will be kept confidential.

Where possible information about you which leaves the NHS site will have your name and address removed and a unique code will be used so that you cannot be recognised from it, however sometimes we need to ensure that we can recognise you to link the research data with your medical records so in these instances we will need to know your name and date of birth.

Your contact information will be kept by the University of Nottingham for 12 months after the end of the study so that we are able to contact you about the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted). This information will be kept separately from the research data collected and only those who need to will have access to it. All other data (research data) will be kept **securely** for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team given permission by the data custodian will have access to your personal data.

In accordance with the University of Nottingham's, the Government's and our funders' policies we may share our research data with researchers in other Universities and organisations, including those in other countries, for research in health and social care. Sharing research data is important to allow peer scrutiny, re-use (and therefore avoiding duplication of research) and to understand the bigger picture in particular areas of research. Data sharing in this way is usually anonymised (so that you could not be identified) but if we need to share identifiable information we will seek your consent for this and ensure it is secure. You will be made aware then if the data is to be shared with countries whose data protection laws differ to those of the UK and how we will protect your confidentiality.

Although what you say to us is confidential, should you disclose anything to us which we feel puts you or anyone else at any risk, we may feel it necessary to report this to the appropriate persons.

What will happen if I don't want to carry on with the study?
Your participation is entirely voluntary, and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw, we will no longer collect any information about you or from you but we will keep the information about you that we have already obtained as we are not allowed to tamper with study records and this information may have already been used in some analyses and may still be used in the final study analyses. To safeguard your rights, we will use the minimum personally-identifiable information possible.

What will happen to the results of the research study?
The results will be written up as partial fulfilment of the requirement for the Trent Doctorate in Clinical Psychology, with an expected completion date of February 2023. It is intended the findings from the study will be submitted to a peer-reviewed journal. Participants will be allocated a code to ensure they **will not** be identifiable in any publications.

If you wish to be informed of the results of the study, please let one of the researchers know and we will take your contact details and store these up until dissemination of the findings. These will be stored separately to the research findings and will be kept **strictly confidential** – only members of the research team will have access to these.

Who is organising and funding the research?
This research is being organised by the University of Nottingham and is being funded by Health Education England.

Who has reviewed the study?
All research in healthcare is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by South Central – Berkshire B Research Ethics Committee.

Further information and contact details

Primary Researcher: Bethany Thompson
Trainee Clinical Psychologist
Bethany.thompson@nottingham.ac.uk

Supervised by: Prof Roshan das Nair (Chief Investigator)
Professor of Clinical Psychology and Neuropsychology
Roshan.dasnair@nottingham.ac.uk

Dr Nima Moghaddam
Research Clinical Psychologist/Senior Lecturer
Nmoghaddam@lincoln.ac.uk

Dr Nikos Evangelou
Consultant Neurologist
Nikos.evangelou@nottingham.ac.uk

Support services: MS Society
https://www.mssociety.org.uk/
Freephone: 0808 800 8000

Appendix I
Informed Consent Form

University of Nottingham
UK | CHINA | MALAYSIA

CONSENT FORM

Nottingham University Hospitals NHS
NHS Trust

(Final version 2: 25.02.22)

Title of Study: Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis: PrEliMS 2

IRAS Project ID: 302587

Name of Researcher: Bethany Thompson

Name of Participant:……

Please initial box

1. I confirm that I have read and understand the information sheet final version number 2, dated 25.02.2022 for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis. ☐

3. I understand that relevant sections of my medical notes and data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential. ☐

4. Consent for storage and use in possible future research (Optional)

   I agree that the information gathered about me can be stored by the University of Nottingham at the Division of Psychiatry and Applied Psychology, for possible use in future studies. I understand that some of these studies may be carried out by researchers other than the current team who ran the first study, including researchers working for commercial companies. Any data used will be anonymised, and I will not be identified in anyway.

   Yes ☐ **No** ☐

5. I understand that the support sessions will be audio recorded. ☐

6. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

3 copies: 1 for participant, 1 for the project notes and 1 for the medical notes

Appendix J
Demographic Data Form

University of Nottingham
UK | CHINA | MALAYSIA

Nottingham University Hospitals NHS
NHS Trust

Participant information

Please answer the following questions about yourself:

1. What is your date of birth?

   _____

2. What is your gender?
   - o Female
   - o Male
   - o Other

3. What is your ethnicity?
   - o White
   - o Black
   - o Mixed/Multiple Ethnic Groups
   - o Asian
   - o Other

4. What is the highest education you attained?
   - o Below GCSE
   - o GCSE
   - o A-Level
   - o Degree
   - o Higher Degree
   - o Not known

