Preface

This report presents the results of the PIMS feasibility trial, focusing on analyses assessing the feasibility of a full-scale trial against pre-defined progression criteria outlined in the Statistical Analysis Plan (version 1.0).

This draft report covers recruitment, patient flow, and baseline demographic and clinical characteristics by group. Analyses related to treatment effects are based on partially blinded group indicator variable. The analyst was fully unblinded for this analysis regression analysis includes facilitator, which is only relevant for the intervention arm.

This was a multicentre, two-arm, randomised feasibility trial evaluating the feasibility and acceptability of the Psychosexual Intervention for Sexual Difficulties in People with Multiple Sclerosis (PIMS). Adults with multiple sclerosis who reported sexual or intimacy difficulties were randomised to receive either PIMS or a control intervention consisting of psychosexual education/usual care. The primary purpose of the study was to assess feasibility outcomes, including eligibility, recruitment, retention, adherence and acceptability, to inform the design of a future definitive trial.

Background

The PIMS trial is a two-armed, parallel-group, multi-centre randomised controlled feasibility trial assessing the effectiveness of a psychosexual intervention for people with Multiple Sclerosis (MS) experiencing sexual or intimacy difficulties.

The primary objective of the PIMS trial is to evaluate the feasibility of conducting a full-scale phase III randomised controlled trial by examining recruitment, retention, and adherence rates, as well as the acceptability of the intervention. Secondary objectives include exploring differences in self-reported sexual function outcomes between trial arms and qualitatively evaluating participant and healthcare provider perceptions of the intervention.

Outcomes

Primary feasibility outcomes include recruitment and retention rates, adherence to the intervention, and participant acceptability as assessed by an 8-item satisfaction inventory. Secondary outcomes focus on sexual function, intimacy-related quality of life, and health economic measures, using validated instruments such as the Sexual Function Evaluation Questionnaire (SFEQ), Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19), and EQ-5D-5L.

Table 1. Outcome completeness and reliability

	Items	Estimable*	Cronbach's Alpha (at baseline)	McDonald's Omega (at baseline)
Sexual Function Evaluation Questionnaire (SFEQ) total score	13	84.6%	.681	.748
Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19)primary subscale score	5	93.6%	.657	.658

Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19)secondary subscale score	9	93.6%	.839	.833
Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19) tertiary subscale score	5	93.6%	.800	.792
Female Sexual Distress Scale-Revised (FSDS-R) total score	13	93.6%	.923	.926
New Sexual Satisfaction Scale – Short form (NSSS-S) total score	12	92.3%	.893	.884
Guy's Neurological Disability Scale (GNDS) total	12	94.9%	.639	-
Guy's Neurological Disability Scale (GNDS) sexual subscale score	1	94.9%	NA	NA
EQ-5D-5L utility	5	96.2%	.711	.727
EQ-5D-5L health	1	96.2%	NA	NA
Patient Health Questionnaire-9 (PHQ-9) total score	9	96.2%	.804	.793
Generalised Anxiety Disorders (GAD7) total score	7	96.2%	.862	.801
Five Facet Mindfulness Questionnaire (FFMQ) awareness of actions total score	8	92.3%	.843	.867
Five Facet Mindfulness Questionnaire (FFMQ) non-judgement total score	8	92.3%	.935	.933
Dyadic Sexual Communication (DSC) total score	13	93.6%	.579	-

