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Home-Based, Square-Stepping Exercise Program Among Older Adults with Multiple Sclerosis: Results of A Feasibility Randomized Controlled Study

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Abstract

There is very little known about exercise rehabilitation approaches for older adults with multiple sclerosis (MS), yet this growing segment of the MS population experiences declines in cognition and mobility associated with disease progression and aging. We conducted a RCT examining the feasibility of a 12-week, home-based Square-Stepping Exercise (SSE) program in older adults with MS. Older adults with MS (*N* = 26) with mild-to-moderate levels of disability were recruited and randomized into the intervention (i.e., SSE) or a minimal activity, attention-control conditions. Participants in the SSE condition received a mat for home-based practice of the step patterns, an instruction manual, and a logbook along with a pedometer for monitoring compliance. Both conditions received weekly Skype™ calls and had biweekly meetings with an exercise trainer. Feasibility was assessed based on process, resource, management and scientific outcomes. Regarding scientific outcomes, participants in both conditions completed in-lab assessments before and after the 12-week period. Twenty-five participants completed the study (96%) and the total cost of the study was $13,387.00 USD. Pedometer data demonstrated good compliance with the SSE intervention condition. Effect sizes calculated for all treatment outcomes ranged from small-to-moderate for both mobility and cognitive variables between the intervention and attention-control conditions, thereby providing preliminary evidence that participation in the SSE program may improve cognition and mobility function. The results support the feasibility, acceptability, and possible efficacy of a home-based SSE intervention for older adults with MS.

Keywords

Cognition, Elderly, Exercise, Mobility, Neurological disease, Rehabilitation

1. Introduction

There are increasing numbers of adults with multiple sclerosis (MS) who are now aging into older adulthood. This is reflected by the shifting age demography of persons with MS whereby there is an expanding prevalence of older adults living with MS [1]. Aging with MS as a disabling disease presents a number of consequences, and older adults with MS present with poor health status and functioning, cognitive and ambulatory difficulty, and dependence for activities of daily living [[2], [3], [4], [5], [6], [7]]. There is further evidence of a faster rate of disability progression among older adults with MS [8], yet there are no approved disease-modifying therapies (DMTs) for adults with MS beyond 65 years of age. This is mostly due to the paucity of research studies including this age group in trials. Nevertheless, some evidence indicates that DMTs have no or very modest effect for slowing disability in this demographic of persons with MS [9].

Researchers and clinicians have become interested in exercise training as an approach for managing the consequences of aging and MS. This is largely based on evidence for benefits of exercise in MS [10] and older adults in the general population [11] separately, but there have been a few interventions focusing on the beneficial effects of exercise for older adults with MS [12]. We further note that the rates of participation in physical activity and exercise are exceedingly low in older adults with this MS [13,14] and that this population does not meet current recommendations of physical activity necessary for accruing health benefits. Several factors may interfere with physical activity and exercise participation in older adults with MS, including increasing age, perception that exercise is too difficult, cost of exercise programs and lack of low-cost and accessible recreational facilities [15]. Such observations must be accounted for in the design of exercise training

programs for older adults that are consistent with recommendations regarding exercise for persons with MS [16].

We recently described and proposed a methodological protocol paper involving a feasibility study of the square-stepping exercise (SSE) in older adults with MS [17]. The SSE program was originally developed by Japanese researchers and focused on improving functional fitness (e.g., lower limb muscle strength, walking ability, balance, reduce the risk of falls) and enhancing cognition in older adults of the general population [18]. To this end, we opted for the SSE intervention for its potential benefit to improve clinical aspects in older adults with MS. The SSE-MS project is a 12-week, home-based, exercise training program developed to be an easy-to-do and fun exercise with the potential to improve mobility and cognition in individuals with MS in the older adulthood. The present manuscript reports results (i.e., outcomes) regarding the process, resource, management, and scientific feasibility metrics on the feasibility of SSE-MS Project in adults with MS aged 60 years and older. The results were reported in accordance with current recommendations and guidelines for feasibility trials [19].

2. Methods

2.1. Ethical approval

This feasibility study was a randomized controlled trial (RCT) conducted between October 2016 and September 2017. The study protocol was approved by a university institutional review board (IRB) and all participants signed an informed consent document before data collection.

2.2. Participant recruitment and eligibility

Participants were recruited from the Midwest region of United States using (i) the North American Research Committee on Multiple Sclerosis (NARCOMS), (ii) a database of people with MS who had previously participated in studies conducted by researchers in the Exercise Neuroscience Research Laboratory, (iii) interactions with potential participants during MS events and MS-specific support groups, (iv) advertisement on the research laboratory's website, and (v) advertisement in local newspapers. Participant recruitment was an ongoing process over the course of the study.

