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Web-based physiotherapy for people affected by multiple sclerosis: a single blind, randomized controlled feasibility study.

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 Web-based Physiotherapy for people affected by Multiple Sclerosis (WEBPaMS); a single
- 4 blind, randomised controlled feasibility study
- 5

6 Introduction

7 People with Multiple Sclerosis benefit from rehabilitation (1), but access is limited in part 8 because of resource limitations (2). Web-based interventions may overcome this since they 9 can provide tailored programmes and improve access to specialist therapists or services 10 particularly for those with work/family commitments, rural location or limited mobility (3–5); 11 but further evidence is needed concerning its effectiveness and costs. Previous research on 12 web-based interventions has examined the effectiveness of general physiotherapy 13 programmes (3,6,7) or specific Multiple Sclerosis impairments such as balance (1,8), strength 14 (9) or reduced physical activity (10,11).

15

16 We previously undertook a 12 week randomised controlled pilot study to investigate web-17 based physiotherapy for people with Multiple Sclerosis (Expanded Disability Status Score 18 (EDSS) 5-6.5) (6). The results showed trends towards improvement in walking speed, 19 symptoms and the physical impact of Multiple Sclerosis (6). Like previous studies, our initial 20 study was limited by small sample size (3,7,8), and short intervention period (7,8). Therefore, 21 the aim of this feasibility randomised controlled trial was to examine a six-month web-based 22 physiotherapy exercise programme compared to a standard home exercise programme 23 (active comparator) in people moderately affected by Multiple Sclerosis. The primary 24 research objective was to estimate the sample size required for a future randomised 25 controlled trial. Secondary objectives included; a) to inform the recruitment strategy for a

future trial; b) estimate attrition rates; c) estimate adherence to the intervention; d) identify baseline factors most strongly associated with outcomes, as potential stratification factors in the definitive trial; e) determine the acceptability and feasibility of web-based physiotherapy; f) help establish the eligibility criteria for a definitive trial; g) undertake an exploratory costeffectiveness analysis of web-based physiotherapy compared to the active comparator.

31

32 Methods and Materials

33 The study was prospectively registered on ClinicalTrials.gov (Identifier: NCT02508961), ethical 34 approval was obtained from the West of Scotland Research Ethics Service (Ref:15/WS/0030; 35 March 2015- January 2016) and University of Glasgow acted as study sponsor. This 36 randomised, controlled, multi-centre feasibility study aimed to recruit 90 people with 37 Multiple Sclerosis from three centres (30 from each centre); NHS Ayrshire and Arran, NHS 38 Lothian and Plymouth Hospitals NHS Trust, over a seven month period (June 2015-December 39 2015). The sample size was based on previous pilot data (6) and the assumption that each 40 centre could recruit participant one per week. 41

42 Potential participants were identified through neurology, Multiple Sclerosis specialist 43 nurse/physiotherapy clinics and from the Multiple Sclerosis regional register/iMED database 44 in Plymouth; and were issued a letter of invitation. To be included participants were required 45 to have a confirmed diagnosis of Multiple Sclerosis (12), an EDSS of 4.0-6.5 (13) and access to 46 a personal computer/tablet with an email address and internet connection. Participants were 47 excluded if they were currently taking part in regular exercise (≥ two times/week) and/or 48 regular physiotherapy programme, had poor cognitive function (Mini Mental State 49 Examination Score <24) (14), any significant change in medication or a relapse within the last

three months, other significant co-morbidities for which exercise would be contra-indicatedor were currently participating in another clinical trial.

52

53 At the initial appointment potential participants were screened for eligibility, written 54 informed consent was obtained and baseline assessments were performed. One week later 55 participants' were given an appointment with an experienced neurological physiotherapist 56 where they received a standardised physiotherapy assessment. Goals were agreed, from 57 which an individualised exercise programme was devised. Participants were then randomised 58 to the intervention or active comparator group using a remote, telephone automated randomisation system within the Glasgow Clinical Trials Unit. Randomisation was stratified by 59 60 study centre and EDSS (4.0-5.0 and 5.5-6.5). Participants were provided with their exercise 61 programme either via web-based physiotherapy or as a printed sheet of exercises. All 62 participants were asked to complete their exercise programme twice weekly and received a 63 weekly telephone call/email for the first two weeks to discuss any issues.

64

65 Outcome measures were performed at baseline, 3 months, 6 months (post intervention) and 66 9 months (follow-up) by a blinded research assistant at each site. Primary outcome measures 67 were adherence and the Two Minute Walk Test (15,16). Adherence was measured from the 68 electronic (web-based physiotherapy) or returned paper diaries (active comparator). 69 Participants were advised to undertake their physiotherapy programme twice per week for 70 six months (2 x 26 weeks = 52 diary entries). Secondary outcome measures included the 71 Timed 25 Foot Walk (17), Timed Up and Go test (18), Berg Balance Scale (19), Multiple 72 Sclerosis Impact Scale v2 (20), MS-Related Symptom Checklist (21), Hospital Anxiety and 73 Depression Scale (22), EQ-5D, (23) and steps taken/day measured objectively worn continuously for one week using the activPAL tri-axial accelerometer (Pal Technologies Ltd,
Glasgow, UK) (24,25). The device was attached to the participant's mid-thigh using a
waterproof Tegaderm dressing and participants kept a diary to record their sleep time.
Healthcare resource use, physiotherapist time, GP visits, nurse visits, other Multiple Sclerosis
or outpatient review, Accident and Emergency attendance and hospital stay, were recorded
by self-report questionnaire.

