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

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1   Web-based Physiotherapy for people affected by Multiple Sclerosis (WEBPaMS); a

2   pragmatic, single blind, randomised controlled feasibility study

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12

13 **Running Heading** Web-based physiotherapy in MS

14 **Acknowledgements**

18 **Conflicts of Interest**

19 The authors declare that there are no conflicts of interest.

20 **Clinical Trial Registration Number**

21 The study was registered on ClinicalTrials.gov (Identifier: NCT02508961).

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24 Web-based Physiotherapy for people affected by Multiple Sclerosis (WEBPaMS); a single

25 blind, randomised controlled feasibility study

26

27 **<u>Abstract</u>**

28 <u>Objective</u>: To examine the feasibility of a trial to evaluate web-based physiotherapy compared

29 to a standard home exercise programme in people with Multiple Sclerosis (MS).

30 <u>Design</u>: Multi-centre, randomised controlled, feasibility study

31 <u>Setting</u>; Three Multiple Sclerosis out-patient centres

32 <u>Participants:</u> Ninety people with Multiple Sclerosis (Expanded Disability Disease Scale 4-6.5),

33 <u>Interventions</u>: Participants were randomised, to a 6 month individualised, home exercise

34 programme delivered via web-based physiotherapy (n=45) (intervention) or a sheet of

35 exercises (n=45) (active comparator).

36 <u>Main outcome measures</u>: Outcome measures (0, 3, 6 and 9 months) included adherence,

37 2min walk test, 25ft walk, Berg Balance Scale, physical activity and healthcare resource use.

38 Interviews were undertaken with 24 participants and 3 physiotherapists.

39 <u>Results</u>: Almost 25% of people approached agreed to take part. No intervention-related

40 adverse events were recorded. Adherence was 40-63% and 53-71% in the web-based

41 physiotherapy and comparator groups. There was no difference in the 2min walk test

42 between groups at baseline (Intervention-80.4(33.91)m, Comparator-70.6(31.20)m) and no

43 change over time (at 6 months Intervention-81.6(32.75)m, Comparator 74.8(36.16)m). There

44 were no significant changes over time in other outcome measures except the EQ-5D at 6

45 months which improved in the active comparator group. For a difference of 8(17.4)m in the

46 2min walk test between groups 76 participants/group would be required (80% power, $p > 0.05$)

47 for a future randomised controlled trial.

48   <u>Conclusion</u>: no changes were found in the majority of outcome measures over time. This

49   study was acceptable and feasible by participants and physiotherapists. An adequately

50   powered study needs 160 participants.

52

53

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;

77   f) help establish the eligibility criteria for a definitive trial; g) undertake an exploratory cost-

78   effectiveness analysis of web-based physiotherapy compared to the active comparator.

79

80   **Methods and Materials**

81   The study was prospectively registered on ClinicalTrials.gov (Identifier: NCT02508961), ethical

82   approval was obtained from the West of Scotland Research Ethics Service (Ref:15/WS/0030;

83   March 2015- January 2016) and University of Glasgow acted as study sponsor. This

84   randomised, controlled, multi-centre feasibility study aimed to recruit 90 people with

85   Multiple Sclerosis from three centres (30 from each centre); NHS Ayrshire and Arran, NHS

86   Lothian and Plymouth Hospitals NHS Trust, over a seven month period (June 2015-December

87   2015). The sample size was based on previous pilot data (6) and the assumption that each

88   centre   could   recruit   one   participant   per   week.

89

90   Potential participants were identified through neurology, Multiple Sclerosis specialist

91   nurse/physiotherapy clinics and from the Multiple Sclerosis regional register/iMED database

92   in Plymouth; and were issued a letter of invitation. To be included participants were required

93   to have a confirmed diagnosis of Multiple Sclerosis (12), an EDSS of 4.0-6.5 (13) and access to

94   a personal computer/tablet with an email address and internet connection. Participants were

95   excluded if they were currently taking part in regular exercise (≥ two times/week) and/or

96   regular physiotherapy programme, had poor cognitive function (Mini Mental State

97   Examination Score <24) (14), any significant change in medication or a relapse within the last

98   three months, other significant co-morbidities for which exercise would be contra-indicated

99   or were currently participating in another clinical trial.

100

101   At the initial appointment potential participants were screened for eligibility, written

102   informed consent was obtained and baseline assessments were performed. One week later

103   participants' were given an appointment with an experienced neurological physiotherapist

104   where they received a standardised physiotherapy assessment. Goals were agreed, from

105   which an individualised exercise programme was devised. Participants were then randomised

106   to the intervention or active comparator group using a remote, telephone automated

107   randomisation system within the Glasgow Clinical Trials Unit. Randomisation was stratified by

108   study centre and EDSS (4.0-5.0 and 5.5-6.5). Participants were provided with their exercise

109   programme either via web-based physiotherapy or as a printed sheet of exercises. All

110   participants were asked to complete their exercise programme twice weekly and received a

111   weekly telephone call/email for the first two weeks to discuss any issues.

