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Telephone-supported Acceptance and Commitment Bibliotherapy for People with Multiple Sclerosis and Psychological Distress: A Pilot Randomised Controlled Trial

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Abstract

A few randomised controlled trials (RCTs) show that Acceptance and Commitment Therapy (ACT) is beneficial for people with Multiple Sclerosis (MS), but the effectiveness of telephone-supported self-help ACT for people with MS with low mood has not been evaluated. We assessed the feasibility of conducting an RCT of an intervention (8 weekly telephone-calls plus a self-help ACT book) compared to treatment-as-usual. Participants' mood, quality of life, and impact of MS were assessed at baseline and 12 weeks post-randomisation. Some were interviewed to assess feasibility and acceptability. Twenty-seven participants were randomised. Most participants found the trial procedures acceptable. We found a large and significant effect at follow-up, favouring the intervention in reducing anxiety (*d*=0.84, 95% CI=0.02-1.66). However, the high attrition rate (33% overall) meant that the trial in its current format was not feasible. The intervention needs to be revised following user-testing and feedback before it can be put to a full trial.

Keywords: Acceptance and Commitment Therapy, Multiple Sclerosis, Teletherapy, Bibliotherapy, Randomised Controlled Trial, Guided Self-help

Introduction

Multiple Sclerosis (MS) is a central nervous system disease, wherein brain-areas are inflamed or destroyed by the immune system. More than 100,000 people in the UK

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are currently diagnosed with MS (MS Trust, 2017): most have a relapsing-remitting form; some stay as relapsing-remitting and a minority remain benign, however, for most, symptoms become permanent and degenerative (termed progressive MS).

MS can have diverse and unpredictable effects on psychological wellbeing (Wilkinson & das Nair, 2013) reflected in high prevalence-estimates for depression (30%) and anxiety (22%) (Boeschoten et al., 2017). Psychological and psychosocial problems frequently arise in relation to physical functioning, fatigue, pain, cognition, and relationships with others (Khan, Turner-Stokes, Ng, Kilpatrick, & Amatya, 2007).

Acceptance and Commitment Therapy (ACT)

ACT is a third-wave of Cognitive-Behavioural Therapy (CBT) underpinned by the theory of psychological flexibility, and is efficacious across a broad range of physical and psychological symptoms (A-tjak et al., 2015; Ruiz, 2010; Hacker, Stone, & MacBeth, 2016). ACT is designed to improve functioning and quality of life (QoL) by enabling individuals to live in accordance with personally-held values (Hayes, Strosahl, & Wilson, 1999). The model views experiential avoidance as a core pathogenic process, and attempts to increase acceptance of aversive experiences: as a means of promoting engagement with valued, and previously avoided, activities (Dahl, Wilson, & Nilsson, 2004).

ACT may be particularly suited to those with chronic physical health conditions, as traditional CBT thought-challenging of illness-beliefs may be limited when such cognitions could be accurate (Dennison, Moss-Morris, & Chalder, 2009). Furthermore, there is evidence that, in MS, avoidant coping strategies predict poor outcomes (Pakenham, 1999), and acceptance is the strongest predictor of adjustment (Pakenham, 2006). There is some preliminary research to suggest that group-based face-to-face ACT can be effective in reducing experiential avoidance and psychological distress in people with MS (Nordin & Rorsman, 2012; Pakenham, Mawdsley, Brown, & Burton, 2017).

Teletherapy

ACT is typically delivered face-to-face, but other delivery-formats warrant evaluation due to the costs of providing face-to-face therapy and because of a lack of services, particularly for those living in remote areas. Furthermore, people with MS may not be

able to access face-to-face therapies due to MS-related fatigue and reduced mobility. Telephone-psychotherapy (teletherapy) facilitates delivery to people in their own home: a recent review found that the teletherapy format could be efficacious for improving psychological outcomes (including depression, fatigue, and quality of life) in people with MS (Proctor, Moghaddam, Vogt, & das Nair, 2018); however, many of the studies were of poor methodological quality, so findings should be interpreted with caution.

