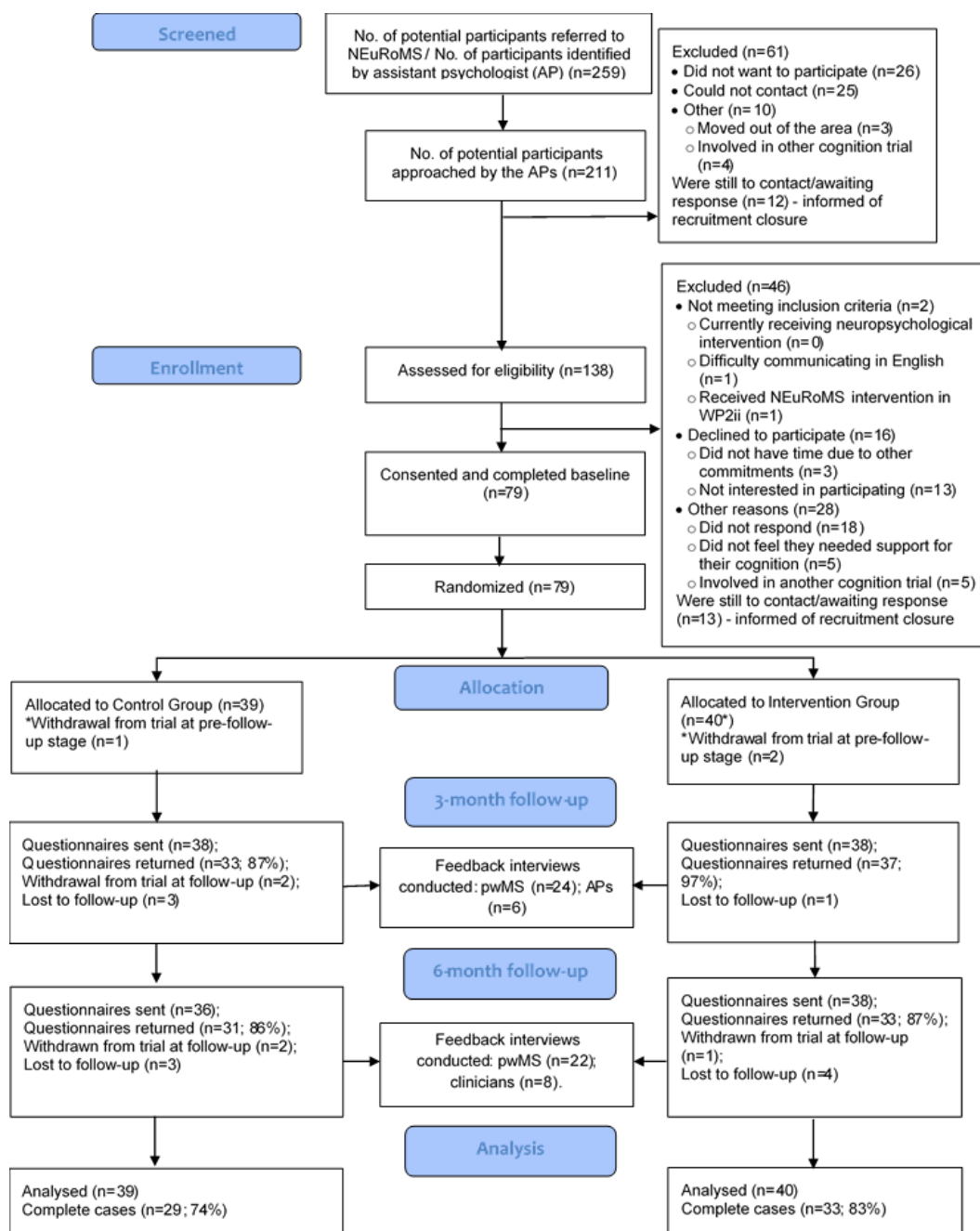


Neuropsychological evaluation and rehabilitation in multiple sclerosis – feasibility study

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Participant Flow

Figure 1. CONSORT diagram.