*Out of a total of 78 completed baseline and follow-up assessments

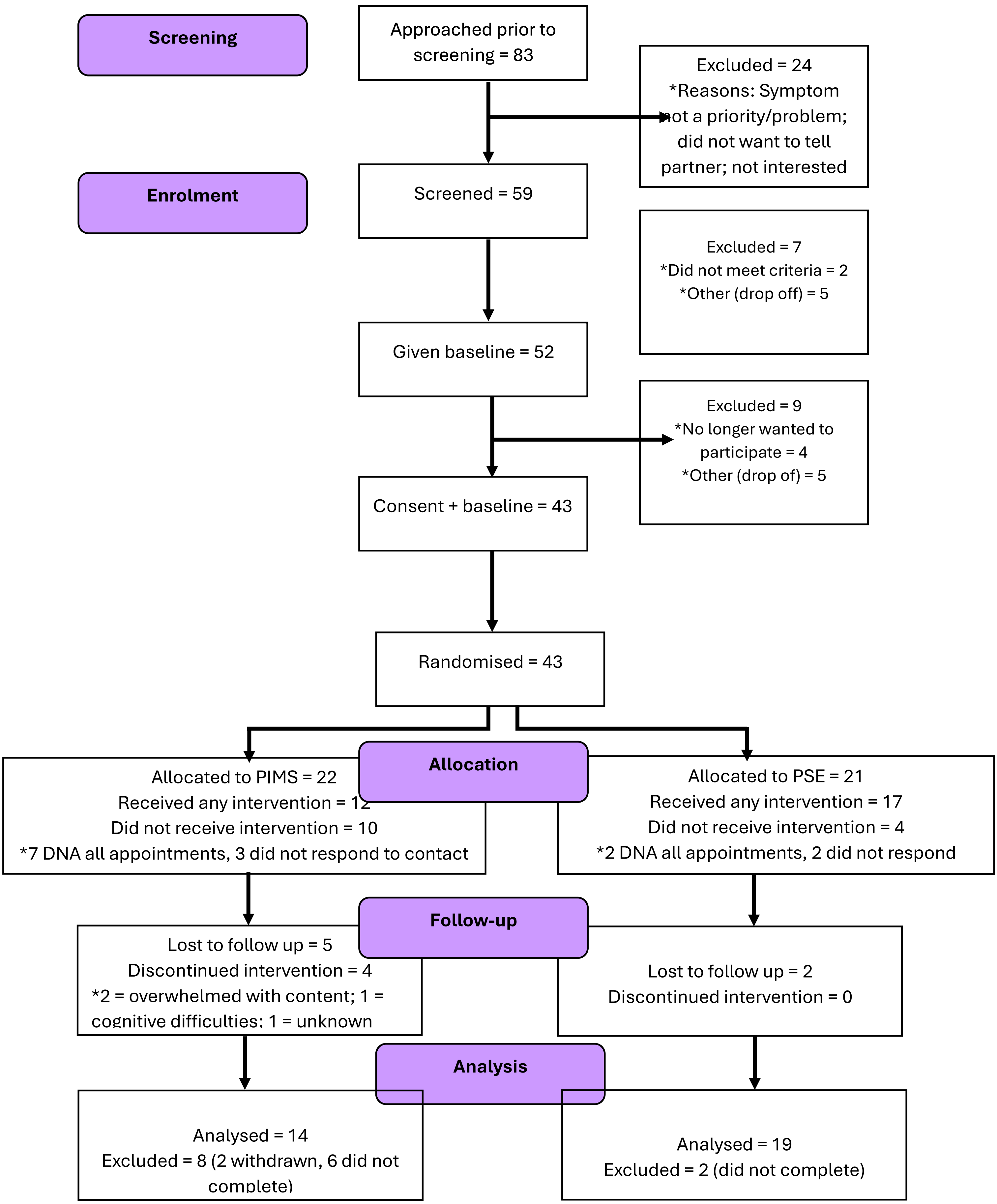
Statistical Analyses

Statistical analyses were conducted according to the Statistical Analysis Plan version 1.0 dated July 2024. Descriptive statistics will summarise recruitment, retention, and baseline characteristics by group. Primary outcomes will be reported with 95% confidence intervals (CIs), and secondary outcomes will explore between-group differences using linear regression models. Treatment efficacy will be assessed using exploratory analyses, with between-group differences expressed as adjusted mean differences and Hedge's g standardised mean difference effect sizes. Missing data will be handled through pro-rating and missing indicator methods, with sensitivity analyses conducted where necessary. Descriptive analyses were conducted in SPSS Statistics 29 and MS Excel and treatment effect analyses in Stata MP 18.

Results

Recruitment and patient flow

Patient flow through the study is presented in Figure 1. Between 11/30/2022 and 03/25/2024, 59 patients were screened and 43 patients were randomised to receive either PIMS plus TAU (N=22) or TAU alone (N=21).