Bibliotherapy

Bibliotherapy (self-help texts) is another common alternative or adjunct to face-to-face therapy, which can be supplemented with teletherapy. Meta-analyses have shown that bibliotherapies – including ACT-based bibliotherapies – can improve psychological outcomes, as compared to control conditions (den Boer, Wiersma, & van den Bosch, 2004; French, Golijani-Moghaddam & Schröder, 2017). A previous trial of an eight-week telephone-supported CBT bibliotherapy for people with MS found significant reductions in depression (Mohr et al., 2000). However, the trial was specific to those with depression diagnoses and did not consider the multitude of other psychological difficulties experienced by people with MS.

A telephone-supported ACT bibliotherapy may therefore provide an appropriate, accessible, and effective way of delivering psychotherapy to people with MS and psychological distress. To date, no studies have examined whether this format of ACT intervention is feasible within this population.

Aims

The primary aim of this study was to explore the feasibility of conducting an RCT of telephone-supported ACT bibliotherapy plus treatment-as-usual (TAU), compared with a TAU control group, for people with MS and psychological distress. Secondary to this, we explored between- and within-group differences to generate parameters for designing a full trial.

Methods

Participants

This study was approved by Institutional and NHS Research Ethics Committees (14/EM/1228). The trial was registered on ClinicalTrials.gov (ID: NCT02596633). Participants did not receive any financial incentive for participation.

We aimed to recruit 25-30 participants: to generate data enabling parameter-estimation for designing a full trial (Julious, 2005). Participants were recruited through a neurology outpatient clinic at an acute National Health Service (NHS) hospital in Nottingham, UK, and through an advertisement placed in a regional MS Society (charity) publication. Participants were adults with MS, diagnosed at least 12 months prior to trial-enrolment. Participants were screened for psychological distress using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). They were eligible if they met 'caseness' criteria on the HADS (scoring >7 for anxiety/depression), which is recommended in MS populations (Honarmand & Feinstein, 2009). Completion of the screening measure occurred in-clinic for those recruited through the NHS-service and via postal-return for those recruited through the MS Society. Participants unable to read and write English, and those receiving other psychotherapy, were excluded. Informed consent was obtained.

Assessment

Basic demographic details, time since MS diagnosis, time since last relapse, most recent Expanded Disability Status Scale (EDSS; Kurtzke, 1983) score, and current medication were noted from clinical records. Participants also self-reported current medications and contacts with health services on a bespoke healthcare-utilisation questionnaire. This is not a validated questionnaire but based on the resources available in the Database of Instruments for Resource Use Measurement (dirum.org; Ridyard & Hughes, 2012), which includes the number and types of primary and secondary care NHS resources used, and changes to employment status.

Baseline assessments were administered to all participants pre-randomisation, and these assessments were repeated at follow-up, 12 weeks post-randomisation. Co-primary outcome measures were the Generalised Anxiety Disorder 7-item (GAD-7) scale (Spitzer, Kroenke, Williams, & Löwe, 2006) and the Patient Health Questionnaire-9 (PHQ-9; Kroenke, Spitzer, & Williams), which captured anxiety and depression, respectively. Secondary outcomes were the Multiple Sclerosis Impact Scale (MSIS-29; Hobart, Lamping, Fitzpatrick, Riazi, & Thompson, 2001) which splits

into physical and psychological sub-scales (Ramp, Khan, Misajon, & Pallant, 2009). The EQ-5D-5L (Herdman et al., 2011) was administered to assess QoL. The Acceptance and Action Questionnaire (AAQ-II; Bond et al., 2011) was included as a process measure, to gauge variability in ACT-targeted processes of experiential avoidance and psychological inflexibility. Measures were administered securely online using www.esurv.org; except the EQ-5D-5L, which was administered and collected via post.

Design

The study was a pilot RCT – as defined by Eldridge et al. (2016). Participants were randomly allocated to intervention or control (1:1 ratio). The randomisation sequence was computer-generated by one researcher (NM), concealed from other researchers, and entered into a standalone web-based system (Cunningham, 2006). The recruiting researcher (BP) used this system to request individual time-stamped allocations at the point of consent, before informing the participant of their allocation.