112

113   Outcome measures were performed at baseline, 3 months, 6 months (post intervention) and

114   9 months (follow-up) by a blinded research assistant at each site. Primary outcome measures

115   were adherence and the Two Minute Walk Test (15,16). Adherence was measured from the

116   electronic (web-based physiotherapy) or returned paper diaries (active comparator).

117   Participants were advised to undertake their physiotherapy programme twice per week for

118   six months (2 x 26 weeks = 52 diary entries). Secondary outcome measures included the

119   Timed 25 Foot Walk (17), Timed Up and Go test (18), Berg Balance Scale (19), Multiple

120   Sclerosis Impact Scale v2 (20), MS-Related Symptom Checklist (21), Hospital Anxiety and

121   Depression Scale (22), EQ-5D, (23) and steps taken/day measured objectively worn

122   continuously for one week using the activPAL tri-axial accelerometer (Pal Technologies Ltd,

123   Glasgow, UK) (24,25). The device was attached to the participant's mid-thigh using a

124   waterproof Tegaderm dressing and participants kept a diary to record their sleep time.

125 Healthcare resource use, physiotherapist time, GP visits, nurse visits, other Multiple Sclerosis

126 or outpatient review, Accident and Emergency attendance and hospital stay, were recorded

127 by self-report questionnaire.

128

129 To determine the acceptability and feasibility of the study semi-structured telephone

130 interviews were undertaken with physiotherapists and participants. The interviewer was a

131 member of the research team unknown to participants. A purposive sample of 24

132 participants, eight from each study site (both groups), consented to take part. The purposive

133 sample was selected using a sampling matrix to include age (<50 years, >50 years), disability

134 (EDSS 4.0-5.0, 5.5-6.5) and gender. Participants were asked their reasons for taking part in

135 the study, their views of the assessments and intervention, any issues faced, perceived

136 benefit and recommendations for a future trial.

137

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

139 Participants randomised to the web-based physiotherapy intervention received an

140 individualised exercise programme delivered via www.webbasedphysio.com. Programmes

141 could consist of cardiovascular, strengthening and balance exercises, as well as warm up, cool

142 down and stretching exercises, at different levels of difficulty and a prescribed number of

143 sets/repetitions individualised to meet the participants' needs. The website contained

144 exercises (videos, text and audio description) and disease-specific advice and education

145 (described in Paul et al. (6)). During the intervention period the physiotherapist reviewed

146 electronic exercise diaries every two weeks and remotely altered programmes in response to

147 a participant's comments. Alterations could include changing exercises, difficulty level or

148 number of repetitions/sets. Participants were informed of any changes by email.

149

<u>Active comparator</u>

151 Participants randomised to the active comparator intervention received a printed sheet of

152 exercises (www.physiotherapyexercises.com). Programmes consisted of similar exercises as

153 above. Participants completed a paper-based exercise diary that was posted to the research

154 team every three months.

155

156 The three physiotherapists also consented to take part in a telephone interview. They were

157 asked regarding their experiences of delivering the interventions, issues in operationalising

158 the protocol and recommendations for a future trial.

159

<u>Data analysis</u>

161 All analyses were performed on an intention to treat basis using SAS for windows v9.3.

162 Categorical variables are summarised as number and percentage (n(%)). Continuous variables

163 were summarised by mean and standard deviation (SD) or median and interquartile range

164 (IQR) as appropriate. Adherence data were considered as those who recorded no exercise

165 sessions per four week period, non-adherence (<75% of completed sessions) and adherence

166 (≥75% of completed sessions) and was compared between intervention groups using Chi-

167 squared tests. Between group differences were assessed using analysis of covariance

168 (ANCOVA) adjusted for baseline value and stratification variables (centre and EDSS) and

169 Cohen's (d) effect sizes were calculated (26).

170

171 Cost-effectiveness was explored using healthcare resource use and valued using UK cost

172 sources (27–29). EQ-5D data were used to derive health utility values and estimate quality-

173   adjusted life-years (QALYs) gained (30). Mean costs and QALYs associated with each

174   treatment group were estimated using generalised linear models. Telephone interviews were

175   audio-recorded, transcribed verbatim and analysed using thematic analysis. One researcher

176   first coded all scripts, then two researchers independently identified emerging themes and

177   sub-themes. Following this, discussion was held between the researchers to agree and finalise

178   themes and sub-themes.

179

180   **Results**

181   Ninety people with Multiple Sclerosis were recruited (Figure 1), however to achieve our target

182   sample size the data collection period was extended from seven to twelve months (June 2015-

183   May 2016) (Figure 2). The sample consisted of 21 males and 69 females; mean age 56.1 (SD

184   9.6) years (Table 1). Eight people (18%) from the intervention group and five (11%) from the

185   active comparator group withdrew from the study (Figure 1) (31). One participant received

186   the web-based physiotherapy intervention rather than the active comparator, although with

187   intention to treat analysis they were considered as having received the comparator

188   intervention.