5. What is your employment status? (Please tick all that apply)
   - o Not employed
   - o Employed full-time
   - o Employed part-time
   - o Retired
   - o Voluntary full-time
   - o Voluntary part-time
   - o In education full-time
   - o In education part-time

6. How long have you been diagnosed with MS?

   _____

7. Type of MS diagnosis:
   - o Relapsing-remitting MS
   - o Primary Progressive MS
   - o Secondary Progressive MS
   - o Not known

8. How long did it take you to get a diagnosis of MS?

   _____

Appendix K
Interview Consent Form

University of Nottingham
UK | CHINA | MALAYSIA

Nottingham University Hospitals NHS
NHS Trust

CONSENT FORM FOR INTERVIEW

(Final version 2.0: 25.02.22)

Title of Study: Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis: PrEliMS 2

IRAS Project ID: 302587

Name of Researcher: Bethany Thompson

Name of Participant:…… **Please initial box**

1. I confirm that I have read and understand the information sheet version number 2, dated 25.02.2022 for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation in the interview is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis. ☐
3. I understand that relevant sections of my medical notes and data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential. ☐
4. I understand that the interview will be recorded and that anonymous direct quotes from the interview may be used in the study reports. ☐
5. I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers. ☐
6. I agree to take part in the interview process. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

3 copies: 1 for participant, 1 for the project notes and 1 for the medical notes

Appendix L
Interview Schedule

University of Nottingham
UK | CHINA | MALAYSIA

Nottingham University Hospitals NHS
NHS Trust

Qualitative Feedback Interview Schedule

(Final Version 1.0: date 16.12.21)

1) What has using the workbook "Better Living with a Diagnosis of MS" been like for you?

   Prompt: are there any positive and negative changes noticed. The timing of the intervention after MS diagnosis i.e., too soon, just right or would have preferred this sooner?

2) How has it felt to be in a support session alongside using the workbook?

   Prompt: Did this add anything? Were they paced in line with workbook progress?

3) Were there aspects you liked or found helpful about the:

   a. **workbook**? If so, please explain these…

   Prompt: Metaphors, exercises on acceptance, mindfulness and values, workbook layout, readability.

   b. **support sessions***?* If so, please explain these…

   Prompt: Consider topics discussed, length of sessions, number of sessions, would more/less have been preferred, would more/less frequent have been preferred

4) Were there aspects you did not like or found difficult about the:

   a. **workbook**? If so, please explain these…

   Prompt: Metaphors, exercises on acceptance, mindfulness and values, workbook layout, readability.

   b. **support sessions**? If so, please explain these…

Prompt: Consider topics discussed, length of sessions, number of sessions, would more/less have been preferred, would more/less frequent have been preferred

5) Do you have any suggestions for us to improve the workbook **and** support sessions?
   Prompt: delivery, intervention content, were they both necessary?

6) Your scores indicated a dip in your mood **XXX**, can you tell me more about what was perhaps going on for you? (i.e., was this MS related?...)

7) Is there anything that is important to talk about that we haven't already? Anything you'd want Beth or the research team to know or take on board?

Appendix M
ACT-FM Description and Scoring

ACT-FM key areas	Description
Therapist stance	The stance taken by the therapist is equal, compassionate and non-judgemental. The therapist should show empathy and warmth and be guided by what the client brings. The therapist does not try to change the client's mind, but to guide noticing of their own experience using experiential techniques. The therapist encourages responsibility, focuses on context, and models psychological flexibility responses and behaviour.
Aware response style	This is the ability to flexibly contact the present moment. This might involve practicing exercises designed to enhance the client's ability to nonjudgementally attend to the present moment. The therapist may encourage the client to take an observer perspective on their psychological experiences, when doing so helps increase the effectiveness of client behaviour.
Open response style	This is the ability to open-up to experiences, and to observe and describe these without becoming entangled in them or trying to diminish them. The therapist might work on skills that promote the client's willingness to sit with difficult thoughts, emotions, or sensations, when in the service of their values and goals. They might use defusion techniques or exercises with the client, giving them the opportunity to notice or distance themselves from their thought.
Engaged response style	This is the ability to identify, clarify and act according to one's values on an ongoing basis. The therapist might give the client opportunities to identify their values. They may help the client to define goals and actions that support their values, and to plan and do these actions.

