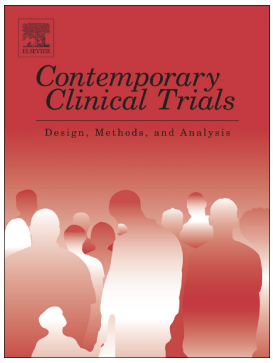

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Results of a feasibility randomised controlled study of the Guidelines for Exercise in Multiple Sclerosis Project

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Abstract

There is increasing recognition that exercise is an efficacious strategy for managing many consequences of multiple sclerosis (MS), yet persons with MS are not engaging in sufficient exercise for accruing health benefits. Poor exercise uptake might be associated with the design of previous research. We conducted a randomised controlled trial (RCT) for examining the feasibility of a 4-month home-based, exercise-training program designed based on recent physical activity guidelines for MS and supplemented by behavioral strategies for compliance. Feasibility was assessed in the domains of process (e.g., recruitment), resource (e.g., monetary costs), management (e.g., personnel time requirements) and scientific outcomes (e.g., treatment effect). We recruited persons with mild-to-moderate MS who were randomised into an intervention or wait-list control condition. Intervention participants received a pedometer, elastic resistance bands, DVD, training manual, calendars, log-book, video coaching calls and newsletters. Participants in both conditions completed home-based assessments before and after the 4-month period. Ninety-nine persons with MS were assessed for eligibility, and 57 were randomised. Fifty-one persons completed the study (90%). Total costs of the study were US $5331.03. Personnel time to conduct the study totaled 263 hours. Participants in the intervention group complied fully with 71% of all exercise sessions. There was a moderate increase in self-reported exercise behaviour of the intervention participants as measured by the Godin Leisure-Time Exercise Questionnaire scores (d≥.5). The results support the feasibility and acceptability of a home-based exercise intervention based on physical activity guidelines and supplemented with behavioral strategies for adults with mild-to-moderate MS.

Key Words

Multiple sclerosis, randomised-controlled trial, exercise, home-based

1. Introduction

Researchers have indicated that exercise training is possibly the single most effective non-pharmacological approach for managing symptoms[1] and improving health-related quality of life (HRQOL) in persons with multiple sclerosis (MS)[2,3]. Such a statement is based on evidence summarized in meta-analyses and systematic reviews[4–6]. Nevertheless, there is substantial evidence that persons with MS are not engaging in sufficient amounts of exercise and physical activity for accruing health benefits[7,8]. This poor uptake of exercise and physical activity is a public health and clinical concern, and might be associated with the design of previous research, as noted in a paper on the 10 most important issues for future research on exercise and MS[9]. Indeed, there are few home-based exercise training feasibility trials that are supplemented with behavioural principles for increasing adherence with change toward physical activity guidelines. Such feasibility trials are necessary for providing information on the process, resource, management and scientific metrics of a study, and critically inform the design and credibility of subsequent research[10–12].

We recently proposed the Guidelines for Exercise in MS Project [13], or Project GEMS, as a feasibility study that overcomes major limitations of previous research on physical activity and exercise in MS. Project GEMS is a 4-month, home-based, exercise training program that is based on recent exercise guidelines[6] and supplemented with behavioural principles for increasing exercise participation, with possibly secondary effects on physical activity and tertiary effects on symptoms and HRQOL in MS. We have previously reported the methodological protocol for this study[13]. This paper reports results on the feasibility of Project GEMS in persons with MS. The outcomes reported are in accordance with current recommendations and guidelines for feasibility trials[15–17], and this manuscript reports the results regarding the process, resource, management, and scientific feasibility metrics of Project GEMS.

2. Methods

Our recent publication provided complete details on the design and methodology of Project GEMS[13]. Ethical approval was granted by a university institutional review board (IRB) and all

participants provided written informed consent. University IRB procedures were followed to manage applicable adverse events (AEs) and serious adverse events (SAE). This feasibility study adopted a randomised controlled trial design, and was conducted between May 2015 and March 2016.

2.1. Participant recruitment and eligibility

As the aim of this study was to assess the feasibility of a future definitive trial, we did not undertake a formal sample size calculation. Participants were recruited from across the USA using (a) a database of 137 persons with MS who had previously taken part in a nationwide questionnaire-based study conducted by researchers in our laboratory, (b) interactions with persons at MS events taking place in the Midwest of the USA, and (c) an advertisement on the research laboratory's website. We recruited participants over a 2-month period in early Summer 2015 using a successive 3-pronged approach of delivering flyers through the United States Postal Service (USPS) followed by email and phone calls.

Recruitment flyers detailed eligibility criteria, provided a 65 word description of the study, and included contact details (telephone and email) for the research site. Participants were eligible to participate in the study based on 7 inclusion criteria[13]: (a) age 18-64 years; (b) diagnosis of MS; (c) Patient Determined Disability Steps (PDDS) scale score ≤ 3.0; (d) relapse free in past 30 days; (e) willing and able to participate in the intervention; (f) non-exercisers (i.e., not participating in 30 or more minutes of structured strength training AND, 30 or more minutes of brisk walking OR moderate exercise in the last 3-months); and (g) a Physical Activity Readiness Questionnaire (PAR-Q) score of 2 or less (physician approval was requested for participants who had a PAR-Q score of 2). We saught a sample size exceeding 12 subjects per group, as this has been deemed acceptable for pilot and feasibility studies involving RCT study designs[18].

2.2. Procedure

Participants received the informed consent document via the USPS and returned it signed through the same mechanism. After the baseline assessment, participants were randomised into the intervention condition or a waitlist control condition. We pre-prepared sealed slips of paper containing group allocation and stored these in a randomisation container. On receipt of

participants baseline assessment a researcher not involved in the study chose a sealed slip of paper from the container, and this determined group allocation. We delivered the intervention over a 16-week period and further collected outcome assessments both during (e.g., communication and safety) and after completion (e.g., monetary costs and treatment effect). All participants received $40 in remuneration.

2.2.1. Intervention condition

The intervention content and timeline are provided in Table 1 and further details are available in our previous publication[13]. The intervention was inspired by guidelines incorporating progressive aerobic and resistance exercise[14] and research including principles of behavioural change based on Social Cognitive Theory (SCT) in persons with MS [19–22]. We further developed our intervention using a "person based approach" [23], by gathering informal feedback regarding our manual and equipment from 4 persons with MS. We received positive and constructive feedback from these persons and this feedback resulted in changes within the program manual (e.g., instructions on programme progression and completion of the log-book).

Table 1 Summary of the 4-month home-based exercise program emphasizing aerobic and resistance training

Intervention element	Component	Further details
Prescribed exercise	Home-based resistance and aerobic training.	Based on the physical activity guidelines for adults with mild-to-moderate disability due to MS. Aerobic-training; 10-30 minutes of moderate-intensity walking (1000 steps/10 minutes) performed 2 days a week. Resistance training; 1-2 sets, 10-15 repetitions of 10 exercises targeting lower body, upper body, and core muscle groups performed 2 days per week.
	Programme variation*	Orange – Aerobic and resistance training time and intensity increased over 16 weeks. Exercise guidelines achieved and maintained after week 5. Blue – As above, exercise guidelines achieved and maintained after week 7. White – As above exercise, guidelines achieved and maintained after week 9.
Materials	Exercise equipment	Aerobic equipment; Pedometer Resistance equipment; Elastic resistance bands varying in 5 degrees of strength.
	DVD	Demonstrations of resistance training exercises including modifications for differing levels of physical capability in order to maximize safety.
	Programme manual	An introduction to the staff, safety information, description of equipment and a detailed description of the resistance and aerobic exercises to be performed and how to progress over 4-months. Comparison tables of orange, blue and white programmes, blank calendars (for exercise planning).
	Calendars	Four undated calendars to facilitate exercise planning.
	Log-book	Annotated booklet for participants to note exercise participation feeling and rating of perceived exertion (RPE) after each session. Aerobic training recorded per session as; length of time (in minutes) walked and number of steps per session, 3 point scale (happy, neutral, frown) to describe feeling after exercise, and RPE on 0-10 scale[24]. Resistance training recorded per session as; number of sets and repetitions of prescribed exercise per session, 3 point scale (happy, neutral, frown) to describe feeling after exercise, and rating of perceived exertion on 0-10 scale[24].
Behavioural change interaction	Video-chats	Designed to provide participants with feedback and information on how to progress through the exercise program as well as to provide social accountability
	Newsletter	Newsletters provide instructional material on specific behavioural change content, websites to visit for more information, testimonials of individuals who have experienced benefits of exercise, and tips for participants to try at home.