Recruitment flyers and newspaper advertisements provided detailed eligibility criteria, and included contact information (i.e., telephone and email) for the researchers. Inclusion criteria for the study included: (a) 60 years and older; (b) clinically definitive diagnosis of MS; (c) relapse-free for the past 30 days; (d) ability to walk with or without an assistive device (e.g., cane); (e) willing and able to participate in the 12-week home-based intervention; (f) non-exerciser (operationalized as not engaging in structured exercise 2 + days/week); (g) asymptomatic (i.e., one or fewer affirmatives on the Physical Activity Readiness Questionnaire (PAR-Q)) or physician approval for undertaking exercise training for those with 2 or more affirmatives on the PAR-Q [20], (h) signed medical release form; and (i) scoring ≥13 points in the Telephone Interview for Cognitive Status, indicating no more than mild cognitive impairment [21]. Participants who did not meet those criteria were excluded from study participation. We sought a sample size exceeding 12 participants per group, as it is believed to be acceptable for pilot and feasibility studies involving RCT study designs [22]. We did not conduct a formal sample size calculation, as this was a feasibility study.

2.3. Procedure

Participants who successfully enrolled in the study were scheduled for a visit to the Exercise Neuroscience Research Laboratory. This visit started with a review and provision of a written informed consent document. Participants then undertook baseline assessments (e.g., functional mobility, walking speed and endurance, cognitive assessments) and were randomized using concealed allocation into the intervention condition or the attention control condition. This involved (a) a research staff member not involved in the study pre-preparing

opaque sealed envelopes with slips of paper containing group allocation and storing these in a randomization container and (b) another research staff member involved in the study choosing an envelope. This determined group allocation. Because of the feasibility pilot nature of the study, outcome assessors were not blind to group allocation. The intervention was delivered over a 12-week period and we further collected outcome assessments both during (e.g., communication and safety) and after (e.g., treatment effect). All participants received $250 as incentive for participation. Participation included two in-laboratory assessment (i.e., pre- and post-intervention), six site visits/encounters with the exercise trainer, weekly skype calls, and the home practice.

2.3.1. Intervention condition

Table 1 and Fig. 1 display intervention progression and step pattern levels examples. SSE was performed on a thin mat of 250 × 100 cm, partitioned into 40 smaller squares (25 cm per side). The program provides sequences of stepping patterns wherein participants learn and practice specific stepping routines by progressively stepping along the mat length direction and avoid treading on the lines of the squares. The exercise intervention group received in-person supervised instruction at a university laboratory setting followed by ongoing home-based practice with weekly Skype™ calls for monitoring and compliance check. Participants further received a pedometer (YAMAX SW-200), which was worn during all SSE home-sessions and a logbook to record the date, start and end time, and the number of steps per SSE session. Importantly, this study was not designed to increase average steps, and participants were not asked to reach or perform a certain number of steps per session. The pedometer was used with the purpose only of monitoring compliance with the program (i.e., participants increased the number of steps as expected based on doing the prescribed step patterns per session). Participants further provided written responses of level of perceived exertion, feeling, enjoyment, and physical and mental fatigue per session in the logbook. This information was retrieved during the biweekly encounters for monitoring compliance with the program. The exercise intervention started with sessions being performed twice a week with a duration between 10 and 15 min and progressed to 5 sessions per week with a duration between 25 and 30 min per session. Participants started with basic step patterns that focused on walking-like movements and gradually progressed to more complex step patterns requiring forward, lateral, diagonal and backwards movements. Over the course of the intervention, participants had a total of six in-person encounters (one every two weeks) with the exercise trainer to be familiarized with and receive verbal and visual instructions about the step patterns. Participants then practiced the sequence of step patterns designated for the two-week period at home until the next meeting. For additional details in the intervention please see reference elsewhere [17].

Table 1. Progression of the arms of the SSE-MS program.

Week	Intervention				Control			
	Frequency (days/week)	Duration (minutes)	Number of step patterns	Level of step patterns	Frequency (days/week)	Duration (minutes)	Stretching exercises	Sets/time for each exercise
1*	2	10–15	4	B1; B1; B1; B2	2	10	H & N	1/30 s
2	2	10–15	+4	B1; B1, B2, B2	2	10	W1 + S	1/30 s
3*	3	15–20	+4	B2; B2; B2; B2; I1	3	15	W1–2 + SR	2/20 s
4	3	15–20	+4	B2; B2; I1; I1; I1	3	15	W1–3 + E	2/20 s
5*	3	15–20	+4	I1; I1; I1; I1; I2	3	15	W1–4 + FE	2/20 s

6	4	20–25	+4	I1; I1; I1; I2; I2; I2	4	20	W1–5 + Ha	2/20 s
7*	4	20–25	+4	I2; I2; I2; I2; I2; I3	4	20	W1–6 + W	3/20 s
8	4	20–25	+4	I2; I2; I2; I3; I3; I3	4	20	W1–7 + T	3/20 s
9*	5	25–30	+4	I3; I3; I3; I3; I3; I3; A1	5	25	W1–8 + Hi	3/20 s
10	5	25–30	+4	I3; I3; I3; I3; A1; A1; A1	5	25	W1–9 + A	4/20 s
11*	5	25–30	+4	A1; A1; A1; A1; A1; A1; A2; A2	5	30	W1–10 + FoE	4/20 s
12	5	25–30	+4	A1; A2; A2; A2; A2; A2; A3; A3	5	30	W11	4/20 s

∗Meeting with SSE/Stretching trainer; B1 = Beginner one; B2 = Beginner two; I1 = Intermediate one; I2 = Intermediate two; I3 = Intermediate three; A1 = Advanced one; A2 = Advanced two; A3 = Advanced three; H = Head; N = Neck; W1, 11 = Week one to eleven; S = Shoulder; SR = Shoulder Range; E = Elbow; FE = Forearm Exercises; Ha = Hand; W = Wrist; T = Trunk; Hi = Hip; A = Ankle; FoE = Foot Exercise.