Feasibility and acceptability feedback was obtained via telephone-interviews, conducted by an independent researcher with a sub-sample of participants, 12-weeks post-randomisation. We followed guidance for maximising the impact of qualitative methods within a pilot trial (O'Cathain et al., 2015) and used maximum variation purposive sampling to select five participants from each arm to capture a diverse range of perspectives within our sample, sufficient to provide elaborative nuance to this primarily quantitative design.

Intervention

The intervention arm consisted of TAU plus the self-help book "Get out of your mind and into your life" (Hayes, 2005) – with guidance on which chapters to read each week. This coincided with eight weekly support-calls, theoretically orientated to the ACT model, from a trainee clinical psychologist (BP), who supported participants in understanding the text and engaging with the model. BP received supervision from an experienced ACT practitioner-researcher (NM). The book covers all components of the ACT model and prompts self-application through multiple semi-structured exercises per chapter – enabling the reader to tailor material to their own

idiosyncratic needs. Participants in this arm received no other psychological therapies.

The control arm consisted solely of TAU, conforming to UK National Institute for Health and Care Excellence guidance for MS symptoms (NICE, 2014), which typically involves referral to psychological services for intervention or medication for mood problems, although none in the TAU group accessed any psychological therapy.

Analysis

To assess feasibility and acceptability, framework analysis (Gale, Heath, Cameron, Rashid, & Redwood, 2013) of interview-data was undertaken by BP. Pre-defined codes about feasibility and acceptability of the study and intervention were assigned to interview-transcripts, then codes were amalgamated into a framework.

Healthcare-utilisation was explored between groups using independent t-tests. Self-report medication was cross-referenced against medication recorded in clinical notes. EQ-5D-5L scores were norm-converted using UK EQ-5D-5L value-sets. Independent t-tests were conducted to explore baseline differences between intervention completers vs. non-completers.

RCT analysis used an intention-to-treat approach. Independent variables of ‘group allocation’ and ‘time point’ were entered into linear mixed models to explore interactions of intervention and time. This method provides unbiased estimates in the presence of missing data, enabling us to use all observed data and include participants who did not return data at all timepoints, so avoiding the need for (and potential biases of) methods of imputation. Given the feasibility-nature of the study, *p* values were not adjusted for multiple comparisons: consistent with recommendations for pilot and feasibility trials (Moore, Carter, Nietert, & Stewart, 2011) we sought to explore potential efficacy (to be tested subsequently in larger trials). To produce standardised estimates of effect for the linear mixed models, we applied Cohen's *d* calculation to the relevant data for estimated marginal means and their pooled standard deviation (Hedges, 2007); we additionally computed 95% confidence intervals around point-estimates of effect-size.

Sample-size estimates for a full trial were computed using the standard deviations of the GAD-7 and PHQ-9 at 12-weeks post-randomisation and published clinically significant change (CSC) values.

Results

Sample

Two participants responded to the advertisement in the MS Society publication. From the outpatient clinic, consultants referred 33 patients, 25 of whom consented, to make up 27 enrolled participants. Demographic and baseline clinical characteristics of the sample are shown in Tables 1 and 2.

Feasibility

To summarise data from interview respondents (n=10) we refer to the number of participants endorsing particular codes using the terms “majority”, “some” and “minority”, meaning more than 75%, 50-75%, and under 50% (respectively) of all participants who referenced a given code.

Recruitment

The majority of interviewed participants found the pathway to recruitment appropriate and the recruitment process straightforward. A minority thought their neurologist using their appointment to discuss the trial was inappropriate. The majority thought the information provided by the recruiter (BP) was clear. A minority wanted more information about the commitment and work required from participants.

Randomisation

Whilst all interviewed participants agreed that randomisation was a fair way to allocate people to intervention or control, some participants reported they did not fully understand minutiae of the process – suggesting that provision of information about randomisation could be enhanced, to ensure that individuals are making suitably informed decisions about participation.