ACT Fidelity Measure (ACT-FM; O'Neill et al., 2019)

ACT-FM Assessment for ACT consistency (completed by NM and AT)

Criteria	Session	Response			
Did the therapist 'check in' with the participant?	1	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	2	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	3	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	4	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	5	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
Did the psychologist refer to and support use of the patient workbook?	1	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	2	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	3	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	4	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	5	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	1	☐ No (0)	☐ Somewhat (1)	☑ Mostly (2)	☐Yes (3)

ACT-FM Assessment for ACT consistency (completed by NM and AT)

Criteria	Session	Response			
Were psychologist contributions consistent with our ACT-based approach to emotional support?	2	☐ No (0)	☐ Somewhat (1)	☐ Mostly (2)	☑ Yes (3)
	3	☐ No (0)	☐ Somewhat (1)	☑ Mostly (2)	☐Yes (3)
	4	☐ No (0)	☐ Somewhat (1)	☐ Mostly (2)	☑Yes (3)
	5	☐ No (0)	☐ Somewhat (1)	☐ Mostly (2)	☑Yes (3)
Was any support inconsistent with this model? [Reverse-scored]	1	☑ No (2)	☐ Somewhat (1)	☐ Yes (0)	
	2	☑ No (2)	☐ Somewhat (1)	☐ Yes (0)	
	3	☑ No (2)	☐Somewhat (1)	☐ Yes (0)	
	4	☑ No (2)	☐Somewhat (1)	☐ Yes (0)	
	5	☑ No (2)	☐Somewhat (1)	☐ Yes (0)	
Was the psychologist suitably flexible and responsive to issues raised by the participant?	1	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	2	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	3	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	4	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	
	5	☐ No (0)	☐ Somewhat (1)	☑ Yes (2)	

Mean ACT consistency score of 28.6 out of 36 (median rating of 3, indicating “therapist consistently enacts ACT-congruent behaviours”.

Appendix N
Supplementary Material to Journal Paper: Table of framework analysis themes and quotations

Participant Quotes from Feedback Interviews

Theme	Participant 1	Participant 2	Participant 4	Participant 5
Utility of ACT processes and techniques	"opened my awareness" (6)	"[sailing boat metaphor]… I found that a little bit patronizing" (9-10)	"you know what your values are and how you can kind of live towards them… and then incorporate them in spite of MS issues" (111-113)	"the breathing exercises… take a minute to just breathe and just be calm" (65-66)
Value of sessions	"the biggest thing for me is having someone totally independent you can really off load to" (275)	"it's nice to see a human being and kind of talk about what you've just unpacked" (171)	"Time to talk to someone who knows about the condition but who isn't family" (205-206)	"[therapist/BT] is incredibly knowledgeable… it's the calm attitude and not afraid to listen" (82-83)
Making use of the workbook	"there was nothing about it I didn't really like. The workbook was easy to follow,… very clear, it wasn't complicated in any way" (73-74)	"a good breadth of things in there [workbook] to kind of tailor how you wanted to use it as well" (209-210)	"having everything sort of strategy-wise written down, so I could do it in my own time rather than just talking about it, that was really helpful" (146-147)	"you could see exactly what was going on in the book, it was very easy to follow the flow of the book and everything else, perfect" (139-140)
Suggestions for improvements	"I can't think of anything that cries out that you would need to change" (109)	"it felt too young… like it was almost written for a child… I can imagine reading that as part of a bedtime story" (246 – 254)	"we arrived at the values section, I think week three… I think doing it at session two might have been a more logical	"two analogies [sky and the weather; beachball] that [therapist/BT] used that weren't in the book, but… I think they probably should be" (21-22)

Participant Quotes from Feedback Interviews

Theme		Participant 1	Participant 2	Participant 4	Participant 5
				way" (101-102)	
Meeting support needs around MS diagnosis	Getting the timing right	"I would say about three or four weeks [after diagnosis]" (308)	"where it's come for me has been good" (147)	"If I had known when I came to hospital that it was there, I would have parked it and then gone back to it when I was ready" (74-75)	"probably pretty much straight away [after diagnosis]" (54)
	Remaining support needs	---	"I've let it out [emotion] and it's kind of hard to put the lid back on" (17)	"ongoing support or top-up of sessions or monthly sessions might be a helpful offering … now like it's a bit of an unknown, where do we go from here" (223-224)	"I've got a decent network of friends… . I've got a podcast that I do where I will just sit and talk and get things out, and OK I'm not talking to anyone in particular, but I'm talking" (174-176)

Note. Dashes indicate no appropriate quotation.

Appendix O
Research Ethics Committee (REC) Approval Letter

NHS
Health Research Authority
South Central - Berkshire B Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Telephone: 0207 104 8253

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

08 March 2022

Professor Roshan das Nair
B19, Institute of Mental Health
Innovation Park, Triumph Road
University of Nottingham
NG7 2TU

Dear Professor das Nair

Study title:	**Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis: PrEliMS 2**
REC reference:	**22/SC/0034**
Protocol number:	**21082**
IRAS project ID:	**302587**

Thank you for your letter of 01 March 2022, responding to the Research Ethics Committee's (REC) request for further information on the above research and submitting revised documentation.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Good practice principles and responsibilities

The UK Policy Framework for Health and Social Care Research sets out principles of good

