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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 blind, randomised controlled feasibility study

Introduction

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

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

Methods and Materials

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

Potential participants were identified through neurology, Multiple Sclerosis specialist nurse/physiotherapy clinics and from the Multiple Sclerosis regional register/iMED database in Plymouth; and were issued a letter of invitation. To be included participants were required to have a confirmed diagnosis of Multiple Sclerosis (12), an EDSS of 4.0-6.5 (13) and access to a personal computer/tablet with an email address and internet connection. Participants were excluded if they were currently taking part in regular exercise (≥ two times/week) and/or regular physiotherapy programme, had poor cognitive function (Mini Mental State 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-indicated or were currently participating in another clinical trial.

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

Outcome measures were performed at baseline, 3 months, 6 months (post intervention) and 9 months (follow-up) by a blinded research assistant at each site. Primary outcome measures were adherence and the Two Minute Walk Test (15,16). Adherence was measured from the electronic (web-based physiotherapy) or returned paper diaries (active comparator). Participants were advised to undertake their physiotherapy programme twice per week for six months (2 x 26 weeks = 52 diary entries). Secondary outcome measures included the Timed 25 Foot Walk (17), Timed Up and Go test (18), Berg Balance Scale (19), Multiple Sclerosis Impact Scale v2 (20), MS-Related Symptom Checklist (21), Hospital Anxiety and 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.

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

Web-based Physiotherapy

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

electronic exercise diaries every two weeks and remotely altered programmes in response to a participant's comments. Alterations could include changing exercises, difficulty level or number of repetitions/sets. Participants were informed of any changes by email.

Active comparator

Participants randomised to the active comparator intervention received a printed sheet of exercises (www.physiotherapyexercises.com). Programmes consisted of similar exercises as above. Participants completed a paper-based exercise diary that was posted to the research team every three months.

The three physiotherapists also consented to take part in a telephone interview. They were asked regarding their experiences of delivering the interventions, issues in operationalising the protocol and recommendations for a future trial.

Data analysis

All analyses were performed on an intention to treat basis using SAS for windows v9.3. 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 Cohen's (d) effect sizes were calculated (26).

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

Results

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

Figure 1 Near Here

Figure 2 Near Here

Table 1 Near Here

Between 40%-63% of participants adhered to the web-based physiotherapy intervention (≥75% completed diaries) and between 53%-71% to the active comparator during each four week period (Table 2). In both groups adherence reduced over time but over 40% of participants were still adhering to their programme at 6 months. The proportion of people who had no diary entries was 16-24% in the intervention group and 22-27% in the comparator group. No significant differences were found between both groups.

Table 2 Near Here

Compared to baseline, there were no changes in the majority of outcome measures, in either group, at three, six and nine months, with the exception of the EQ-5D at six months in the active comparator group (Table 3).

Table 3 Near Here

Sixty adverse events were recorded; intervention group (n=27), active comparator group (n=33) and 42 of these were falls. Two participants had skin reactions due to the Tegaderm. None of the adverse events were deemed to be related to the intervention.

Telephone interviews were completed by 8 men and 16 women (mean age 56.2 (SD 9.6) years, 11 received web-based physiotherapy and 13 the comparator intervention (EDSS 4.0 n=4, EDSS 4.5 n=3, EDSS 5.0 n=1, EDSS 6.0 n=11, EDSS 6.5 n=5)). Analysis of the interview transcripts yielded three themes and 13 subthemes (Table 4). Participants had a variety of 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.

Table 4 Near Here

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

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

review diaries through web-based physiotherapy and suggested being able to retrospectively add diary entries would have been useful. The therapists reported initial goals were not reviewed, and stated that another appointment would have been useful. Participants rarely left comments in their diaries which meant that the physiotherapists were unable to change/progress their programme. When changes were made it tended to be a change in the dose of the exercise rather than add/change the exercise.

