The effects of a twelve week leisure centre based, group exercise intervention for people moderately affected with Multiple Sclerosis: a randomised controlled pilot study.

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Abstract

Objective: To establish the effects of a twelve week, community based, group exercise intervention for people moderately affected with Multiple Sclerosis (MS) (Extended Disability Status Score 5-6.5).

Design: Randomised controlled pilot trial

Setting: Two community leisure centres.

Participants: 32 subjects with MS were randomised into an intervention or control group.

Intervention: The intervention group received twelve weeks of twice weekly, 60 minute group exercise sessions, which included mobility, balance and resistance exercises. The control group received usual care.

Main Outcome measures: An assessor blinded to group allocation assessed participants at baseline, after eight weeks and after twelve weeks (i.e after the intervention period). The primary outcome measure was 25 Foot Walk time (T25FW), secondary outcomes assessed walking endurance, balance, physical function, leg strength, body mass index, activity levels, fatigue, anxiety and depression, quality of life and goal attainment.

Results The intervention led to an improvement in all outcome measures. Physical activity results showed a significant group effect ($p<0.001$) and interaction effect ($p=0.009$), post hoc analysis revealed this was significant at week eight ($p<0.001$) and week twelve ($p=0.005$). Balance confidence results showed a significant group effect ($p=0.001$). Good effect sizes were found for activity levels ($d=1.05$), dynamic balance ($d=0.80$), perceived balance ($d=0.94$) and leg strength ($d=1.33$).

Conclusion: Although further research is required, the results of the study suggest that community based group exercise classes are a feasible option for people moderately affected with MS, and offer benefits such as improved physical activity levels, balance and leg strength.

Introduction

For those with MS, a long-term condition which often strikes individuals in early adulthood[1], it is important to encourage exercise as part of a healthy lifestyle. Doing so may help manage the many disabling symptoms often associated with the disease including muscle weakness[2], reduced balance[3,4], reduced mobility[3], reduced exercise tolerance[5,6] and fatigue[7]. Cumulative evidence suggests that exercise may help improve some of these symptoms[8-10].

The benefits of exercise in those with MS has been investigated in relation to aerobic interventions[11-15], resistance interventions[16-21] or balance interventions[3,22]. Some studies have investigated combined exercise which includes aerobic, resistance and/or balance components in each session[23-28]. In addition the optimum length of the intervention has yet to be clarified, as previous studies have evaluated interventions varying in length from three weeks to over three months.

Few studies have investigated combined exercise specifically with subjects who are moderately affected with MS[23,27,28]. Freeman and Allison[23] reported that ten weeks of weekly sessions, comprising 30 minutes of general standing exercises, and 30 minutes of floor-based stretching exercises, increased balance, mobility and improved fatigue in their subjects. However only 10 subjects participated and no control group was included. Hayes et al[27]carried out a randomised controlled study comparing two groups of subjects, both undertook 12 weeks of combined exercise (aerobic, upper limb resistance, stretching and balance exercise) for 45-60 minutes thrice weekly, with the intervention group also doing lower limb strengthening exercises. They found improvements in strength, fatigue and balance in both groups of subjects. Cakt et al[28] reported, from a randomised controlled trial, that two months of resisted cycling exercises followed by balance exercises twice weekly for around 60 minutes improved many assessed outcomes including participants' mobility, physical function and fatigue levels. Thus combined exercise programmes appear to offer an effective training option for those moderately affected with MS.

MS is a chronic condition and rehabilitation forms a key component of the long term support and management. With finite health care resources, hospital or health centre exercise may not always be viable or available on an on-going basis. In addition the UK has seen an increased provision of rehabilitation programmes for people with long term conditions within local leisure or community centres; most notably cardiac[29] and pulmonary[30] rehabilitation. However there is little evidence of similar programmes for those with MS.

Current healthcare practice highlights the need for those with long term conditions to remain as active as possible[31-33]. This is particularly relevant for those moderately affected by their MS symptoms who, due to problems such as mobility impairments, may not be able to easily access standard community based exercise options aimed at those more able-bodied.

This study then aimed to evaluate the feasibility and effectiveness of a group, leisure centre based, combined exercise (aerobic, resistance and balance exercises) intervention for people moderately affected with MS. Furthermore from the pilot data generated from this study was used to establish the number of subjects required for a definitive trial.

Methods

A pre-test post test, randomised, controlled experimental design was used to compare the effects of twelve weeks of twice weekly, community based exercise with twelve weeks of usual care in people moderately affected by MS. People were recruited from the Managed Clinical Network (MCN) for MS within NHS Ayrshire and Arran. Subjects had a confirmed diagnosis of MS, an Extended Disability Status Scale (EDSS)[34] score of 5 (ambulatory without aid or rest for about 200 metres) to 6.5 (constant bilateral assistance required to walk about 20m without resting), stable rehabilitation and drug therapy for 30 days before entry into the study, cognitive scores of over 24 on the Mini Mental State Examination (MMSE)[35] and access to the intervention sites using their own or public transport. Potential subjects were excluded if they had experienced exacerbation of their MS symptoms three months prior to the study, or had any medical condition which may preclude them from taking part in the exercise intervention. Ethical approval was provided by the West of Scotland Research Ethics Committee and all subjects provided written informed consent.