Appendix P
Health Research Authority (HRA) Ethical Approval Letters

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Professor Roshan das Nair
B19, Institute of Mental Health
Innovation Park, Triumph Road
University of Nottingham
NG7 2TUN/A

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

08 March 2022

Dear Professor das Nair

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis: PrEliMS 2**
IRAS project ID:	**302587**
Protocol number:	**21082**
REC reference:	**22/SC/0034**
Sponsor	**University of Nottingham**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Appendix Q
Nottingham University Hospitals Letter of Access

We Listen
We Care

NHS
Nottingham
University Hospitals
NHS Trust

Research & Innovation
Nottingham Integrated Clinical Research Centre
C Floor, South Block
QMC Campus
Derby Road
Nottingham
NG7 2UH

Tel: 0115 970 9049

RSCH1060

Date 04/APR/2022

Bethany Thompson

Trent DClinPsy Course
Division of Psychiatry and Applied Psychology
School of Medicine
University of Nottingham
B14 Yang Fujia Building
Jubilee Campus
Nottingham,
NG7 2TU

Dear Bethany Thompson
As an existing NHS employee you do not require an additional honorary research contract with this NHS organisation. We are satisfied that the research activities that you will undertake in this NHS organisation are commensurate with the activities you undertake for your employer. Your employer is responsible for ensuring such checks as are necessary have been carried out. This letter confirms your right of access to conduct research through **Nottingham University Hospitals** for the purpose and on the terms and conditions set out below. This right of access commences on **04/APR/2022** and ends on **30/SEP/2023** unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from this NHS organisation. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving permission to conduct the project.

You are considered to be a legal visitor to **Nottingham University Hospitals,** premises. You are not entitled to any form of payment or access to other benefits provided by this organisation to employees and this letter does not give rise to any other relationship between you and this NHS organisation, in particular that of an employee.

While undertaking research through **Nottingham University Hospitals,** you will remain accountable to your employer **Nottingham Healthcare NHS Foundation Trust,**but you are required to follow the reasonable instructions of your nominated manager **Roshan Das Nair,** in this NHS organisation or those given on her/his behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by this NHS organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with **Nottingham University Hospitals** policies and procedures, which are available to you upon request, and the Research Governance Framework.

Appendix R
Nottingham University Ethics Committee Approval

Research and Innovation
University of Nottingham
East Atrium, Jubilee Conference Centre
Triumph Road
Nottingham
NG8 1DH

Our reference: R&I: 21082
IRAS Project ID: 302587

0115 8467906
sponsor@nottingham.ac.uk

Health Research Authority
Research Ethics Committee

Professor Roshan das Nair
Professor of Clinical Psychology and Neuropsychology
Division of Psychiatry & Applied Psychology
School of Medicine
University of Nottingham
B19, Institute of Mental Health
Innovation Park
Triumph Road
Nottingham NG7 2TU

11th January 2022

Dear Sir or Madam,

Sponsorship Statement

Re: Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis: PrEliMS 2

I can confirm that this research proposal has been discussed with the Chief Investigator and agreement to sponsor the research is in place.

An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.*
Any necessary indemnity or insurance arrangements will be in place before this research starts. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
Wording has been included in the participant information sheets to address the requirements of GDPR for transparency information and has been drafted by the sponsor to ensure consistency and compliance with the University's privacy notice, HRA guidance and the expectations of other organisations, therefore the HRA template wording has not been used verbatim.
Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

The duties of sponsors set out in the UK Policy Framework for Health and Social Care Research will be undertaken in relation to this research.**
* Not applicable to student research (except doctoral research).
** Not applicable to research outside the scope of the Research Governance Framework.

Yours faithfully

Angela Shone
Head of Research Governance
University of Nottingham

Appendix S
IRAS Confirmation of Non-Substantial Amendment

IRAS 302587. Amendment

NI New IRAS Dev <no-reply-iras@hra.nhs.uk>
To Bethany Thompson
01/07/2022

You forwarded this message on 01/07/2022 16:22.

IRAS Project ID: 302587
Sponsor amendment reference: 21082 NSA01

Thank you for submitting your study amendment. In accordance with the outcome of your completed amendment tool, this amendment requires no further regulatory review. Please now share this amendment with your UK research sites, in accordance with the instructions in your completed amendment tool.

For studies with more than one UK research site, your amendment will now be automatically shared with the R&D offices of any NHS/HSC research sites in Scotland and Northern Ireland, but you should share the amendment by email directly with those Research team/s.

For all NHS research sites in England and Wales, please now share this amendment by email directly with those sites, including both the R&D offices and research teams.

Do not reply to this email as this is an unmonitored address and replies to this email cannot be responded to or read.