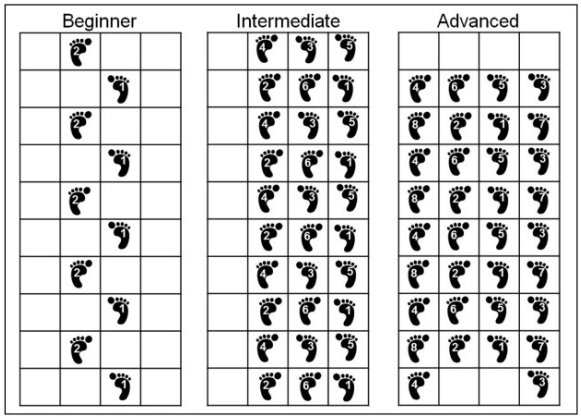

Fig. 1. Examples of the three different levels of patterns available in the square-stepping exercise program.

2.3.2. Control condition

The stimulus was a light intensity stretching and minimal muscle strengthening program based on an illustrated manual for persons with MS developed by the National Multiple Sclerosis Society that involves major muscle groups of the upper and lower body. This stimulus is common in RCTs of exercise training in older adults [4] and serves as an attention-control condition to account for social interaction with the exercise trainers. Participants received graphical instructions on the designated stretching exercises and the intervention progressed with the inclusion of more exercises and sets over the course of the program (i.e., 12-week period). Participants in the control group were involved in the same hybrid of biweekly, in-person supervised instruction as the intervention group, followed by ongoing home-based practice (i.e., 2–5 days/week) with weekly Skype™ monitoring. Compliance for the control group was monitored through the weekly Skype™ calls and through the five scales

(i.e., level of perceived exertion, feeling, enjoyment, and physical and mental fatigue) that were completed at the end of each home-based session.

2.4. Feasibility metrics

This study assessed outcomes based on process, resource, management and scientific metrics of feasibility. All feasibility metrics components assessed in this study are summarized in Table 2 along with the methods for collecting and assessing relevant data.

Table 2. Feasibility metrics; proposed methodology and importance to future research in MS.

Metric	SSEMS monitored and assessed	Data source	Outcome variable computational method
Process; assesses participant recruitment and retention	a. Recruitment and refusal rates b. Retention, attrition and adherence rates	a. Central database recording number of participants recruited via each recruitment method (i.e., telephone, email, participation in MS-related events and newspaper); number of excluded participants and reason b. Central database recording adherence to study completion (i.e., logbook, weekly phone calls, and step count during SSE home sessions), participants completing the study (i.e., follow up); attrition and reason.	a. Recruitment rate was calculated dividing total number of participants enrolled from each method adopted by total number of participants contacted b. Retention rate was calculated as the number of participants who completed follow-up assessments from those who were randomized. Attrition rates was calculated as the number of participants who did not complete follow-up assessments. Adherence was calculated as the total number of consenting participants who received intervention allocation
Resources; assesses communication and monetary requirements of the study	c. Communication with participants d. Communication needs of participants and staff e. Monetary costs of research	c. Central database recording length of initial recruitment, weekly phone calls and meetings with exercise trainer. d. Central database for intervention participants recording preferred communication method (i.e., Skype video calls, regular telephone calls) and call time e. Expenditure spread sheet recording overall costs of	c. Recruitment time was calculated based on the mean time pend during phone calls/screening time for participation, time for medical release forms to be signed and returned by their physicians d. Preferred time of communication method was calculated as the number of participants opting for skype video calls or regular telephone calls e.