Of the 873 patients on the MS database 159 patients were deemed suitable for the study and were sent invitation letters and participant information sheets. Forty-three potential subjects expressed an interest in participating. From initial telephone consultation five people did not fit the inclusion criteria; three had relatively high levels of mobility, and two were interested but could not commit the time. Thus thirty-six were invited for screening.

The screening appointment established eligibility; adequate cognition using the MMSE[35] and disability using the EDSS[34,34], a frequently used measure of disability in MS research which bases scores primarily on mobility. Four potential subjects were excluded; two with EDSS scores of 4.5, one who was suffering relapse and one who could not commit the time. Thus 32 people with MS, 23 female and nine male, participated in the study. Demographic information, including gender, age, EDSS level and time since disease onset are shown in Table 1.

Table 1 near Here

The intervention took place at two different geographical locations (Site A & Site B). From those living near Site A a list of potential participants (n=16) was created and to maximise class occupancy, ten potential participants were to be allocated to Site A's intervention group. A computer programme (Microsoft Excel 2003) was set-up to randomly assign the ten places against ten of the 16 subjects, leaving six subjects in the control group. A similar system was used for Site B, (which had a class capacity of 12), for which a list of potential participants (n=20) was created.

Outcome measures

Outcome measures were carried out within the local hospital's rehabilitation unit. They were taken at baseline, after eight and twelve weeks of the intervention period (i.e. either the exercise class or usual care). One assessor, an experienced physiotherapist, blinded to group allocation, carried out all physical assessments.

The 25 Foot Walk test (T25FW) [36] was chosen as the primary outcome measure. The T25FW measures walking speed over a short distance and has shown good reliability and validity in the MS population as an individual component of the Multiple Sclerosis Functional Composite disability assessment[37,38]. Two lines 25ft apart were marked on the floor, to allow for acceleration and deceleration subjects started walking one step behind one marked line and walked past the second line. The time taken to walk the marked 25ft distance was recorded with a stop watch. This was repeated three times and the mean of the three times recorded.

The following were included as secondary outcome measures. Body Mass Index (BMI) (weight (kg)/[height^2](m)) was calculated on each testing occasion. The six minute walk test (6MWT) test[39], a test of endurance, was undertaken following established protocol[40]. The distance walked during the six minutes was recorded.

Dynamic balance was assessed using the Berg Balance Scale (BBS)[41]. Fourteen functional balance tasks were performed and rated by the assessor, using a four-point scoring scale, producing a total score between 0-56, higher scores being indicative of better dynamic balance. Physical function was measured with the 'Timed Up and Go' test (TUG)[42]. The time to stand up from a standard chair, walk around a cone placed three metres away and return to sit on the chair was recorded. This was repeated three times and the mean of the three times recorded

Quadriceps strength (QPW) of the weaker leg (established at baseline) was measured using a "break-test"[43] with a hand-held dynamometer (Lafayette, IN 27904, USA, Manual Muscle Tester, Model 01163). Subjects sat with their back and feet unsupported, the dynamometer was placed anterior to their ankle joint with length of the lever arm, i.e. the distance from the proximal surface of the dynamometer to the apex of their patella, recorded. The maximum isometric force generated by the subject over four seconds was recorded in kg. At each assessment three scores from the weaker leg were recorded and converted to torque in Nm ((kg output x 9.81) x lever-arm length) and the mean score was recorded.

Activity levels were measured using the PhoneFITT (PF) questionnaire[44], this interview format asks subjects to provide information on the time spent and how often they undertake, six specific common household tasks and eleven particular forms of physical activity in a typical month, with the option to include other personal activities not included in the questionnaire. Higher scores indicate higher levels of activity.

Self-perceived balance confidence was assessed using the Activities Balance Confidence (ABC) questionnaire[45]. Fifteen questions ask subjects to rate on a 10-point Likert scale their confidence in their balance when performing daily tasks, yielding a total score 0-150. Higher scores are indicative of better self-confidence in balance. Fatigue was assessed with the Fatigue Severity Scale (FSS)[46], on which subjects rate their agreement to nine fatigue-related questions on a seven-point Likert scale, producing a score between 0-63. This score was then divided by nine and that figure was used for analysis, lower scores are indicative of lower fatigue. The Hospital Anxiety and Depression Scale (HADS)[47] was used to assess anxiety and depression. Subjects rate 14 items on a four-point scale, generating a total score of 0-42. Higher scores indicate more anxiety and depression. Quality of life was assessed using the Leeds Multiple Sclerosis Quality of Life (LMSQOL) scale[48] which asks subjects to rate eight health related questions on a four-point scale, in relation to the past month, producing a score between 0-24. With lower scores indicative of higher quality of life.