Behavioural Change Session Content	Week 1 Introduction to programme	*Video-chat 1* - Clarification of materials received and initial questions - Explanation of program - Planning exercise schedule - Using the log-book
	Week 2 Outcome expectations	*Video-chat 2* - Compliance with programme - Using the manual and log-book - Identifying personal outcomes *Newsletter 1* - Exercise expectations - Exercise outcomes - Importance of this knowledge
	Week 3 Choosing a programme	*Video-chat 3* - Compliance with programme - Comparison of orange, blue and white programme - Choosing a programme
	Week 4 Self-monitoring	*Video-chat 4* - Compliance with programme - Using your pedometer - Understanding exercise intensity *Newsletter 2* - Self-monitoring defined - Benefits of self-monitoring - Importance of this knowledge
	Week 6 Goal-setting	*Video-chat 5* - Compliance with programme - Setting SMAART goals - Performing resistance training exercises correctly - Tracking progress *Newsletter3* - Specific, measurable, adjustable, action-oriented, realistic, and time-limited exercise related goals defined.

	- Importance of this knowledge
Week 9 Self-efficacy	*Video-chat 6* - Finding your self-confidence - What to do when you feel like quitting - Involving family *Newsletter 4* - Self-efficacy defined - Experiencing success, choosing role models, accepting encouragement & managing physical and emotional responses - Reminder that programme is specific for persons with MS
Week 12 Overcoming Barriers	*Video-chat 7* - Identifying your barriers - Making plans to overcome obstacles - Dealing with MS symptoms *Newsletter 5* - Exercise barriers defined - Common barriers (facilities, social & symptoms) - Strategies to overcome barriers
Week 15 Identifying facilitators	*Video-chat 8* - How to keep going on your own - Making adjustments as needed - Setting future goals *Newsletter 6* - Exercise facilitators defined - Common facilitators (having a goal, enjoyment, social support, knowledge) - Using facilitators long term

- Note: *Further details of programme variation available in Adamson et al 2016[13]

Participants in the exercise intervention condition received a pedometer, elastic resistance bands, DVD, training manual, calendars, and log-book. The training manual detailed the exercises and 4-month progression[13]. The aerobic training was 10-30 minutes of moderate-intensity walking 2 days a week. The pedometer was used to monitor and track the intensity of walking per bout. Participants monitored exercise intensity using a step rate of 100 steps per minute, as measured by the pedometer. This stepping rate corresponds with moderate-intensity exercise in persons with MS[40]. The strength training consisted of 1-2 sets, 10-15 repetitions of 10 exercises targeting lower body, upper body, and core muscle groups performed 2 days per week. Exercises were performed using elastic resistance bands (Black Mountain Products, McHenry, IL). The DVD provided demonstrations of all the resistance training exercises and included modifications for differing levels of physical capability in order to maximise safety. Demonstations were performed by 2 persons with MS who were both compensated $50 for participation. Importantly, we offered 3 separate arms of the program that varied in terms of progression to meeting the physical activity guidelines. All groups reached the guidelines after 10 weeks of participation in the program (i.e., orange group achieved guidelines at week 6, blue group achieved guidelines at week 8, and white group achieved guidelines at week 8). The decision on an appropriate arm of progression was made after the first two weeks of the program based on a discussion between the participant and behavioral coach. We further provided 6 newsletters based on SCT which were delivered in a titrated fashion (i.e, weeks 2,4,6,9,12 and 15), and these were delivered through email and USPS. On the same schedule, participants engaged in one-on-one Skype sessions with a behavioural coach for discussing the newletter content as well as progress with the exercise program.

2.2.2. Control condition

We included a waitlist control. Participants in the waitlist control condition received all programme materials after return of follow-up assessments.

2.3. Feasibility metrics

We gathered data based on the feasibility metrics of process, resource, management and scientific outcomes. These metrics, monitoring and assessment strategy, data source and outcome variable computation method are summarised in Table 2.

Table 2. Feasibility metrics; monitoring and assessment strategy, data source and outcome variable computation method.

Metric	Monitoring and assessment strategy	Data source	Outcome variable computation method
Process; assesses participant recruitment.	a. Recruitment and eligibility rate.	a. Central database recording number of participants recruited via each recruitment method (i.e., USPS, phone and electronic mail); number of excluded participants and reason.	a. Recruitment rate was calculated for USPS letter, email letter or phone call by dividing the number of participants enrolled from each method by the total number of participants contacted for each method. Eligibility rate was calculated as the number of potential participants excluded from the total number of interested participants.
Resources; assesses participation, communication and monetary requirements of the study.	b. Adherence, retention and attrition rates c. Communication with participants. d. Communication needs of participants and staff. e. Monetary costs of research	b. Central database recording; adherence to study completion (i.e., receiving intervention) participants completing study (i.e., return of follow-up data); attrition time point and reason. c. Central database recording length of initial recruitment telephone call (i.e., <5 min, 5-10 min, >10 min); length of mail turn-around-time for assessment packets through the USPS (i.e., days). d. Central database for intervention participants recording preferred communication method (i.e, internet video call or telephone	b. Adherence rate was calculated as the total number of consenting participants who received the allocated intervention. Retention rate was calculated as the number of participants who completed follow-up testing from those who were randomised. Attrition rate was calculated as the number of participants who did not return follow-up testing materials or discontinued participation during the 16 week study period. c. Recruitment time was calculated as number of calls lasting <5 min, 5-10 min, or >10 min. Mail turn-

call), call time (i.e., morning, afternoon or evening), length of video coaching calls and technical issue with calls (i.e., connection, participant technical knowledge, staff technical problem, participant technical problem).
e. Expenditure spreadsheet recording overall cost of intervention (i.e., instructional materials, postage, exercise equipment, participant remuneration)

around-time was calculated as the mean time for participants assessment packets to leave our laboratory, be completed by participants (including the 7-day wear time of accelerometers), and be received by our laboratory.
d. Preferred type of communication method was calculated as the number of participants choosing video chats or telephone chats, and preferred time of day was calculated as number of participants choosing morning, afternoon or evening; coaching call time was calculated as mean time for all intervention participants over all coaching calls; technical issue was calculated as the total number of technical issues.
e. The costs of the study were calculated as the total monetary cost in US dollars of producing materials (i.e., paper outcome assessments, program manuals, and log-books, and DVDs), postage and packaging (i.e., delivery and return of outcome assessments, and delivery of program materials), exercise materials (i.e., pedometer and resistance bands) and

			participant remuneration.
Management; assesses data management and safety reporting during the study.	f. IRB approval procedures. g. Staff time requirements. h. Missing data items.	f. Record of time (i.e., days) to achieve initial IRB approval, and count sheet of total number and type of IRB amendments. g. Preparation time spreadsheet recording recruitment database preparation time (min), material preparation time (min), recruitment and database preparation time (min), missing data and group allocation calls (min), material purchasing (min), staff meetings (min); time to enter and check participants data (min). h. Data entry spreadsheet recording missing data items in the database.	f. IRB approval time was calculated as the total number of days from submission to approval notification. IRB amendment details were calculated as number of amendment submissions and approvals. g. Staff preparation and reporting time were calculated as the time to: progress the study (i.e., staff meetings), prepare the recruitment database (i.e., Access database (Microsoft Corporation 2013, Indianapolis, IN)), recruit participants, liaise with participants over the telephone (i.e., group allocation, answering study questions and gathering missing data), prepare participant materials (i.e., ordering and mailing materials and exercise equipment), and enter and check all participant data (i.e., total min). h. Missing data items (i.e., questions not answered, and accelerometer wear days) were established for the baseline and follow-up assessments.