80

81 To determine the acceptability and feasibility of the study semi-structured telephone 82 interviews were undertaken with physiotherapists and participants. The interviewer was a 83 member of the research team unknown to participants. A purposive sample of 24 84 participants, eight from each study site (both groups), consented to take part. The purposive 85 sample was selected using a sampling matrix to include age (<50 years, >50 years), disability 86 (EDSS 4.0-5.0, 5.5-6.5) and gender. Participants were asked their reasons for taking part in 87 the study, their views of the assessments and intervention, any issues faced, perceived 88 benefit and recommendations for a future trial.

89

90 <u>Web-based Physiotherapy</u>

Participants randomised to the web-based physiotherapy intervention received an individualised exercise programme delivered via www.webbasedphysio.com. Programmes could consist of cardiovascular, strengthening and balance exercises, as well as warm up, cool down and stretching exercises, at different levels of difficulty and a prescribed number of sets/repetitions individualised to meet the participants' needs. The website contained exercises (videos, text and audio description) and disease-specific advice and education (described in Paul et al. (6)). During the intervention period the physiotherapist reviewed

98	electronic exercise diaries every two weeks and remotely altered programmes in response to
99	a participant's comments. Alterations could include changing exercises, difficulty level or
100	number of repetitions/sets. Participants were informed of any changes by email.
101	
102	Active comparator
103	Participants randomised to the active comparator intervention received a printed sheet of
104	exercises (www.physiotherapyexercises.com). Programmes consisted of similar exercises as
105	above. Participants completed a paper-based exercise diary that was posted to the research
106	team every three months.
107	
108	The three physiotherapists also consented to take part in a telephone interview. They were
109	asked regarding their experiences of delivering the interventions, issues in operationalising
110	the protocol and recommendations for a future trial.
111	
112	Data analysis
113	All analyses were performed on an intention to treat basis using SAS for windows v9.3.
114	
	Categorical variables are summarised as number and percentage (n(%)). Continuous variables
115	Categorical variables are summarised as number and percentage (n(%)). Continuous variables were summarised by mean and standard deviation (SD) or median and interquartile range
115 116	Categorical variables are summarised as number and percentage (n(%)). Continuous variables were summarised by mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Adherence data were considered as those who recorded no exercise
 115 116 117 	Categorical variables are summarised as number and percentage (n(%)). Continuous variables were summarised by mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Adherence data were considered as those who recorded no exercise sessions per four week period, non-adherence (<75% of completed sessions) and adherence
 115 116 117 118 	Categorical variables are summarised as number and percentage (n(%)). Continuous variables were summarised by mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Adherence data were considered as those who recorded no exercise sessions per four week period, non-adherence (<75% of completed sessions) and adherence (≥75% of completed sessions) and was compared between intervention groups using Chi-
 115 116 117 118 119 	Categorical variables are summarised as number and percentage (n(%)). Continuous variables were summarised by mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Adherence data were considered as those who recorded no exercise sessions per four week period, non-adherence (<75% of completed sessions) and adherence (≥75% of completed sessions) and was compared between intervention groups using Chi- squared tests. Between group differences were assessed using analysis of covariance
 115 116 117 118 119 120 	Categorical variables are summarised as number and percentage (n(%)). Continuous variables were summarised by mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Adherence data were considered as those who recorded no exercise sessions per four week period, non-adherence (<75% of completed sessions) and adherence (≥75% of completed sessions) and was compared between intervention groups using Chi- squared tests. Between group differences were assessed using analysis of covariance (ANCOVA) adjusted for baseline value and stratification variables (centre and EDSS) and

123 Cost-effectiveness was explored using healthcare resource use and valued using UK cost 124 sources (27–29). EQ-5D data were used to derive health utility values and estimate quality-125 adjusted life-years (QALYs) gained (30). Mean costs and QALYs associated with each 126 treatment group were estimated using generalised linear models. Telephone interviews were 127 audio-recorded, transcribed verbatim and analysed using thematic analysis. One researcher 128 first coded all scripts, then two researchers independently identified emerging themes and 129 sub-themes. Following this, discussion was held between the researchers to agree and finalise 130 themes and sub-themes.

131

132 <u>Results</u>

133 Ninety people with Multiple Sclerosis were recruited (Figure 1), however to achieve our target 134 sample size the data collection period was extended from seven to twelve months (June 2015-135 May 2016) (Figure 2). The sample consisted of 21 males and 69 females; mean age 56.1 (SD 136 9.6) years (Table 1). Eight people (18%) from the intervention group and five (11%) from the 137 active comparator group withdrew from the study (Figure 1) (31). One participant received 138 the web-based physiotherapy intervention rather than the active comparator, although with 139 intention to treat analysis they were considered as having received the comparator 140 intervention.