189

190   Figure 1 Near Here

191   Figure 2 Near Here

192   Table 1 Near Here

193

194   Between 40%-63% of participants adhered to the web-based physiotherapy intervention

195   (≥75% completed diaries) and between 53%-71% to the active comparator during each four

196   week period (Table 2). In both groups adherence reduced over time but over 40% of

197   participants were still adhering to their programme at 6 months. The proportion of people

198   who had no diary entries was 16-24% in the intervention group and 22-27% in the comparator

199   group. No significant differences were found between both groups.

200

201   Table 2 Near Here

202

203   Compared to baseline, there were no changes in the majority of outcome measures, in either

204   group, at three, six and nine months, with the exception of the EQ-5D at six months in the

205   active comparator group (Table 3).

206

207   Table 3 Near Here

208

209   Sixty adverse events were recorded; intervention group (n=27), active comparator group

210   (n=33) and 42 of these were falls. Two participants had skin reactions due to the Tegaderm.

211   None of the adverse events were deemed to be related to the intervention.

212

213   Telephone interviews were completed by 8 men and 16 women (mean age 56.2 (SD 9.6) years,

214   11 received web-based physiotherapy and 13 the comparator intervention (EDSS 4.0 n=4,

215   EDSS 4.5 n=3, EDSS 5.0 n=1, EDSS 6.0 n=11, EDSS 6.5 n=5)). Analysis of the interview

216   transcripts yielded three themes and 13 subthemes (Table 4). Participants had a variety of

217   reasons for taking part in the study, most wanted to get back to exercise to improve their

218   physical condition but for some a realistic goal was to maintain their physical ability. Taking

219   part in the study was stated as a way of getting more therapy, providing a sense of purpose

220   and to help others with Multiple Sclerosis.

221

222   Table 4 Near Here

223

224   In general, participants were very positive about the study, some people had a preference in

225   terms of group allocation, often determined by previous experience, but no-one felt very

226   strongly. A number of people suggested an additional appointment with the physiotherapist

227   to review progress would have been beneficial. Participants from both groups appreciated

228   the individualised nature of their programme. There was notable variation in the number of

229   exercises participants reported and very few instances of exercise programmes being

230   changed or progressed. Most people reported some benefit from exercising and gave

231   examples of both Multiple Sclerosis (e.g. fatigue) and non- Multiple Sclerosis related factors

232   (e.g. holidays or surgery) which affected their adherence. Participants in the comparator

233   group reported that completing the exercise diary was motivating. Finally some suggestions

234   were proposed to improve the web-based physiotherapy website including being able to

235   retrospectively complete exercise diaries.

236

237   Analysis of the transcripts from the physiotherapists' interviews resulted in three themes and

238   nine sub-themes (Table 5). There were some challenges with recruitment mentioned as other

239   studies were recruiting at the same time. All three therapists commented that some

240   participants had a significant distance to travel for assessments which may have affected the

241   outcomes due to fatigue. The physiotherapists reported that it only took a few minutes to

242   review diaries through web-based physiotherapy and suggested being able to retrospectively

243   add diary entries would have been useful. The therapists reported initial goals were not

244   reviewed, and stated that another appointment would have been useful. Participants rarely

245 left comments in their diaries which meant that the physiotherapists were unable to

246 change/progress their programme. When changes were made it tended to be a change in the

247 dose of the exercise rather than add/change the exercise.

248

249 Table 5 Near Here

250

251 The results of the within-trial analysis found that the web-based intervention was associated

252 with lower costs (£954), compared to standard treatment (£1,076). This was associated with

253 a small QALYs gain in the intervention group (0.557), compared with the comparator group

254 (0.517). We undertook a bootstrap analysis to explore uncertainty associated with our results.

255 The results estimated a mean cost difference between treatment groups of -£122 (95% CI: -

256 583.856, 339,206) and a mean difference in QALYs of 0.03 (95% CI: -0.012, 0.072). Although

257 the web-based intervention had the potential to dominate the standard treatment, as it

258 provides additional QALYs for a lower cost, there is substantial uncertainty associated with

259 these estimates.

260

261 **Discussion**

262 Adherence to the intervention was good, 40-63% in the web-based physiotherapy group and

263 53-71% in the comparator group, with the lowest adherence during the last month of the

264 study. Direct comparison with previous studies is challenging due to different methods of

265 defining adherence, although all demonstrated that adherence to web-based physiotherapy

266 reduces over time (9,10,32). Tallner et al. (9) reported that 73% of participants completed

267 80% or more of their programme during months 1-3 which reduced to 36% during months 4-

268 6, Motl et al. (10) reported 96% of participants logged on to the website in weeks 1-2 which

269   reduced to 52% at week 8, and Conroy et al. (3) reported only half of participants adhered to

270   their programme and almost one quarter completed no exercise diaries.