Scientific; assesses the safety, burden and treatment effect of the study.	i. AEs, SAEs and clinical emergencies. j. Participants demographic information, experience, burden, and compliance during the intervention. k. Treatment effect.	i. Database recording reported health problems, relapses or adverse events (AEs) occurring during the study. j. Central database recording participants age, sex, SR-EDSS , MS type and duration of MS. Database storing participants' written feedback and transcribed interviews. Central database recording primary (exercise participation), secondary (physical activity), and tertiary (symptoms and HRQOL) outcome measures. ActiGraph GT3X accelerometers (Actigraph, Pensacola, FL) and accelerometers wear time reported on log sheets. Intervention participant log-books reporting exercise sessions and perceived exertion (RPE; using Modified Borg 0-10 scale) after aerobic and resistance exercise each week. Central database recording compliance with video calls. k. Primary outcome of exercise participation (Godin Leisure-Time Questionnaire (GLTEQ)[35]. Secondary outcome of free-living physical activity participation (i.e., time in	i. Health problems experienced by the participants over the course of the intervention were categorised as MS symptom exacerbations (e.g. increased fatigue or heat sensitivity), MS relapse (e.g. an acute onset of new or worsening neurological symptoms[40]), injury (e.g. back and joint pain, fracture), and illness (e.g. respiratory tract infection, migraine). j. Demographic data was established via a self-report questionnaire. Written feedback data from intervention participants were captured via a feedback survey (survey questions listed in Table 3). We used 5-point Likert scales; for satisfaction (1 representing completely unsatisfied and 5 representing completely satisfied) and programme recommendations, continuation plans and programme suitability (1 representing strongly disagree and 5 representing strongly agree). We used open-ended written responses for research experience and programme satisfaction. Verbal feedback was gathered using semi-

	moderate to vigorous physical activity (MVPA). Tertiary outcomes of mobility (Multiple Sclerosis Walking Scale (MSWS)[27]); balance (Activities-Specific Balance Confidence Scale (ABC)[28]); fatigue (Fatigue Severity Scale)[29]; function (Late-Life Function and Disability Instrument(LLFDI)[30]); anxiety and depression (Hospital Anxiety and Depression Scale(HADS)[31]); pain (Short-form McGill Pain Questionnaire(MPQ)[32]); health-related quality of life (Multiple Sclerosis Impact Scale(MSIS)[33]; Leeds MS Quality of Life Scale(LMSQOL)[34]); exercise related social cognitive factors (Exercise Self-Efficacy Scale(ESES)[36], Exercise Goal Setting and Planning Scale(EGSPS)[37], Multidimensional Outcome Expectancies for Exercise Scale(MOEES)[38], Exercise Benefits and Barriers Scale(EBBS)[39], and Social Provisions Scale(SPS)[39]).	structured telephone interviews (interview topics listed in Table 3). Compliance with the intervention reported via; 1. Participant individual log sheets, and we considered three categories of compliance with exercise sessions (i.e., full (85% of sessions), partial (i.e., defined as <4 days per week or 4 days/week partial sessions), no compliance (i.e., 0 days/week), and 2. Record of number of video calls attended. k. Primary and tertiary outcomes gathered via standardised questionnaire forms. Standardised protocols were followed as published. Secondary outcome of free-living physical activity participation gathered via ActiGraph GT3X accelerometers; standardised processing protocols were followed as published[41].

2.4. Data analysis

Data were analysed in SPSS Statistics, Version 22 (IBM Corporation, Armonk, NY). Descriptive data are presented as mean value and standard deviation (i.e., age, mean duration of MS); median, range and IQR (i.e., self-reported Expanded Disability Status Scale (SR-EDSS)); and total number (i.e., sex and MS Type). Process feasibility data are described as total number and percentage (i.e., recruitment). Resource feasibility data are described as total number and percentage (i.e., retention, communication), total cost (i.e., monetary requirements), and mean value, standard deviation (SD) and range (i.e., communication). Management feasibility data are described as total time (i.e., obtaining ethical approval, data management; personnel time requirement), and total number and percentage (i.e., data management; missing data). Scientific feasibility data are described as total number and percentage (i.e., safety, and experience, burden and compliance), and effect size estimates from the univariate *F*-ratios to establish the magnitude of interactions. *F*-ratios are expressed as partial Eta^2 and Cohen's *d* (i.e., Treatment effect for primary, secondary and tertiary outcomes per group). Data were analysed for all persons who completed the study (i.e., a completers analysis). To allow for missing data per outcome scale/measure, missing data items were substituted using a conservative process of item imputation (i.e., "last value carried forward") and analysis was performed on the scale item mean score. Further scientific feasibility data associated with written and interview feedback from intervention participants were analysed for themes and quotations related to intervention participant questionnaire feedback for satisfaction on research experience and programme satisfaction. Qualitative content analysis was undertaken on feedback data; and this involved basic principles of qualitative content analysis [42] including reading all feedback data, creating a coding frame related to topics described in Table 3, and categorising material relevant to these topics of interest.

2.4.1. Table 3 Intervention participants feedback survey questions and feedback interview topics

Feedback source	Question or Topic area
Feedback Survey (Likert scale) – Satisfaction with programme	Overall, how satisfied were you with the GEMS program? How satisfied were you with; - the program manual? - the log-book? - the calendars? - the DVD? - the resistance bands? - the pedometer? - the newsletters? - the calls?
Feedback Survey (Likert scale) – Programme suitability, recommendation and continuation questions	The programme was appropriate considering; - how MS affects me? - my fitness level? - the time commitment? - the progression of the exercises? I would recommend the GEMS program to others with MS? I would participate in a program like this again? I will continue using the GEMS materials to keep exercising.
Feedback Survey (Written responses) – Satisfaction and recommendations for improvement	What did you like most about the GEMS programme? What did you like least about the GEMS programme? How would you improve the programme in the programme?
Telephone Interview topics - Satisfaction and recommendations for improvement	Expectations prior to the programme Overall program evaluation Let's discuss more details of the exercises, programme materials, newsletters and coaching calls How do you think we could improve the program?

3. Results

3.1. Participant demographic details

Participant were mainly female (88%) and Caucasian (66%), and the mean age was 48.4 years (± 9.7 years). Participants self-reported a median SR-EDSS score of 1.5 (range 1-6, interquartile range 3.5). Type of MS was mainly relapsing remitting (98% of participants), and mean duration of MS was 13.9 years (±8.1 years) (Table 4). There were no significant baseline differences in any demographic or clinical metrics between conditions.

Table 4: Patient demographic information

	Overall (n=57)	Allocated to intervention condition (n=29)	Allocated to control condition (n=28)
Mean age (SD)	48.4 (9.7)	48.7 (10.4)	48.2 (9.1)
Male: Female	2:55	1:28	1:27
Caucasian:African American:American Indian:Latino/a	38:17:1:1	20:9:0:0	18:8:1:1
Median SR-EDSS (Range, IQR)	1.5 (0-6, 3.5)	1.25 (0-6, 2.5)	2 (0-5.5, 3)
MS Type* (RR:SP)	51:1	26:0	25:1
Mean duration of MS*(SD)	13.9 (8.1)	14.8 (8.5)	13.0 (7.7)

Note: One-way ANOVA indicated no significant difference in age (p=0.865) and SR-EDSS (p= .201) between groups at baseline. * Data collected at follow up (intervention condition n=26; control condition n=26).

3.2. Process feasibility; Recruitment

The consort diagram in Figure 1 details the participant flow through the trial. One hundred and thirty-seven persons with MS were directly contacted to participate in the study; all 137 via USPS, 80 of the 137 via email, and 54 of the 137 via telephone. Across the three methods, the recruitment rate was 52% (n=71). Recruitment via the USPS yielded 35 interested participants (25%), recruitment via email yielded 24 interested participants (30%), and recruitment via telephone yielded 12 interested participants (22%). Our secondary "word of mouth" recruitment method was at MS events and from our website, this method yielded a further 28 interested participants. There were 99 total interested participants; 71 (72%) from our database source, and 28 (28%) from our "word of mouth" source. Thirty-two potential participants were excluded during telephone screening. Twenty-three persons did not meet the inclusion criteria; 14 participants were too active (i.e., engagement in 30 or more minutes of structured strength training and 30 or more minutes of brisk walking or moderate aerobic exercise on 2 or more days per week), 5 potential participants who were excluded for having a PDDS score > 2, and 4 other participants were excluded for other reasons. Nine persons declined to participate during the screening process. Sixty-seven (94%) of the interested participants were eligible to participate and were sent a consent document. Three addition participants were sent a clearance and approval form to be completed by a personal physician as these participants had provided 2 affirmative responses on the PAR-Q during telephone screening. Four persons who qualified did not return a signed consent form and were not included in the study. Sixty-three participants signed and returned the consent document, and were sent baseline testing materials. Six of these participants did not return the baseline testing materials and were not included in the study. This yielded a final sample of 57 persons with MS.

3.3.