		intervention (i.e., SSE mats, instructional materials, pedometers, participant compensation)	The costs of the study were calculated as the total monetary cost in US dollars of producing materials (i.e., manual, paper-pencil tests materials, log-books); SSE materials (i.e., mats, pedometers); and participant compensation
Management; assesses data management and safety reporting during the study	f. IRB approval procedures g. Staff preparation and report time for participant communication h. Time and accuracy in data collection/entry i. Reporting and handling of adverse events (AE), serious adverse events (SAE) and clinical emergencies	f. Record of time (i.e., days) to achieve initial IRB approval g. Preparation spread sheet recording recruitment database preparation time (min), material preparation time (min) recruitment and database preparation; staff meetings (min) h. Preparation spread sheet recording assessment time (min) and time to data enter and check (min) i. Preparation spread sheet recording adverse events (AE), serious adverse events (SAE) and clinical emergencies as wells actions taken	f. IRB approval time was calculated as the amount of days taken from submission to approval notification g. Staff preparation and reporting time were calculated as the time with staff meetings, create recruitment database, recruit participants, conversation with participant over the phone (i.e., study explanation, answering questions), preparation of participants' materials; and entering and checking study's data h. This was calculated based on the time taken for each participant assessment and information to be entered and checked in the database i. Health problems reported by the participants over the course of the study period was computed. This included: MS symptoms exacerbation (e.g., increased fatigue, pain), MS relapse (e.g., acute worsening of neurological symptoms), injury (e.g, sprains, fracture), and illness (e.g., infections)
Scientific; assesses the safety, burden and treatment effect of the study	j. AEs, SAEs and clinical emergencies k. Participants experience, burden, and compliance	j. Database recording reported adverse health problems, relapses and AEs occurring during the study period k.	j. same as item i k. This study adopted scales for physical and mental fatigue, enjoyment, feelings and program intensity

	during the intervention l. Treatment effect	Database recording exercise participation and burden reported by participants during the intervention (i.e., scales measuring level of mental and physical fatigue, level of enjoyment, feelings and perceived exertion) l. Mobility outcomes (i.e., T25FW, TUG, 6 MW); Functional Fitness outcome (i.e., SPPB); cognitive outcomes (i.e., SDMT, CVLT, BVMT)	l. Outcomes were collected using valid, reliable and recommended test to be adopted in exercise trials involving persons with MS

2.4.1. Physical and cognitive outcome measures

We included measures of walking mobility, cognition, and physical function for capturing possible beneficial effects of the SSE protocol. The Timed 25-foot Walking (T25FW) [24,25], Six-minute Walk (6 MW) [26,27] and Timed Up and Go (TUG) [[28], [29], [30]] represented standard performance measures of walking mobility. The Brief International Cognitive Assessment for MS, including the oral version of the Symbol Digit Modalities Test (SDMT), Brief Visuospatial Memory Test (BVMT), and the California Verbal Learning Test (CVLT) represented the cognitive endpoints [31]. The Short Physical Performance Battery (SPPB) represented a measure of physical function for older adults with MS [32].

2.5. Data analysis

Data were analyzed using SPSS version 24.0 (SPSS Inc. Armonk, NY: IBM Corp.). Basic descriptive statistics (mean, median, standard deviation (SD), interquartile range) were used to present the data regarding demographic (e.g., age) and clinical characteristics (e.g., MS duration, Expanded Disability Status Scale (EDSS)). Process feasibility data were described as total number and percentage (i.e., recruitment). Resource feasibility data were described as total number and percentage (i.e., retention and communication). The scientific metrics of efficacy were examined using mixed-factor ANOVA. Condition was the between-subjects factor and time was within-subjects factor. Due to the nature of the study (i.e., feasibility), covariates were not included and statistical analysis served primarily for the observation of Eta-squared (η^2) values rather than statistical significance. Effect sizes associated with *F*-statistics were expressed as η_p^2. Effect sizes were based on a difference in mean scores over time between groups were expressed as Cohen's *d* [33].

3. Results

3.1. Participant demographic and clinical characteristics

Detailed demographics and clinical characteristics of the overall sample and sample by conditions (i.e., intervention and attention-control) are presented in Table 3. The average age of participants was 64.3 (SD = 4.5) years. The majority of the sample was female (88.5%) and married (77.3%). Further, all participants self-identified as Caucasian. Thirty-five percent of the sample reported having a master's degree, 58% of the participants reported being retired, and 69% reported an annual income of $40,000 or greater. Relapsing-remitting MS was reported by 88.5% of participants with an average duration of the disease of 21.1 (SD = 10.7)

years. The sample had a moderate level of disability (EDSS = 4.0, IQR = 2.5). No significant differences were observed in any demographic or clinical metrics between conditions.

Table 3. Baseline demographic and clinical characteristics of the sample.

	Overall (n = 25)	**Intervention condition (n = 15)**	**Control condition (n = 10)**
Age, mean (SD)	64.3 (4.5)	63.8 (4.1)	65.1 (5.2)
Sex, %Female	88.5	87.5	90
Race, %Caucasians	100	100	100
Marital Status, %Married	73.1	75	70
EDSS, mdn (IQR)	4.0 (2.5)	3.75 (2.75)	4.25 (2.13)
MS Type, RRMS/SPMS/BGMS	23/2/1	14/1/1	9/1/0
Disease duration, mean(SD)	21.1 (10.7)	21.9 (10.7)	19.9 (11.2)

Note. SSE: Square-stepping exercise; SD: Standard deviation; EDSS: Expanded Disability Status Scale; Mdn: Median; IQR: (Interquartile range); MS: Multiple sclerosis; RRMS: Relapsing-remitting multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; BGMS: benign Multiple sclerosis.