This message may contain confidential information. If you are not the intended recipient please inform the sender that you have received the message in error before deleting it. Please do not disclose, copy or distribute information in this e-mail or take any action in relation to its contents. To do so is strictly prohibited and may be unlawful. Thank you for your co-operation..

Appendix T
REC Approval for Substantial Amendment

Health Research Authority

South Central - Berkshire B Research Ethics Committee

The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Tel: +442071048276

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

30 September 2022

Miss Bethany Thompson
Trainee Clinical Psychologist
Nottinghamshire Healthcare NHS Foundation Trust
Institute of Mental Health
Innovation Park, Triumph Road
University of Nottingham
NG7 2TU

Dear Miss Thompson

Study title:	**Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis: PrEliMS 2**
REC reference:	**22/SC/0034**
Protocol number:	**21082**
Amendment number:	**21082 SA01**
Amendment date:	**13 September 2022**
IRAS project ID:	**302587**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Appendix U
HRA Approval for Substantial Amendment



berkshireb.rec@hra.nhs.uk <noreply@harp.org.uk>
30/09/2022 15:59

To: Roshan Nair (staff); Bethany Thompson; sponsor@nottingham.ac.uk



22.SC.0034.AM02 IRAS Project I...
106.59 KB

Dear Professor das Nair

IRAS project ID:	302587
REC reference:	22/SC/0034
Short Study title:	PrEliMS2 v1
Date complete amendment submission received:	13 September 2022
Amendment No./ Sponsor Ref:	21082 SA01
Amendment Date:	13 September 2022
Amendment Type:	**Substantial**
Outcome of HRA Assessment	**This email also constitutes HRA and HCRW Approval for the amendment, and you should not expect anything further.**

I am pleased to confirm that this amendment has been reviewed by the Research Ethics Committee and has received a Favourable Opinion. Please find attached a copy of the Favourable Opinion letter.

HRA and HCRW Approval Status

As detailed above, **this email also constitutes HRA and HCRW Approval for the amendment**. No separate confirmation of HRA and HCRW Approval will be issued.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/.

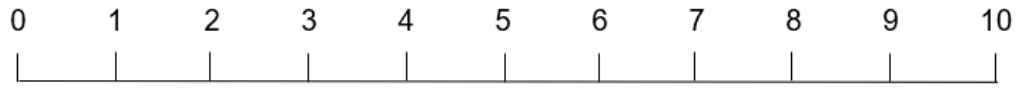
If you require further information, please contact me.

Kind regards

Sarah Ferry
The Old Chapel | Royal Standard Place | Nottingham Centre | NG1 6FS

Appendix V
Visual Analogue Scales

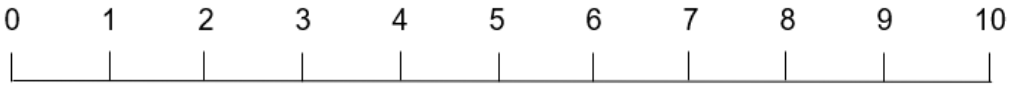
1. **How much of your current psychological distress is related to receiving a diagnosis of Multiple Sclerosis? (Please circle)**



Not at all

All of my current distress

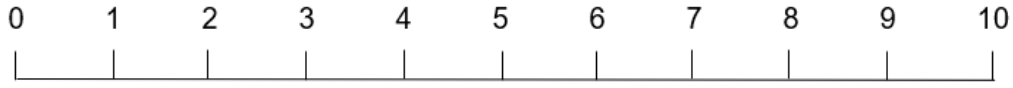
2. **How confident do you feel in managing the physical impact of Multiple Sclerosis day-to-day? (Please circle)**



Not at all

Very confident

3. **How confident do you feel in managing the psychological impact of Multiple Sclerosis day-to-day? (Please circle)**



Not at all

Very confident

Appendix W
Examples of Pages from the Workbook: 'Better Living with a Diagnosis of MS'