Measures

At follow-up, 25 of 27 participants (93%) completed online-questionnaires, and 24 participants (89%) completed postal-questionnaires (EQ-5D-5L only). On average, online-questionnaires took 14 minutes to complete (SD=9).

The majority of interviewees found the questionnaire-items clear, easy and quick to complete, and appropriate for the study. Some participants reported wanting to add text to clarify their responses, because response-options did not adequately capture their experiences.

Self-reported healthcare-utilisation

At follow-up, 25 of 27 participants (93%) reported their frequency of MS-related service contacts over the preceding three months. In the intervention group, the mean number of contacts was 10.8 (SD=6.6) versus 7.4 (SD=6.2) in the control group, which was not a statistically significant difference (p=0.2) but represented a moderate effect-size (d=0.53). Across 23 participants' self-reporting medication use, there were 45 instances where clinical notes described a medication a participant had not listed – and 20 instances where participants self-reported a drug that was unlisted in clinical notes.

Attrition

Overall, 9 of 27 (33%) participants dropped out of the study. All nine were participants randomised to receive the intervention (within-group attrition of 64%). Of non-completers, six did not start the book and three dropped out after reading the first few chapters and receiving one support-call. Table 3 summarises reasons for non-completion.

Baseline comparisons of completers versus non-completers revealed that non-completers scored higher on the MSIS-physical and -psychological subscales and the AAQ-II at baseline (Table 4).

Support-calls

Of the five participants who completed the self-help book: 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 (one took 10 weeks to complete the book and the other took 12 weeks).

The average support-call length was 14 minutes (SD=6). Intervention participants rescheduled the timing of their support-calls on 8 of 42 occasions (19%); and there was one occasion where a scheduled call was missed.

The majority of participants agreed that support-calls were helpful and appropriate in length, and that the researcher was supportive. However, they felt that either less text to read each week, or calls spaced further apart would have been a better pace for the intervention.

Self-help text

The majority of interviewed participants found the language used in the self-help text understandable, although a few found it too complex. The majority thought that the language was "Americanised", and a considerable amount of re-reading was required.

Regarding helpfulness of specific book-elements, there was variability across the sample. For example, one participant found the 'Values' chapter most helpful; one found the 'Mindfulness' chapter most helpful, and one found it unhelpful. The majority of interviewed participants thought that other people with MS would find the book and the phone-support helpful.

Effectiveness

As shown in Table 5, the intent-to-treat[2] linear mixed model[3] analyses found a significant interaction effect for time and allocation on the GAD-7 in favour of the intervention at follow-up (F=10.34, p=0.004). No statistically-significant comparisons were identified for depression, QoL, or MSIS outcomes.

Effect-sizes at follow-up, with 95% confidence intervals (CI), are displayed in Table 5. A large and significant effect-size (d=0.84, 95% CI=0.02-1.66) was found in favour of the intervention on one of the co-primary outcomes measure of GAD-7 at follow-up, but not the other (PHQ-9 [d=0.2, 95% CI=-0.59-0.99]). The strengths of the

[2] Per protocol analysis results were similar in that a significant interaction of time and group allocation for the GAD-7 (anxiety) was found (F=8.7, p=0.011) with a large effect size (d=2.054, 95% CI=0.8-3.3).

[3] Mixed ANOVAs of all dependent variables were also conducted. A similar trend of results was found to the linear mixed models in that there was a significant interaction of time and group allocation for the GAD-7 (anxiety) and no other significant effects.

effect-estimates vary across measures; however, all estimates were positive and favoured intervention.

Sample Size Estimation

In a full trial, a total of 34 participants (i.e., 17 per arm) would be required to have a 90% chance of detecting, as significant at the 5% level, a clinically significant decrease of five points on the GAD-7. With the same criteria, 76 participants (38 per arm) would be required to detect clinically significant decrease on the PHQ-9. These figures would need to be higher to account for attrition.