3.2. Process feasibility: recruitment and retention

Details on participant flow through the trial are provided in the CONSORT diagram in Fig. 2. There were 129 older adults with MS who were directly contacted to participate in the study; 66 via email and 63 via telephone. Recruitment via email yielded 23 interested participants, and recruitment via telephone yielded 40 interested participants. Based on these two methods, recruitment rate was 49% (*n* = 63). We further recruited through MS-related events, the laboratory website, and local newspapers as additional approaches for recruitment. These methods yielded 11 interested participants. Across all recruitment methods, there were 74 interested participants in total. Thirty-six potential participants were excluded during telephone screening. Twenty-three persons did not meet the inclusion criteria, with 19 being too active (engagement in structured activity for >2 times per week) and 4 potential participants not meeting age requirements (i.e., younger than 60 years of age)). Thirteen potential participants declined to participate during the screening process. Thirty-eight (51%) of the interested participants were eligible to participate and were sent a medical release form to be signed by a personal physician. Eight medical release forms were not returned and participants were excluded. Thirty participants were enrolled and scheduled for the baseline laboratory visit. Four out of 30 dropped out before baseline testing. This yielded a final sample of 26 people with MS who were randomized and enrolled into the intervention (*n* = 16) or control condition (*n* = 10); resulting in nearly 87% retention rate. Twenty-five out of 26 participants completed the study and post-intervention assessments (96% completion rate). Regarding attrition, one participant randomized into the intervention condition did not complete the study. This participant dropped out of the study at week 6 (i.e., due to hospitalization followed by death unrelated to the study). Data from this participant were not included in our analysis of intervention outcomes.

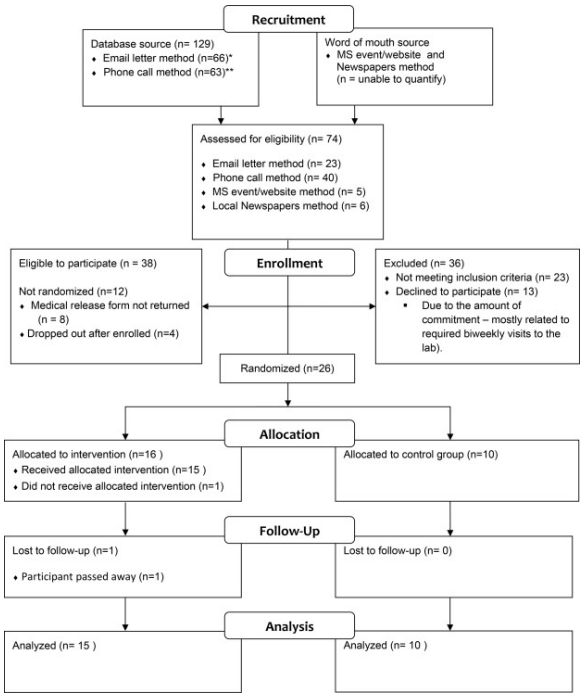

Fig. 2. CONSORT diagram. Note: In addition there were *27 invalid emails and **11 invalid phone numbers.

3.3. Resources feasibility; communication and monetary requirements

The phone calls conducted for recruitment purposes (i.e., study presentation) took on average <10 min. Phone calls for recruitment plus screening ranged between 12 and 15 min. The mean time to receive signed medical release forms was 7 days, and 30% of the sample required a follow-up phone call with the personal physician for receipt of medical clearance. The majority (*n* = 14; 93%) of participants in the intervention condition received all weekly Skype™ calls. One participant in the intervention group had problems with the computer and the weekly interaction was done via regular phone call. Seventy percent of the participants (*n* = 7) in the control group received the weekly interactions through Skype calls. Three participants in the control condition did not feel comfortable using a computer and preferred to do the weekly interaction via regular phone calls.

The total study cost was $13,387.00 USD. This total included costs related to equipment (i.e., SSE customized mats and pedometers; $6982.00 USD), materials (i.e., colored photocopies and binders; approximately $155.00 USD), and participant incentive ($6250.00 USD). The total costs do not include personal costs (i.e., research assistants and investigators).

3.4. Management feasibility: data management and safety reporting during the study

The study protocol was submitted to the university IRB on November 29th, 2015 and received approval on January 11, 2016. This represented 43 days from initial submission through approval.

The time necessary to complete the study totaled 349 h (h). This time was distributed across discussions and meetings between investigators and staff (48 h), recruitment (database creation, email preparation, journal and website advertisement creation, participation in MS-related event; 35 h), recruitment phone calls (40 h); material preparation (36 h), data entry and checking (41 h), weekly Skype™ calls (33h) and visits with the exercise trainer (112*h*). Of note, three participants in the intervention group only made it to the first visit with the exercise trainer due to the distance from their residence to the laboratory (3 to 3.5 h) and the lack of someone to drive them. For these participants, new step patterns were sent by email and participants were asked to print a hardcopy to be included in their binder. A research staff was responsible to follow up with participants through phone/video call and proceed as close as possible to a normal laboratory visit with the

exercise trainer (please refer to item 2.2.1 intervention condition). Nevertheless, the 112 h mentioned above include the hours of these three participants. An additional 4 h were necessary to retrieve the mats from three participants who were unable or forgot to return the mat in the post-assessment session.