- 142Figure 1 Near Here143Figure 2 Near Here144Table 1 Near Here
- 145

146	Between 40%-63% of participants adhered to the web-based physiotherapy intervention
147	(≥75% completed diaries) and between 53%-71% to the active comparator during each four
148	week period (Table 2). In both groups adherence reduced over time but over 40% of
149	participants were still adhering to their programme at 6 months. The proportion of people
150	who had no diary entries was 16-24% in the intervention group and 22-27% in the comparator
151	group. No significant differences were found between both groups.
152	
153	Table 2 Near Here
154	
155	Compared to baseline, there were no changes in the majority of outcome measures, in either
156	group, at three, six and nine months, with the exception of the EQ-5D at six months in the
157	active comparator group (Table 3).
158	
159	Table 3 Near Here
160	
161	Sixty adverse events were recorded; intervention group (n=27), active comparator group
162	(n=33) and 42 of these were falls. Two participants had skin reactions due to the Tegaderm.
163	None of the adverse events were deemed to be related to the intervention.
164	
165	Telephone interviews were completed by 8 men and 16 women (mean age 56.2 (SD 9.6) years,
166	11 received web-based physiotherapy and 13 the comparator intervention (EDSS 4.0 $n=4$,
167	EDSS 4.5 n=3, EDSS 5.0 n=1, EDSS 6.0 n=11, EDSS 6.5 n=5)). Analysis of the interview
168	transcripts yielded three themes and 13 subthemes (Table 4). Participants had a variety of
169	reasons for taking part in the study, most wanted to get back to exercise to improve their

physical condition but for some a realistic goal was to maintain their physical ability. Taking
part in the study was stated as a way of getting more therapy, providing a sense of purpose
and to help others with Multiple Sclerosis.

- 173
- 174

Table 4 Near Here

175

176 In general, participants were very positive about the study, some people had a preference in 177 terms of group allocation, often determined by previous experience, but no-one felt very 178 strongly. A number of people suggested an additional appointment with the physiotherapist 179 to review progress would have been beneficial. Participants from both groups appreciated 180 the individualised nature of their programme. There was notable variation in the number of 181 exercises participants reported and very few instances of exercise programmes being 182 changed or progressed. Most people reported some benefit from exercising and gave 183 examples of both Multiple Sclerosis (e.g. fatigue) and non- Multiple Sclerosis related factors 184 (e.g. holidays or surgery) which affected their adherence. Participants in the comparator 185 group reported that completing the exercise diary was motivating. Finally some suggestions 186 were proposed to improve the web-based physiotherapy website including being able to 187 retrospectively complete exercise diaries.

188

Analysis of the transcripts from the physiotherapists' interviews resulted in three themes and nine sub-themes (Table 5). There were some challenges with recruitment mentioned as other studies were recruiting at the same time. All three therapists commented that some participants had a significant distance to travel for assessments which may have affected the outcomes due to fatigue. The physiotherapists reported that it only took a few minutes to

194	review diaries through web-based physiotherapy and suggested being able to retrospectively
195	add diary entries would have been useful. The therapists reported initial goals were not
196	reviewed, and stated that another appointment would have been useful. Participants rarely
197	left comments in their diaries which meant that the physiotherapists were unable to
198	change/progress their programme. When changes were made it tended to be a change in the
199	dose of the exercise rather than add/change the exercise.
200	
201	Table 5 Near Here
202	
203	The results of the within-trial analysis found that the web-based intervention was associated
204	with lower costs (£954), compared to standard treatment (£1,076). This was associated with
205	a small QALYs gain in the intervention group (0.557), compared with the comparator group
206	(0.517). We undertook a bootstrap analysis to explore uncertainty associated with our results.
207	The results estimated a mean cost difference between treatment groups of -£122 (95% CI: -
208	583.856, 339,206) and a mean difference in QALYs of 0.03 (95% CI: -0.012, 0.072). Although
209	the web-based intervention had the potential to dominate the standard treatment, as it
210	provides additional QALYs for a lower cost, there is substantial uncertainty associated with
211	these estimates.
212	
213	Discussion
214	Adherence to the intervention was seed. 40 C20/ in the web based shoristly around and

Adherence to the intervention was good, 40-63% in the web-based physiotherapy group and 53-71% in the comparator group, with the lowest adherence during the last month of the study. Direct comparison with previous studies is challenging due to different methods of defining adherence, although all demonstrated that adherence to web-based physiotherapy

reduces over time (9,10,32). Tallner et al. (9) reported that 73% of participants completed 80% or more of their programme during months 1-3 which reduced to 36% during months 4-6, Motl et al. (10) reported 96% of participants logged on to the website in weeks 1-2 which reduced to 52% at week 8, and Conroy et al. (3) reported only half of participants adhered to their programme and almost one quarter completed no exercise diaries.