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Baseline characteristics

Table 1. Part 2 Baseline Characteristics:

Characteristic	Descriptive	Intervention Group (Group 1)	Control Group (Group 2)	Total
Age (years)	N (Missing)	40 (0)	39 (0)	79 (0)
	Mean (SD)	56.0 (11.2)	52.9 (11.7%)	54.5 (11.5)
	Median [IQR]	55.5 [49, 63]	55 [44, 61]	55 [48, 62]
	Min, Max	22, 77	21, 72	21, 77
Gender	Woman	27 (67.5%)	28 (71.8%)	55 (69.6%)
	Man	12 (30.0%)	10 (25.6%)	22 (27.9%)
	Other	1 (2.5%)	0 (0%)	1 (1.3%)
	Prefer not to say	0 (0%)	1 (2.6%)	1 (1.3%)
	Missing	0 (0%)	0 (0%)	0 (0%)
Ethnicity	White	38 (95.0%)	33 (84.6%)	71 (89.9%)
	Asian/Asian British	0 (0%)	1 (2.6%)	1 (1.3%)
	Black/ African/ Caribbean/ Black British	2 (5.0%)	4 (10.3%)	6 (7.6%)
	Other ethnic group	0 (0%)	0 (0%)	0 (0%)
	Mixed/Multiple Ethnic Groups	0 (0%)	1 (2.6%)	1 (1.3%)
	Missing	0 (0%)	0 (0%)	0 (0%)
Education	Below GCSE	4 (10.0%)	4 (10.3%)	8 (10.1%)
	GCSE	6 (15.0%)	6 (15.4%)	12 (15.2%)
	A-Level	10 (25.0%)	6 (15.4%)	16 (20.3%)
	NVQ	4 (10.0%)	1 (2.6%)	5 (6.3%)
	Degree	11 (27.5%)	17 (43.6%)	28 (35.4%)
	Higher Degree	3 (7.5%)	4 (10.3%)	7 (8.9%)
	Not known	2 (5.0%)	1 (2.6%)	3 (3.8%)
	Missing	0 (0%)	0 (0%)	0 (0%)
Employment	Not employed	10 (25.0%)	9 (23.1%)	19 (24.1%)
	Employed full-time	8 (20.0%)	8 (20.5%)	16 (20.3%)
	Employed part-time	3 (7.5%)	6 (15.4%)	9 (11.4%)
	Voluntary full-time	0 (0%)	0 (0%)	0 (0%)
	Voluntary part-time	2 (5.0%)	2 (5.1%)	4 (5.1%)
	In education full-time	0 (0%)	0 (0%)	0 (0%)
	In education part-time	1 (2.5%)	0 (0%)	1 (1.3%)
	Retired	16 (40.0%)	14 (35.9%)	30 (38.0%)
	Missing	0 (0%)	0 (0%)	0 (0%)
Time since diagnosis (years)	N (Missing)	40 (0)	39 (0)	79 (0)
	Mean (SD)	17.8 (10.2)	15.3 (11.4)	16.6 (10.8)
	Median [IQR]	16 [10.5, 23.5]	12 [7, 22]	14 [7, 23]
	Min, Max	1, 53	1, 42	1, 53
Type of MS	Relapsing-remitting MS	18 (45.0%)	24 (61.5%)	42 (53.2%)
	Primary Progressive MS	5 (12.5%)	19 (23.1%)	14 (17.7%)
	Secondary Progressive MS	15 (37.5%)	35 (12.8%)	20 (25.3%)
	Not known	2 (5.0%)	1 (2.6%)	3 (3.8%)
	Missing	0 (0%)	0 (0%)	0 (0%)
Comorbidities	No	33 (82.5%)	34 (87.2%)	67 (84.8%)
	Yes	7 (17.5%)	5 (12.8%)	12 (15.2%)
	Missing	0 (0%)	0 (0%)	0 (0%)
	N (Missing)	40 (0)	39 (0)	79 (0)
	Mean (SD)	28.5 (3.8)	28.1 (4.3)	28.3 (4.0)

Symbol Substitution Task Score	Median [IQR]	29 [26,31]	28 [25,32]	29 [26, 31]
	Min, Max	20, 34	21, 34	20, 34
Cognitive Impairment Category	Mild	33 (82.5%)	31 (79.5%)	64 (81.0%)
	Moderate	7 (17.5%)	8 (20.5%)	15 (19.0%)

Outcome measures

Table 2. Primary Outcomes – RAG (Red/Amber/Green) ratings for progression to a definitive trial, by feasibility area.