3.5. Scientific; assesses the safety, burden and treatment effect of the study

3.5.1. Safety

Two participants in the intervention condition reported adverse events that were unrelated to the study during the 12-week intervention period. One person reported a fall (i.e., slipped in the wet garage) and another person was hospitalized during the study due to a generalized infection and passed away. One person in the control condition reported a discomfort during one of the stretch exercises (i.e., neck stretching) and the specific exercise was removed from participant's exercises by the exercise trainer.

3.5.2. Burden

The mean time to complete baseline assessment for all participants was 115 min (SD = 17 min) and the mean time to complete follow-up assessments for all participants was 89 min (SD = 11 min). The average time for the weekly Skype™ calls per participant was 7 min (± 3 min). The average time for the biweekly meeting with the exercise trainer per participant was 45 min (± 6 min).

3.5.3. Compliance

Four (27%) participants in the intervention condition asked to reschedule the weekly Skype™ calls, but the rescheduled calls were within 2 days from the original scheduled date. Seven (47%) participants in the intervention condition missed at least one of the biweekly meetings with the exercise trainer (range: 1–3 meetings). Compliance in the intervention group was further verified through the SSE home practice (i.e., average steps per week of session) and through the logbook where information on data and time of practice were available. Fig. 3 displays the average steps per week performed during the SSE sessions. Paired samples *t*-tests indicated a statistically significant difference on the average number of steps between weeks 1 and 6 [t(14) = −15.670; P < 0.001] and between weeks 6 and 12 [t(14) = −11.293; P < 0.001]. The average difference in steps per week from week 1 to 12 was approximately 8073 steps. Such difference was also found to be statistically significant [t(14) = −18.203; P < .001].

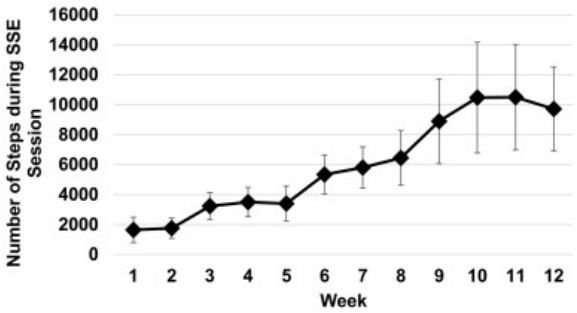

Fig. 3. Average number of steps accumulated per week of square-stepping exercise home practice.

Regarding the control group, one participant (10%) could not be reached for the first scheduled weekly skype call due to traveling. Three (30%) participants in the control group missed one biweekly face-to-face meeting each with the exercise trainer. Compliance in the control group was further verified through a date and time sheet form that was provided to the participants and checked during the biweekly laboratory visits.

3.5.4. Scientific metrics of treatment outcomes

Table 4 presents the effect sizes (η_p^2) associated with the time by condition interaction for all of the outcome variables included in the study. Regarding physical functioning outcomes, there were no statistically significant

time by group interactions on T25FW (F = .398, P = .534, η_p^2 = .017), TUG (F = .306, P = .586, η_p^2 = .014), 6 MW (F = .001, P = .983, η_p^2 = .001), or SPPB (F = .1.347, P = .258, η_p^2 = .055). The lack of significance is likely due to the small sample size and associated impact on statistical power for a feasibility study. However, effect sizes as Cohen's d demonstrate a small-to-moderate improvement for these outcomes in the SSE condition, with the largest effect size for the T25FW (d = −.34) and SPPB (d = .30). Similar results were observed for cognitive functioning outcomes. There was no statistically significant time by group interactions on SDMT (F = .163, P = .691, η_p^2 = .007), CVLT (F = .764, P = .391, η_p^2 = .032) or BVMT (F = 2.417, P = .134, η_p^2 = .095). However, effect sizes highlight the small-to-moderate improvements in the SSE condition, with the largest effect sizes for the CVLT (d = .40) and BVMT (d = .34).

Table 4. Outcomes at baseline and follow-up in the intervention (n = 15) and control (n = 10) groups.

Outcome assessment	Baseline		Post-intervention		Intervention Effect (***d***)	Control Effect (***d***)	η_p^2	***F***-value
	Intervention Mean (SD)	Control Mean (SD)	Intervention Mean (SD)	Control Mean (SD)				
T25FW, ***sec***	6.9 (3.1)	8.8 (3.7)	6.0 (1.6)	8.5 (4.1)	−0.34	−0.07	.017	.398
TUG, sec	10.4 (3.5)	15.1 (8.0)	9.7 (2.7)	14.0 (7.3)	−0.22	−0.14	.014	.306
6 MW, ft.	1303.4 (362.3)	969.5 (423.5)	1392.6 (415.4)	1050.8 (514.5)	0.23	0.17	.001	.001
SPPB, pts	8.8 (2.6)	7.2 (3.3)	9.5 (2.1)	7.1 (4.0)	0.30	−0.03	.055	1.347
SDMT, pts	52.8 (10.7)	42.1 (15.8)	53.3 (10.9)	42.0 (17.1)	0.05	−0.01	.007	.163
CVLT, pts	53.6 (10.5)	53.1 (13.9)	58.1 (12.3)	54.9 (14.9)	0.40	0.12	.032	.764
BVMT, pts	23.9 (4.8)	22.5 (6.2)	25.6 (5.1)	20.3 (4.6)	0.34	−0.40	.095	2.417