271

272   Adherence to home-based exercise is affected by factors such as low motivation, pain and

273   past experience of exercise (33). Participants in the active comparator group reported that

274   completing and returning the exercise diaries improved their adherence. Return of exercise

275   diaries is not part of usual care and may have inflated adherence in this group. Although our

276   adherence was better than previous studies it is clear that other strategies to improve

277   adherence e.g. more contact with a health care professional and more frequent updates are

278   required (32). Specific strategies are needed to engage those with no diaries entries.

279

280   In terms of recruitment, 24% of those invited to participate took part in the study. There were

281   no issues raised around the eligibility criteria. The recruitment rate of around two per month

282   was less than the anticipated four per month per centre. Recruitment was generally on target

283   for the first six months, however this recruitment rate was not maintained partly due to this

284   study 'competing' for participants with other studies. The most common pathway to

285   recruitment was via the nurses or consultants. Thus, the recruitment strategy of a future trial

286   would consider that around 1 in 4 of those invited will be recruited, would be predicated on

287   an anticipated recruitment rate of two participants per month and would favour recruiting

288   participants directly from clinics/health care staff.

289

290   Although there were no significant changes in outcome measures, participants in both groups

291   maintained their clinical outcomes over the intervention period and, during interview, a

292   number of participants reported improvements in e.g. walking, balance and strength.

293 Multiple Sclerosis is a progressive neurological condition and some participants reported their

294 goal was to maintain their functional status rather than improve. Similarly, Conroy et al. (3)

295 recruited people with Multiple Sclerosis with levels of disability similar to the current study

296 and reported no significant improvement in outcomes following a six month web-based

297 physiotherapy intervention. Web-based exercise may have the potential to maintain the

298 clinical status of people with Multiple Sclerosis with higher levels of disability, however

299 further investigation with the inclusion of a control group with no exercise intervention, to

300 assess the natural history of participants, is required.

301

302 The dose of exercise prescribed may explain the lack of improvement in outcome measures.

303 Similar to Conroy et al. (3), our study took place within the context of available resources,

304 with exercise programmes reflecting physiotherapy practice (including aerobic,

305 strengthening, cardiovascular and functional exercises). Only one similar, small, uncontrolled,

306 short-term (12 week) web-based physiotherapy study found some improvements in people

307 with Multiple Sclerosis (7). In contrast, previous web-based studies in Multiple Sclerosis that

308 have focussed on a single impairment e.g. strengthening (9), physical activity (10) or balance

309 (8) have reported positive results. It is possible that with a combined programme, the dose of

310 exercise for any one component is insufficient for physiological changes to take place thus

311 web-based interventions need to focus on specific impairments in order to achieve

312 meaningful change.

313

314 Few participants left comments in their exercise diaries therefore therapists had no clinical

315 rationale to change programmes, which resulted in a lack of exercise progression. The

316 physiotherapists were reluctant to add exercises without seeing the participant to ensure

317   they were doing new exercises correctly and any progress tended to be an increase in

318   repetitions of the same exercises, this was also raised by Conroy et al. (3). Delivering

319   physiotherapy programmes remotely is a different service delivery model, which appears to

320   challenge professional practice and values.

321

322   From the data of this study and clinical experience it is estimated that the difference in Two

323   Minute Walk Test between intervention and comparator groups would be 8m, assuming a

324   standard deviation of 17.4m. Therefore, for 80% power at the 0.05 significance level 76

325   participants per group would be required for a future definitive randomised controlled trial.

326   However, attrition across the study period was 18% in the intervention group and 11% in the

327   active comparator group which is notably less than previous web-based interventions of

328   similar duration; 39% attrition Tallner et al. (9) and 35% attrition Conroy et al. (3). Thus,

329   allowing for a conservative dropout rate of 20%, 95 participants per group would be required.

330

331   The estimated differences in costs and QALYs between groups were small and further

332   research to reduce the uncertainty associated with these estimates would be beneficial. The

333   association between changes in functional status and changes in Health-related Quality of Life

334   remains unclear in the literature, particularly given the questionable sensitivity of the EQ-5D

335   in people with Multiple Sclerosis (34). While some studies have found some improvement in

336   Health-related Quality of Life in people with Multiple Sclerosis (8,35,36), others found no

337   change (6,7,11). Further research is required to determine the impact of web-based

338   physiotherapy on Health-related Quality of Life in people with Multiple Sclerosis and the

339   suitability of EQ-5D.

340

341 This study has a number of limitations. Paper exercise diaries were used in the active

342 comparator group to measure adherence however this is not part of usual care and may have

343 increased adherence levels. The study did not include a non-exercising control group

344 therefore comparisons to the natural history of Multiple Sclerosis cannot be made. Exercise

345 programmes were individually tailored to participants to reflect clinical practice, however this

346 meant that dose of exercise varied greatly and there were few examples of progression of

347 programmes. This lack of progression was due to the paucity of diary comments and therefore

348 a reluctance on the part of the therapists to progress exercises without face-to-face contact.