The Goal Attainment Scale (GAS)[49] is a method of assessing individual subjects' goals. A list of eleven possible goals, with a 12th "personal goal", related to the study were created. Expected achievement of each goal was established from the literature and through discussion with the research team, thus creating a five-point scale (between -2 and +2) for each goal. The subject chose three goals, from the list of twelve, to be achieved by the end of the twelve week intervention. Each subject also listed their chosen goals in order of importance (from 1-3) and weighed the possibility of achievement (from 1-3). The overall goal attainment scale score was calculated using an automated Microsoft Excel spreadsheet which applies a standard mathematical formula[49]; to produce baseline scores and, after the twelve week intervention, achieved scores. The difference between these (achieved minus baseline) was used for analysis with higher scores indicative of greater personal goal achievement.

Intervention

Subjects assigned to the intervention group attended a leisure centre based exercise class, twice weekly for twelve weeks, led by a physiotherapist and a fitness instructor. The same physiotherapist was present at both sites. The group session involved a 10 minute warm-up of aerobic and stretching components, 30-40 minutes of circuit exercises (Appendix 1), designed to train aerobic endurance, resistance and balance, and a 5-10 minute cool down, involving aerobic work, stretching and relaxation[50]. Subjects completed a circuit of 8-12 different exercises for one minute each, having a rest before moving to the next exercise. Not all exercises were performed at all classes, and in week nine a fifth level of difficulty was added to some of the exercises to encourage progress Instruction cards, with photographs, demonstrating the four different levels of skill/difficulty were used at both sites. Subjects were provided with exercise progress cards and they were asked to record which level they performed each exercise at each session. Attendance of subjects as each class was recorded.

Subjects assigned to the control group were advised to continue their usual routine, seeking any healthcare as required. They were asked to avoid beginning any new exercise regime for the twelve weeks of the study.

Statistical analysis

Data were analysed using Minitab v 16 and SPSS v 16 statistical packages. For demographic variables which were found to be parametric (e.g. BMI) independent sample t-tests were used to determine differences, and for non-parametric outcomes (e.g. Age) a Mann-Whitney *U* test was used. All outcome measures were analysed on the basis of intention to treat, with all variables summarised and comparisons made between groups and over time. Data were analysed using a univariate General Linear Model (GLM) ANOVA which allowed for missing data, possible interaction effects over time (baseline, week 8 and week 12) and between groups (intervention and control) were assessed. A Kolmoroff-Smirnoff test was used to assess the distribution of the data, for any results found not to be normally distributed, data were transformed to Natural Logarithms and these are presented, significance was set at $p<0.05$. The impact of the intervention effect size (ES) was calculated using Cohen's *d* analysis with weak ES<0.5, moderate ES 0.5<0.8 and good ES>0.8 being used[51]. Clinical effectivness was also calculated, as percentage change, for all outcome measures after the twelve weeks for both groups.

Results

Twenty subjects were allocated to the intervention group with twelve subjects to the control group. The intervention group comprised of five men and fifteen women, with four men and eight women in the control group. Table 1 shows that, at baseline, there were no statistical differences between the two groups in terms of age (p=0.893), years since disease onset (p=0.687) or any of the assessed outcome measures. The recruitment, withdrawals and missing data are presented in Figure 1. At week eight three subjects discontinued participation, with missing data for a further three continuing subjects. At week twelve one other subject discontinued participation, with missing data for three other subjects.

Figure 1 near here

Including those who discontinued participation, attendance at the classes was 69% with subjects missing classes due to other appointments, family/work commitments, transport problems, holidays or mild ill health (eg. common cold).

For most outcome measures the intervention group improved to a greater extent than the control group (Table 2), for example weaker leg strength almost doubled in the intervention group (95%) compared with a smaller improvement (21%) in the controls.

For the primary outcome measure, the T25FW, mean scores improved by 7.2 seconds (24%) compared with the 3 seconds (19%) in the control group, although for both groups large standard deviations were present (Table 2). GLM ANOVA results demonstrated no group ($p=0.710$) or time effect ($p=0.778$) and no group/time interaction ($p=0.428$). After eight weeks and twelve weeks of the intervention weak effect sizes of $d=0.30$ and $d=0.23$ respectively were seen for the T25FW.

Table 2 near here

The results of the GLM ANOVA revealed a significant group effect for both activity levels (PF) ($p<0.001$) and perceived balance confidence (ABC) ($p=0.001$), with a trend toward a significant group effect for LMSQOL ($p=0.063$) and BMI ($p=0.083$) scores (Table 2). Post hoc analysis of the PF results from the intervention group revealed a statistical difference between baseline and week 8 ($p<0.001$) and baseline and week 12 ($p=0.005$), and for the ABC between baseline and week 12 ($p=0.013$).