Note: η_p^2: partial eta-squared. T25FW: Timed 25-ft Walk Test; TUG: Timed Up and Go Test; 6 MW: 6-min Walk Test, SPPB: Short Physical Performance Battery; SDMT: Symbol Digits Modality Test; CVLT: California Verbal Learning Test; BVMT: Brief Visual Memory Test.

4. Discussion

This manuscript reports results of process, resource, management and scientific feasibility of a home-based, SSE program in older adults with MS. The SSE was chosen as the intervention because of its great potential to improve common impairments of older adults with MS (e.g., balance, walking, and cognition). The SSE program was developed by a group of Japanese researchers with the main goal to prevent falls, improve lower limb physical functioning, and enhance aspects of cognition such as memory [18,34]. However, this intervention has not been tested for its feasibility in older adults with MS. This exercise method has been effective in improving physical functioning in older adults of the general [35,36]. The SSE is a low-cost, indoor or outdoor exercise method that is easy to perform. This is mostly due to the fact that the movements/step patterns performed by individuals over the SSE mat mimics walking movements. The potential benefits for improving clinical outcomes among older adults with MS, similar to those reported in the general population, motivated our adoption the SSE program. However, this intervention had not previously been tested for its feasibility in older adults with MS. The outcome of process feasibility focused on recruitment and retention rates. The two main approaches adopted for recruitment in this study (i.e., email and phone calls), without taking into consideration newspaper advertisements and MS-related events, resulted in an overall recruitment rate of 49%. This is comparable with

the 52% recently observed by researchers in a different home-based study in younger and middle-aged adults with MS [37] and higher than previous studies with similar characteristics [[38], [39], [40]] that reported rates ranging between 11 and 34%. Our strong recruitment rate indicates that similar processes would be applicable in a subsequent phase II trial. Our study further had 87% retention rate (i.e., older adults enrolled and randomized into one of the two arms of the study). This number is comparable with previous studies [38,41] and demonstrates overall positive study acceptability.

Regarding metrics of resource feasibility (i.e., communication and monetary requirements), our study provided important information for designing a future phase II trial. Regarding communication, our study demonstrated that overall Skype™ calls were well accepted by the participants. However, we faced the challenge of some participants not being comfortable using computers with Skype™. In those cases, a video call connection could not be established and those participants received weekly contact through regular phone calls. This should be anticipated in future trials so precautions can be taken to help avoid potential delays in the communication with participants. A potential solution would be offering multiple means of communication to participants at the beginning of the study. We did not experience any technical issues in terms of Internet connectivity during the Skype™ calls or other logistical problems, such as participants not having a computer/tablet/smartphone to communicate with the research team. One participant in the control group required an instructional sheet with instruction on how to download and use Skype™ and this should be included in future trials. Regarding our communication with physicians to obtain the signed medical release, it may be important to plan for extra time and/or develop a different approach to accelerate this part of the process. We recruited older adults with MS for the current study, and this necessitated medical approval for undertaking the exercise program. Our approach was to fax the medical approval form to the physician's office. Members of the research team had to call the physician's office for approximately one third of the sample to remind them to complete and sign the form. A potential solution to minimize this issue would be asking the participant to bring a hardcopy of the medical approval form to the physician's appointment. However, it is important to note that this may necessitate cost to the participant to ensure timely enrollment. Gathering information on the costs related to the study was crucial to better inform future grant proposals for large-scale research efforts. Our study was accomplished with slightly over $13,000 and the majority of this cost was related to the manufacturing of the mats (~$7000) and participant's payment (~$6000). The costs related to the mat can be significantly reduced by opting for a different material. Our mats used an industrial material which may not be necessary for the purposes of the mat. The majority of participants might require travel for the laboratory visits, so this was taken into consideration when offering the large incentive. A multi-site study could be a potential way to reduce participant's payment in future large-scale trials; but this would come with its own set of challenges and quality control that will need to be addressed before hand. The $250 USD paid to participants as an incentive can arguably be seen as a potential bias for participation in this study. However, we believe that this amount was necessary when considering the costs of transportation. We further do recognize that the cost may limit translation into clinical practice, and further research is necessary for examining the SSE intervention under conditions amenable for translation into a clinical setting.