349 As such the exercise dose may have been insufficient to induce physiological changes and

350 hence outcome measures.

351

352 This study has established the recruitment strategy for a definitive RCT of web-based

353 physiotherapy for people moderately affected by Multiple Sclerosis. There are however a few

354 uncertainties which require to be addressed before progressing to a full RCT. These include

355 strategies to reduce the variation in prescribed exercise dose e.g. manualising the

356 intervention, determining the number and format of contacts with healthcare staff to

357 optimise adherence and outcomes, and providing staff education/training in the remote

358 delivery of services.

359

364

365 **Conflicts of Interest**

366 The authors declare that there are no conflicts of interest.

367

368 **Clinical Messages**

369 • The web-based physiotherapy based intervention was piloted and found to be feasible

370 and acceptable to both participants and physiotherapists, with no intervention-

371 related adverse events

372 • The Two Minute Walk Test and other secondary outcome measures were suitable

373 however further consideration of the sensitivity of EQ-5D in Multiple Sclerosis is

374 required

375 • Based on the Two Minute Walk Test, for 80% power, at the 0.05 significance level, 76

376 participants per group would be required for a future definitive randomised controlled

377 trial

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References

382   **References**

383   1.   Ortiz-Gutiérrez R, Cano-de-la-Cuerda R, Galán-del-Río F, Alguacil-Diego IM, Palacios-

384   Ceña D, Miangolarra-Page JC. A telerehabilitation program improves postural control

385   in multiple sclerosis patients: a Spanish preliminary study. Int J Environ Res Public

386   Health. 2013;10(11):5697–710.

387   2.   Huijgen BCH, Vollenbroek-Hutten MMR, Zampolini M, Opisso E, Bernabeu M, Van

388   Nieuwenhoven J, et al. Feasibility of a home-based telerehabilitation system

389   compared to usual care: arm/hand function in patients with stroke, traumatic brain

390   injury and multiple sclerosis. J Telemed Telecare. 2008;14(5):249–56.

391   3.   Conroy SS, Zhan M, Culpepper WJ, Royal W, Wallin MT. Self-directed exercise in

392   multiple sclerosis : Evaluation of a home automated tele-management system. J

393   Telemed Telecare. 2018;24(6):410–9.

394   4.   Brennan DM, Mawson S, Brownsell S. Telerehabilitation: Enabling the Remote

395   Delivery of Healthcare, Rehabilitation, and Self Management. Stud Health Technol

396   Inform. 2009;145:231–48.

397   5.   Khan F, Amatya B, Kesselring J, Galea M. Telerehabilitation for persons with multiple

398   sclerosis. A Cochrane Review. Eur J Phys Rehabil Med. 2015;51(3):311–25.

399   6.   Paul L, Coulter EH, Miller L, McFadyen A, Dorfman J, Mattison PGG. Web-based

400   physiotherapy for people moderately affected with Multiple Sclerosis; quantitative

401   and qualitative data from a randomized, controlled pilot study. Clin Rehabil.

402   2014;28(9):924–35.

403   7.   Finkelstein J, Lapshin O, Castro H, Cha E, Provance PG. Home-based physical

404   telerehabilitation in patients with multiple sclerosis: A pilot study. J Rehabil Res Dev.

405   2008;45(9):1361–73.

406   8.   Frevel D, Mäurer M. Internet-based home training is capable to improve balance in

407   multiple sclerosis: a randomized controlled trial. Eur J Phys Rehabil Med.

408   2015;51(1):23–30.

409   9.   Tallner A, Streber R, Hentschke C, Morgott M, Geidl W, Mäurer M, et al. Internet-

410   Supported Physical Exercise Training for Persons with Multiple Sclerosis — A

411   Randomised , Controlled Study. Int J Mol Sci. 2016;17(10):E1667.

412   10.   Motl RW, Dlugonski D, Wójcicki TR, McAuley E, Mohr DC. Internet intervention for

413   increasing physical activity in persons with multiple sclerosis. Mult Scler.

414   2011;17(1):116–28.

415   11.   Pilutti LA, Dlugonski D, Sandroff BM, Klaren R, Motl RW. Randomized controlled trial

416   of a behavioral intervention targeting symptoms and physical activity in multiple

417   sclerosis. Mult Scler. 2014;20(5):594–601.

418   12.   Polman CH, Reingold SC, Edan G, Filippi M, Hartung H, Kappos L, et al. Diagnostic

419   Criteria for Multiple Sclerosis : 2005 Revisions to the "McDonald Criteria." Ann

420   Neurol. 2005;58(6):840–6.

421   13.   Kurtzke J. Rating neurologic impairment in multiple sclerosis: an expanded disability

422   status scale (EDSS). Neurology. 1983;33(11):1444–52.