Discussion

This is the first study to evaluate the feasibility of conducting a telephone-supported ACT bibliotherapy for people with MS and psychological distress. Regarding the primary aim, whilst some aspects of trial design appeared viable (e.g., recruitment, randomisation, and outcome measurement) the high level of attrition in the intervention arm identified problems with the piloted approach to implementing telephone-supported ACT bibliotherapy. However, preliminary effect-estimates were promising, and warrant further testing.

Trial procedures

Recruitment was straightforward, and the required number of participants was recruited within three months. Some additional information regarding the commitments required to participate is needed. Participants did not object to being randomised, but additional information about the rationale and need for randomisation may improve understanding of this process. With good completion of online- and postal-questionnaires (>89%), most participants found the questionnaires easy to understand and complete. We attempted to collect healthcare-utilisation information in a non-validated self-report questionnaire. However, when compared to clinical records, there were marked discrepancies in both directions, with no consistent pattern. Both sources of information may be limited (Byford et al., 2007). On balance, in a future trial, we recommend collecting this information from patients, but by supplementing data collection with a telephone support from a researcher (Heinrich et al., 2011). Designing a validated healthcare utilisation measure may also be prudent.

Attrition

Of most concern was the attrition rate. All the participants who dropped out from the study (33%) were from the intervention group. The mean attrition rate from a meta-analysis of telephone-administered psychotherapy for depression was 7.6% (95% CI=4.23–10.90), across all studies (Mohr, Vella, Hart, Heckman, & Simon, 2008). Methodological differences notwithstanding, the level of attrition from the intervention group in our study therefore clearly suggests problems that participants had in engaging with the intervention. There were, however, a mixture of external factors and trial-related factors influencing participant drop-out. Most participants dropped out due to illness-related factors (e.g., episodes of worsening in clinical symptoms) or not being able to commit to the programme, and some dropped out as they found the self-help text too generic for their diagnosis of MS.

Participants who dropped out tended to have higher baseline rates of MS-related physical and psychological distress compared to intervention-completers – suggesting that those who could benefit most from psychological intervention may be those most likely to disengage. Engagement with psychotherapy requires effort and concentration, and problem confrontation may initially increase distress and established avoidance responses (Bystedt, Rozental, Andersson, Boettcher, & Carlbring, 2014). People with higher rates of physical and psychological distress were potentially unable to tolerate and/or engage with the intervention, because of their illness-related distress or because of MS-related cognitive decline.

Non-completers also had significantly higher baseline scores on the AAQ-II than completers. Therefore, ACT-based interventions may be less acceptable to people with high rates of experiential-avoidance, the very process that ACT attempts to reduce. People with lower rates of experiential-avoidance may find that the ACT model is more consistent with their pre-existing coping styles, facilitating engagement and building on established skills. For those higher in experiential avoidance, it may be important to provide more intensive therapist input at an early stage: supporting acculturation to an approach that markedly differs from established coping responses. Incorporation of more comprehensive measures of psychological flexibility (e.g., Francis, Dawson, & Golijani-Moghaddam, 2016) could enable greater

insight into whether/how differential functioning in ACT-targeted processes influences treatment engagement.

Those who were able to engage with the self-help text (persisting beyond the early chapters) found the content to be beneficial and perceived that others with MS could benefit from it. However, interview feedback and completion-time data suggested that pacing should be revisited: allowing more time and flexibility to complete the materials (in the context of illness-related burden). The telephone support component was well-received: most calls were made as scheduled, and call durations were brief, suggesting that this form of adjunctive support would be acceptable and feasible to provide within limited resources. Based on responses indicating that some of the UK participants found (1) the language to be 'Americanised' and overly complex/academic, and (2) the content to be sometimes difficult to relate to their (e.g., MS-specific) experiences, we would recommend the following adaptations: (1) UK-regionalisation and simplification of language and (2) either (i) additional guidance and support to self-apply the generic self-help materials (particularly early on; e.g., through an initial orientation meeting to set expectations and clarify relevance) or (ii) revision of the text to include more relatable (e.g., MS-specific) examples. Any revisions should be made with iterative feedback from individuals with relevant lived experience, and with checks for fidelity to the core components of the ACT model (to ensure, for example, that changes to the form of language do not disrupt intended functions).