Screening
Approached prior to screening = 83
Excluded = 24
*Reasons: Symptom not a priority/problem; did not want to tell partner; not interested
Enrolment
Screened = 59
Excluded = 7
*Did not meet criteria = 2
*Other (drop off) = 5
Given baseline = 52
Excluded = 9
*No longer wanted to participate = 4
*Other (drop of) = 5
Consent + baseline = 43
Randomised = 43
Allocation
Allocated to PIMS = 22
Received any intervention = 12
Did not receive intervention = 10
*7 DNA all appointments, 3 did not respond to contact
Allocated to PSE = 21
Received any intervention = 17
Did not receive intervention = 4
*2 DNA all appointments, 2 did not respond
Follow-up
Lost to follow up = 5
Discontinued intervention = 4
*2 = overwhelmed with content; 1 = cognitive difficulties; 1 = unknown
Lost to follow up = 2
Discontinued intervention = 0
Analysis
Analysed = 14
Excluded = 8 (2 withdrawn, 6 did not complete)
Analysed = 19
Excluded = 2 (did not complete)

Eligibility and recruitment rates: This will allow us to determine whether our eligibility criteria are appropriate, and whether those eligible to participate (i.e., complete screening) are willing to be randomised.

- Eligibility rate: proportion of those screened who meet inclusion criteria
    - 57/59: 96.6% 95%CI 88.3% to 99.6%
- Recruitment rate: proportion of eligible PwMS consented to trial
    - 43/57: 75.4% 95%CI 62.2% to 85.9%

Follow up/retention rates: Proportion of participants who were randomised that completed the follow up assessment

- Retention rate: % participants randomised who complete 14-week follow up
    - Started follow-up 35/43: 81.4% 95%CI 66.6% to 91.6%
    - Provided sufficient data for at least one outcome 33/43: 76.7% 95%CI 61.4% to 88.2%
        - TAU 2/21: 90.5% 95%CI 69.6% to 98.8%
        - PIMS 14/22: 63.4% 95%Ci 40.7% to 82.8%
    - Withdrew
        - PIMS 4/22: 18.2% 95%CI 5.2% to 40.3%