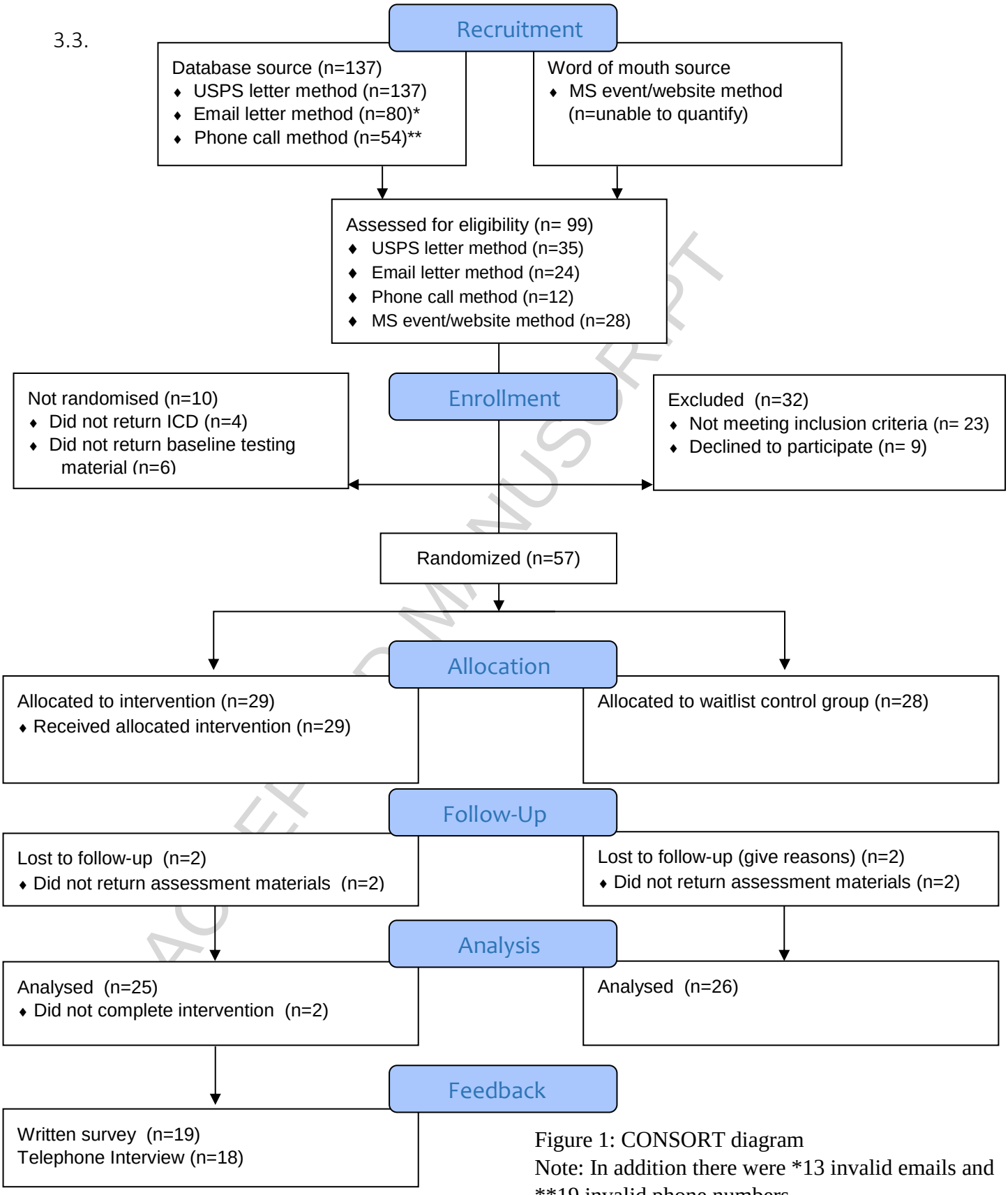


Figure 1: CONSORT diagram
Note: In addition there were *13 invalid emails and **19 invalid phone numbers.

3.4. Resources feasibility; Retention, communication and monetary requirements of the study

3.4.1. Retention

Fifty-seven of the participants who consented to participate returned the baseline testing materials and were randomised into the intervention (n=29) or control condition (n=28) (adherence rate; 90%). Fifty-one participants completed the study and returned the follow-up testing materials (retention rate: 89%). Regarding attrition, 2 participants randomised to the intervention condition did not complete the study. These participants dropped out of the study at either week 4 (i.e., due to lack of time) or week 12 (due to an unrelated health condition). Four participants did not return the follow-up testing materials. Data from these 6 participants are considered in our analysis of missing data, but are not included in our analysis of intervention outcomes.

3.4.2. Communication

The initial recruitment phone call took more than 10 minutes for 100% of the sample. The mean turn-around-time for assessment packets to leave our laboratory, be completed by participants (including the 7-day wear time of accelerometers), and be received by our laboratory was 24 days (±18, range 11-145). The majority (n=22, 76%) of participants in the intervention condition preferred to be contacted using a video call over the internet, and others preferred to be contacted via the telephone. Fifteen participants in the intervention condition preferred to be contacted for coaching calls in the afternoon (12 noon-4pm), 7 preferred the morning (8am -12 noon) and 5 preferred the evening (4pm-8pm). The mean duration of the coaching calls was 12 minutes (±4, range 7-23). Technical issues occurred on 12 (6%) calls over the course of the intervention (i.e., connection problems with the internet video call) and on each occasion coaches utilised telephones to undertake the communication.

3.4.3. Monetary requirements

Total study costs were $5331.03 USD (mean cost per person = $93.53 USD). This total included costs for materials (i.e., paper and DVDs; $140.04 USD), postage ($1911.56 USD), equipment (i.e., pedometers and resistance bands; $2479.43 USD) and participant remuneration ($800

USD). The total costs do not include personnel costs or accelerometer costs ($225 USD per unit).

3.5. Management feasibility; data management and safety reporting during the study

3.5.1. Obtaining ethical approval

The time necessary to receive approval from the university IRB for our initial study application was 41 days. We subsequently made four amendments. These amendments reflected the following; additional remuneration for retesting (3 days to receive approval), voluntary feedback questionnaire and telephone interview (4 days to receive approval), clarification of separate mailing for voluntary feedback (13 days to receive approval), and additional clinical demographic questions on follow-up testing material (8 days to receive approval). Participants signed new consent document to reflect participation in the feedback portion of the study.

3.5.2. Data management; Personnel time requirement

Personnel time to complete the study totaled 263 hours across the four staff who were directly involved in administering this study. This time involved the following; discussions and meeting between staff (72 hours), recruitment (database creation, letter preparation and mailing, emailing; 25 hours), recruitment phone calls (25 hours); material ordering and preparation (71 hours), and data entry and checking (61 hours). Additional phone calls were made to notify participants of group allocation (i.e., intervention condition or control condition), and to gather missing data (9 hours).

3.5.3. Data management; missing data

There were missing data (e.g., non-answered questions, non-completed accelerometer log sheets, and unworn accelerometers) at both time points and these are detailed in Table 5. At baseline, there were no missing data for our primary outcome measure of exercise participation. Missing data were most prevalent for the question on time to complete all questionnaires (14%). Regarding weartime recorded by the accelerometer, 16% of data were invalid (i.e., <10 hours of wear time), and the frequency of valid days was as follows; 7 days, 27 participants, 6 days; 10 participants; 5 days, 7; 4 days, 6 participants; 3 days, 1 participant; 2

days, 2 participants; 1 day, 1 participant. Participants self-reported accelerometer wear time by recording the time the accelerometer was put on and the time it was taken off (including breaks), and 9% of these data were invalid (i.e., wear time <10 hours). This result reflects inaccurate self-reporting of accelerometer usage. Regarding questionnaires, 3.0% of tertiary outcome measures data were missing on initial return; follow-up calls to capture missed data reduced the missed data number to 2.5%, and missing data were most prevalent for the Hospital Anxiety and Depression Scale (4%) and Late-Life Function and Disability Instrument (9%).