In terms of effect sizes, most of the outcome measures improved more so after twelve weeks, for example after eight weeks leg strength (QPW) showed a weak effect size (*d*=0.2), but after the twelve weeks a good effect was found (*d*=1.33); however this was not true for all the outcomes, with some showing a better effect at the week eight assessments e.g. ???. In addition to leg strength after twelve weeks the effect sizes were also good for dynamic balance (BBS) (*d*=0.8), activity levels (PF) (*d*=1.05) and perceived balance confidence (ABC) (*d*=0.94), with a moderate effect size in walking endurance (6MWT) (*d*=0.68) and fatigue (FSS) (*d*=0.67).

Table 3 summaries the collective goals chosen by the subjects via the GAS. Improving fatigue scores was the priority goal for most participants (n=7), closely followed by improving weaker leg strength, balance and walking endurance. There was an overall improvement in mean group scores for set goals, with a 31% clinical improvement in fatigue (FSS) scores, however t-test analysis did not find this to be significant (p=0.703).

Table 3 near here

Discussion

This study aimed to evaluate the effects of a leisure centre based combined exercise intervention for people moderately affected with MS comparing results against a cohort of age, gender, and disability level matched controls with MS who received usual care. Findings suggest improvement in all outcome measures for those in the intervention group, with participation in the exercise intervention leading to statistically significant improvements in physical activity levels (PF) and perceived balance confidence (ABC). Good effect sizes were also found for activity levels (PF), dynamic balance (BBS) and leg strength (QPW).

One of the key findings of the present study was an increase in physical activity levels following the intervention. Surprisingly few studies looking at exercise interventions for people with MS have included physical activity levels within their outcome measures. Mostert and Kesselring[12] used the Baecke Activity questionnaire to investigate the effects of aerobic exercise specifically on activity levels in people with MS. Activity levels increased in their participants by on average 4% i.e. to a lesser degree than in our study. An increase in activity may be beneficial to a disease population previously found to be more sedentary than their healthier peers[12,52], helping to manage both MS related symptom deterioration, such as muscle weakness and reduced balance, and also to aid prevention of other co-morbidities associated with inactivity, such as cardiovascular problems, obesity, diabetes, psychological ill heath and cancer[53].

Results from our study suggest that both balance confidence (ABC) and dynamic balance (BBS) improve with the exercise intervention. We found a good effect size in our intervention participants BBS, although we failed to find a significant improvement over time (p=0.969), or between groups (p=0.575). Previous studies on the effect of exercise on balance in people with MS have reported differing results. Freeman and Allison[23], found a significant improvement in BBS scores (p=0.02) at the end of their ten-week, twice weekly, combined exercise intervention in participants who had an average EDSS of 5. Hayes et al[27] demonstrated significant improvements in balance improvements following 12 weeks of combined exercise in subjects with a mean EDSS score of 5.2. Cattaneo et al[3] studied three groups of MS sufferers who had balance problems (<53 points on the BBS), of whom less than half required walking aids. Two groups received in-patient balance related rehabilitation (either motor and sensory training, or motor training only) and one in-patient group acted as controls. They found BBS scores were significantly different between groups following the three weeks of ten to twelve 45 minute sessions. However subjects in these studies had lower levels of disability than those in our study.

Other studies[3,22] which have used the ABC questionnaire have reported differing results to the present study. Cattaneo et al[3] did not find any significant difference in the results of the ABC questionnaire over time, nor did Freeman et al[22] whose participants (with a similar disability level to our subjects) followed eight weeks of one to one out-patient physiotherapy core balance sessions, with additional home exercises. The ABC includes questions in relation to everyday experiences (e.g. “get into or out of a car”) and as the study by Cattaneo et al[3] investigated in-patients the ABC may not have been an appropriate outcome measure. As balance is noted as being a common problem amongst those with MS[4] and an important goal for many of the subjects involved in this study, it is desirable that more emphasis be placed on both the assessment of balance and exercise interventions to improve individuals' balance and prevent falls, a common problem for those with MS[54].

From the GAS reducing fatigue was a goal of many of the study participants. However, although our exercise intervention failed to significantly improve fatigue scores over time, perhaps due to a ceiling effect with baseline scores, a moderate effect size was noted. Furthermore the exercise intervention did not appear to increase subjects' levels of fatigue. These findings link to other studies[23,26-28] involving combined exercise interventions. Cakt et al[28], found a significant improvement in fatigue scores following two months of resisted cycling and balance exercises in people with MS. With similar significant improvements in FSS results also being found by others[27]. Therefore whilst further research is required to determine if exercise reduces levels of fatigue in people with MS, it is important to note there is no evidence that combined exercise increases levels of fatigue.