Effectiveness

A lack of power, multiple comparisons and large attrition rate make the detection of significant differences unlikely, yet a significant large effect was found for anxiety in favour of the intervention group at follow-up in intention-to-treat analysis. Ostensibly, this suggests initial evidence for the ‘success’ of the intervention and the strong effect of the intervention-completers in the analysis. Our study is the first to demonstrate a substantive effect of ACT on anxiety in people with MS, given non-significant and small effect-magnitudes for this outcome in previous MS-specific ACT studies (Nordin & Rosman, 2011; Pakenham et al., 2017). Notably, our observed effect-size is similar to the pooled-estimate from a meta-analytic review of ACT on anxiety (0.84; Vøllestad, Nielsen, & Nielsen, 2012).

Less impact was evident on measures of depression. There were higher levels of anxiety than depression in this sample; whereas most research reports the reverse (Korostil & Feinstein, 2007; Mohr & Cox, 2001). Participants may have focally used the intervention to manage their primary presenting concern (anxiety).

The high attrition-rate has limited the confidence with which we can estimate parameters for a full trial. However, the mixed-methods design of this pilot-trial was a strength; enabling more detailed exploration of practical issues and reason for withdrawal, with implications for improving participant retention in future studies.

Conclusions

Overall, we found that the current intervention design was not feasible for trialling telephone-supported ACT bibliotherapy for people with MS and psychological distress. Preliminary evidence indicates that the intervention may be effective in reducing anxiety, but high attrition suggests that the treatment cannot be evaluated on a larger scale without further user-testing and refinement. Such a process could be usefully informed by User-Centred Design principles and practices (Lyon & Koerner, 2016), and might include cognitive interviewing with prospective users (persons with MS) focussed on intervention content, format, and ease of understanding (Willis, 2015) with a view to maximising the acceptability of (and potential engagement with) the self-help materials.

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Table 1. Baseline demographic characteristics of the control and intervention groups.

Characteristic	TAU group (n=13) *Mean (SD)*	Intervention group (n=14) *Mean (SD)*	p value
Age, years, mean *(SD)*	45.8 *(8.8)*	46 *(12.4)*	0.984a
Male/Female	0/13	3/11	0.22b
Diagnosis, *n* (%)			0.61c
Relapsing Remitting	10 (77%)	9 (64%)	
Primary Progressive	2 (15%)	2 (14%)	
Secondary Progressive	1 (8%)	3 (21%)	
Years since MS diagnosis *(SD)*	6.2 *(4.7)*	9.7 *(7.5)*	0.16a
Years since last relapse *(SD)*	2.5 *(1.9)*	2.2 *(3.9)*	0.83a
Marital Status			0.152c
Single	3	2	
Married/Civil Partnership	7	12	
Divorced/Dissolved Partnership	2	0	
Widowed	1	0	
Employment Status			0.746c
Full Time	3	2	
Part Time	3	3	
Unpaid Work	0	1	
Not Employed	6	5	
Retired	1	2	
In Education	0	1	

a=Independent t-test, b=Fisher's exact test, c=Pearson's chi squared.

Table 2. Baseline clinical characteristics of the control and intervention groups.

Characteristic	TAU (n=13) *Mean (SD)*	Intervention group (n=14) *Mean (SD)*	p value
HADS	18.5 *(5.5)*	20.8 *(4.8)*	0.24a
EDSS	4.9 *(2)*	5.4 *(1.6)*	0.51a
GAD-7	16.8 *(4.8)*	18.3 *(5)*	0.45a
PHQ-9	21.2 *(5.9)*	22.1 *(7.1)*	0.72a
MSIS-Physical	63.8 *(14.3)*	60.6 *(20.2)*	0.63a
MSIS-Psych	28.7 *(7.8)*	29.9 *(8.9)*	0.7a
EQ-5D-5L	0.356 *(0.253)*	0.408 *(0.292)*	0.62a
AAQ-II	23.8 *(12.9)*	27.4 *(9.5)*	0.41a

HADS: Hospital Anxiety and Depression Scale, EDSS: Expanded Disability Status Scale, EQ-5D: Quality of Life Measure, GAD: Generalised Anxiety Disorder scale, PHQ: Patient Health Questionnaire, MSIS-Physical: Multiple Sclerosis Impact Scale - Physical health subscale, MSIS-Psych: Multiple Sclerosis Impact Scale - Psychological subscale, AAQ-II: Acceptance and Action Questionnaire, a: Independent t-test.