Table 5: Missing data items

Questionnaire or task (total no. of questions per participant; total number of questions for entire sample)	Baseline		Follow-up	
	Missing items on return (% of sample) n=57	Missing items post phone call (% of sample) n=57	Missing items on return (% of sample)) n=57^	Missing items post phone call (% of sample) n=57^
Time to complete all questionnaires (1;57)	12 (21%)	8 (14%)	10 (18%)	10 (18%)
Demographic information (11; 627)	20 (3%)	15 (2%)	86 (14%)	59 (9%)
SR-EDSS (9;513)	19 (4%)	13 (3%)	54 (11%)	54 (11%)
Primary Outcome Measure				
GLTEQ (4; 228)	1 (<0%)	0 (0%)*	16 (7%)*	16 (7%)*
Secondary Outcome Measure				
Accelerometer valid self report data (7; 399)	34 (9%)	-	77 (19%)	-
Accelerometer valid wear days (7:399)	62 (16%)	-	136 (34%)	-
Tertiary Outcome Measures				
MSWS (12; 684)	23 (3%)	22 (3%)	73 (11%)	48 (7%)*
ABC (15; 855)	16 (2%)	15 (2%)	106 (12%)	61 (7%)
FSS (9; 513)	9 (2%)	9 (2%)	54 (11%)	36 (7%)*
LLFDI (31; 1767)	80 (5%)	69 (4%)	194 (11%)	132 (7%)
HADS (14; 798)	43 (5%)	28 (4%)	112 (14%)	59 (7%)
MPQ (16; 912)	22 (2%)	17 (2%)	193 (21%)	64 (7%)*

MSIS (29; 1539)	35 (2%)	31 (2%)	174 (11%)	119 (8%)
LMSQOL (8; 456)	8 (2%)	8 (2%)	48 (12%)	32 (7%)*
ESES (6; 342)	6 (2%)	6 (2%)	36 (11%)	30 (9%)*
EGSPS (20; 1140)	24 (2%)	23 (2%)	120 (11%)	81 (7%)
MOEES (10; 570)	10 (2%)	10 (2%)	40 (7%)	40 (7%)*
SPS (6; 342)	6 (2%)	6 (2%)	24 (7%)	24 (7%)*
EBBE (43; 2451)	49 (2%)	47 (2%)	304(12%)	178 (7%)
Total tertiary outcome items	331 (3.0%)	304 (2.5%)	1506 (11.9%)	904 (7.2%)

Note: ^ Missing followup data is inclusive of participants who did not return followup outcome assessments (n=4). *Complete dataset from all returned assessments. SR-EDSS-Self reported Expanded Disability Status Scale, GLTEQ - Godin Leisure-Time Questionnaire, MSWS- Multiple Sclerosis Walking Scale, ABC- Activities-Specific Balance Confidence Scale, FSS- Fatigue Severity Scale, LLFDI - Late-Life Function and Disability Instrument, HADS- Hospital Anxiety and Depression Scale, MPQ- Short-form McGill Pain Questionnaire, MSIS-Multiple Sclerosis Impact Scale, LMSQOL - Leeds MS Quality of Life Scale, ESES - Exercise Self-Efficacy Scale, EGSPS - Exercise Goal Setting and Planning Scale, MOEES - Multidimensional Outcome Expectancies for Exercise Scale, SPS – Social Provisions Scale, , EBBE - Exercise Benefits and Barriers Scale.

At follow-up, 4 participants did not return any data and this was considered missing data. Taking these 4 participants missing data into consideration we note there was no missing data from our primary outcome measure for all participants who returned outcome assessments. Missing data were most prevalent for the question on time to complete all questionnaires (18%). Regarding weartime recorded by the accelerometer, 34% of data were invalid (i.e., <10 hours of wear time). The frequency of valid days was as follows; 7 days, 18 participants, 6 days; 14 participants; 5 days, 3 participants; 4 days, 5 participants; 3 days, 4 participant; 2 days, 1 participant; 1 day, 0 participants; 0 days; 12 participants. 19% of participants self-reported accelerometer wear time was invalid (i.e., wear time <10 hours). This result reflects inaccurate self-reporting of accelerometer usage. For tertiary outcome measures, 11.9% of data were missing on initial return; follow-up calls to capture missed data reduced the missed data number to 7.2% and missing data were most prevalent for the Exercise Self-Efficacy Scale (9%). We further note that when considering all returned follow-up outcome assessments there were no missing data for the majority of outcomes (refer to Table 5), and this suggests an overall improved compliance with data collection for those who completed the study.

Twenty-four participants returned log-books at the end of the intervention (83% of intervention participants), and these data were used to determine participant experiences and compliance with the programme. Eighteen participants completed the orange exercise programme (i.e., prescribed exercise guidelines achieved at week 6), 4 participants completed the blue exercise programme (i.e., prescribed achievement of exercise guidelines at week 8), and 2 participants completed the white exercise programme (i.e., prescribed achievement of exercise guidelines at week 10).

3.6. Scientific; Safety, burden and treatment effect.

3.6.1. Safety

Eight participants in the intervention condition reported instances of health problems during the 4-month intervention period. Two persons (7%) reported injury (i.e., snowboarding injury

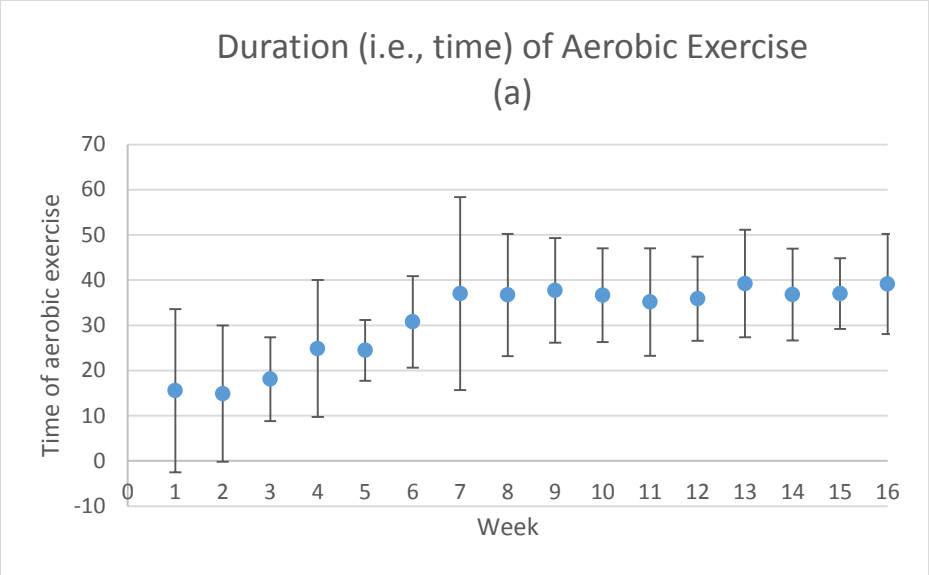
and fall during everyday activity) unrelated with the study or intervention. Four persons (14%) reported a temporary increase in MS symptoms during the intervention (i.e., 2 persons reported increased fatigue, 1 person reported vision problems, and 1 person reported drop-foot) and these persons continued with the prescribed programme. Two persons (7%) self-reported experiencing symptom exacerbation and took a break from the programme; both participants completed the program after this break.

3.6.2. Experience, burden, and compliance.

The mean time to complete baseline questionnaires for all participants was 40 minutes (±22 minutes), the mean time to complete follow-up questionnaires for all participants was 48 minutes (±50 minutes).

Participants in the intervention condition complied fully with 228 (75%) of the total possible aerobic exercise sessions (304); 57 sessions (19%) were partially completed, and 19 (6%) were not completed or not reported in participants' log-books. Participants complied fully with 206 (68%) of the total possible resistance exercise sessions (304); 72 sessions (24%) were partially completed, and 26 (9%) were not completed or not reported in participants' log-books. All participants in the intervention condition progressively increased the volume of aerobic and resistance activity over the 4-months of the programme (Figures 3 and 4). The mean volume (i.e., time duration and number of steps) of the aerobic component of the intervention progressed from an average 15.5 minutes ± 18 minutes, and 1568 steps ± 1356 steps per session in the first week of the programme to an average of 39.1 minutes ± 11.1 minutes, and 3966 steps ± 1076 steps per session in the final week of the programme. We further note that participants were achieving an average time of 30.76 minutes ± 10.1 minutes, and 3388.7 steps ± 922.1 steps per session at week 6 of the programme, and continued to increase this intensity for the duration of the programme. The mean volume (i.e., number of exercises completed) of the resistance component of the intervention progressed from 5 exercises ± .2 per exercise session to 9.3 exercises ± 1.4 per exercise session. Figure 5 indicates that following the first 2 weeks of the programme participants maintained a mean exercise intensity which represented moderate exercise (i.e., a RPE score of 4-6 on the Modified Borg 0 to 10 scale). All persons in the intervention condition complied with 3 or more video calls, and 17 persons (59%) complied

with all 8 calls. The mean duration of video calls were 12 minutes (±3.5 minutes). During the baseline assessment week (7 days), the mean accelerometer wear time for all participants was 773 minutes, and the mean self-reported accelerometer wear time was 798. This information may be considered alongside accelerometer missing data items (Table 5) which indicated 84% of accelerometer recorded data were valid compared with 91% of self-reported accelerometer data. At the follow-up assessment week (7days), the mean accelerometer wear time for all participants was 738 minutes, and the mean self-reported accelerometer wear time was 779 minutes. This information may be considered alongside accelerometer missing data items (Table 5) which indicated 66% of accelerometer data were valid compared with 81% of self-reported accelerometer data. Taken together this result indiated reduced compliance with the accelerometer at the follow-up data collection, and separately this result indicates inaccurate reporting of accelerometer wear time.