Our results also indicated that the exercise intervention increased the muscle strength of participants' weaker leg, although this failed to reach statistical significance. This finding is similar to Hayes et al[27] who reported clinical improvements in their participants leg strength. Others using a resistance specific intervention have found more significant results. White et al[19] and Gutierrez et al[18] reporting results from the same study, showed that eight weeks of twice weekly progressive lower limb strengthening, in a fitness centre, resulted in significant strength gains for knee extensor and ankle plantar flexor muscles. Taylor et al[16] found significant gains in general leg muscle performance following an eight week, thrice weekly intervention which focused solely on upper and lower body resistance training. This evidence suggests that whilst strength gains are possible from a combined exercise programme, a resistance specific exercise programme is required to achieve significant improvements in muscle strength.

The present study was undertaken in two community leisure settings; the classes were led by local authority employed exercise instructors, with a physiotherapist providing assistance. This is one of the first studies to utilise this format and, as there is a trend toward longer term rehabilitation and symptom management in the community throughout the UK[32,33], the results of this study are timely. It is particularly relevant that, due to the positive feedback and attendance at our class the local leisure services decided to continue the MS exercise class. Thus one of the main benefits of this study has been the establishment of a regular, local, MS specific exercise class.

The initial interest in the study was not as good as anticipated, and thus group numbers were not equal and the sample size was disappointing, perhaps due to the commitment of a twice weekly class for twelve weeks. Despite this the class attendance rates were reasonable, with reasons such as other appointments, family/work commitments, transport problems, holidays or mild ill health (eg. common cold) given for non attendance or discontinued study participation. On initial inspection our attendance rates (69%) appear lower than other studies with similar class based methodology[16,21,26,28] all of whom reported greater than 80% attendance. Our data were analysed on an intention to treat basis, however if data from the three subjects who discontinued participation was excluded, our attendance rates were 77% and thus almost comparable with other similar studies. Furthermore subjects in these other studies[16,21,26,28] had less mobility problems, and all but one[16] took place in hospital rehabilitation clinics thus access and attendance may have been easier.

People with moderate MS present with a wide range of balance and mobility problems, consequently large standard deviations were seen throughout the results. Other studies[12,17,22,23] who have included subjects with similar levels of disability have also reported large standard deviations. Thus even with a narrow EDSS range (5-6.5) heterogeneity was event within the sample. For studies of people moderately affected by MS it may be advisable to narrow the EDSS range further. For example using the results of the present study but narrowing the EDSS range to 5-6 only 30 subjects in each group would be required to achieve a power of 92% (with significance set at $p<0.05$), for a within group improvement of more than two seconds in the T25FW results.

Past studies have evaluated interventions varying in length from three weeks[3] to over three months[15]. By taking outcome measures at week eight and week twelve our study aimed to assess the optimum length of exercise intervention required. Although no conclusive findings emerged, perhaps due to the small sample size and thus it is not possible to make specific recommendations more of the outcome measures improved after twelve weeks of the intervention, than were improved after only eight weeks, suggesting a longer exercise period may be more beneficial.

This study demonstrated that a leisure centre based group exercise class combining aerobic, resistance and balance exercises is feasible, with participants reporting in post intervention focus groups that they enjoyed the social aspect, found many benefits and planned to continue exercising. Results suggested the intervention was effective in improving activity levels, balance and strength in people moderately affected with MS, with no worsening of their fatigue levels. Larger scale studies in those moderately affected with MS are required.

Clinical messages

- Combined, aerobic, resistance and balance exercise have a positive effect on people with MS especially in relation to activity levels, balance and muscle strength.
- A leisure centre based group exercise is a feasible option for those with MS

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Competing Interests

The Authors declare that there is no conflict of interest.

Contributions

YL initiated the study. LP, PM, and YL acquired funding. YL managed all aspects of the project, with support and advice from LP, PM, LM and AM. AM and YL undertook statistical analysis. LP, YL and AM wrote the draft manuscript. PM, and LM revised the manuscript and all gave approval of the final version submitted. YL takes responsibility for the accuracy and honesty of the report and the morality of the study.

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Table 1 Demographic and baseline characteristics of subjects.

