Calling Out MS Fatigue: Feasibility and Preliminary Effects of a Pilot Randomized Telephone-Delivered Exercise Intervention for Multiple Sclerosis Fatigue

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Background and Purpose: Fatigue is a common and debilitating symptom of multiple sclerosis (MS). Exercise therapy is effective in reducing MS-related fatigue; however, its feasibility, acceptability, and effectiveness when delivered over the telephone remain unknown. This randomized study aimed to determine the feasibility and acceptability of a telephone-delivered exercise intervention for MS-related fatigue. In addition, pre-/postchange in fatigue and secondary outcomes were compared with an otherwise identical in-person delivered exercise intervention.

Methods: Twenty participants with MS and clinically significant fatigue were randomized to 8 sessions of either telephone (n = 10) or in-person (n = 10) delivered exercise therapy. Primary outcome measures concerned feasibility (number of sessions attended), acceptability (Client Satisfaction Questionnaire), and fatigue (Fatigue Severity Scale and two 11-point numeric rating scales: fatigue intensity and interference). Data on a range of secondary outcome measures were also collected.

Results: There was no difference in average session attendance by group (telephone group: 7.6 ± 1.3 sessions; in-person 7.8 ± 0.42). Acceptability and reductions in fatigue were observed regardless of group, and improvements in a range of secondary outcomes were comparable.

Discussion and Conclusions: A telephone-delivered exercise intervention that targets MS-related fatigue is both feasible and acceptable. Primary and secondary outcome measures signaled that telephone-delivered exercise may be an effective mode of delivery that overcomes barriers to care in persons with MS and warrants testing in larger efficacy trials.

Video Abstract available for more insights from the authors (see Video, Supplemental Digital Content 1, http://links.lww.com/JNPT/A293).

Key words: *aerobic training, exercise, fatigue, multiple sclerosis, resistance training, telehealth*

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INTRODUCTION

Fatigue is a prominent and debilitating symptom of multiple sclerosis (MS); up to 92% of individuals report fatigue[1] that manifests as lack of energy, exhaustion, or worsening of MS symptoms and ultimately contributes to increasing disability. Fatigue severely impacts participation in daily life activities and predicts employment status.[2,3] Available pharmaceutical treatments fail to fully control fatigue in most individuals with MS. Nonpharmacologic therapies, such as exercise therapy, offer additional options for combating MS fatigue.

The presence of fatigue negatively impacts participation in physical activity, and levels of fatigue have been shown to correlate with depressive symptoms, sleep disturbance, and pain intensity.[4,5] Exercise therapy, specifically endurance (eg, walking, cycling) and mixed training (ie, endurance and strength training), is effective in reducing MS fatigue.[6-8] However, these exercise trials have been implemented only via traditional one-on-one, in-person delivery method, and access to these therapies is seriously limited for many individuals with MS due to geographical location, limited resources (eg, financial, transportation), and/or disability.[9] The development and evaluation of an alternative delivery method for exercise therapy to target MS-related fatigue that increases participation and reduces barriers are critical.

Telephone-delivered exercise interventions have the potential to increase participation in exercise and physical activity, as has been shown in other clinical populations where retention rates were 96% at a 12-month follow-up.[10,11] A behavioral intervention was effective at reducing fatigue in persons with MS regardless of whether delivered in-person or via telephone,[12] and group teleconference calls focusing on energy conservation principles have been shown to improve fatigue impact.[13] To date, however, no studies have investigated the feasibility and acceptability of telephone-delivered exercise interventions to target MS fatigue or compared the effects of telephone-delivered exercise therapy to traditional one-on-one, in-person-delivered exercise therapy.

To address this gap in the literature, we conducted a phase IIa pre-/postintervention study, according to the ORBIT (Obesity-Related Behavioral Intervention Trials) model, which provides a stepwise framework for developing behavioral treatments for chronic disease.[14] The specific objectives of this study were to determine (*a*) the feasibility and acceptability of a telephone-delivered exercise intervention to target fatigue in persons with MS; and (*b*) how the telephone-based exercise intervention compared in absolute terms to an otherwise identical in-person–delivered exercise intervention in pre- to posttreatment changes in fatigue and secondary outcomes.

METHODS

Subjects

Participants were recruited through the clinicaltrials.gov Web site (NCT03256851), the local chapter of the National Multiple Sclerosis Society, the Wayne State University (WSU) neurology clinic, and the University of Michigan neurology clinic.