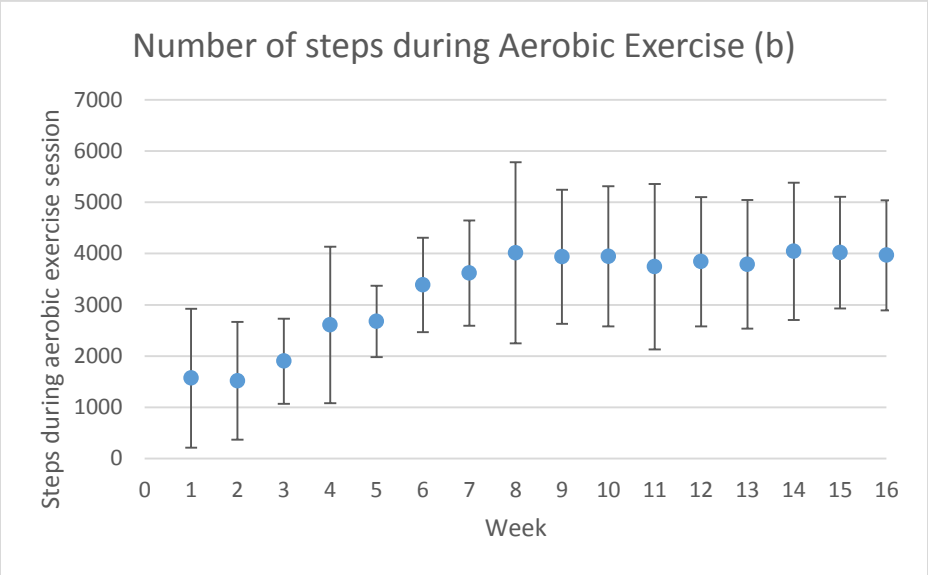


Figure 3 Intervention participant aerobic exercise progression over the 16 weeks of the study; time duration (a) and number of steps (b).

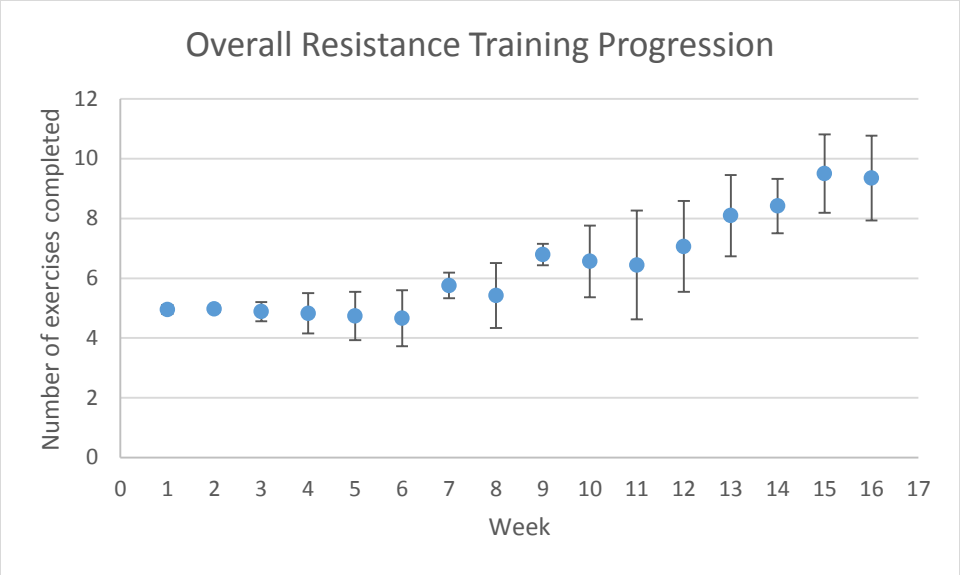


Figure 4. Intervention participants resistance exercise progression over the 16 weeks of the study; number of exercise completed.

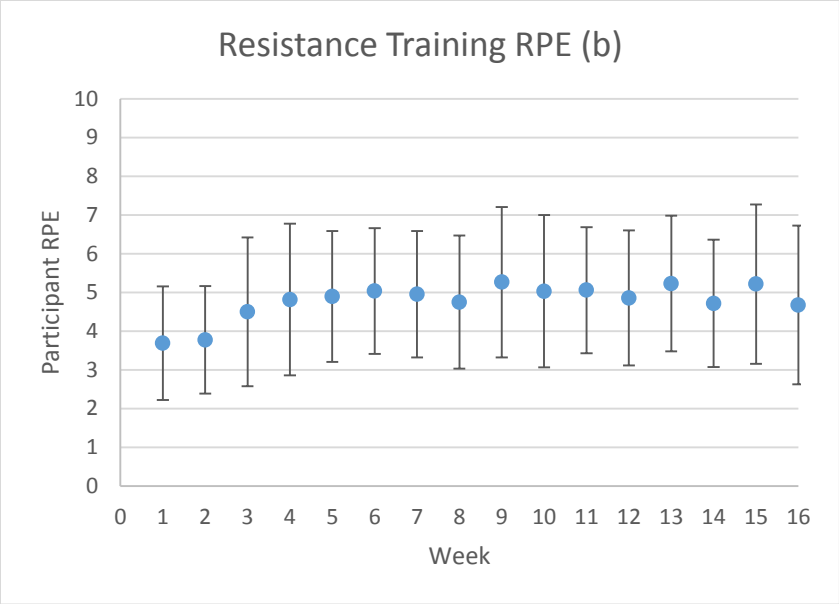


Figure 5. Intervention participants rating of perceived exertion following aerobic (a) and resistance (b) exercise.
Note: RPE – Rating of Perceived Exertion.

Nineteen participants in the intervention condition completed feedback questionnaires. Eighteen participants completed telephone interviews and we established examples of participant satisfaction with the programme and recommendations for future improvement. Example quotes from participants are displayed in Table 6. Participants commented upon research experiences, and reported that recruitment and communication were good, however many participants felt completing the large questionnaire battery and wearing the accelerometer were burdensome. Overall, participants were satisfied with all aspects of the intervention (all mean scores >4 out of 5), and comments indicated that the aerobic exercise was enjoyed most by participants. Participants would recommend the program to others with MS, continue the programme, and felt the programme was suitable for personal needs (all mean scores >4.6 out of 5) (Figure 2).

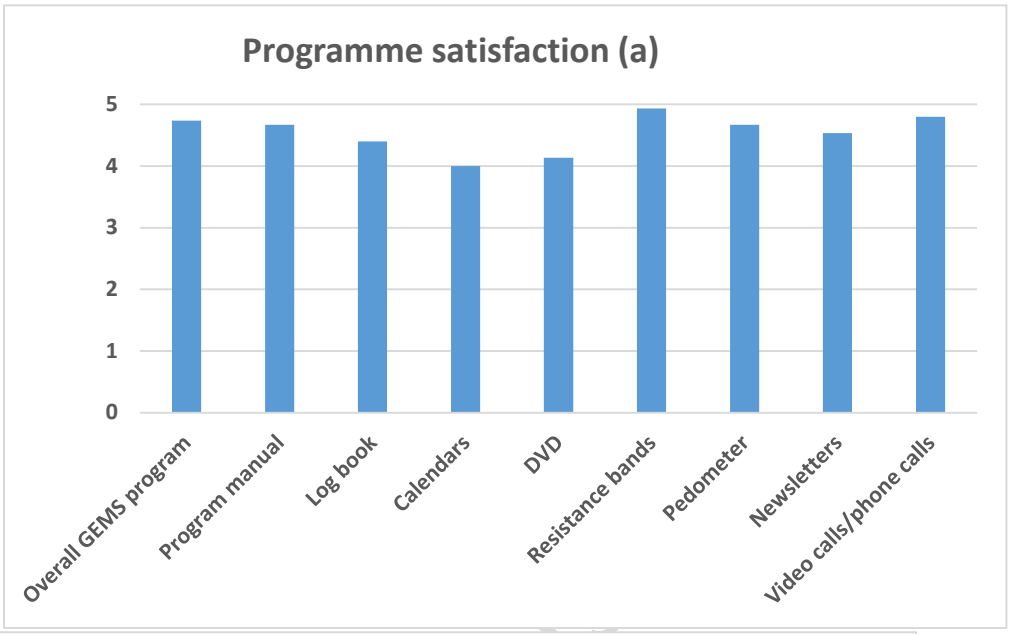
Table 6: Grouped examples of participants written and verbal feedback following completion of the intervention