University of Nottingham
UK | CHINA | MALAYSIA

PrEliMS
Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis

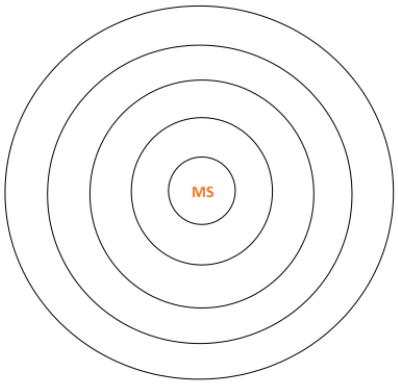
Better living with a diagnosis of MS

Patient Workbook

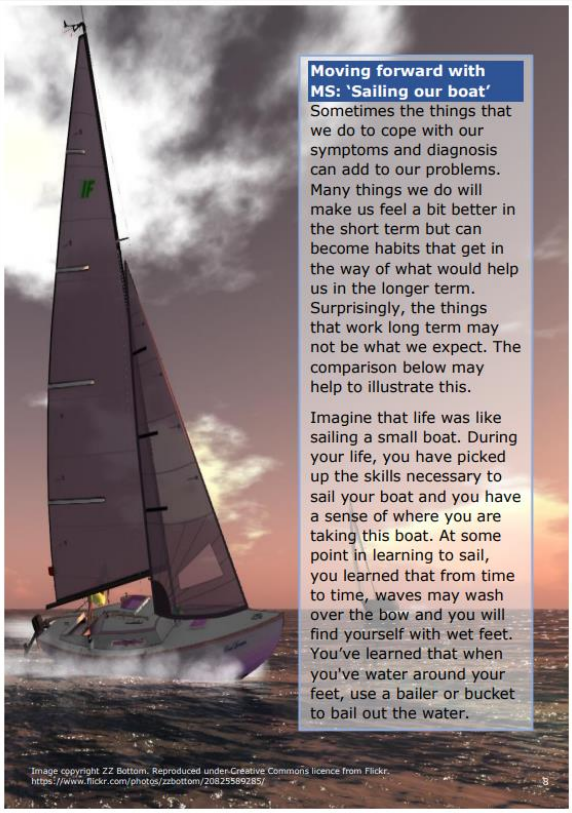
This workbook was developed by the PrEliMS Research team members at the University of Nottingham in collaboration with the MS Society and University of Lincoln. July 2018. The PrEliMS project is funded by the MS Society UK.

MS-related distress– and how we respond to it

Your MS could cause you distress. This is something that we sometimes can't do a lot about. Take a few minutes to think about the difficult responses that you have had to MS. Think about your emotional reaction to your illness and diagnosis, how you are not doing the things that are important to you, the impact your illness has had on your relationships. Write the things that come along with MS that also cause you distress in the circles around the MS circle.



6



Moving forward with MS: 'Sailing our boat'

Sometimes the things that we do to cope with our symptoms and diagnosis can add to our problems. Many things we do will make us feel a bit better in the short term but can become habits that get in the way of what would help us in the longer term. Surprisingly, the things that work long term may not be what we expect. The comparison below may help to illustrate this.

Imagine that life was like sailing a small boat. During your life, you have picked up the skills necessary to sail your boat and you have a sense of where you are taking this boat. At some point in learning to sail, you learned that from time to time, waves may wash over the bow and you will find yourself with wet feet. You've learned that when you've water around your feet, use a bailer or bucket to bail out the water.

Image copyright ZZ Bottom. Reproduced under Creative Commons licence from Flickr. https://www.flickr.com/photos/zzbottom/20825589285/

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Section 2.1 Acceptance: *Allowing for difficult experiences*

Acceptance refers to experiencing the unwanted thoughts, feelings, and sensations without evaluating them or trying to change them. This doesn't mean that you have to like or want the experiences. It is more to do with acknowledging that you are having these experiences ("there's that feeling again…") and that pushing it away may not be very helpful. Has it worked yet? Or if it works sometimes does it seem to work in the longer term for you? For example, have you noticed that when you try not to think about something (or someone) that you end up thinking more about it? Distraction may help for a few minutes or hours, but does it make the thoughts and feelings go away in the long term?



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Appendix X
Examples of Exercises from the Workbook: 'Better Living with a Diagnosis of MS'

Exercise 2.1.1

Quick Steps to acceptance of feelings and physical sensations

1. OBSERVE. Bring awareness to the feelings in your body.
2. BREATHE. Take a few deep breaths. Breathe into and around them.
3. EXPAND. Make room for these feelings. Create some space for them.
4. ALLOW. Allow them to be there. Make peace with them

Some people find it helpful to silently say to themselves, '*I don't like this feeling, but I have room for it,*' or '*It's unpleasant, but I can accept it.*'