423   14.   Folstein M, Folstein S, McHugh P. "Mini-mental state". A practical method for grading

424   the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189–98.

425   15.   Gijbels D, Eijnde BO, Feys P. Comparison of the 2- and 6-minute walk test in multiple

426   sclerosis. 2011;17(10):1269–72.

427   16.   Gijbels D, Dalgas U, Romberg A, De V, Bethoux F, Vaney C, et al. Which walking

428   capacity tests to use in multiple sclerosis ? A multicentre study providing the basis for

429   a core set. Mult Scler. 2012;18(3):364–71.

430   17.   Cutter GR, Baier ML, Rudick RA, Cookfair DL, Fischer JS, Petkau J, et al. Development

431   of a multiple sclerosis functional composite as a clinical trial outcome measure. Brain.

432   1999;122:871–82.

433   18.   Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility

434   for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142–8.

435   19.   Berg K, Wood-Dauphinée S, Williams JI. The Balance Scale: reliability with elderly

436   residents and patients with an acute stroke. Scand J Rehabil Med. 1995;21(1):27–36.

437   20.   Hobart J, Cano S. Improving the evaluation of therapeutic interventions in multiple

438   sclerosis: the role of new psychometric methods. Health Technol Assess (Rockv).

439   2009;13(12).

440   21.   Gulick E. Model confirmation of the MS-Related Symptom Checklist. Nurs Res.

441   1989;38(3):147–53.

442   22.   Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr

443   Scand. 1983;67(6):361–70.

444   23.   Brazier J, Ratcliffe J, Tsuchiya A, Salomon J. Measuring and Valuing Health Benefits for

445   Economic Evaluation. Oxford: Oxford University Press; 2007.

446   24.   Ryan CG, Grant PM, Tigbe WW, Granat MH. The validity and reliability of a novel

447   activity monitor as a measure of walking. Br J Sports Med. 2006;40(9):779–84.

448   25.   Grant PM, Ryan CG, Tigbe WW, Granat MH. The validation of a novel activity monitor

449   in the measurement of posture and motion during everyday activities. Br J Sports

450   Med. 2006;40(12):992–7.

451   26.   Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale, NJ:

452   Erlbaum; 1988.

453   27.   Curtis L, Burns A. Unit Costs of Health & Social Care 2016. Canterbury: Personal Social

454   Services Research Unit, University of Kent; 2016.

455   28.   Information Services Division Scotland. Scottish Health Service Costs [Internet]. 2016.

456   Available from: http://www.isdscotland.org/Health-

457   Topics/Finance/Publications/2016-11-22/2016-11-22-Costs-Report.pdf

458   29.   Department of Health. Reference Costs 2015-16 [Internet]. 2016. Available from:

459   https://www.gov.uk/government/publications/nhs-reference-costs-2015-to-2016

460   30.   Dolan P. Modeling valuations for EuroQol health states. Med Care. 1997;35(11):1095–

461   108.

462   31.   Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Lancaster GA, et al.

463   CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ.

464   2016;24(355):i5239.

465   32.   Kelders SM, Gemert-pijnen JEWC Van, Werkman A, Nijland N. Effectiveness of a Web-

466   based Intervention Aimed at Healthy Dietary and Physical Activity Behavior : A

467   Randomized Controlled Trial About Users and Usage. J Med Internet Res.

468   2011;13(2):e32.

469   33.   Lambert TE, Harvey LA, Avdalisa C, Chen LW, Jeyalingama S, Pratt CA, et al. An app

470   with remote support achieves better adherence to home exercise programs than

471   paper handouts in people with musculoskeletal conditions: a randomised trial. J

472   Physiother; 2017;63(3):161–7.

473   34.   Kuspinar A, Mayo NE. Do generic utility measures capture what is important to the

474   quality of life of people with multiple sclerosis? Health Qual Life Outcomes.

475   2013;11(71):1–10.

476   35.   Egner A, Phillips VL, Vora R, Wiggers E. Depression, fatigue, and health-related quality

477   of life among people with advanced multiple sclerosis: results from an exploratory

478   telerehabilitation study. NeuroRehabilitation. 2003 Jan;18(2):125–33.

479   36.   Moss-Morris R, McCrone P, Yardley L, van Kessel K, Wills G, Dennison L. A pilot

480   randomised controlled trial of an Internet-based cognitive behavioural therapy self-

481   management programme (MS Invigor8) for multiple sclerosis fatigue. Behav Res Ther.

482   2012;50(6):415–21.