Topic	Written Feedback	Verbal feedback
Research experiences	-The questionnaires were not hard to fill out or answer. I was glad when the week was over so I didn't have to wear the accelerometer -How this program was set-up, to me worked perfectly. From answering a few question, receiving and sending the information in the mail (all with correct postage), wearing the accelerometer/pedometer and having a log-book to keep track of everything.	-If it (the study recruitment information) was online, I might have seen it or I might have just glossed over it... The mail was probably the best way, because I was actually opening the envelope and looking at it. - I liked that it was a little more involved and pretty in-depth 'cause I wanted to do, I wanted to give something a chance to see if I could make any kind of change in my life with a program. -The questionnaires were a bit daunting at first, and the accelerometer I took that out and I pinned it to my clothes, the clothes that I wear don't allow for that belt you put it in.
Overall programme satisfaction	-I thought everything went seamlessly. It was all self-explanatory. It was put together well. I enjoyed the program very much. - I initially wasn't crazy about the rigidity of the frequency and intensity of the workout but I now understand that the incremental progression was necessary for best results	-I think that it the exercise programme is not only safe but I think it is important. It helped me with not only my physical strength, but also cognitively it helped me. It helped my mood, my confidence, my muscle tone, everything. I also now feel that even if I do have periods of times that I can't exercise; say if I am having an exacerbation that I know where to start now. - I thought it was a good program. Maybe not for my level. I think I was pretty physically fit for the program but I think for people that are starting out or starting to begin exercises, I think it would be very useful for them. I really do.
Satisfaction with exercise	I liked the resistance training. I had never done that before since I didn't	-I like both of them (the resistance and aerobic exercises) and I also like the variety of muscle groups

prescription	know enough about it. I feel stronger in my arms because of it.	to work on. -I think (the exercise programme was appropriate). Not that one size doesn't fit everybody obviously, but I think that (the progression of exercises are) a very reasonable expectation, and I think it is something that can be accomplished by most people.
Satisfaction with programme materials	-Receiving everything I needed and by having the needed items I could do what I needed to do, without worrying or having to go purchase items. The log-book was very helpful with keeping me on track. -Having everything I needed to complete the program was great. I appreciated the different bands so I could work up as I got stronger.	-I'm a big fan of those exercise bands because they're so easy to take with you anywhere, where you could throw it in your car and have it with ya. I'm probably always going to be a band user now. -Because it's simple manual with the pictures and all the descriptions, it was so self-explanatory that I didn't even, I didn't even bother with the DVDs.
Satisfaction with behavioural change interactions	-I enjoyed the interaction with my coach via video calls. I feel like I opened up more with her because of the face-to-face time. - I really enjoyed the video calls with the coach. She was insightful and full of great information and ideas about health/exercise in general.	-It was very positive. Everything was very relevant and she responded to my questions, my concerns, and she was genuine. I felt like she was there and not doing multitasking. She was there when our session was going on. I had her hundred percent attention. I like that we talked about the newsletters which I think was very important. She pointed out certain things in the newsletter that I should pay attention to and I think she also used the newsletter to help me make sense of everything that's going on. - I don't know that I really gained a whole lot of extra

		information out of newsletters and things like that. I'm really an internet kind of person so I gain more information using the internet in general.
Recommendations for improvement	- Wish it (the exercise programme) would go longer… Perhaps some way to log into an app or page where we could document exercise, symptoms, mood, etc. on an ongoing basis… Something interactive… more MS-related -If anything change-up the exercises every 3 weeks or so or have choices of exercises to do each week. I personally would have liked choices.	-If the (assessment) questionnaire was something that I could have filled on the computer rather than putting it in the mail. -I think that, in general, the program is pretty good. It might be nice if there were a group Skype. Not once a week, but maybe once a month or whatever. Now you've got several people that are doing the same thing and have base talking about it and all of that.

3.6.3.



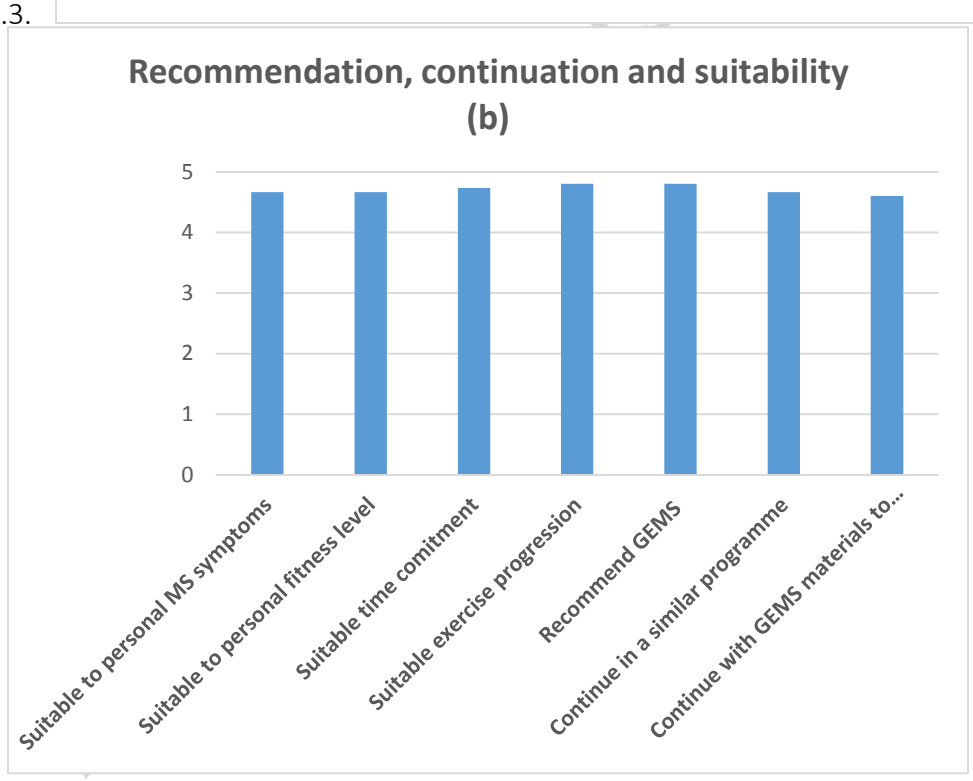


Figure 2: Intervention participant feedback; satisfaction with each aspect of the programme (a), and recommendation, continuation and suitability of the programme (b).
Note: 0 indicates low agreement/suitability, 5 indicates high agreement/suitability

3.6.4. Treatment effect

Table 7 presents the effect sizes associated with the baseline to follow-up differences for all of the outcome variables. Regarding our main outcome, there was a statistically significant time by group interaction on Godin Leisure-Time Exercise Questionnaire scores ((GLTEQ); F=6.94, P <0.01, η_p^2 = 0.12); this corresponded with a moderate increase (d≥.5) in self-reported exercise behaviour for the intervention condition and tracked with the aforementioned log-book data. There was no interaction on the secondary outcome of free-living physical activity (MVPA from accelerometer), and this is logical considering that Project GEMS did not target free-living physical activity behaviour. Regarding our other outcome measures, there were significant time by group interactions on the exercise goal-setting component of the Exercise Goal Setting and Planning Scale (F=10.5, P <0.05, η_p^2 = 0.18), and the barriers component of the Exercise Benefits and Barriers Scale (F=5.5, P <0.05, η_p^2 = 0.10). These results in our tertiary outcome measures indicate that the intervention may have influenced exercise goal setting and overcoming exercise barriers, and these were key behavioural components of GEMS.

Table 7: Outcomes at baseline and follow-up in the intervention (n=29) and control (n=28) groups.