Table 3. Completers and non-completers in the intervention group.

	Intervention group (n=14)
Completed Intervention	5 (36%)
Non-completers:	9 (64%)
Too busy	4 (29%)
Lost to follow-up	2 (14%)
Book described as inappropriate	2 (14%)
Too unwell	1 (7%)

Table 4. Baseline characteristics of intervention completers and non-completers.

	Group		
	Completers (n=5)	**Non-completers (n=9)**	
Characteristic/Measure	Mean *(SD)*	Mean *(SD)*	p value
Age, (years)	51.8 *(6)*	42.7 *(14)*	0.2a
Years since MS diagnosis	11.2 (7.8)	8.9 (7.7)	0.62a
Years since last relapse	2.2 (2.6)	2.3 (4.4)	0.96a
Diagnosis, *n* (%)			0.9c
Relapsing Remitting	3	6	
Primary Progressive	1	1	
Secondary Progressive	1	2	
HADS	19.4 (4.6)	21.7 (5)	0.42a
EDSS**	4.5 (2)	5.8 (1.1)	0.3a
GAD-7	15.2 (2.9)	20 (5)	0.85a
PHQ-9	18.8 (6.9)	24 (6.9)	0.2a
MSIS-Physical	45.2 (15)	69 17.9)	0.027a*
MSIS-Psych	22.6 (7.6)	34 (6.9)	0.014a*
EQ-5D-5L	0.49 (0.18)	0.36 (0.33)	0.44a
AAQ-II	19.6 (6.9)	31.8 (7.9)	0.014a*
Service use (no of contacts)	8.4 (5)	12.2 (7.2)	0.28a

a=Student's t test, b=Fisher's exact test, c=Pearson's chi squared.

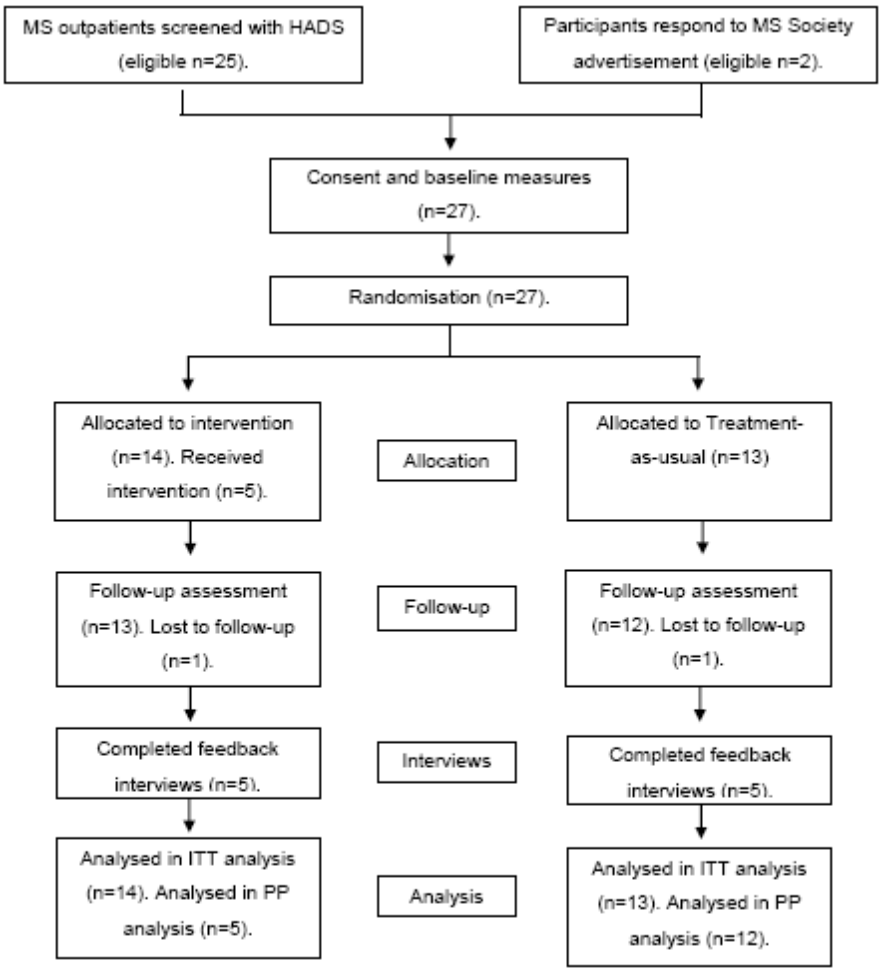
**completers: n=5; non-completers: n=8. *= significant at p=0.05