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Exercise 2.2.1

'Simply noticing' exercise

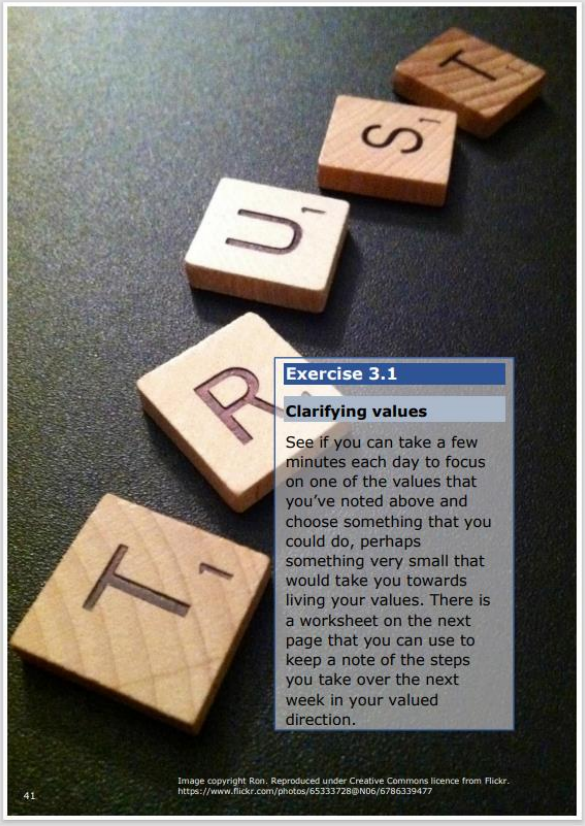
Let's try simply noticing the things that are occurring right now. Take a moment to get comfortable and sit quietly. Begin to notice sounds around you. Pay attention to anything making a noise in the room, the sound of the radio, the hum of a light. Listen out for any noises coming from other rooms, the sound of a washing machine, the boiler, a fan. Now focus on sounds coming from outside, cars passing by, people talking, birds... Are some sounds louder than others? Do some sounds come and go? Notice the weather, can you hear rain on the window or the wind blowing through trees? Are there lots of sounds? Is it noisy? Or is it generally quite quiet? If it's quiet, can you hear your own body? Can you hear your breathing or the sound your body makes as you move?



Now pay attention to what you can see. How many different things are there in the room that you are in? Spend some time looking at them. Is anything moving? Pets, people passing by the window, birds in the sky? What's the lighting like? Does the room look dark or light? Notice any colours that are in the room. Focus on one object and spend a couple of minutes really looking at it. Notice its shape, colour, size. Does it look heavy or light? Can you see any marks on it, any dust or any faults? Does it have lots of intricate parts to it or is it a relatively plain object? Does it look hard or soft?

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Exercise 3.1

Clarifying values

See if you can take a few minutes each day to focus on one of the values that you've noted above and choose something that you could do, perhaps something very small that would take you towards living your values. There is a worksheet on the next page that you can use to keep a note of the steps you take over the next week in your valued direction.

Image copyright Ron. Reproduced under Creative Commons licence from Flickr. https://www.flickr.com/photos/65333728@N06/6786339477

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Exercise 3.3

Remembering what's important

Create some blank cards, about the same size as business cards and write an area of life (as outlined on page 38) at the top of each one. On each card, write down your values. Carry these cards around with you as a reminder of what you stand for. If, at any point, you feel like your values are changing or you remembered something else that you value, take out your cards and either cross off or add to them. At the end of each day make time to take out your cards and ask yourself whether you have been living according to your values. If you have, be proud of yourself. If you haven't, don't worry about it: use this opportunity to reflect on what made it difficult for you to stick to your values. Also, think about any changes you could make in the future to make your week more consistent with what you value. Either way, you may want to start a journal to remind you of how far you have come, what you found difficult and what worked well for you.



Image copyright John Hain. Reproduced under Creative Commons licence from Pixabay. https://pixabay.com/en/man-standing-qualities-celebration-1207687/

44

Providing Emotional Support Around the Point of Multiple Sclerosis Diagnosis (PrEliMS-2): A multiple single case series

Bethany Thompson, Roshan das Nair, Anna Tickle, Henrietta Hall & Nima Moghaddam

Trent Doctorate in Clinical Psychology, Universities of Nottingham & Lincoln

Nikos Evangelou

Nottingham University Hospitals NHS Foundation Trust

Introduction

Multiple Sclerosis (MS) is a chronic, long-term condition. Diagnosis is fraught with a "rollercoaster" of emotion: uncertainty, fear, relief, anger and sadness[1].

Support at diagnosis plays a key role in coping with and adjusting to the disease, leading to better outcomes for quality of life and psychological health[2]. However, this is currently lacking from clinical service provision[3].

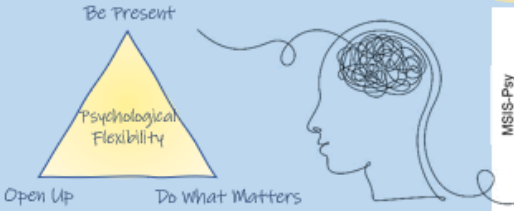
A recent feasibility randomised controlled trial aimed to test how best to provide this support (PrEliMS)[4]. The PrEliMS intervention is based on Acceptance and Commitment Therapy (ACT), which is a therapeutic approach focusing on acceptance, mindfulness and values-based action. ACT improves psychological health through psychological flexibility[5]. The approach has shown promising results for improving positive mental and physical health related-outcome in long-term conditions, including MS[6,7].