Inclusion/Exclusion Criteria

A trained research coordinator completed a telephone screening form with each participant. The study principal investigators (AK, NF) then determined whether the individual met the study inclusion and exclusion criteria. Participants were included if they had a diagnosis of MS,[15] were independently ambulatory with or without an assistive device for at least 5 minutes at a time, had significant fatigue as indicated by a score of 36 or more (of 63 possible points, for an average fatigue score of 4/7 points) on the Fatigue Severity Scale (FSS),[16] and were able to follow study-related commands. Participants were excluded if they were experiencing any of the following: MS exacerbation within the past 30 days, an additional neurological condition that affected walking, or pregnancy. This study was approved by the Institutional Review Board at WSU, and all participants completed informed consent before enrolling in the study.

Randomization and Allocation Concealment

Eligible participants were consented and randomly assigned into the telephone-delivered exercise group (telephone; n = 10) or the in-person–delivered exercise group (in-person; n = 10). Simple randomization (ie, single random number sequence) using SPSS was performed by the University of Michigan study team, who were not involved in participant testing or training. To ensure concealed allocation, sealed envelopes with group assignment were given to the study team at WSU and pulled sequentially at the time of randomization.

Outcome Measures

Primary Outcome Measures

Feasibility. To measure feasibility, adherence rates (number of sessions completed) were calculated for each group.

Acceptability. The Client Satisfaction Questionnaire (CSQ-8),[17] an 8-item measurement of the participant's perceptions of the value of and general satisfaction with the services received, was assessed at the final testing session after the intervention had been completed. Items are rated from 1 (poor/quite dissatisfied) to 4 (excellent/very satisfied), with a maximal score of 32.

Ecological Momentary Assessment Fatigue Intensity and Fatigue Interference. Fatigue intensity and fatigue interference scores were entered directly into the PRO-Diary (CamNTech, Cambridge, United Kingdom), which provides a more reliable and sensitive assay of symptoms compared with traditional recall measures.[18] The PRO-Diary wrist-worn accelerometer is enhanced with a user interface that allows for self-report. During the pre- and postintervention home monitoring periods, participants wore the PRO-Diary continuously for 7 consecutive days. Five times a day (upon waking, 11 AM, 3 PM, 7 PM, and bedtime), participants were prompted to enter self-reported ratings of fatigue intensity and fatigue interference. *Fatigue intensity*, defined for respondents as tiredness or weariness, was measured with the item: "What is your level of fatigue right now?" rated on a scale from 0 = "no fatigue" to 10 = "extremely severe fatigue." *Fatigue interference*, was measured with the item: "How much is your fatigue interfering with what you are doing right now?" rated on a scale from 0 = "no interference" to 10 = "totally interfering."

Fatigue Severity Scale. Participants completed the FSS,[16] a 9-item questionnaire, rated from 1 (strong disagreement) to 7 (strong agreement). Higher scores indicate greater fatigue and a sum score of 36 and greater out of a possible 63 points (average score 4/7) is used as a cut point for clinically significant fatigue.

Secondary Outcome Measures

Accelerometer Measures. Physical activity was measured with the PRO-Diary, which passively collects physical activity data, calculating daily activity counts, number of active minutes, and percentage of time sedentary. Average activity counts per minute from the PRO-Diary were aggregated across the entire home monitoring period to produce a measure of average activity count per minute over the entire pre- and posttreatment assessment periods. The PRO-Diary accelerometer has shown good construct validity for measuring differences in physical activity from sedentary to moderate-level physical activity in individuals with and without mobility impairments.[19] The PRO-Diary measures physical movement with a triaxial

micro electromechanical systems accelerometer. The PRO-Diary was programmed to record activity in 15-second epochs. Raw acceleration measurements were processed with onboard software to generate "activity counts" where higher activity counts related to more physical activity. Participants entered the time they woke up/went to bed into the PRO-Diary, which helped in identifying periods of wake/sleep in the data. All accelerometer data went through extensive data cleaning using a standardized protocol to identify invalid data and to classify sleep/wake activity data.

Participant-Determined Effectiveness. The Patient Global Impression of Change (PGIC)[20] Scale was used to determine the participants' perspective on the effectiveness of the intervention. The PGIC is one question that asks how the participant would describe the change (if any) in activity limitations, symptoms, emotions, and overall quality of health related to their fatigue since beginning treatment. Respondents choose from 1 (no change) to 7 (a great deal better and considerable improvement that has made all the difference) for a maximal score of 7.