Variable/Outcome measure	Intervention group	Control group	Test	p-value
Number of subjects	20	12	-	-
Gender M:F	5:15	4:8	FE	0.696
Age (years)	51.4 (8.06)	51.8 (8.0)	MW	0.893
EDSS	6.14 (0.36)	5.82 (0.51)	MW	0.387
Years since onset	13.4 (6.4)	12.6 (8.1)	MW	0.687
T25FW (sec)	22.1 (21.8)	16.1 (13)	MW	0.289
6MWT (m)	191.1 (102.2)	221.2 (120.0)	MW	0.431
BBS	41.4 (11.8)	44.7 (11.1)	MW	0.289
TUG (sec)	22.3 (16.9)	19.66 (14.93	MW	0.526
QPW (Nm)	27.9 (16.1)	28.3 (14.7)	MW	0.744
BMI (kg/m^2)	28.7 (5.1)	31.4 (5.9)	T-test	0.138
PF	53.3 (20.6)	54.6 (26.6)	T-test	0.155
ABC	56.2 (16.6)	51.8 (23.5)	MW	0.578
FSS	5.3 (1.7)	5.7 (1.2)	T-test	0.108
HADS	15.9 (6.5)	15.8 (9.3)	MW	0.578
LMSQOL	12.9 (4.9)	14.1 (3.9)	T-test	0.481

Results are shown as mean and standard deviations

FE – Fisher's Exact, MW – Mann-Whitney, T-test – Independent samples t-test, EDSS-Extended disability Status Scale, T25FW – Timed 25ft Walk, 6MWT – Six minute walk test, BBS, Berg Balance Scale, TUG-Timed Up and Go test, QPW-weakest quadriceps strength, BMI-Body Mass Index, PF-PhoneFITT, ABC-Activities Balance Confidence, FSS-Fatigue Severity Scale, HADS-Hospital Anxiety and Disability Scale, LMSQOL-Leeds MS Quality of Life.

Table 2 Summary of results, Mean (and standard deviation) at baseline, after eight weeks and after twelve weeks of the intervention/control period, results of GLM ANOVA , Cohen's *d* tests and percentage change.

Outcome Measure	Baseline	Week 8	Week 12	Group effect p-value	Time effect p-value	Group/time interaction p-value	Effect Size at…		Clinical Effect (Baseline – Week 12)
							Week 8	Week 12	
T25FW (sec)* Intervention Control	 22.1 (21.8) 16.1 (13)	 16.7 (11.8) 15.4 (10.1)	 14.9 (13.6) 13.1 (8.6)	0.778	0.71	0.428	0.30	0.23	 24% 19%
6MWT (m) Intervention Control	 191.1 (102.2) 221.2 (120.1)	 228.6 (118.7) 260 (128.9)	 262.2 (127.4) 215.8 (175.7)	0.544	0.649	0.465	0.02	0.68	 37% -2%
BBS Intervention Control	 41.4 (11.8) 44.7 (11.1)	 47.4 (9.7) 47.9 (8.1)	 46.7 (10.6) 40.9 (15.2)	0.575	0.969	0.115	0.25	0.80~	 12% -9%
TUG (sec)* Intervention Control	 22.3 (16.9) 19.66 (14.93)	 19.82 (14.6) 19.51 (12.1)	 18.4 (14.95) 16.22 (11)	0.971	0.471	0.688	0.15	0.03	 17% 17%
QPW (Nm)* Intervention Control	 27.9 (16.1) 28.3 (14.7)	 36.3 (20) 33.6 (16.5)	 54.5 (49) 34.3 (24.6)	0.144	0.352	0.464	0.20	1.33~	 95% 21%
BMI (kg/m^2) Intervention Control	 28.7 (5.1) 31.4 (5.9)	 27.9 (5.1) 30.7 (6.7)	 27.5 (6) 29.6 (6.2)	0.083	0.618	0.796	-0.02	0.17	 3% 6%
PF Intervention Control	 53.3 (20.6) 54.6 (26.6)	 69.7 (23.6) 38.3 (23.1)	 78.2 (35.5) 54.6 (16.7)	<0.001^	0.220	0.009^	1.37~	1.05~	 47% 0.2%
ABC Intervention Control	 56.2 (16.6) 51.8 (23.5)	 69.7 (23.6) 58.7 (35.6)	 79.8 (28.3) 60.9 (35.6)	0.001^	0.059	0.408	0.33	0.94~	 42% 8%
FSS Intervention	 5.5 (1.7)	 5 (2)	 5 (1.8)	0.741	0.100	0.261	0.30	0.67	 9%

Control	5.7 (1.2)	5.7 (2.1)	6.2 (0.7)						-8%
HAD Intervention Control	15.9 (6.5) 15.8 (9.3)	11.6 (5.4) 14.2 (7.9)	11.7 (5.9) 13.8 (6.6)	0.097	0.263	0.838	0.02	0.08	16% 12%
LMSQOL Intervention Control	12.9 (4.9) 14.1 (3.9)	11 (4.22) 12.3 (4.1)	10.9 (3.9) 12.4 (3.1)	0.063	0.208	0.922	0.34	0.27	26% 13%