Table 5. Baseline and follow-up means between and within groups, results of linear model analyses of interaction effects of allocation and time, and effect sizes of intervention vs TAU at follow-up.

	Time					
	Pre-randomisation			**Follow-up**			
Measure	TAU (n=13) Mean *(SD)*	Intervention (n=14) Mean *(SD)*		TAU (n=12) Mean *(SD)*	Intervention (n=13) Mean *(SD)*	F *(p value)* Interaction effect	Effect size *(95% CIs)* at follow-up
GAD-7	16.8 *(4.8)*	18.3 *(5)*	GAD-7	16.8 *(4.6)*	12.7 *(5.2)*	10.34 *(0.004)*	0.84 *(0.02-1.66)*
PHQ-9	21.2 *(5.9)*	22.1 *(7.1)*	PHQ-9	19.6 *(6.3)*	18.4 *(7.5)*	0.74 *(0.39)*	0.2 *(-0.59-0.99)*
MSIS-Physical	63.8 *(14.3)*	60.6 *(20.2)*	MSIS-Physical	60.6 *(16.7)*	57.5 *(21.7)*	0.016 *(0.9)*	0.14 *(-0.65-0.92)*
MSIS-Psych	28.7 *(7.8)*	29.9 *(8.9)*	MSIS-Psych	28.1 *(9.3)*	24.5 *(10.6)*	3.82 *(0.063)*	0.46 *(0.34-1.25)*
EQ-5D-5L	0.36 *(0.25)*	0.41 *(0.29)*	EQ-5D-5L*	0.44 *(0.2)*	0.45 *(0.22)*	0.099 *(0.756)*	0.11 *(-0.71-0.93)*
AAQ-II	23.8 *(12.9)*	27.4 *(9.5)*	AAQ-II**	23.4 *(12.5)*	20.9 *(13.2)*	2.868 *(0.105)*	0.23 *(-0.58-1.03)*

*: n for TAU = 11, n for Intervention = 12, **: n for TAU = 11, n for Intervention = 13.

HADS: Hospital Anxiety and Depression Scale, EDSS: The Expanded Disability Status Scale, EQ-5D-5L: Quality of Life Measure, GAD: Generalised Anxiety Disorder scale, PHQ: Patient Health Questionnaire, MSIS-Physical: Multiple Sclerosis Impact Scale - Physical health subscale, MSIS-Psych: Multiple Sclerosis Impact Scale - Psychological subscale, AAQ-II: Acceptance and Action Questionnaire.



MS: Multiple Sclerosis, HADS: Hospital Anxiety and Depression Scale, ITT: Intention-to-treat, PP: Per-protocol.

Fig. 1: Flow of participants through the study.

Highlights

- Preliminary evidence that the intervention can reduce anxiety in those with MS
- Low adherence and high attrition suggest the current trial-design lacks feasibility
- Further user-testing and design adaptation is warranted, given preliminary evidence