Mobility. Walking was measured with the Timed 25 Foot Walk. Participants were asked to walk at their quickest safe speed for 25 ft. Two trials were completed and the average of the 2 was used as the final score.

MS-Specific Factors. Disease severity was determined using the Patient Determined Disease Steps, which has established concurrent validity with the Expanded Disability Status Scale.[21,22]

Self-reported physical activity was assessed with the Godin Leisure-Time Exercise Questionnaire,[23] a 4-item measure of the frequency and intensity of exercise during "a typical week" that has been frequently used in MS clinical research and has even been used to validate accelerometer measures of physical activity in MS.

Self-efficacy for managing fatigue was assessed with the MS Fatigue Self Efficacy Scale,[24] an 8-item measure that assesses the respondent's confidence to manage fatigue intensity and impact on a 10 (very uncertain) to 100 (very certain) scale. A summary score is calculated as the average of the 8 responses, ranging from 10 to 100 with higher scores indicating greater self-efficacy.

Pain intensity was assessed using the PROMIS Pain Intensity Short Form 3a,[25] which consists of 3 items that assess worst, average, and current pain on a 5-point Likert scale (1 = no pain, 5 = very severe pain). Summed scores are converted to a T-score metric with mean = 50, SD = 10; higher scores indicate higher pain intensity.[26]

Sleep disturbance was assessed with the PROMIS Sleep Disturbance Short Form 8a,[27] which contains 8 items rated on a scale of 1 (very good or very much) to 5 (very poor or not at all). Summed scores are converted to a T-score metric with mean = 50, SD = 10; higher scores indicate greater sleep disturbance.

Depressive symptoms were assessed with the Patient Health Questionnaire—8[28] that records the frequency of 8 depressive symptoms in the past 2 weeks. It provides clinical cut points ranging from no depression to severe depression (range: 0-24).

Testing Sessions. At baseline visit 1, participants completed informed consent procedures and surveys using Qualtrics, a free online research tool licensed by WSU that enables the creation of study-specific Web sites for securely entering and storing participant data. Gait speed was assessed and resting heart rate (HR) was obtained for calculation of target HR for week 1. Participants were outfitted with a PRO-Diary accelerometer and asked to continue their usual activities for the next week. One week after visit 1, participants returned to the laboratory for baseline visit 2 where they returned their accelerometer and were randomized into either telephone or in-person group. Eight weeks later, after the intervention was finished, participants completed a posttreatment testing session, which included Qualtrics surveys, gait speed assessment, and donning of a PRO-Diary to wear for the next week. Participants returned PRO-Diaries to the laboratory in a prepaid box.

Intervention Sessions. All participants then received intervention materials, a binder of weekly educational modules (Table 1) and resources, and the following equipment: yoga mat, 1 set of 5 resistance bands attached to a carabiner, 1 leg strap with carabiner, a door anchor for securing resistance bands, weekly exercise logs, and a wrist-worn pedometer/HR monitor. Participants received instruction on performance of each exercise and had the opportunity to practice in the exercise, receive feedback on form, and ask questions. The trainer then set goals (ie, resistance level and target HR) for week 1 of exercise based on the participant's individual abilities. Both manualized exercise interventions consisted of endurance and strength training components, in line with current evidence for one-on-one exercise interventions to target MS fatigue.[6,7] Wrist-worn HR monitors ensured that endurance training occurred within the prescribed target range HR range, which was progressed over the course of the study to reach 60% to 70% of maximal HR. Participants in both groups were instructed to complete 30 minutes of endurance training (eg, cycling, treadmill, or overground walking) 2 times per week and a lower extremity strength training program using resistance bands 3 times per week for 8 weeks. Strength training focused on lower extremity muscles (hip flexion, extension and abduction, and knee flexion and extension) using resistance bands, following the methods of Keller et al.[29] All participants were assigned 2 functional exercises to complete each week (see Supplemental Digital Content 2C, available at: http://links.lww.com/JNPT/A294, which describes the functional exercises). These functional exercises allowed participants to translate the lower extremity strength training into functional movements, including transfers (sit-to-stand) and balancing. The majority of participants chose to perform resistance training on Mondays, Wednesdays, and Fridays; aerobic training on Tuesdays and Thursdays; and functional exercises over the weekend. Participants recorded their progress (ie, number of repetitions performed, number of minutes of endurance activity) and daily step counts in an activity log provided by the study team. Regardless of group allocation, the trainer used a set