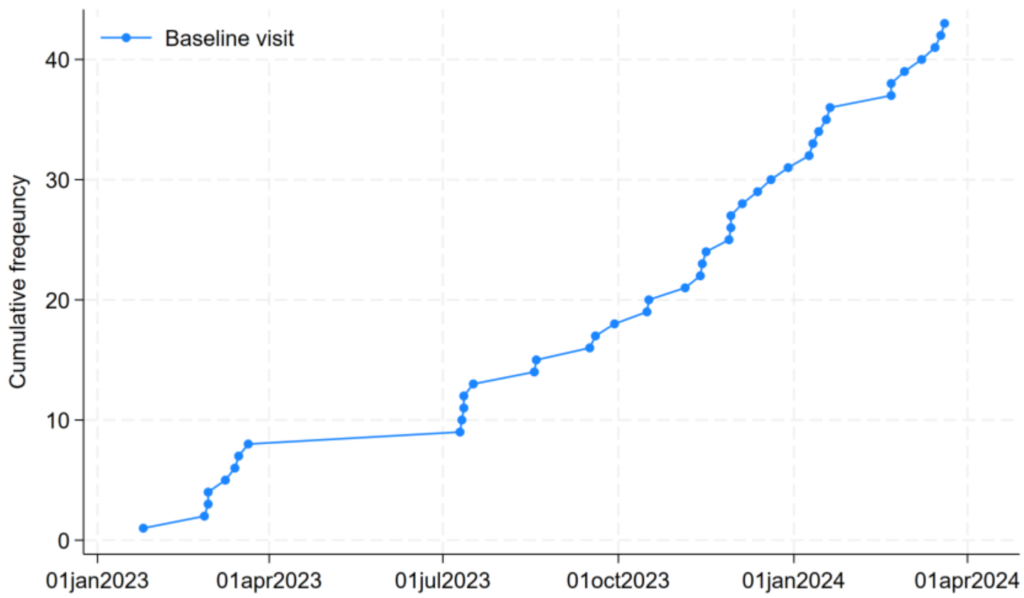


Figure 1. Timing of recruitment and randomisation events

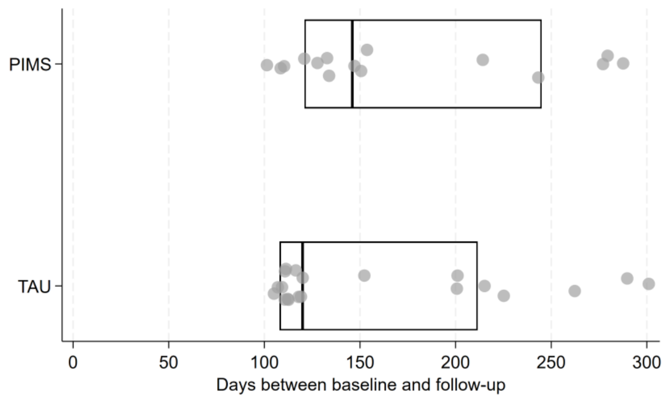


Figure 2. Timing of follow-up assessment

Baseline data by treatment group

Table 2. Baseline demographic variables by treatment group

	TAU N=21	PIMS N=22
Age in years (median, IQR)	43.3 (33.9-58.3)	48.1 (37.6-53.5)
Gender		
Male	9 (42.9%)	9 (40.9%)
Female	11 (52.4%)	13 (59.1%)
Unknown	1 (4.8%)	0 (0.0%)
Sex assigned at birth		
Male	9 (42.9%)	9 (40.9%)
Female	12 (57.1%)	13 (59.1%)
Sexual orientation		
Heterosexual	19 (95.0%)	20 (90.9%)
Bisexual	1 (5.0%)	0 (0.0%)
Gay/Lesbian	0 (0.0%)	1 (4.5%)
Asexual	0 (0.0%)	1 (4.5%)
Relationship status		
Single (not dating)	2 (9.5%)	1 (4.5%)
Single (currently dating)	4 (19.0%)	0 (0.0%)
Long-term partner (including married)	13 (61.9%)	21 (95.5%)
Other/unknown	2 (9.5%)	0 (0.0%)
Education		
GCSE/O Level or equivalent	5 (26.3%)	5 (22.7%)
A-Level or equivalent	4 (21.1%)	2 (9.1%)
Some college or university, no degree	5 (26.3%)	3 (13.6%)
Bachelor's degree	3 (15.8%)	6 (27.3%)
Master's degree	2 (10.5%)	6 (27.3%)
Ethnicity		
White	17 (81.0%)	14 (63.6%)
Asian	1 (4.8%)	1 (4.5%)
Black	1 (4.8%)	5 (22.7%)
Mixed	1 (4.8%)	1 (4.5%)

Other	0 (0.0%)	1 (4.5%)
Unknown	1 (4.8%)	0 (0.0%)
MS type		
Relapsing-remitting	18 (85.7%)	20 (90.9%)
Primary progressive	1 (4.8%)	0 (0.0%)
Secondary progressive	1 (4.8%)	1 (4.5%)
Unknown	1 (4.8%)	1 (4.5%)
Years since diagnosis (median, IQR)	4.0 (2.0-8.0)	11.5 (8.0-16.0)

Baseline data by loss to follow-up

Table 3. Baseline variables for those completing at least one post-randomisation assessment vs not