223

Adherence to home-based exercise is affected by factors such as low motivation, pain and past experience of exercise (33). Participants in the active comparator group reported that completing and returning the exercise diaries improved their adherence. Return of exercise diaries is not part of usual care and may have inflated adherence in this group. Although our adherence was better than previous studies it is clear that other strategies to improve adherence e.g. more contact with a health care professional and more frequent updates are required (32). Specific strategies are needed to engage those with no diaries entries.

231

232 In terms of recruitment, 24% of those invited to participate took part in the study. There were 233 no issues raised around the eligibility criteria. The recruitment rate of around two per month 234 was less than the anticipated four per month per centre. Recruitment was generally on target 235 for the first six months, however this recruitment rate was not maintained partly due to this 236 study 'competing' for participants with other studies. The most common pathway to 237 recruitment was via the nurses or consultants. Thus, the recruitment strategy of a future trial 238 would consider that around 1 in 4 of those invited will be recruited, would be predicated on 239 an anticipated recruitment rate of two participants per month and would favour recruiting 240 participants directly from clinics/health care staff.

241

242 Although there were no significant changes in outcome measures, participants in both groups 243 maintained their clinical outcomes over the intervention period and, during interview, a 244 number of participants reported improvements in e.g. walking, balance and strength. 245 Multiple Sclerosis is a progressive neurological condition and some participants reported their 246 goal was to maintain their functional status rather than improve. Similarly, Conroy et al. (3) 247 recruited people with Multiple Sclerosis with levels of disability similar to the current study 248 and reported no significant improvement in outcomes following a six month web-based 249 physiotherapy intervention. Web-based exercise may have the potential to maintain the 250 clinical status of people with Multiple Sclerosis with higher levels of disability, however 251 further investigation with the inclusion of a control group with no exercise intervention, to 252 assess the natural history of participants, is required.

253

254 The dose of exercise prescribed may explain the lack of improvement in outcome measures. 255 Similar to Conroy et al. (3), our study took place within the context of available resources, 256 with exercise programmes reflecting physiotherapy practice (including aerobic, 257 strengthening, cardiovascular and functional exercises). Only one similar, small, uncontrolled, 258 short-term (12 week) web-based physiotherapy study found some improvements in people 259 with Multiple Sclerosis (7). In contrast, previous web-based studies in Multiple Sclerosis that have focussed on a single impairment e.g. strengthening (9), physical activity (10) or balance 260 261 (8) have reported positive results. It is possible that with a combined programme, the dose of 262 exercise for any one component is insufficient for physiological changes to take place thus 263 web-based interventions need to focus on specific impairments in order to achieve 264 meaningful change.

265

Few participants left comments in their exercise diaries therefore therapists had no clinical rationale to change programmes, which resulted in a lack of exercise progression. The physiotherapists were reluctant to add exercises without seeing the participant to ensure they were doing new exercises correctly and any progress tended to be an increase in repetitions of the same exercises, this was also raised by Conroy et al. (3). Delivering physiotherapy programmes remotely is a different service delivery model, which appears to challenge professional practice and values.

273

274 From the data of this study and clinical experience it is estimated that the difference in Two 275 Minute Walk Test between intervention and comparator groups would be 8m, assuming a 276 standard deviation of 17.4m. Therefore, for 80% power at the 0.05 significance level 76 277 participants per group would be required for a future definitive randomised controlled trial. 278 However, attrition across the study period was 18% in the intervention group and 11% in the 279 active comparator group which is notably less than previous web-based interventions of 280 similar duration; 39% attrition Tallner et al. (9) and 35% attrition Conroy et al. (3). Thus, 281 allowing for a conservative dropout rate of 20%, 95 participants per group would be required. 282

The estimated differences in costs and QALYs between groups were small and further research to reduce the uncertainty associated with these estimates would be beneficial. The association between changes in functional status and changes in Health-related Quality of Life remains unclear in the literature, particularly given the questionable sensitivity of the EQ-5D in people with Multiple Sclerosis (34). While some studies have found some improvement in Health-related Quality of Life in people with Multiple Sclerosis (8,35,36), others found no change (6,7,11). Further research is required to determine the impact of web-based

290 physiotherapy on Health-related Quality of Life in people with Multiple Sclerosis and the291 suitability of EQ-5D.

292

293 This study has a number of limitations. Paper exercise diaries were used in the active 294 comparator group to measure adherence however this is not part of usual care and may have 295 increased adherence levels. The study did not include a non-exercising control group 296 therefore comparisons to the natural history of Multiple Sclerosis cannot be made. Exercise 297 programmes were individually tailored to participants to reflect clinical practice, however this 298 meant that dose of exercise varied greatly and there were few examples of progression of 299 programmes. This lack of progression was due to the paucity of diary comments and therefore 300 a reluctance on the part of the therapists to progress exercises without face-to-face contact. 301 As such the exercise dose may have been insufficient to induce physiological changes and 302 hence outcome measures.