Table 1. Summary of Two 8-Week Interventions: Telephone and Person-Delivered Exercise Training

Intervention Components	Person-Delivered	Phone-Delivered
Approach	Receive binder with weekly modules. Immediately following randomization, all participants received instruction on performance of aerobic and resistance exercises, with the opportunity to try each exercise, receive feedback on form, and ask questions.	
Treatment goals	Engage participants in a regular exercise program consisting of aerobic, resistance, and functional exercises. Educate participants on the importance of exercise for combating fatigue.	
Interaction with trainer	1×/week: in-person meeting with trainer, performing aerobic training (exercise bike, treadmill, or over ground walking) and resistance exercises.	1×/week: telephone call with trainer.
Session content (8 weekly sessions)	Trainer reviewed of the following modules: Week 1: Barriers and facilitators to exercise • Identify barriers to exercise success • Identify facilitators to help overcome these barriers Week 2: Strengthening for walking and movement • The role of specific leg muscles in walking and movement • Discuss how these strengthening exercises carry over to functional activities Week 3: Effect of resistance training on fatigue • Recommended dosage of resistance training • Importance of proper form during resistance training • Evidence supporting resistance training for fatigue Week 4: Effect of aerobic training on fatigue • Recommended dosage of aerobic training • FITT principle target heart rates • Evidence supporting aerobic training for fatigue Week 5: Energy conservation and fatigue • Principles of energy conservation • How energy conservation might apply to daily life • Evidence supporting energy conservation for fatigue Week 6: Lifelong Wellness • Components of physical wellness • Evidence supporting the positive effects of exercise in MS Week 7: Community safety and mobility • Transitioning exercise from home to community • Develop a plan for exercising in the community Week 8: Revisiting goal setting/long-term exercise planning • Review goals and progress over the 8-week intervention • Review plan for maintaining future exercise • Evidence supporting exercise for fatigue in MS	
Home exercise program	Tailored goals for aerobic training, resistance training, and functional exercises. Participants reported their progress to the trainer at the next telephone or in-person session. The trainer then progressed individual resistance and aerobic training programs and set goals for the next week according to a predetermined progression schedule (see Supplemental Digital Content A-C, available at: http://links.lww.com/JNPT/A294).	

Abbreviations: FITT, frequency, intensity, time, and type; MS, multiple sclerosis.

progression schedule to determine each participant's goals for the upcoming week (see Supplemental Digital Content 2A-C, available at: http://links.lww.com/JNPT/A294, which describes the progression of aerobic, resistance, and functional exercises). No specific safety monitoring was performed for the home exercise programs. Specific information regarding safe performance of exercises was included in the study binder and the trainer reviewed this information during the baseline 2 visit. Participants were instructed to stop an exercise if it caused pain and contact their trainer for instructions.

In-person Training. Participants in the in-person group received 1 time per week training with a physical therapist or trained member of the research team (eg, doctoral physical therapy student). Training sessions consisted of 30 minutes of endurance training and 30 minutes of strength training, focusing on progression of exercises, and review of weekly module. Participants followed a home exercise program for the remainder of the week.

Telephone Training. Participants in the telephone group received a 1 time per week telephone call from a physical therapist. Participants reviewed the weekly module, reported their progress from the prior week, discussed any issues or problems, and received progressions of exercises for the upcoming week.

Statistical Analyses

All analyses were performed using Stata (version 15.1, StataCorp LLC, College Station, Texas). Normally distributed continuous variables were described by means and SD, nonnormally distributed variables by medians and interquartile ranges, and categorical variables by number and percentages. Mean change scores (SD) (pre-/postintervention) were calculated for each variable by intervention group and Cohen *d* effect sizes were computed (mean change divided by SD of