The PrEliMS-1 study did not find a signal of efficacy however some difficulties with delivery and practicality were identified by the nurses delivering the intervention.

Aims

To have a trainee clinical psychologist (TCP) deliver a four-session PrEliMS intervention to assess:

- signals of efficacy; particularly on the principle primary outcome (MSIS-Psy)
- change observed compared to PrEliMS-1
- improvements to be made to PrEliMS-2
- possible mechanisms of change.



Methods

We used a mixed-method, multiple single case AB design. Five participants completed all study phases.

Outcome measures:

Weekly

- Multiple Sclerosis Impact Scale – Psychological Subscale (MSIS-Psy; principle primary outcome)
- Comprehensive Assessment of Acceptance and Commitment Therapy Processes (CompACT-8)
- Generalised Anxiety Disorder (GAD-7)
- Patient Health Questionnaire (depression; PHQ-9)

Pre-, post-, 1-month follow-up

- Health Related Quality of life (EQ-5D-5L)
- Perceived Stress Scale (PSS-10)
- Multiple Sclerosis Self Efficacy Scale (MSSES)
- Modified Impact Fatigue Scale (MFIS-5)



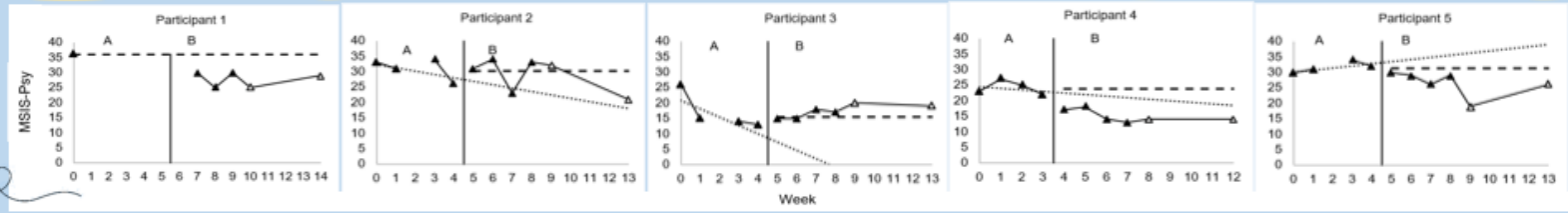
Analysis: Visual, Reliable and Clinically Significant Change, Standardised Difference Test and Framework Analysis.

Recruitment	Baseline	Intervention	Follow-up
•Clinician obtain consent to be contacted by researcher •Eligibility criteria applied •Consent obtained	•Three to five weeks •Primary measures completed weekly •Secondary measures pre-obtained	•Workbook received •Four weekly sessions with TCP •Primary outcome measures weekly	•At 1-week and 1-month post-intervention, repeat all outcome measures •Option qualitative feedback interview

Results

Two men and three women (*n* = 5), aged between 18-59 years, completed all study phases. Participants were recruited from an NHS MS Outpatient service in the United Kingdom.

- All five participants demonstrated reliable improvements in MSIS-Psy.
- Reliable and clinically significant improvement was observed in ACT-processes (*n* = 1), anxiety (*n* = 1), depression (*n* = 2), stress (*n* = 2), and self-efficacy (*n* = 3). No participant showed clinically significant change in health-related quality of life or fatigue.
- One participant (P3) showed clinically significant deterioration in stress and self-efficacy.
- One participant (P2) demonstrated change on the MSIS-Psy that was significantly larger ($p = 0.02$) in direct comparison to that observed in the first PrEliMS study.
- Recommended improvements included moving the values-based action to sooner in the intervention, having either longer or more sessions, and offering this as a group-based intervention.



Qualitative Feedback

"it's opened my awareness"

"non-judgemental supportive structure was so important"

"a good breadth of things in there [workbook] to kind of tailor how you wanted to use it"

"talking about that [acceptance] was when the penny dropped"

"a little more time would be beneficial"

Discussion

Reliable change was observed for all participants on the MSIS-Psy. We observed three demonstrations of an effect on the MSIS-Psy, meeting the criteria for inferring an effective intervention for reducing the psychological impact of MS. This key finding is in line with the primary focus of ACT in improving quality of life, as opposed to targeting symptom reduction.

Participants presenting with a clinical level of psychological distress (on the PHQ-9 and/or GAD-7) appeared to benefit more from the intervention.

All participants experienced reliable change in at least one outcome.

Direct comparison to PrEliMS-1 is limited, however findings from the current study are promising for TCP-delivered PrEliMS.

Participants overall found the intervention a positive experience, noting common therapeutic factors (i.e., non-judgemental interaction) as a salient factor.

Due to the small sample within this study, future research is warranted to test this intervention on a larger scale.

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