303

This study has established the recruitment strategy for a definitive RCT of web-based physiotherapy for people moderately affected by Multiple Sclerosis. There are however a few uncertainties which require to be addressed before progressing to a full RCT. These include strategies to reduce the variation in prescribed exercise dose e.g. manualising the intervention, determining the number and format of contacts with healthcare staff to optimise adherence and outcomes, and providing staff education/training in the remote delivery of services.

311

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314	physiotherapists and assessors (Kim Algie, Nicholas Campbell, Rachel Dennett, Hayley
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316	
317	Conflicts of Interest
318	The authors declare that there are no conflicts of interest.
319	
320	<u>Clinical Messages</u>
321	The web-based physiotherapy based intervention was piloted and found to be feasible
322	and acceptable to both participants and physiotherapists, with no intervention-
323	related adverse events
324	• The Two Minute Walk Test and other secondary outcome measures were suitable
325	however further consideration of the sensitivity of EQ-5D in Multiple Sclerosis is
326	required
327	• Based on the Two Minute Walk Test, for 80% power, at the 0.05 significance level, 76
328	participants per group would be required for a future definitive randomised controlled
329	trial
330	
331	
332 333	

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436 Table 1. Demographic characteristics of participants.

	Intervention group	Active control	All
	(n=45)	(n=45)	(n=90)
Age (years)	55.6 (10.2)	56.5 (9.1)	56.1 (9.6)
Gender	13 M, 32 F	8 M, 37 F	21 M, 69 F
BMI (kg/m ²)	25.8 (5.1)	26.4 (5.6)	26.1 (5.3)
Type of MS			
Benign	0 (0%)	1 (2%)	1 (1%)
PPMS	11 (24%)	5 (11%)	16 (18%)
SPMS	14 (31%)	17 (38%)	31 (34%)
RRMS	15 (33%)	15 (33%)	30 (33%)
Unknown	5 (11%)	7 (16%)	12 (13%)
TSD(years)			
Median [IQR]	10[6-18]	15 [10-23]	12 [6-20]
EDSS (median [IQR])	6.0 [6-6]	6.0 [6-6]	6.0 [6-6]

437 Data values are mean (SD) for continuous variables and n (%) for categorical variables unless438 otherwise stated.

439 Abbreviations- n-number; BMI: Body Mass Index; MS: Multiple Sclerosis; PPMS: Primary

440 Progressive MS; SPMS: Secondary Progressive MS; RRMS: Relapsing Remitting MS; TSD:

441 Time Since Diagnosis; EDSS: Expanded Disability Disease Steps; IRQ: Interquartile Range

	Adherence	Intervention (n=45)	Active Comparator (n=45)
Week 1-4	0 times	7 (16)	10 (22)
	<75%	11 (24)	3 (7)
	≥75%	27 (60)	32 (71)
Week 5-8	0 times	8 (18)	12 (27)
	<75%	9 (20)	5 (11)
	≥75%	28 (62)	28 (62)
Week 9-12	0 times	10 (22)	11 (24)
	<75%	14 (31)	7 (16)
	≥75%	21 (47)	37 (60)
Week 13-16	Withdrawn	5 (11)	3 (7)
	0 times	11 (24)	9 (20)
	<75%	6 (13)	7 (16)
	≥75%	23(51)	26 (58)
Week 17-20	Withdrawn	5 (11)	3 (7)
	0 times	11 (24)	8 (18)
	<75%	9 (18)	6 (13)
	≥75%	20 (47)	28 (62)
Week 21-24	Withdrawn	5 (11)	3 (7)
	0 times	10 (22)	12 (27)
	<75%	12 (27)	6 (13)
	≥75%	18 (40)	24 (53)

Table 2. Adherence rates to the exercise programme in both intervention and active comparator groups.

445

446 Data values are presented as n(%). P-values from Chi-squared, withdrawn category not included. 0

times refers to those who recorded no exercise sessions per four week period, non-adherence (<75%

448 of completed sessions) and adherence (\geq 75% of completed sessions)