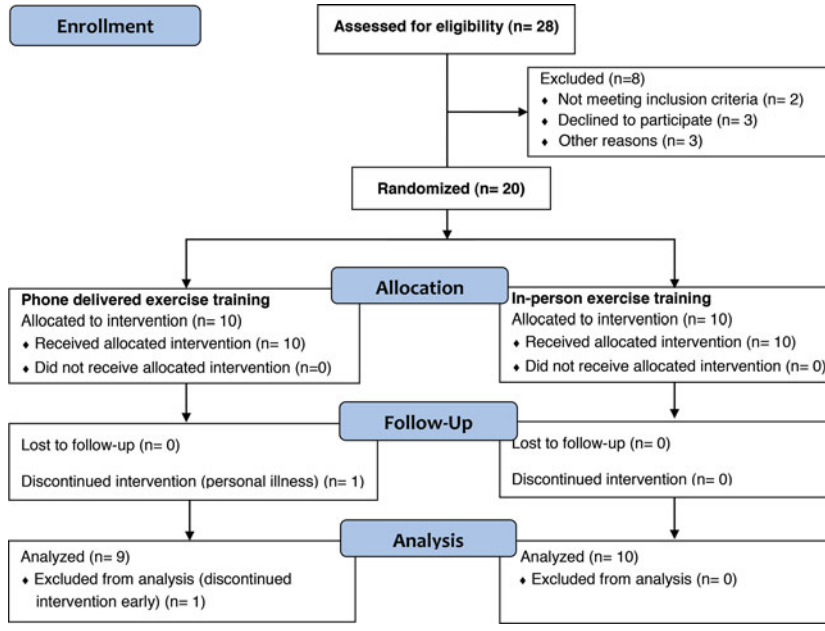

Figure 1. CONSORT flow diagram demonstrating the flow of participants through the study.

the mean change). Effect sizes for fatigue-related outcome measures were used to calculate a minimum sample size for a 2-tailed *t* test study with a probability level of .05 and desired statistical power of 0.8. Between-group differences were analyzed using a 2-sample *t* test to generate mean differences and 95% confidence intervals. Pre- and postintervention fatigue scores (fatigue intensity, interference, and FSS) were plotted by group for each participant and for the group mean.

RESULTS

Twenty participants were enrolled in the study (Figure 1), with 10 randomized to the telephone group and 10 randomized to the in-person group (Table 2). There were no baseline differences between groups on age, race, education level, disability level on the Patient Determined Disease Steps, number of comorbid conditions, depression on the Patient Health Questionnaire—8, pain on the PROMIS-Pain, self-efficacy on the MS Fatigue Self Efficacy Scale, self-reported fatigue on the FSS, or self-reported physical activity on the Godin Leisure Time Exercise Questionnaire. Baseline data from the PRO-Diary revealed no baseline differences in activity counts, sleep, fatigue intensity, or fatigue interference between groups. There were no adverse events reported for either the telephone or the in-person groups. Individuals in both groups demonstrated improvements in the intensity of

Table 2. Baseline Descriptive Statistics

	Total Sample n = 20	Person-Delivered Intervention n = 10	Phone-Delivered Intervention n = 10
Age, y			
Mean, SD	48.3 (7.9)	50.7 (7.4)	45.9 (8.0)
Median, IQR	48.5 (41.0-54.5)	49.5 (48-55)	44.5 (40-52)
Range	36-62	38-62	36-61
Female, n (%)	18 (90)	9 (90)	9 (90)
BMI, median (IQR)	32.9 (27.8-36.4)	29.1 (27.1-34.7)	33.8 (30.8-38.7)
Years since diagnosis, median (IQR)	8 (4-13.5)	4.5 (4-9)	13.5 (5-16)
MS type, n			
RRMS	16	7	9
PPMS	1	0	1
Unsure	2	2	0
SPMS	1	1	0
Right dominant, n (%)	16 (80)	8 (80)	8 (80)
Fatigue Severity Scale			
Mean (SD)	49.5 (7.3)	51.1 (4.1)	47.8 (9.5)
Median (IQR)	51 (46-54)	52 (47-54)	48.5 (37-54)
PDDS, median (IQR)	3 (1-4)	3.5 (3-5)	2 (1-3)

Abbreviations: BMI, body mass index; IQR, interquartile range; MS, multiple sclerosis; PDDS, patient-determined disease steps; PPMS, primary progressive multiple sclerosis; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

aerobic and resistance training exercises over 8 weeks. In week 8, 78% of individuals (7/9) in the telephone group achieved their target heart rate during aerobic exercise, while 60% of individuals (6/10) in the in-person group reported achieving their target heart rate. From week 1 to week 8, individuals in the telephone group increased their exercise band resistance by 113% for hip flexion, 170% for hip extension, 283% for hip abduction, 122% for knee flexion, and 190% for knee extension while individuals in the in-person group increased their exercise band resistance by 86% for hip flexion, 83% for hip extension, 117% for hip abduction, 64% for knee flexion, and 96% for knee extension.