483

484   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]

485   Data values are mean (SD) for continuous variables and n (%) for categorical variables unless
486   otherwise stated.
487   Abbreviations- n-number; BMI: Body Mass Index; MS: Multiple Sclerosis; PPMS: Primary
488   Progressive MS; SPMS: Secondary Progressive MS; RRMS: Relapsing Remitting MS; TSD:
489   Time Since Diagnosis; EDSS: Expanded Disability Disease Steps; IRQ: Interquartile Range
490

491 Table 2. Adherence rates to the exercise programme in both intervention and active
492 comparator groups.
493

	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)

494 Data values are presented as n(%). P-values from Chi-squared, withdrawn category not included. 0
495 times refers to those who recorded no exercise sessions per four week period, non-adherence (<75%
496 of completed sessions) and adherence (≥75% of completed sessions)
497

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

Outcomes	N	Intervention (n=45) Mean (SD)	Mean change (SD)	N	Active control (n=45) Mean (SD)	Mean change (SD)	Difference between groups 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

	N	Mean (SD)	Change (SD)	N	Mean (SD)	Change (SD)	Difference (95% CI)	Effect size
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

499 *Adjusted for baseline value and stratification variables (centre and EDSS). Abbreviations- CI: Confidence Interval, n-number; MS- Multiple Sclerosis; MSIS v2-
500 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
501 Anxiety and Depression Scale; A- Anxiety subscale, D – Depression subscale. ** statistically significant ($p \leq 0.05$).
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504   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)

28

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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Table 5. Findings of interviews with physiotherapists.

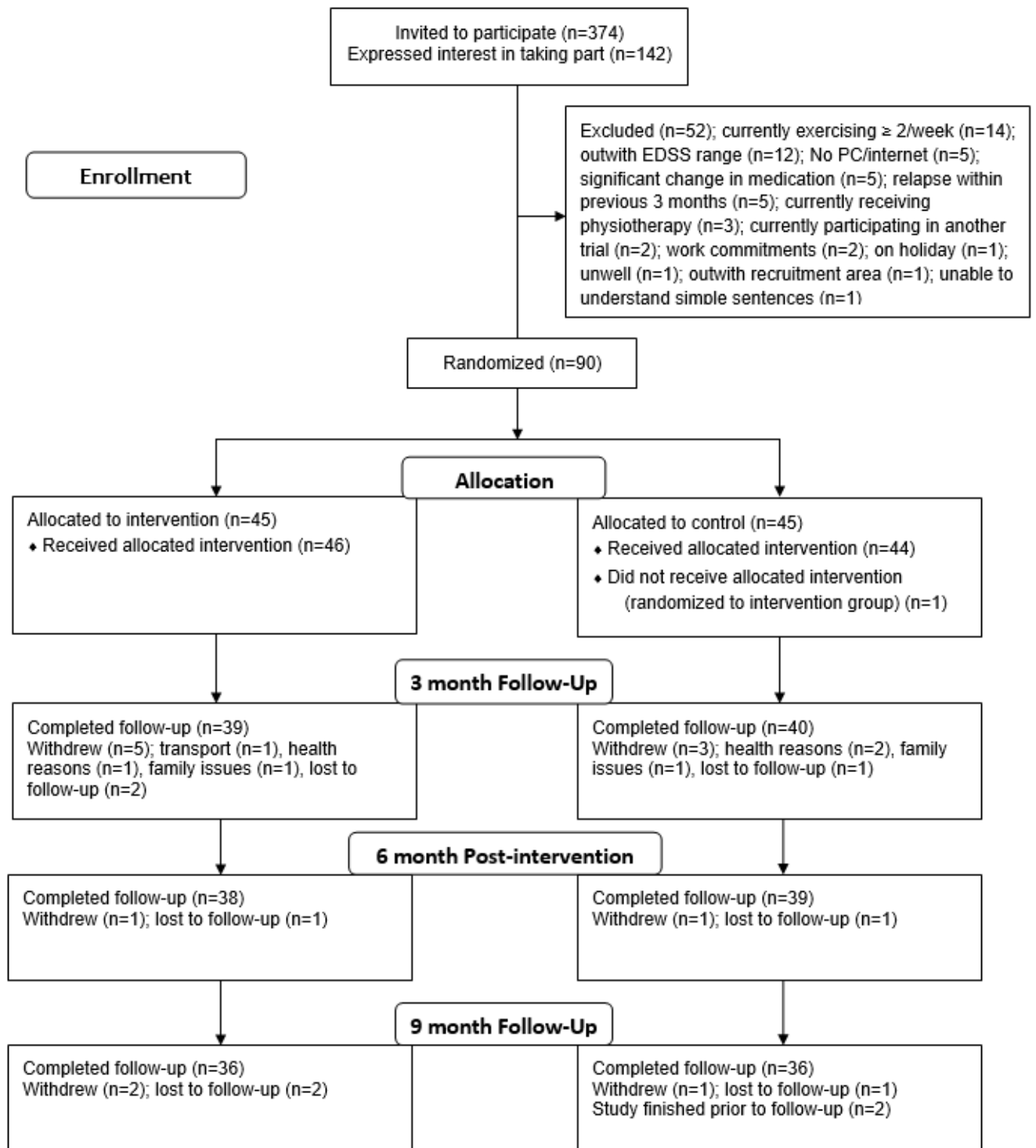| Theme	Subtheme	Indicative quotes
Study logistics/Feasibility	Training of staff	*"I think it really helps with rapport building… the trial is feeling like a team"* (T3) *"Handouts we got from the training were great to refer back to… meant a bit more when I was actually involved and doing it"* (T2) *"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)