	Intervention (n=45)				Active co	ntrol (n=45)	Difference between groups	
Outcomes	Ν	Mean (SD)	Mean change (SD)	Ν	Mean (SD)	Mean change (SD)	Mean difference (95% CI)*	Effect size (d)
2 minute walk	test (n	n)						
Baseline	45	80.4 (33.91)		45	70.6 (31.20)			
3 months	39	87.0 (32.88)	5.18 (17.81)	40	77.3 (33.82)	4.85 (17.33)	2.23 (-5.54, 10.01)	0.07
6 months	37	81.8 (33.22)	0.77 (15.12)	39	74.8 (36.16)	3.32 (19.48)	-1.14 (-9.49, 7.21)	-0.04
9 months	35	81.6 (32.75)	-2.61 (16.19)	36	77.6 (33.64)	5.05 (20.43)	-5.83 (-14.61, 2.95)	-0.19
MS Symptom	Checkli	st						
Baseline	45	34.5 (13.47)		45	37.5 (13.45)			
3 months	39	31.0 (13.05)	-2.95 (8.10)	40	34.8 (13.22)	-1.55 7.56)	-1.87 (-5.35, 1.62)	-0.14
6 months	38	33.3 (14.90)	-1.45 (9.11)	39	36.1 (13.33)	-0.25 (8.87)	-1.47 (-5.59, 2.64)	-0.11
9 months	36	31.8 (11.99)	-1.45(9.09)	36	34.4 (11.49)	-0.45 (6.53)	-1.41 (-4.88, 2.07)	-0.12
MSIS 29 v2 (pł	nysical)							
Baseline	45	51.3 (10.83)		45	51.3 (10.46)			
3 months	39	49.9 (11.32)	-2.00 (7.22)	40	49.6 (10.95)	-1.59 (5.51)	-0.36 (-3.20, 2.48)	-0.03
6 months	38	52.6 (11.54)	0.55 (9.94)	39	50.6 (12.44)	-0.17 (8.34)	1.05 (-3.09, 5.18)	0.10
9 months	36	49.9 (11.28)	-2.06 (8.18)	36	49.2 (11.46)	-1.01 (8.16)	-0.77 (-4.56, 3.01)	-0.07
MSIS 29 v2 (ps	ycholo	gical)						
Baseline	45	19.2 (4.51)		45	19.7 (6.03)			
3 months	39	19.0 (4.96)	-0.21 (3.03)	40	19.4 (5.68)	-0.30 (3.14)	0.06 (-1.28, 1.41)	0.01
6 months	38	20.2 (5.58)	0.76 (3.15)	39	20.0 (5.68)	0.44 (4.08)	0.47 (-1.12, 2.08)	0.09
9 months	36	18.8 (5.16)	-0.35 (3.92)	36	18.2 (5.13)	-0.57 (4.02)	0.38 (-1.37, 2.14)	0.08
BBS								
Baseline	43	42.3 (10.92)		44	40.3 (10.30)			
3 months	39	43.7 (11.2)	1.36 (4.21)	40	42.8 (9.22)	3.06 (5.76)	-1.26 (-3.45, 0.93)	-0.12
6 months	37	43.2 (11.20)	0.81 (6.31)	39	42.3 (8.30)	1.86 (6.74)	-0.52 (-3.40, 2.36)	-0.05
9 months	36	43.1 (11.93)	0.41 (6.86)	36	43.8 (8.98)	3.75 (6.69)	-2.87 (-5.98, 0.24)	-0.28
T25ftW (ft/sec	:)							
Baseline	43	2.97 (1.26)		42	2.86 1.37)			
3 months	32	3.14 (1.20)	0.08 (0.51)	33	3.04 (1.32)	0.05 (0.73)	0.03 (-0.24, 0.30)	0.03

450	Table 3. Mea	n values and cl	hange in o	utcomes at three.	six months and	nine months from	baseline.

6 months	28	3.01 (1.27)	-0.06 (0.62)	28	3.06 (1.71)	0.12 (1.43)	-0.04 (-0.60, 0.53)	-0.03
9 months	27	3.02 (0.93)	-0.03 (0.53)	32	2.99 (1.33)	0.13 (0.80)	-0.05 (-0.38, 0.29)	-0.04
EQ-5D								
Baseline	45	0.73 (0.16)		45	0.70 (0.16)			
3 months	39	0.73 (0.13)	0.02 (0.12)	40	0.71 (0.16)	0.00 (0.17)	0.02 (-0.03, 0.08)	0.16
6 months	38	0.74 (0.14)	0.03 (0.13)	39	0.65 (0.25)	-0.06 (0.21)	0.10 (0.02, 0.17)**	0.61
9 months	36	0.71 (0.16)	-0.01 (0.10)	36	0.73 (0.18)	0.01 (0.14)	-0.02 (-0.07, 0.04)	-0.11
EQ-5D VAS								
Baseline	45	64.8 (17.47)		45	63.1 (18.56)			
3 months	39	66.8 (18.79)	4.41 (15.40)	40	63.4 (19.87)	-0.35 (17.12)	5.36 (-1.61, 12.34)	0.29
6 months	38	66.2 (19.38)	0.68 (16.95)	39	60.28 (21.09)	-4.56 (17.97)	5.27 (-2.28, 12.81)	0.29
9 months	36	67.4 (17.93)	0.97 (16.97)	36	65.3 (19.19)	-1.13 (16.27)	2.13 (-4.76, 9.02)	0.12
TUG (s)								
Baseline	44	16.1 (8.98)		45	18.9 (11.47)			
3 months	35	14.3 (7.62)	-0.90 (2.44)	40	19.0 (17.15)	0.07 (8.19)	-0.06 (-2.77, 2.65)	-0.01
6 months	33	14.7 (6.55)	-0.33 (3.39)	37	18.0 (10.66)	-0.15 (4.20)	-0.64 (-2.51, 1.23)	-0.07
9 months	34	14.6 (6.57)	-1.43 (5.11)	36	16.6 (10.67)	-1.20 (6.03)	-1.00 (-3.32, 1.33)	-0.10
HADS - A								
Baseline	45	6.6 (3.35)		44	6.5 (3.87)			
3 months	39	6.2 (3.13)	-0.33 (2.92)	39	6.4 (4.46)	-0.05 (2.68)	-0.33 (-1.51, 0.85)	-0.09
6 months	38	6.2 (3.60)	-0.34 (3.18)	39	6.4 (4.72)	-0.05 (3.15)	-0.22 (-1.56, 1.13)	-0.06
9 months	36	5.8 (3.45)	-0.62 (3.63)	36	5.5 (3.94)	-0.45 (3.06)	-0.06 (-1.49, 1.37)	-0.02
HADS - D								
Baseline	45	7.0 (3.57)		44	6.7 (4.01)			
3 months	39	6.9 (2.93)	-0.01 (2.47)	39	6.3 (3.56)	-0.64 (2.76)	0.68(-0.33, 1.67)	0.18
6 months	38	6.6 (3.48)	-0.32 (2.74)	39	6.9 (3.98)	0.23 (3.32)	-0.41 (-1.70, 0.89)	-0.11
9 months	36	6.5 (2.85)	-0.03 (3.30)	36	6.0 (3.75)	-0.29 (2.98)	0.38 (-0.86, 1.61)	0.11
Steps/day								
Baseline	44	4451 (2511)		43	4584 (2788)			
3 months	29	3989 (2286)	-296 (1560)	32	4303 (2633)	319 (1600)	-551.2 (-1300.1, 197.8)	-0.23
6 months	33	4017 (2493)	-454 (911)	35	4271 (2272)	-54 (1830)	-318.6 (-979.4, 342.1)	-0.13
9 months	29	3960 (2323)	-570 (1177)	33	4410 (2910)	-166 (1777)	-381.7 (-1137.5, 374.2)	-0.15