Feasibility outcome	Progression criteria ^a	Rating
Recruitment rate	Go: average 12/month; Review: average 6-11/month; Stop: average ≤ 5/month 79 recruited over 9 months = 9/month	Review
Retention rate	Go: ≥ 80% participants retained; Review: 50-79% retained; Stop: ≤ 49% retained 3-month: 70/79 (88.6%) 6-month: 64/79 (81.0%)	Go
Suitability of outcome measures (measured by level of completeness)	Go: ≥ 80% participants completed MSIS-Psych; Review: 50-79%; Stop: ≤ 49% 3-month: 70/76 (92.1%) 6-month: 64/74 (86.5%)	Go
Randomisation	79/79	Go
NEuRoMS intervention	Feasibility of delivery - 93% of participants randomised to the treatment group completed the intervention.	Go
	Intervention fidelity - <u>Content of sessions</u> : Time-sampling of intervention session recordings for 9 participants: ≥85% of time coded spent discussing intervention-specific content. Intervention content	Go

	<p>mostly discussed - goal setting / progress on goals (26% of time) and discussing cognition and cognitive problems experienced (17% of time);</p> <p><u>Therapist competency:</u> All intervention providers received a competency rating of delivering the intervention of at least “adequately well”</p>	
Health economics	<p>Approximately 90% of participants completed health economic outcome measures and over 80% of service use questionnaires were returned (87.3% at 3-months and 81.0% at 6-months).</p> <p>Economic outcome measures: EQ-5D 5L: 91.1% at 3-months and 87.3% at 6-months; ICECAP-A: 91.1% at 3-months and 87.3% at 6-months.</p>	Go

Table 3. Descriptive Statistics for secondary outcome measures:

Measure	Time	N	Min	Max	Mean (SD)	Median [IQR]	95% Confidence Interval
Perceived Difficulties Questionnaire (PDQ-20)	Baseline G1	40	3	71	34.3 (17.5)	33 [21, 42]	28.7, 39.9
	3m FU G1	37	2	61	29.3 (14.9)	31 [17, 39]	24.3, 34.3
	6m FU G1	33	2	60	28.7 (14.7)	29 [18, 39]	23.5, 33.9
	Baseline G2	39	5	69	38 (19.0)	42 [20, 53]	31.8, 44.2
	3m FU G2	33	5	68	34.9 (19.5)	33 [20, 52]	28.0, 41.8
	6m FU G2	31	5	69	37.4 (19.5)	37 [18, 54]	30.3, 44.6
	Baseline Total	79	3	71	36.1 (18.2)	36 [21, 50]	32.0, 40.2
	3m FU Total	70	2	68	31.9 (17.3)	31.5 [17, 43]	27.8, 36.1
	6m FU Total	64	2	69	32.9 (17.6)	34 [18, 45.5]	28.5, 37.3
Multiple Sclerosis Impact Scale (MSIS) – Physical Subscale	Baseline G1	40	23	90	51.3 (18.2)	50.5 [35, 62.5]	45.5, 57.1
	3m FU G1	37	22	81	50.4 (17.3)	49 [34, 62]	44.6, 56.1
	6m FU G1	33	21	81	48.9 (18.6)	44 [31, 68]	42.3, 55.5
	Baseline G2	39	20	89	51.9 (20.5)	49 [33, 67]	45.3, 58.5
	3m FU G2	33	20	94	50.3 (19.7)	49 [34, 65]	43.3, 57.3
	6m FU G2	32	20	100	52.0 (20.3)	48.5 [36.5, 65]	44.6, 59.3
	Baseline Total	79	20	90	51.6 (19.2)	50 [35, 64]	47.3, 55.9
	3m FU Total	70	20	94	50.3 (18.3)	49 [34, 65]	46.0, 54.7
	6m FU Total	65	20	100	50.4 (19.4)	48 [32, 65]	45.6, 55.2
Multiple Sclerosis Impact Scale	Baseline G1	40	12	43	23.8 (8.0)	22.5 [18.5, 28]	21.3, 26.4
	3m FU G1	37	12	42	22.3 (8.0)	21 [15, 27]	19.6, 24.9
	6m FU G1	33	11	43	21.3 (8.0)	19 [15, 27]	18.5, 24.1
	Baseline G2	39	9	40	25.1 (8.5)	27 [17, 32]	22.3, 27.9