We gathered and provided data on the management requirements of the study. This feasibility trial was conducted with the assistance of eight persons, including the PI, Co-PI, two consultants, two graduate students, and two undergraduate students, with the majority of the work performed by the PI and two graduate students. Twenty-five out of the 26 enrolled and randomized (96%) completed the study, with one participant in the intervention condition not completing the follow up assessment. This rate is higher than rates observed in previous trials [42]. This is also higher than the normally high dropout rates observed clinical trials in diseased populations [43]. Completing and bringing the logbook with the required information during the biweekly meetings with the trainer revealed to be a challenge for some participants. In few occasions, the expected information was retrieved by phone or by email. This does not seem to be unique to our study as previous work

reported the needed to follow up with participants to retrieve information [37]; however, strategies should be implemented to minimize the potential loss of information. For example, the development of a website linked to the program where participants would be able to upload the necessary information. The assessments adopted in the study were performed in the laboratory and data were collected by a member of the research team. To this end, missing data in this study were related to participants not been able to complete one or more of the assessments.

Participants in the intervention group did not report health problems or adverse events (e.g. relapses) associated with the SSE practice. This indicates that home-based SSE is safe to be practiced by older adults with MS. This finding is similar to those observed in previous exercise interventions conducted in younger and middle-aged adults with MS in terms of safety. A previous systematic review that examined the safety of exercise training in persons with MS observed a relapse rate as small as of 4.6% and 6.3% for the exercise and control group, respectively [44]. Further, the rates of adverse events were 2% and 1.2% for exercise and control, respectively [44]. Overall compliance with the intervention was reasonable, as less than half of participants missed a meeting with the exercise trainer. Although important, the meetings with the trainer were a small part of the program as the majority of it was performed in the participants' own home without supervision. Compliance, measured through steps per session with the use of a pedometer, demonstrated that participants complied with the study protocol and the majority of participants were reaching on average 10,000 steps per week at the 10th week of the program (Fig. 3). By week 10th week of the program, participants were practicing SSE five times per week with a duration of 25–30 min per session. This equates to 2000 steps per session of SSE practice by the 10th week of the program. Although this was not our goal/outcome, the 2000 steps accumulated during the SSE session could be a significant contributor in helping this population to achieve the recommended 10,000 steps per day promoted by public health agencies.

We did not observe nor expect statistically significant effects of the home-based SSE on physical and cognitive functioning outcomes. We instead focused on effect sizes (Cohen's *d*) for the interaction effect from the ANOVAs on study outcomes. The partial eta-squared values (η_p^2) indicated the interaction between time and condition accounted for small variability in the physical functioning (i.e., T25FW, TUG, 6MW, SPPB; 0.1 to 5.5%) and cognitive functioning performance tests (i.e., SDMT, CVLT, BVMT; 0.7 to 9.5%). We further focused on Cohen's *d* effect sizes and these indicated a small-to-moderate effect. The largest effects we observed for physical and cognitive functions were for T25FW, SPPB, CVLT and BVMT, respectively. This is somewhat expected considering that the intervention targeted multiple factors involved in the SPPB (e.g., walking and balance) as well as learning and memorizing visuomotor tasks that would translate into changes in the BVMT. Overall, the magnitude of the effect sizes ranged from small-to-moderate for both ambulatory/mobility and cognitive variables and provides preliminary evidence that participation in the intervention may improve cognition and physical function performance in older adults with MS. Similar findings have been observed in older adults for the general population [45]. We further note that the next stage of research may focus on SPPB and BVMT as primary outcomes of a phase II trial that focuses on the efficacy of the home-based SSE for improving physical and cognitive function in older adults with MS.

Participant satisfaction with the programs deserves a brief discussion, although such information was not collected systematically. Based on informal conversations with participants enrolled in the SEE program during the biweekly visits in the laboratory, participants reported a positive perception of the program. This was based on the easy to perform type of exercise, the fact the SSE program was a fun way to increase physical activity that focused on MS-related symptoms, and the fact that the hybrid approach provided participants with a flexibility in terms of time of the day they could perform the exercise at home. However, some participants reported that as they moved forward with the program in terms of frequency and duration (i.e., 4–5 times per week and 25–30 min per day) the exercise became too repetitive and “boring”. Based on this, potential changes would include

a fixed frequency (e.g., 3 times per week) and program progression only in terms of duration (i.e., time per session) and difficulty of step pattern (i.e., beginner, intermediate, and advanced). Similarly, a positive perception regarding the program was also reported by participants in the stretching and minimal muscle strengthening control group. Some participants reported that the stretching exercises improved walking and reduce stiffness. Participants further mentioned that the stretching program focused on the whole body was a positive point. Despite no negative comments, a potential change for a future trial would be to provide participants with a yoga mat and a log book for more similarities to the SSE condition.

5. Conclusion

This home-based, SSE program for older adults with MS (i.e., 60 years and over) was safe and feasible. The program showed great acceptability and no program-related adverse events or MS-related symptoms exacerbation was observed. Overall, results from this feasibility study suggest that the SSE-MS intervention can be moved toward a phase II trial of its efficacy for improving physical and cognitive functions [46]. Researchers might further consider a similar feasibility study design when developing intervention programs for persons with MS in this stage of life (i.e., older adulthood).

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