451 *Adjusted for baseline value and stratification variables (centre and EDSS). Abbreviations- CI: Confidence Interval, n-number; MS- Multiple Sclerosis; MSIS v2-

452 Multiple Sclerosis Impact Scale version 2; BBS- Berg Balance Scale; T25ftW- Timed 25ft Walk; VAS- Visual Analogue Scale; TUG- Timed Up and Go; HADS – Hospital

453 Anxiety and Depression Scale; A- Anxiety subscale, D – Depression subscale. ** statistically significant ($p \le 0.05$).

454

456 Table 4. Findings of interviews with participants.

Themes	Subthemes	Indicative quotes
Reason for taking part	Getting back to exercise	"I used to go to the gym and, um, then I was unwell and I stopped goingso I thought this
		would be a good chance, sort of, ease in to sort of exercising again!" (P314)
	To 'give something	"I thought I owed something back, you know. I have had a lot of care and support and I thought
	back'/help others	I'd better give something back" (P123)
		"Why not? It might not help me but might help other people in the future" (P128)
	A sense of purpose	"Often when you have MS you feel as if you're being totally ignored It's good that somebody is
		trying to do something positive for you" (P309)
	To get individualised	"recognised that it was a way to get access to physiotherapydelay in trying to get seen by the
	physiotherapy	community physiotherapist" (P210)
		"I'm not a sort of a group person eitherbut taking part too much with people with MS, it
		sounds sad but it just reinforces the misery sometimes" (P120)
	To improve/maintain	"Tightening up the core muscles" (P227)
	physical fitness and/or	"Just to try and get some strength back into my muscles" (P129)
	function	"I am getting older anyway, I just want to keep the joints really as supple as I can (P316)
		and maybe feel a bit fitter" (P121)
		"I was hoping to increase or no slow down or stop the declining mobile function" (P210)
Study logistics	Assessment/Outcome	"They don't always tell the full truth of how you are, to be honest" (P121)
	measures	"[walking assessments] were difficult because I get good days and bad days" (P309)
		"[questionnaires]would have been more appropriate for people who, dare I say it, are slightly
		more disabled than myself are you depressed? Yeah just because of the football results" (P123)
	Outcome of	<i>"I didn't mind – either or"</i> (P128)
	randomisation	"I wanted the web of course. I am sure everyone wants the web! Because I am very ofay with
		using the laptop" (P114)
		"I've been given exercises by physios before, paper based and they're not so motivating" (P316)
		"I was quite glad to get that one [control] I get 'splitty' head so I can't sit on a computer" (A121)
	Need for an additional	"At least a second session with the physio after to try and cement it in a little better" (P324)
	appointment	
	with the physiotherapist	