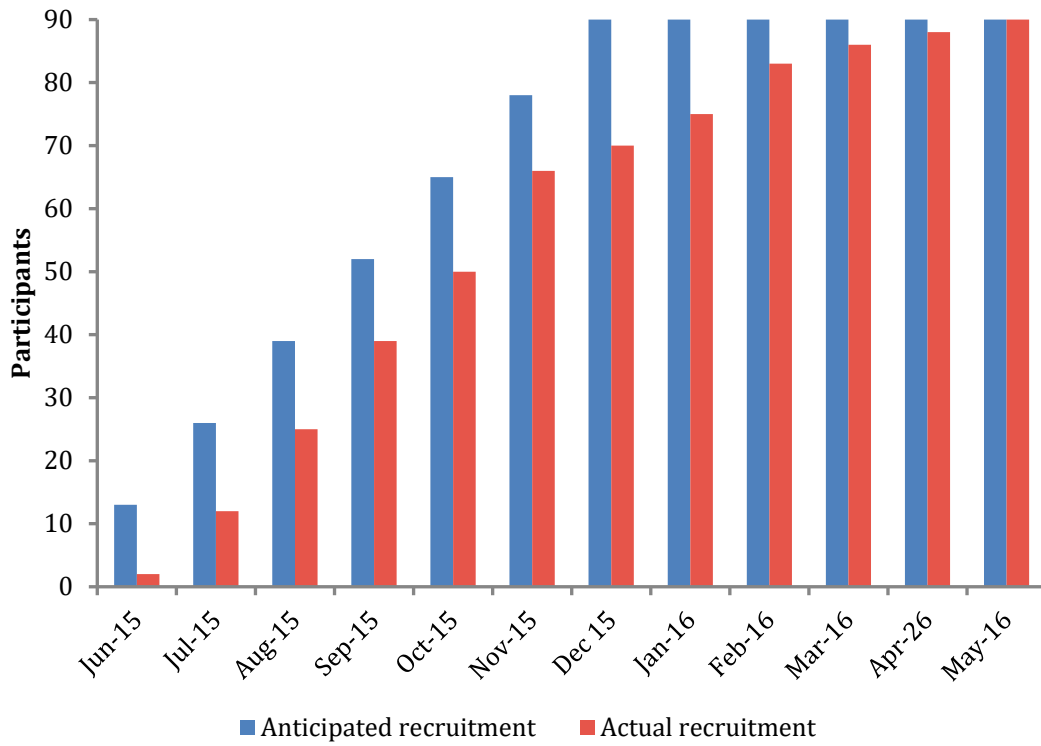|	Time to set up and review participants	*"So control group... maybe easily an hour [appointment with physiotherapist]. The intervention group probably... three quarters of an hour"* (T2) *"If there were lots of changes then [reviewing the programme] maybe 10 or 15 minutes but maybe only … 4-5 minutes 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)

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

Invited to participate (n=374)
Expressed interest in taking part (n=142)

Enrollment

Excluded (n=52); currently exercising ≥ 2/week (n=14); outwith EDSS range (n=12); No PC/internet (n=5); significant change in medication (n=5); relapse within previous 3 months (n=5); currently receiving physiotherapy (n=3); currently participating in another trial (n=2); work commitments (n=2); on holiday (n=1); unwell (n=1); outwith recruitment area (n=1); unable to understand simple sentences (n=1)

Randomized (n=90)

Allocation

Allocated to intervention (n=45)
♦ Received allocated intervention (n=46)

Allocated to control (n=45)
♦ Received allocated intervention (n=44)
♦ Did not receive allocated intervention (randomized to intervention group) (n=1)

3 month Follow-Up

Completed follow-up (n=39)
Withdrew (n=5); transport (n=1), health reasons (n=1), family issues (n=1), lost to follow-up (n=2)

Completed follow-up (n=40)
Withdrew (n=3); health reasons (n=2), family issues (n=1), lost to follow-up (n=1)

6 month Post-intervention

Completed follow-up (n=38)
Withdrew (n=1); lost to follow-up (n=1)

Completed follow-up (n=39)
Withdrew (n=1); lost to follow-up (n=1)

9 month Follow-Up

Completed follow-up (n=36)
Withdrew (n=2); lost to follow-up (n=2)

Completed follow-up (n=36)
Withdrew (n=1); lost to follow-up (n=1)
Study finished prior to follow-up (n=2)

512

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

514