	ltf = 0 N=35	ltf = 1 N=8	p-value
Age in years (median, IQR)	44.4 (35.7-56.9)	45.0 (36.0-52.0)	0.57
Gender			
Male	13 (37.1%)	5 (62.5%)	0.40
Female	21 (60.0%)	3 (37.5%)	
Unknown	1 (2.9%)	0 (0.0%)	
Sex assigned at birth			
Male	13 (37.1%)	5 (62.5%)	0.19
Female	22 (62.9%)	3 (37.5%)	
Sexual orientation			
Heterosexual	32 (94.1%)	7 (87.5%)	0.19
Bisexual	1 (2.9%)	0 (0.0%)	
Gay/Lesbian	1 (2.9%)	0 (0.0%)	
Asexual	0 (0.0%)	1 (12.5%)	
Relationship status			
Single	1 (2.9%)	0 (0.0%)	0.88
Casually dating	3 (8.6%)	1 (12.5%)	
With a monogamous partner	4 (11.4%)	3 (37.5%)	
Living together with a monogamous partner	4 (11.4%)	1 (12.5%)	
Married and monogomous	18 (51.4%)	3 (37.5%)	
Separated from spouse, no current relationship	1 (2.9%)	0 (0.0%)	
Divorced, no current relationship	1 (2.9%)	0 (0.0%)	
In a non-monogamous relationship of any kind	1 (2.9%)	0 (0.0%)	
Other	1 (2.9%)	0 (0.0%)	
Unknown	1 (2.9%)	0 (0.0%)	
Education			
GCSE/O Level or equivalent	6 (18.2%)	4 (50.0%)	0.12
A-Level or equivalent	6 (18.2%)	0 (0.0%)	
Some college or university, no degree	8 (24.2%)	0 (0.0%)	
Bachelor's degree	6 (18.2%)	3 (37.5%)	
Master's degree	7 (21.2%)	1 (12.5%)	
Ethnicity			
White	25 (71.4%)	6 (75.0%)	0.81
Asian	2 (5.7%)	0 (0.0%)	
Black	4 (11.4%)	2 (25.0%)	
Mixed	2 (5.7%)	0 (0.0%)	
Other	1 (2.9%)	0 (0.0%)	
Unknown	1 (2.9%)	0 (0.0%)	
MS type			
Relapsing-remitting	26 (74.3%)	8 (100.0%)	0.46
Primary progressive	1 (2.9%)	0 (0.0%)	
Secondary progressive	1 (2.9%)	0 (0.0%)	

Unknown	7 (20.0%)	0 (0.0%)	
Years since diagnosis (median, IQR)	7.0 (3.0-10.0)	11.5 (7.0-14.5)	0.22
Trial arm			
TAU	20 (57.1%)	1 (12.5%)	0.02
PIMS	15 (42.9%)	7 (87.5%)	

Feasibility outcomes

- Treatment adherence rates
  - Total number of appointments attended/completed: 22
  - Number of appointments attended with facilitator:
    - 22 (M = 1/person)
  - Number of self-guided sessions completed: at least on activity completed for a session will be considered partial completion for the session
    - M = 4; SE = .70; SD = 2.5
  - Adherence defined as at least one session with a facilitator and at least 3 out of 6 self-guided sessions: % at least 3 self guided AND one appointment:
    - 53.8% of those who provided data; 31.8% of whole sample (10 missing)
- Acceptability: This will be evaluated based on theoretical framework for acceptability that have been developed into an 8-item scale for use in feasibility trials [51-53]. Items are on 5-point Likert response scales, though scale point labels differ based on the item. Wording of the items have been adapted for this study, as is directed by the scale authors (see Appendix A).

  - Average acceptability ratings for the TFA Scale items in the intervention group
    - Like: M = 3.79, SD = 0.58
    - Effort to engage: M = 3.64, SD = 1.00
    - Moral/ethical consequences: M = 1.93, SD = 0.83
    - Improved SDs: M = 3.36, SD = 0.84
    - Clear how PIMS can help: M = 3.50, SD = 1.02
    - Confidence in engagement: M = 3.07, SD = 1.07
    - Interference with priorities: M = 2.36, SD = 1.15
    - Acceptability: M = 4.36, SD = 0.63

Secondary feasibility parameter

Other feasibility objectives include determining the following for research sites or HCPs

- Recruitment rates
  - Number of NHS sites recruiting for trial: 3
  - Number of facilitators recruited from neurology services: 5

Treatment effects[1]