Exercise programme	Exercise prescription and	"She took into consideration all my weak points which I wanted to improve. So I've got weakness
	progression	in my hips so we have exercises to try to counteract that" (P309)
		"Takes on average an hour a day" (P117)
		"Only had 4 exercises to do" (P218)
		"I don't think it was hard enough I 'm just doing the same exercises" (P218)
	Adherence	"Did it a couple of times then became ill. And then I broke my foot" (P218)
		"Had a long period when I did nothing went on holiday to Australia I was in patchy WiFi"
		(P330)
		"When there are other things on in the day I get tired and tend not to do exercise that day"
		(P314)
		"Didn't do very much when it was the very hot weather, it was too much" (A129)
	Changes due to the	"I think my legs are a bit stronger. I can do the getting up and sitting down with control" (P328)
	exercise programme	"Found myself walking better" (P227)
		"Very confidence boosting" (P322)
		"I am finding them [exercises] harder now. I don't know if that's just a progression of the
		disease" (P121)
		"Difficult to tellI think to sort of make much difference I would have to have more intensive
		exercise" (P314)
	Comparator Group	"It [sheet of exercise] was good. I thought that, you know the explanation and that was very
		<i>clear"</i> (P314)
		"Yeah there was a picture and an explanation of what each exercise was and [physiotherapist]
		went through it at the beginning you know if I wasn't doing it 100% right she could explain how
		<i>to do it"</i> (P210)
		"I think the fact that someone is looking at the sheet [exercise diary] helps you complete themit
		gives you more of an impetus to do more exercise when you're filling in a form" (P218)
	Web-based Physio Group	"It's good, its good it's very easy and you could follow it and comment on what you were
		doing it's made me feel more open to using things [computers] now than I would have done
		before" (P322)
		"If you see a video of somebody doing what you're actually supposed to be doing then it's like oh
		year I think I've got that" (P213)
		"I'd have liked to have been able to say 'yesterday I did this' but I couldn't go back on the date
		and put anything in" (P113)

458 Table 5. Findings of interviews with physiotherapists.

Theme	Subtheme	Indicative quotes
Study	Training of staff	"I think it really helps with rapport building the trial is feeling like a team" (T3)
logistics/Feasibility		"Handouts we got from the training were great to refer back to meant a bit more when I
		was actually involved and doing it" (T2)
		"Emails went out to the three of us that were the treating therapists those kind of
		questions that needed teasing out, we did that all via email" (T3)
		"Having a mock patient would be good – to have someone as a practice" (T1)
	Participant recruitment	"Most of them [participants] came through either the nurses or the consultantsI don't think
		there were that many people who didn't want to be involved" (T1)
		"We have the SMART drug trial here at the same time with the same EDSS, and people
		obviously couldn't be part of both" (T3)
		"We had a couple who had very patchy or no internet access one was in a rural area" (T2)
	NHS issues	"Our manager has left again We never quite knew who was dealing with what or how it
		had been left" (T1)
		"I ended up having to do a lot of work from home. A lot of it was down to [NHS area] security
		policies and things like that – IT stuff. I couldn't access Dropbox and emails" (T1)
		"So we'd have sometimes use the corridor for the walk tests, but then you'd stop in between
		[people] coming and all kinds of practicality" (T3)
		"Me and [the assessor] had issues sometimes because we were sharing the office clinical
		space" (T2)
	Attendance and Adherence	"A few of them [participants] had quite long journeys for us they are always tired by the
		time they get here" (T1) "One person had a two hour drive to come for their assessment" (T3)
		"Constant juggling of appointments that was a challenge. That worked because she
		[assessor] was flexible" (T3)
		"People were on holiday or the laptop was being used by their son A few people became
		unwell which you would expect, non-related things like sickness bugs" (T2)
Web-based	Setting up a new patient	"I think that was very easy to use actually. Very straightforward to set up a patient and
physiotherapy		modify it" (T2)
		"Trying to find an exercise that you knew in your head trying to find if it was on the list.
		That took a bit of time" (T1)

	Time to set up and review participants	"So control group maybe easily an hour [appointment with physiotherapist]. The intervention group probably three quarters of an hour" (T2) "If there were lots of changes then [reviewing the programme] maybe 10 or 15 minutes but
	Suggested changes/additions to WBP	<i>maybe only</i> 4-5 minutes if everything was OK" (T1) "The main thing would be if you could communicate through the website" (T1) "Because you cant log it [exercise] retrospectively I think sometimes the adherence data weren't probably reflective of actually how much they'd done" (T2) "I had a few patients who were fairly disabled and could have really benefitted from perhaps some stretches but more in lying, like prolonged stretches and then at the top end some dual tasking" (T3)
Progressing the programme and reviewing goals	Progressing the programme	"If people made comments then I could change things. But if people made no comments then I couldn't change things. I had to assume they were okay" (T3) "I felt like I'd abandoned them a bit" (T2) "I felt I should be doing more with them" (T1) "Sometimes the comments that were made weren't guiding me in any way as to how they were getting on with it [programme]" (T2) "I think the temptation was to take out something that you thought it might be, but it was more difficult I think to add stuff in without ever seeing that person do the exercise So I think the natural reaction was to not add something, just to go up on the reps on the other things they still had in" (T3)
	Reviewing goals	"If I say you at, I don't know, six weeks in when you'd started to see some of those physiological changes would things have improved enough that I could then yes push things up a bit? You don't ever have that conversation" (T3) "We did set goals but we never reviewed them we should really review them" (T1)

463 Figure 1. Consort Diagram for pilot and feasibility trials for the WEBPAMS study.





465 Figure 2. Anticipated and actual recruitment across the study period.