Feasibility

There was no difference between groups in the number of sessions attended. Out of a possible 8 sessions, individuals in the telephone group attended an average of 7.6 ± 1.3 sessions, while individuals in the in-person group attended an average of 7.8 ± 0.42 sessions.

Acceptability

Telephone-delivered exercise is acceptable. The CSQ-8 was evaluated postintervention, and both groups rated the intervention as highly acceptable. Out of a possible 32 points, the telephone group scored 30.3 ± 2.8 on the CSQ-12, while the in-person group scored 30.3 ± 2.2.

Preliminary Efficacy

Individuals in both telephone and in-person exercise groups demonstrated improvements in fatigue. Both FSS and ecological momentary assessment data demonstrated decreases in reported fatigue intensity and interference regardless of group (Figure 2). The average FSS (total score/9) change was 1.9/7 points (in-person) and 1.4/7 points (telephone), which are either at or near the established minimal detectable change of 1.9/7 points for FSS in MS.[30] The mean change in fatigue intensity was 0.7 points (10-point scale) in the in-person group and 1.9 points in the telephone group. Fatigue interference decreased slightly in the in-person group (0.4 points) and also decreased (1.2 points) in the telephone group (Table 3). Furthermore, participants felt that the intervention was helpful, with 50% (n = 10) reporting feeling "a great deal better and a considerable improvement" (n = 4 phone; n = 6 in-person, corresponding to a PGIC 7/7), and 25% reporting feeling "better and a definite improvement (n = 3 phone; n = 2 in-person, corresponding to a PGIC 6/7) on the PGIC. On this scale, only 2 participants reported no improvement (n = 1 phone: "almost the same, hardly any change," and n = 1 in-person "no change or condition has gotten worse," corresponding to PGIC 1/7 and 2/7, respectively).

There were also secondary effects of exercise training in persons with MS. Exercise training improved activity counts and reduced the percentage of time spent immobile in both groups as demonstrated by accelerometry. Participants in both groups reported improvements in self-reported physical activity on the Godin Questionnaire regardless of group (Table 3). Individuals in both groups demonstrated improvements in Timed 25 Foot Walk speed (0.7 seconds in-person and 0.3 seconds telephone) and walk velocity (0.2 m/s in-person and 0.1 m/s telephone) but these did not reach established minimal detectable change (2.7 seconds for the Timed

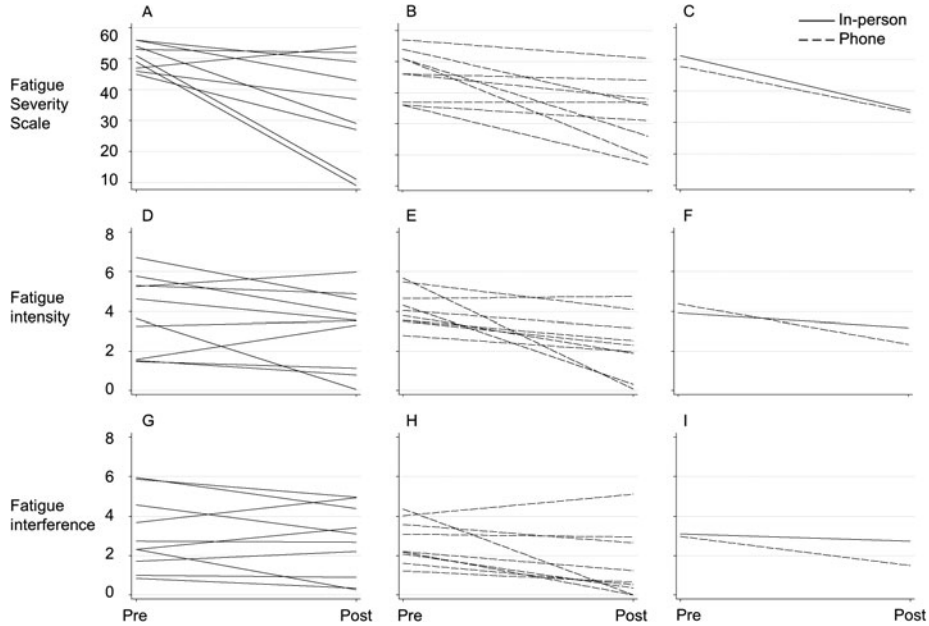

Figure 2. Changes in fatigue following training. Both person-delivered (solid line) and phone-delivered (dashed line) exercise resulted in improvements in fatigue as reported on the Fatigue Severity Scale score (A-C) as well as on EMA measures of fatigue intensity (D-F) and interference (G-I). Individual participant pre- and postratings are represented in panels A and B, D and E, and G and H, while the mean group ratings are represented in panels C, F, and I.