	Baseline		Follow-up					
Outcome Assessment	Intervention Mean (SD)	Control Mean (SD)	Intervention Mean (SD)	Control Mean (SD)	Intervention Effect (*d*)	Control Effect (*d*)	Partial Eta^2	F-value
Primary Outcome Measure								
GLTEQ	20.38 (15.64)	19.64 (20.78)	29.36 (19.68)	16.85 (19.54)	0.57	-0.13	0.12	6.94**
Secondary Outcome Measure								
Accelerometer Time in MVPA	25.54 (18.05)	21.05 (18.78)	26.64 (15.49)	22.55 (22.46)	0.06	0.08	0.01	0.40
Tertiary Outcome Measures								
MSWS-12	15.66 (17.17)	24.73 (17.96)	17.33 (22.81)	28.77 (26.45)	-0.10	-0.22	0.01	0.47
ABC	8.30 (2.08)	6.48 (2.31)	7.61 (2.79)	6.09 (2.47)	-0.33	-0.17	0.01	0.50
FSS	4.21 (1.66)	4.88 (1.59)	4.01 (1.68)	4.87 (1.51)	0.12	0.01	0.00	0.04
LLFDI-Function	65.07 (8.58)	58.95 (10.13)	64.52 (11.06)	57.42 (11.13)	-0.06	-0.15	0.00	0.03
LLFDI-Disability Frequency	31.59 (3.40)	31.05 (3.41)	32.40 (3.96)	32.40 (3.96)	0.24	-0.13	0.04	2.06
LLFDI-Disability Limitations	35.59 (5.25)	31.04 (6.74)	36.52 (5.11)	32.12 (7.12)	0.18	0.16	0.00	0.00
HADS-Anxiety	5.03 (3.74)	4.89 (3.71)	4.24 (4.02)	5.62 (4.24)	0.21	-0.20	0.06	3.20
HADS-Depression	4.10 (3.62)	5.67 (3.87)	3.64 (3.84)	5.88 (4.51)	0.13	-0.06	0.01	0.49
MPQ	6.31 (6.74)	9.86 (8.33	6.28 (6.28)	8.35 (6.24)	0.00	0.18	0.01	0.41
MSIS-Physical	30.93 (10.77)	41.37 (13.74)	32.64 (12.74)	42.00 (17.36)	-0.16	-0.05	0.00	0.05
MSIS-Psychological	16.62 (6.91)	19.83 (7.75)	16.36 (7.69)	20.25 (8.70)	0.04	-0.05	0.01	0.31
LMSQOL	1.00 (0.58)	1.29 (0.52)	0.92 (0.63)	1.26 (0.66)	0.14	0.06	0.00	0.04
ESES	86.09 (18.68)	77.56 (22.08)	73.61 (32.06)	60.13 (33.55)	-0.67	-0.79	0.01	0.25
EG	23.31 (8.90)	22.87 (10.81)	27.92 (12.29)	18.52 (8.74)	0.52	-0.40	0.18	10.50*
EP	25.83 (5.29)	25.71 (4.15)	27.38 (5.97)	25.12 (5.05	0.29	-0.14	0.03	1.37
MOESS	4.33 (0.35)	4.15 (0.64)	4.38 (0.48)	4.27 (0.54)	0.12	0.18	0.01	0.31
EBBE-Barriers	27.73 (5.11)	30.26 (6.02)	25.89 (5.11)	31.72 (5.83)	0.36	-0.24	0.10	5.50*

EBBE-Benefits	51.10 (9.04)	54.00 (12.10)	49.25 (11.65)	54.96 (10.34)	0.21	-0.08	0.01	0.70
SPS	19.52 (2.77)	17.64 (3.70)	20.08 (3.35)	17.56 (3.96)	0.20	-0.02	0.01	0.52

Note: Follow up data inclusive of all participants who returned follow up data. Positive ES indicate an improvement on the scale. GLTEQ - Godin Leisure-Time Questionnaire, MVPA – Moderate to Vigorous Physical Activity, MSWS- Multiple Sclerosis Walking Scale, ABC- Activities-Specific Balance Confidence Scale, FSS- Fatigue Severity Scale, LLFDI - Late-Life Function and Disability Instrument, HADS- Hospital Anxiety and Depression Scale, MPQ- Short-form McGill Pain Questionnaire, MSIS-Multiple Sclerosis Impact Scale, LMSQOL - Leeds MS Quality of Life Scale, ESES - Exercise Self-Efficacy Scale, EG - Exercise Goal Setting and Planning Scale (Goal Setting component); EP - Exercise Goal Setting and Planning Scale (Planning component), MOEES - Multidimensional Outcome Expectancies for Exercise Scale, SPS – Social Provisions Scale, , EBBE - Exercise Benefits and Barriers Scale.

*Indicates significance at 0.05 level.

**Indicates significance at 0.01 level.

4. Discussion

This study determined the process, resource, management and scientific feasibility of a home-based, exercise training program based on recent physical activity guidelines and supplemented by behavioral principles for increasing exercise participation in persons with MS. Our outcome of process feasibility addresses recruitment. Our successive three-pronged approach to recruitment (postal mail followed by email, followed by telephone) yielded a higher overall recruitment rate (52%) than previous studies which range from 11% to 36% [19,43,44], indicating similar recruitment processes would be applicable in a larger study. Regarding outcomes of resource feasibility (i.e.., participation, communication and costs), our eligibility rate (94%) was higher than in previous studies where eligibility ranged 18% to 75% [19,43,45,46]. Our eligibility rate indicates that our inclusion criteria are appropriate for our target population. Our retention rate (89%) was comparable with past research[19,43–46], suggesting overall study acceptibility.

We provide information regarding the communication, time, equipment, and personnel requirements for a larger RCT. For example, the average assessment turn-around-time was over 3 weeks; this timeframe must be incorporated into future funding proposals. There were few technical issues experienced during behavioural coaching sessions, however, minor technical events (e.g., Internet connectivity problems) must be anticipated in future studies. Determining the cost of the research was also vital for informing future large-scale research efforts.

We provide data on the management requirements of the study. Of note, there was a larger percentage of missing accelerometer data in comparison with GLTEQ data and tertiary outcome measures data. The slight incongruity between actual accelerometer wear time and self-reported wear time that we observed has been noted by previous researchers in older adults[47], but is a unique finding in persons with MS. Feedback surveys indicated that wearing the accelerometer was burdensome. Our intervention was not designed to change free-living physical activity, and results did not indicate an intervention effect for this secondary outcome measure. Therefore, inclusion of MVPA measured via accelerometry may not be necessary in a future study.

The completion rate of >90% at both time points for tertiary outcome data is higher than in many past trials[48]. Seven percent of follow-up data were not returned by participants, despite efforts to contact these participants. Lost testing materials incurred additional cost, which must be considered in future research.

Participants reported fewer health problems than previous exercise interventions in MS[49] providing a strong indication of the safety of our study in persons with mild-to-moderate MS. Qualitative feedback indicated a high level of acceptability of the research. Compliance with the intervention was higher for aerobic exercise than for resistance exercise, and qualitative feedback indicated that participants greatly enjoyed walking but requested more variety in resistance training.

There was a moderate treatment effect on our primary outcome measure, namely exercise participation measured via the GLTEQ. Participants in the intervention condition self-reported an increase in exercise behaviour. Furthermore, participants achieved the exercise guidelines[14] by week 6 of the programme, and maintained this throughout the programme. Further results indicated a moderate effect on outcomes of goal-setting and exercise barriers providing preliminary evidence that participation in the intervention may increase one's ability to set exercise goals and overcome exercise barriers.

Our intervention was successful at increasing exercise participation, however, there were no significant changes in other outcomes. This may be due to the multi-faceted nature of the intervention resulting in a broad improvement in tertiary outcomes only. This may further be associated with the lack of a focal inclusion of outcomes measures. Indeed, the inclusion of an excessive number of outcomes might have been burdensome and intrusive for participants in this study and resulted in patient overload (i.e., this would dominate signal with noise). We believe future trials should identif a primary outcome and a selective and smaller number of secondary outcomes that are well justified by the study population, design, and focus.

Our feasibility study highlights important considerations for future large-scale trials. Outcomes of exercise participation, exercise goal setting and overcoming exercise barriers should be of high focus in our future large-scale trials. To that end, we acknowledge that other important

problems in MS, for example fatigue, may be addressed with targeted recruitment, specific intervention content, and relevant primary outcome. Future studies might consider removal of free-living physical activity using accelerometry as this was burdensome. Regarding delivery of the intervention, considerations will be made to add a variety of resistance exercises in consultation with healthcare professionals.

5. Conclusion

The GEMS home-based exercise intervention is safe and feasible for persons with mild-to-moderate MS and yielded positive changes in exercise behaviour. We cautiously suggest that persons with MS can increase exercise participation by engaging in the GEMS intervention. Overall, results of this feasibility study suggest that the GEMS intervention be moved towards a main evaluative trial[50,51] where researchers can examine treatment efficacy and effectiveness on outcomes of MS[17,52]. Other researchers might consider a similar feasibility study design when developing and planning intervention research in the MS population.

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