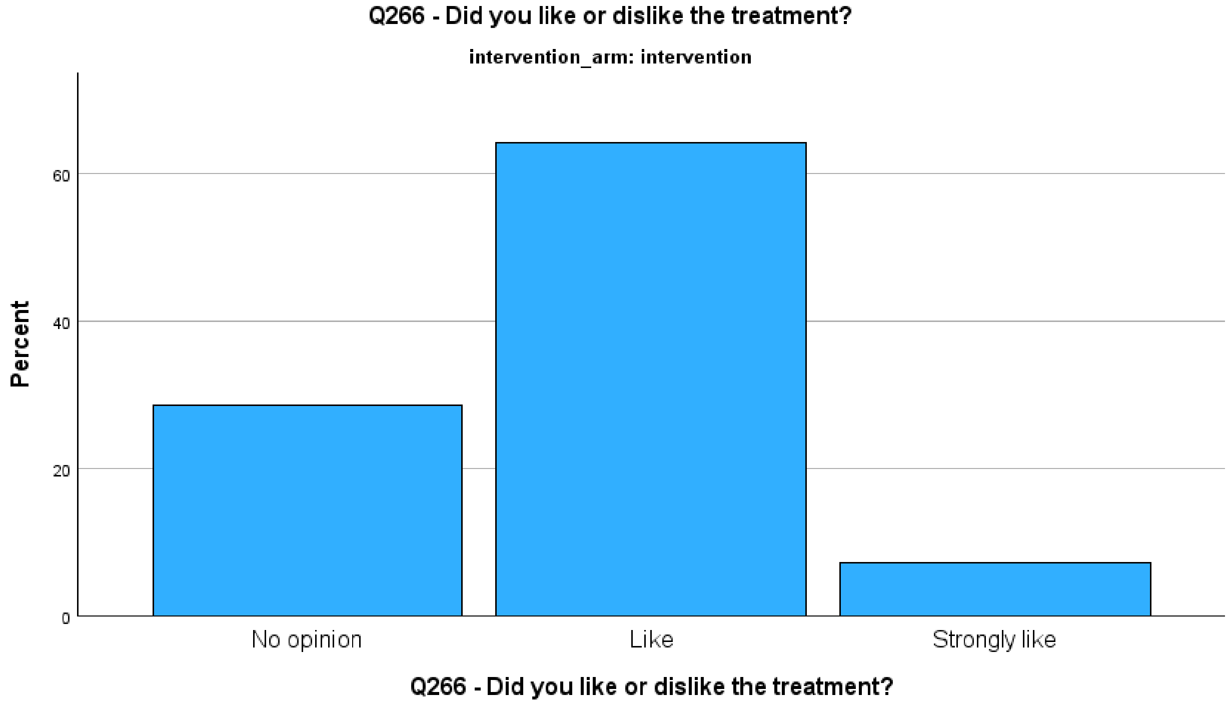
Figure 3. Boxplots with individual observations indicating baseline versus follow-up score for outcome variables. Boxes represent interquartile range with median