Table 3. Pre- and Postintervention Performance on Survey, Walking, and Activity Monitor Measures

	Person-Delivered				Telephone-Delivered				Between-Group
Measure	Pre, Mean (SD)	Post, Mean (SD)	Mean Change (SD)	Effect Size, Cohen *d*	Pre, Mean (SD)	Post, Mean (SD)	Mean Change (SD)	Effect Size, Cohen *d*	Mean Difference (95% CI)
Fatigue Severity Scale	51.1 (4.1)	34.0 (16.0)	17.1 (15.6)	1.1	47.8 (9.5)	33.2 (11.2)	12.8 (11.1)	1.2	−4.3 (−17.6 to 9.0)
Fatigue Intensity Numeric Rating Scale	3.9 (1.9)	3.2 (1.9)	0.7 (1.5)	0.5	4.4 (1.1)	2.3 (1.5)	1.9 (1.8)	1.0	1.1 (−0.5 to 2.7)
Fatigue Interference Numeric Rating Scale	3.1 (1.9)	2.7 (1.8)	0.4 (1.1)	0.3	3.0 (1.3)	1.5 (1.7)	1.2 (1.5)	0.8	0.8 (−0.5 to 2.1)
Average Activity Count/Minute	221.5 (68.4)	245.2 (71.0)	23.8 (89.1)	0.3	263.6 (55.9)	260.2 (65.4)	7.1 (48.9)	0.1	−16.6 (−87.4 to 54.1)
% Immobile	37.9 (12.0)	37.0 (9.6)	0.9 (11.9)	0.08	33.5 (6.5)	34.4 (8.9)	0.1 (5.7)	0.02	−0.8 (−10.0 to 8.4)
Godin Leisure-Time Exercise Questionnaire	19.3 (18.0)	42.6 (27.3)	23.3 (16.2)	1.4	20.6 (31.0)	40.7 (12.6)	18.5 (26.0)	0.7	−4.8 (−26.0 to 16.4)
Timed 25 Foot Walk (s)	7.0 (3.1)	6.3 (3.4)	0.7 (1.2)	0.6	5.2 (1.1)	4.8 (1.3)	0.3 (0.4)	0.9	−0.4 (−1.2 to 0.5)
PHQ-8	8.2 (6.4)	4.3 (4.6)	3.9 (5.1)	0.8	9.3 (6.4)	4.2 (3.6)	4.0 (4.0)	1.0	0.1 (−4.6 to 4.8)
PROMIS-Pain (T-score)	49.4 (9.8)	44.3 (9.6)	5.0 (6.9)	0.7	44.6 (8.6)	39.8 (9.5)	4.9 (9.4)	0.5	−0.2 (−8.4 to 8.1)
PROMIS-Sleep (T-score)	57.1 (10.6)	47.4 (7.8)	9.8 (10.6)	0.9	56.5 (11.2)	50.4 (12.8)	6.1 (10.2)	0.6	−3.7 (−13.4 to 6.1)
MS-Fatigue Self Efficacy	5.0 (1.6)	6.6 (2.9)	1.6 (3.0)	0.5	5.4 (1.0)	7.0 (1.4)	1.6 (2.0)	0.8	0.04 (−2.4 to 2.5)

Abbreviations: CI, confidence interval; MS, multiple sclerosis; PHQ-8, Patient Health Questionnaire—8.

25 Foot Walk) for persons with MS.[31] The effects of training in both groups were also seen in depression, pain, sleep, and self-efficacy (Table 3), with both groups meeting the minimally important difference established for the PROMIS Pain in other populations (3.5-4.5 T-score points).[32] Effect sizes for fatigue-related outcome measures were moderate to large for the person-delivered exercise group and consistently large for the telephone-delivered exercise group (Table 3). Taking the most conservative effect size for telephone-delivered exercise for a fatigue-related variable (0.8 effect size, fatigue interference numeric rating scale), with 0.8 desired statistical power and a probability level of .05, the estimated sample size for a 2-tailed *t* test study is 52.