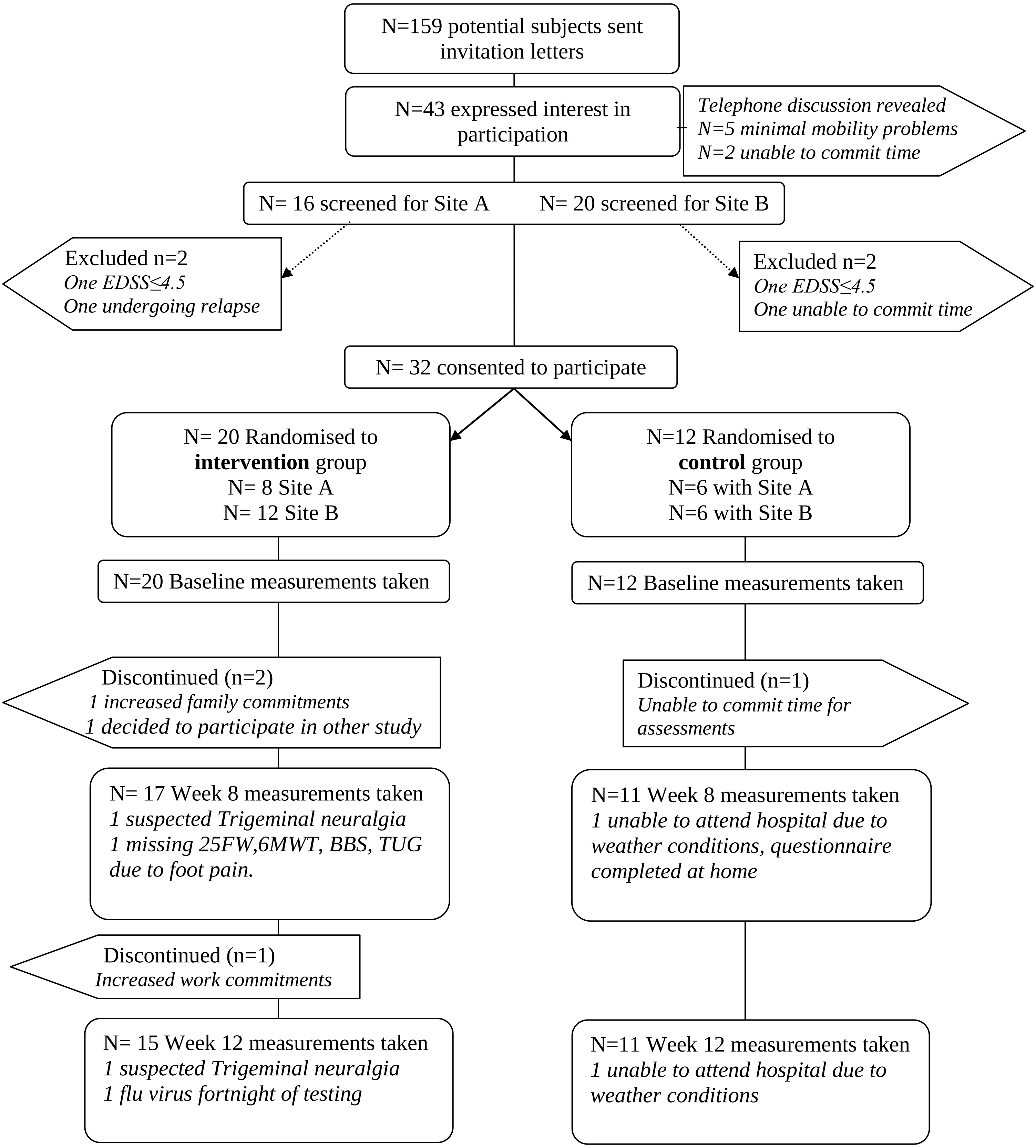
***Data transformed to Natural Logarithm for group effect, time effect and group/time interaction results, ^ p<0.05, ~d=≥0.8, T25FW – Timed 25ft Walk, 6MWT – Six minute walk test, BBS, Berg Balance Scale, TUG-Timed Up and Go test, QPW-weakest quadriceps strength, BMI-Body Mass Index, PF-PhoneFITT, ABC-Activities Balance Confidence, FSS-Fatigue Severity Scale, HADS-Hospital Anxiety and Disability Scale, LMSQOL-Leeds MS Quality of Life.**

Table 3 Goals for the GAS chosen by the subjects (n=32), at baseline.

Related outcome	Goal 1	Goal 2	Goal 3	Total
FSS	7	4	5	16
OS*	7	3	2	12
6MWT	6	2	5	13
BBS	5	7	1	13
Attend class	2	5	4	11
T25FW	2	1		3
QPW	1	8	8	17
ABC	1	1	2	4
LMSQOL		1	1	2
TUG	1		1	2
HADS			1	1
Single leg balance**			1	1
Weight loss**			1	1

***OS-Overall Stability (assessed on a balance plate), data not presented in this paper, **Personal (12th) goal. FSS-Fatigue Severity Scale, 6MWT – Six minute walk test, BBS- Berg Balance Scale, T25FW – Timed 25ft Walk, QPW-weakest quadriceps strength, ABC-Activities Balance Confidence, LMSQOL-Leeds MS Quality of Life, TUG-Timed Up and Go test, HADS-Hospital Anxiety and Disability Scale.**

Figure 1. Flow chart of recruitment, group allocation and experimental protocol.