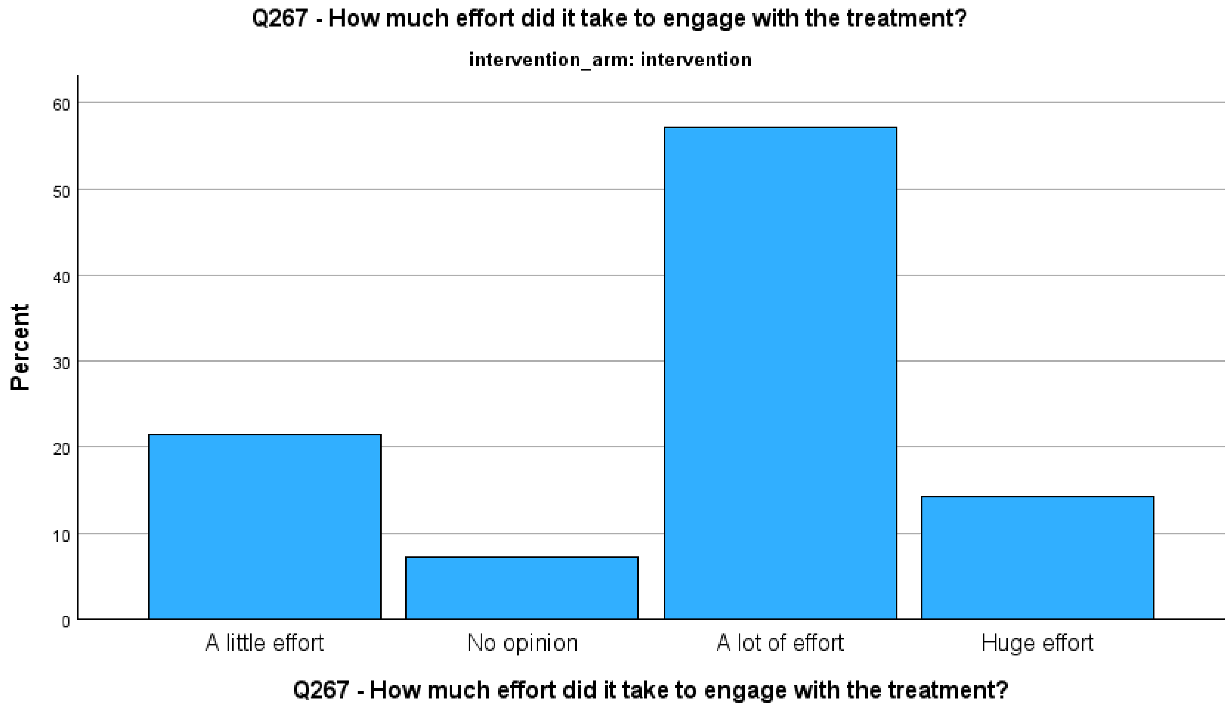
[1] The SFEQ scoring used in the analysis was incorrect, so is not presented here. This secondary outcome is now being correctly analyzed in the blinded dataset and will be presented in publication, to be linked to the trial registry.

Progression criteria

Progression criteria	Criteria	Estimate
1. Eligibility: Meeting eligibility estimates (PwMS)	Green: ≥33% of those screened meet eligibility criteria Amber: 10-32% of those screened meet eligibility criteria Red: <10% of those screened meet eligibility criteria	57/59: 96.6% 95%CI 88.3% to 99.6%
2. Recruitment: Meeting recruitment targets (sites and PwMS)	Green: Two or more research sites recruited & ≥33% of eligible PwMS consent to take part in the trial. Amber: Two or more research sites recruited & 5-32% of eligible PwMS consent to take part in the trial. Red: Fewer than two research sites recruited OR two or more research sites recruited & <5% of eligible PwMS consent to take part in the trial.	3 research sites 43/57 eligible PwMS consented: 75.4%
3. Retention: Assessments made with satisfactory follow-up rates (PwMS)	Green: ≥80% complete the 14-week post randomisation follow-up assessment Amber: 50-79% complete the 14-week post randomisation follow-up assessment Red: <50% complete the 14-week post randomisation follow-up assessment	Started follow-up 35/43: 81.4% Provided sufficient data for at least one outcome 33/43: 76.7% TAU 19/21: 90.5% PIMS 14/22: 63.4%
4. Adherence: Completion of sufficient number of intervention sessions (PwMS)	Green: If ≥80% complete at least one session with a facilitator and at least 3 out of 6 self-guided sessions Amber: If 50-79% complete at least one session with a facilitator and at least 3 out of 6 self-guided sessions Red: If <50% complete at least one session with a facilitator and at least 3 out of 6 self-guided sessions	% at least 3 self guided sessions: 66.6% of those who provided data 36.3 of whole sample (10 = missing) % at least 3 self guided AND one appointment: 53.8% of those who provided data 31.8% of whole sample (10 missing)
5. Satisfaction: Rating of overall satisfaction with	Green: If ≥80% of participants report satisfaction with the intervention package, i.e., select ‘agree’ or ‘strongly agree’ to the overall satisfaction question. (Participants who drop out and do not provide data will be assumed to not be satisfied)	Acceptability: 92.9% Liked treatment: 71.4%

intervention package (PwMS)	Amber: If 50-79% of participants report satisfaction with the intervention package Red: If <50% of participants report satisfaction with the intervention package	




Q267 - How much effort did it take to engage with the treatment?
intervention_arm: intervention
Percent
60
50
40
30
20
10
0
A little effort
No opinion
A lot of effort
Huge effort
Q267 - How much effort did it take to engage with the treatment?