DISCUSSION

Our data indicates that telephone-delivered exercise to target MS fatigue is both feasible and acceptable. Attendance rates were high for the telephone-delivered intervention and participants rated the intervention as highly acceptable. Eight weeks of both in-person and telephone-delivered exercise resulted in reductions in fatigue severity and intensity. Both groups neared or met the established minimal detectable change for the FSS of 1.9 points.

Our results add to the literature showing that exercise improves MS fatigue.[6-8,33-35] The frequency, intensity, time, and type of this study are comparable with other person-delivered exercise studies in MS that utilized a 3 times per week schedule for strength training.[33,34] Similarly, our study is in line with other exercise studies in MS targeting aerobic training at an intensity of 60% to 70% HRmax.[35,36]

To our knowledge, this is the first telephone-delivered exercise program for persons with MS. Other telemedicine approaches have been utilized; the protocols for exercises delivered, including frequency, intensity, type of exercise, or tracking confirmation of performed exercises, were heterogeneous. A 12-week study with the Internet delivery of content recommending 2 times per week of strength training and 1 time per week of endurance training targeting health-related quality of life resulted in improved fatigue[37] but included individuals who were both fatigued and not fatigued. Similarly, a 12-week smartphone-delivered program targeting physical activity in persons with MS fatigue resulted in improved fatigue severity[38] but only reminded participants to stay active and did not specifically recommend exercises or guidelines. Finally, a 6-week group teleconference course in persons with MS fatigue resulted in improved fatigue[13] but did not deliver exercise interventions; the intervention included mediated group conversations about a variety of topics similar to the modules in our manual (Table 1). None of these studies utilized one-on-one telephone delivery, and none of these studies had an active control group. Our data demonstrate improvements in fatigue severity and intensity in both groups, as both were exercising and completing the same prescribed home exercise program. The only difference was the method of delivery (Table 1). Furthermore, this study was not limited to persons with relapsing-remitting MS,[37,38] those taking a particular disease-modifying therapy,[38] and those with a score of less than 4 on Expanded Disability Status Scale,[37,38] as was common in other telemedicine studies. Finally, prior

studies using telemedicine approaches have utilized only survey measures of fatigue, measured at a single time point pre- and postintervention. Rather than measuring with survey measures only, we also utilized ecological momentary assessment measures of fatigue to gain a better understanding of the person's fatigue over the course of a week before and after the intervention. In addition to improvements in fatigue, participants in both groups also experienced improvements in activity levels, self-reported physical activity, depression, pain, sleep, and self-efficacy.

Our a priori criteria for determining whether there would be sufficient evidence supporting telephone-delivered exercise therapy to warrant testing in larger trials included (*a*) feasibility of the telephone-delivered exercise intervention as indicated by adherence and retention rates equivalent to or greater than in-person–delivered exercise therapy; (*b*) acceptability of the telephone-delivered exercise intervention indicated by ratings by 75% of participants or more, indicating moderate to high acceptability on the Client Satisfaction Questionnaire; and (*c*) efficacy of the telephone-delivered exercise therapy, indicated by equivalent or greater reductions in fatigue, compared with in-person–delivered exercise therapy. Although this pilot study was limited by a small sample that was not powered for efficacy, the results provide reassurance for proceeding with larger trials, including comparative effectiveness trials. Indeed, sample size calculation from our effect sizes indicates that a sample of 52 is needed for a 2-tailed *t* test study. The approach used in this study may also be of relevance for other neurologic populations, such as stroke, in whom fatigue is known to impair performance.[39]

Limitations

This trial was limited to a small sample size of ambulatory individuals with MS. Although our inclusion criteria allowed for individuals of all disease subtypes, only 3 individuals with progressive disease enrolled (Table 2), so we cannot generalize these findings to individuals with a progressive disease course. No follow-up was performed; future studies should include a follow-up assessment and determine the long-term impact of this intervention on fatigue.

CONCLUSIONS

The findings from our feasibility study of telephone-delivered exercise for persons with MS indicate that the approach was feasible and acceptable to participants, with adherence and preliminary efficacy comparable to an in-person program. Telephone-delivered exercise is a promising alternative delivery method that may overcome barriers to exercise experienced by persons with MS, including distance from major medical centers offering specialty care, transportation, and limited financial resources. Large-scale efficacy trials are needed to determine the efficacy of telephone-delivered exercise therapy on fatigue for persons with MS.

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