WAYNE STATE UNIVERSITY

EUGENE APPLEBAUM COLLEGE OF PHARMACY AND HEALTH SCIENCES

Study Title: Telephone-Delivered Exercise for Multiple Sclerosis Fatigue

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Study Protocol

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 post-treatment changes in fatigue and secondary outcomes.

Inclusion/Exclusion Criteria. A trained research coordinator completed a telephone screening form with each participant. The study PIs then determined whether the individual met the study inclusion and exclusion criteria. Participants were included if they had a diagnosis of MS, 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 $\geq$ 36 (of 63 possible points, for an average fatigue score of 4/7 points) on the Fatigue Severity Scale (FSS), 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.

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 (i.e., single random number sequence) using SPSS was performed by the UM 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.

Testing Sessions. At baseline visit 1, participants completed informed consent procedures and surveys using Qualtrics, a free online research tool licensed by WSU which enables the creation of study-specific websites 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 lab 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 post-treatment 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 lab in a pre-paid box.

In-person Training. Participants in the in-person group received 1x/wk training with a physical therapist or trained member of the research team (e.g., 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 1x/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 Analysis Plan

All analyses were performed using Stata (version 15.1, StataCorp LLC, College Station, TX). Normally distributed continuous variables were described by means and standard deviations (SD), non-normally distributed variables by medians and interquartile ranges (IQR), and categorical variables by number and percentages. Mean change scores (SD) (pre-post intervention) were calculated for each variable by intervention group and Cohen's *d* effect sizes were computed (mean change divided by standard deviation of the mean change). Effect sizes for fatigue-related outcome measures were used to calculate a minimum sample size for a two-tailed t-test study with a probability level of 0.05 and desired statistical power of 0.8. Between-group differences were analyzed using a two-sample t test to generate mean differences and 95% confidence intervals. Pre- and post-intervention fatigue scores (fatigue intensity, interference) were plotted by group, for each participant and for the group mean.