(MSIS) – Psychological Subscale	3m FU G2	33	9	44	20.9 (8.9)	24 [19, 29]	20.9, 27.2
	6m FU G2	31	9	43	23.9 (9..0)	24 [16, 32]	20.6, 27.2
	Baseline Total	79	9	43	24.5 (8.2)	24 [17, 31]	22.6, 26.3
	3m FU Total	70	9	44	23.1 (8.4)	21.5 [17, 29]	21.1, 25.1
	6m FU Total	64	9	43	22.6 (8.5)	21.5 [15.5, 29]	20.4, 24.7
Patient Health Questionnaire – 9 (PHQ-9)	Baseline G1	40	0	24	8.9 (5.5)	8 [5, 13]	7.1, 10.7
	3m FU G1	37	0	25	7 (5.4)	5 [3, 9]	5.2, 8.8
	6m FU G1	33	1	25	7.0 (5.4)	6 [3, 9]	5.1, 8.9
	Baseline G2	39	0	25	9.9 (6.8)	11 [4, 14]	7.8, 12.1
	3m FU G2	33	0	25	10.2 (7.6)	9 [5, 16]	7.5, 12.9
	6m FU G2	31	0	26	9.2 (7.5)	7 [2, 15]	6.5, 12.0
	Baseline Total	79	0	25	9.4 (6.2)	8 [5, 14]	8.0, 10.8
	3m FU Total	70	0	25	8.5 (6.7)	6.5 [3, 13]	6.9, 10.1
	6m FU Total	64	0	26	8.1 (6.5)	7 [2.5, 12]	6.5, 8.9
Generalised Anxiety Disorder Scale – 7 (GAD-7)	Baseline G1	40	0	20	5.9 (5.0)	5 [1.5, 8.5]	4.3, 7.5
	3m FU G1	37	0	20	4.7 (5.0)	3 [1, 6]	3.0, 6.4
	6m FU G1	33	0	20	4.2 (4.6)	3 [1, 6]	2.6, 5.9
	Baseline G2	39	0	21	7.0 (5.4)	6 [3, 12]	5.3, 8.8
	3m FU G2	33	0	21	7.1 (5.6)	6 [4, 10]	5.1, 9.1
	6m FU G2	31	0	19	6.9 (5.2)	6 [3, 11]	5.0, 8.9
	Baseline Total	79	0	21	6.4 (5.2)	5 [2, 10]	5.3, 7.6
	3m FU Total	70	0	21	5.8 (5.4)	5 [2, 9]	4.5, 7.1
	6m FU Total	64	0	20	5.5 (5.1)	4 [1, 8.5]	4.3, 6.8
Nottingham Extended Activities of Daily Living (NEADL)	Baseline G1	40	0	22	14.6 (5.6)	15.5 [12, 19]	12.8, 16.4
	3m FU G1	37	0	22	14.8 (5.7)	15 [12, 20]	12.9, 16.7
	6m FU G1	33	0	22	15.1 (5.7)	16 [12, 20]	13.1, 17.1
	Baseline G2	39	2	22	16.3 (5.3)	17 [11, 21]	14.6, 18.0
	3m FU G2	33	2	22	16.6 (5.2)	18 [14, 21]	14.8, 18.5
	6m FU G2	31	8	22	16.3 (4.4)	18 [13, 19]	14.7, 17.9
	Baseline Total	79	0	22	15.4 (5.4)	17 [12, 20]	14.2, 16.6
	3m FU Total	70	0	22	15.7 (5.5)	16 [13, 21]	14.3, 17.0
	6m FU Total	64	0	22	15.7 (5.1)	16.5 [12.5, 19.5]	14.4, 17.0
MSSE	Baseline G1	40	16	73	46.9 (13.6)	46.5 [38.5, 55.5]	42.5, 51.3
	3m FU G1	37	23	71	48.6 (12.2)	49 [40, 57]	44.6, 52.7
	6m FU G1	33	28	70	50.4 (12.0)	49 [42, 59]	46.2, 54.7
	Baseline G2	39	24	67	46.5 (12.7)	46 [36, 58]	42.3, 50.6
	3m FU G2	33	23	73	46.8 (13.6)	45 [37, 59]	42.0, 51.7
	6m FU G2	31	20	70	47.3 (13.1)	43 [40, 59]	42.5, 52.1
	Baseline Total	79	16	73	46.7 (13.1)	46 [37, 57]	43.8, 49.6
	3m FU Total	70	23	73	47.8 (12.8)	48 [38, 58]	44.7, 50.1
	6m FU Total	64	20	70	48.9 (12.5)	47.5 [41, 59]	45.8, 52.0
MSWDQ	Baseline G1	11	3	55	28.3 (18.0)	30 [5, 46]	16.2, 40.4
	3m FU G1	10	11	49	28.0 (14.9)	26.5 [13, 43]	17.4, 38.6
	6m FU G1	9	0	43	21.6 (15.0)	22 [9, 30]	10.1, 33.1
	Baseline G2	15	3	64	25.5 (22.2)	14 [9, 49]	13.2, 37.8
	3m FU G2	12	1	65	28.5 (23.9)	24 [7, 55]	13.3, 43.7
	6m FU G2	11	0	55	21.6 (21.3)	19 [1, 48]	7.3, 36.0
	Baseline Total	26	3	64	26.7 (20.2)	27.5 [9, 46]	18.5, 34.8
	3m FU Total	22	1	65	28.3 (19.9)	25 [13, 48]	19.5, 37.1
	6m FU Total	20	0	55	21.6 (18.3)	20.5 [4, 34.5]	13.1, 30.2
Single item work	Baseline G1	25	1	5	3.2 (1.4)	3 [2, 4]	3, 4
	3m FU G1	21	1	5	3.1 (1.2)	3 [3, 4]	3, 4