Table 5 Near Here

The results of the within-trial analysis found that the web-based intervention was associated with lower costs (£954), compared to standard treatment (£1,076). This was associated with a small QALYs gain in the intervention group (0.557), compared with the comparator group (0.517). We undertook a bootstrap analysis to explore uncertainty associated with our results. The results estimated a mean cost difference between treatment groups of -£122 (95% CI: -583.856, 339,206) and a mean difference in QALYs of 0.03 (95% CI: -0.012, 0.072). Although the web-based intervention had the potential to dominate the standard treatment, as it provides additional QALYs for a lower cost, there is substantial uncertainty associated with these estimates.

Discussion

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.

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.

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

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

The dose of exercise prescribed may explain the lack of improvement in outcome measures. Similar to Conroy et al. (3), our study took place within the context of available resources, with exercise programmes reflecting physiotherapy practice (including aerobic, strengthening, cardiovascular and functional exercises). Only one similar, small, uncontrolled, short-term (12 week) web-based physiotherapy study found some improvements in people 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 (8) have reported positive results. It is possible that with a combined programme, the dose of exercise for any one component is insufficient for physiological changes to take place thus web-based interventions need to focus on specific impairments in order to achieve meaningful change.

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.

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

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

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

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

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.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

Clinical Messages

- The web-based physiotherapy based intervention was piloted and found to be feasible and acceptable to both participants and physiotherapists, with no intervention-related adverse events
- The Two Minute Walk Test and other secondary outcome measures were suitable however further consideration of the sensitivity of EQ-5D in Multiple Sclerosis is required
- Based on the Two Minute Walk Test, for 80% power, at the 0.05 significance level, 76 participants per group would be required for a future definitive randomised controlled trial

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436 Table 1. Demographic characteristics of participants.

	Intervention group (n=45)	Active control (n=45)	All (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 unless
438 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
442

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

	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)

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% of completed sessions) and adherence (≥75% of completed sessions)

450 Table 3. Mean values and change in outcomes at three, six months and nine months from baseline.

	Intervention (n=45)			Active control (n=45)			Difference between groups	
Outcomes	**N**	**Mean (SD)**	**Mean change (SD)**	**N**	**Mean (SD)**	**Mean change (SD)**	**Mean difference (95% CI)***	**Effect size (*d*)**
2 minute walk test (m)								
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 Checklist								
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 (physical)								
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 (psychological)								
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

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

*Adjusted for baseline value and stratification variables (centre and EDSS). Abbreviations- CI: Confidence Interval, n-number; MS- Multiple Sclerosis; MSIS v2- 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 Anxiety and Depression Scale; A- Anxiety subscale, D – Depression subscale. ** statistically significant ($p \leq 0.05$).

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 going….so I thought this would be a good chance, sort of, ease in to sort of exercising again!"* (P314)
	To 'give something back'/help others	*"I thought I owed something back, you know. I have had a lot of care and support and I thought 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 physiotherapy	*"..recognised that it was a way to get access to physiotherapy…delay in trying to get seen by the community physiotherapist"* (P210) *"I'm not a sort of a group person either…but taking part too much with people with MS, it sounds sad but it just reinforces the misery sometimes"* (P120)
	To improve/maintain physical fitness and/or function	*"Tightening up the core muscles"* (P227) *"Just to try and get some strength back into my muscles"* (P129) *"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 measures	*"They don't always tell the full truth of how you are, to be honest"* (P121) *"[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 randomisation	*"I didn't mind – either or"* (P128) *"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 appointment with the physiotherapist	*"At least a second session with the physio after to try and cement it in a little better"* (P324)

Exercise programme	Exercise prescription and progression	*"She took into consideration all my weak points which I wanted to improve. So I've got weakness 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 exercise programme	*"I think my legs are a bit stronger. I can do the getting up and sitting down with control"* (P328) *"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 tell …I 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 clear"* (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 to do it"* (P210) *"I think the fact that someone is looking at the sheet [exercise diary] helps you complete them…it 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)

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458 Table 5. Findings of interviews with physiotherapists.

Theme	Subtheme	Indicative quotes
Study logistics/Feasibility	Training of staff	*"I think it really helps with rapport building… the trial is feeling like a team"* (T3) *"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 consultants….I 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 physiotherapy	Setting up a new patient	*"I think that was very easy to use actually. Very straightforward to set up a patient and 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 maybe only … 4-5 minutes if everything was OK"* (T1)
	Suggested changes/additions to WBP	*"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.