Appendix1. Circuit components of the exercise class.

Exercise	Main Type	Description and options
Shuttle Walk	Aerobic	Chairs set 10m apart 1.Rest at each end of the shuttle (having a seat) 2.Walk continuously without resting at each end 3.Walk continuously with a small weight in each hand 4.Walk continuously with a small weight in each hand, swinging arms
Upper Body	Resistance	Near a chair 1.In sitting, shoulder raises (no dumbbells) 2.As above, with light dumbbells 3.In standing, shoulder raises (no dumbbells) 4.As above, with light dumbbells
Side Steps	Aerobic	Near supporting surface 1. Holding onto a stable surface, take one step to the side, and bring feet together, step back. 2. Not holding on, take one step to the side, and bring feet together, step back. 3. As 3, lifting arms out to the side, in time with step. 4.As 4, but taking two-steps to the side before changing direction * 5. Grapevine (two steps crossing one leg behind the other)
Up and Go	Resistance	Sitting on a chair 1. In a chair (with arms) stand up fully, and sit down again, repeat. 2. Stand from chair, walk to other chair and sit down, repeat. 3. Stand from chair, walk around other chair, and return to sit in first chair, repeat. 4. As 3, but with arms folded when standing.
Take-off	Balance	With balance cushion 1. Sitting on chair (with a back), lean forward (simulating 1st part of standing up), and reach forward with arms. 2. As above sitting on stool. 3. As above sitting on sit fit, on chair. 4. As above sitting on sit fit, on chair, lifting one leg (swap legs after 30 secs).
Leg extensions	Resistance	Sitting on a chair 1. Straighten leg as best as possible, point your toes to the sky, hold for a second then swap legs. Repeat. 2. As above, hold for a FIVE seconds then swap legs. Repeat. 3. As above, hold for a TEN seconds then swap legs. Repeat. 4. As above, hold for a FIFTEEN seconds then swap legs. Repeat. *5. As above, small pulses at the end.
Step-ups	Aerobic	Using 20cm step 1.Sit down, with step in front, lift alternate legs up/down 2.Standing, step alternate feet forward and back (not on step 3.Standing, step alternate feet forward and back onto step 4. As 3, but lifting opposite arms up to the sky. *5. Straddle step
Single leg stance	Balance	Near supporting surface 1.Hold onto a stable surface and stand on one leg (aim to maintain for 10 seconds) 2.As above, not holding on, with arms out to side for balance 3. As above, not holding on, with arms into side. 4. As above, with arms into side, slightly bending supporting leg, and then stand up straight, repeat.
Side-kicks	Resistance	Near supporting surface 1. Holding onto a stable surface, lift one leg out to side (as wide as is safe) swap legs, hold for a second swap legs. Repeat. 2. As above, hold for a FIVE seconds then swap legs. Repeat. 3. As above, hold for a TEN seconds then swap legs. Repeat. 4. As above, hold for a FIFTEEN seconds then swap legs. Repeat. *5. As above, small pulses at the end.
Tick-tack toe	Balance	Near supporting surface 1. Walk between tramlines, using wall if required, turn and repeat. 2.Walk between tramlines, not using wall 3.Walk on line, using wall if required 4. Walk on line, not using wall.
Squats	Resistance	Near a chair 1.Holding on, bending legs half-way to ground 2.Not holding on, bending legs half-way to ground 3.As above holding light dumbbells 4.As above, slightly heavier dumbbells *5. As 4, going up on toes.
Cushion standing	Balance	Near supporting surface 1.In the corner of the room, try and maintain your balance without holding on. 2. As 1 standing on a mat. Come off, then go back on, when required. 3. As 2, standing on sit fit. Come off, then go back on, when required.

		4. As 3, moving straight arms slightly (about 4 inches) at sides.
Runner’s arms	Aerobic	Near a chair 1.Sitting down, moving arms in a running style. 2. Sitting down, moving arms in a running style, holding weights. 3. Standing, moving arms in a running style. 4. Standing, moving arms in a running style, holding weights.
Calf raises	Resistance	Near supporting surface 1.Holding onto a stable surface, lift heels from floor, repeat. 2. Lift heels from floor, not holding on, repeat. 3.Lift heels from floor, holding a light weight, repeat 4. Lift heels from floor, holding a heavier weight, repeat.
Bike	Aerobic	On exercise bike or foot pedals 1.Sitting down, use pedals only. 2. Sitting down, use pedals, and lifting arms up and down too. 3. Sitting on bike pedalling with no resistance. 4. Sitting on bike pedalling against resistance. *5. As above, standing out of saddle

*Option added at week 9.