and education question	6m FU G1	22	1	5	2.8 (1.0)	3 [2, 3]	2, 3
	Baseline G2	24	1	5	3.0 (1.3)	3 [2, 4]	2, 4
	3m FU G2	21	1	5	2.8 (1.3)	3 [2, 4]	2, 3
	6m FU G2	20	1	5	2.6 (1.5)	3 [1, 4]	2, 3
	Baseline Total	49	1	5	3.1 (1.4)	3 [2, 4]	3, 3
	3m FU Total	42	1	5	3.0 (1.2)	3 [2, 4]	3, 3
	6m FU Total	42	1	5	2.7 (1.2)	3 [1, 3]	2, 3
Single item medication question	Baseline G1	39	1	5	2.0 (1.2)	2 [1, 3]	2, 2
	3m FU G1	36	1	5	1.8 (1.0)	1 [1, 2]	1, 2
	6m FU G1	33	1	5	1.7 (0.9)	2 [1, 2]	1, 2
	Baseline G2	39	1	4	2.0 (0.9)	2 [1, 3]	2, 2
	3m FU G2	31	1	4	1.8 (0.9)	2 [1, 2]	1, 2
	6m FU G2	31	1	4	2.1 (1.0)	2 [1, 3]	2, 3
	Baseline Total	78	1	5	2.0 (1.0)	2 [1, 3]	2, 2
	3m FU Total	68	1	5	1.8 (1.0)	2 [1, 2]	2, 2
	6m FU Total	64	1	5	1.9 (1.0)	2 [1, 2]	2, 2

Adverse events

Table 4. Adverse events

Serious Adverse Events (SAEs)	No SAEs
Adverse events (AEs)	There were four participants who responded 'Nearly every day' to question 9 on the Patient Health Questionnaire-9, which asks about suicidal thoughts. Of these four participants, two also gave this response at three-month follow up and six-month follow up. None of these AEs was related to study participation, but rather related to other life circumstances (e.g., employment), MS symptoms (e.g., fatigue) or pre-existing mood problems. The events were dealt with in line with the study protocol and have been resolved.