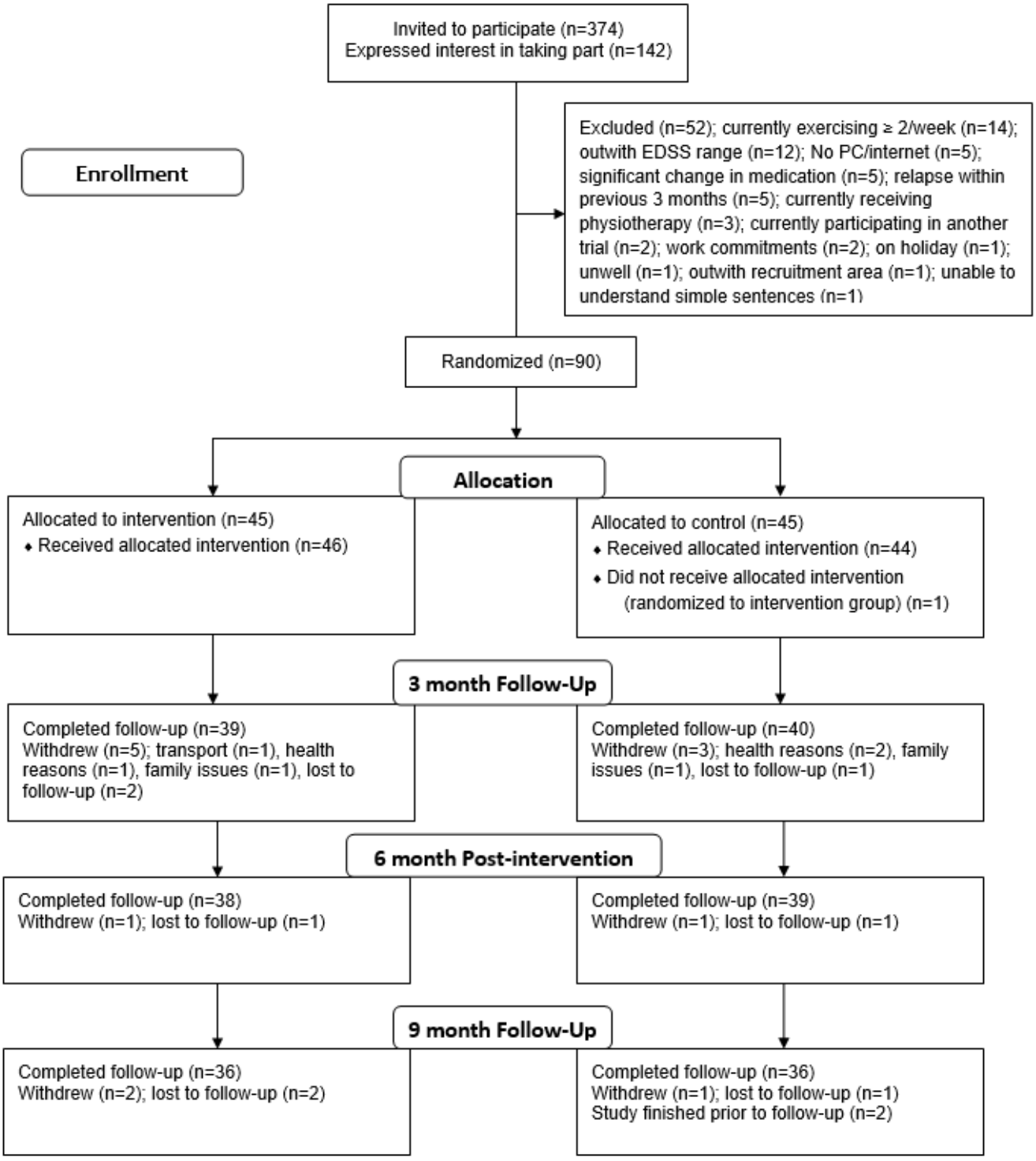

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Figure 2. Anticipated and actual recruitment across the study period.