Feasibility and initial efficacy of a wheelchair exercise-training intervention for persons with multiple sclerosis

NCT05888727

Version Date: 06/17/2024

UTHealth Houston
IRB NUMBER: HSC-SPH-23-0719
IRB APPROVAL DATE: 06/17/2024

Protocol Title:	Feasibility and initial efficacy of a wheelchair exercise-training intervention for persons with multiple sclerosis
Principal Investigator:	Stephanie Silveira, PhD
Co-Investigators:	Robert W. Motl, PhD & Katherine Froehlich-Grobe, PhD
Study Coordinator:	Angela Piasecki
Population:	Twenty-four adults with multiple sclerosis who use wheelchairs for mobility in Texas
Number of Sites:	UTHealth Houston
Study Duration:	2 years
Subject Duration:	6 months

General Information

- The proposed study will examine the feasibility of a stakeholder-informed, home-based, remotely supported and supervised exercise training program for wheelchair users with multiple sclerosis (MS). The proposed exercise training program was developed in partnership with community members using semi-structured interviews, a community advisory board, and focus group feedback wherein community members provided insights to develop and refine an exercise training program that suit the needs and preferences of wheelchair users with MS.

Background Information

- Dr. Silveira recently initiated a targeted agenda for creating an exercise training intervention that could be assist in managing MS consequences and optimizing health and well-being among wheelchair users with MS (1-3). Dr. Silveira first conducted a qualitative study that explored the needs and preferences for exercise training among 20 wheelchair users with MS (1). Participants expressed interest in a home-based, remotely supported and supervised exercise program that included strength and aerobic training. This provided a foundation for Dr. Silveira's NIH F32 fellowship, guided by Prof. Motl and Prof. Froehlich-Grobe, that created the first wheelchair exercise training program for persons with MS. The F32 research included two phases of community-engaged feedback to refine and finalize the stakeholder-informed exercise training program. In Phase I, we convened a Community Advisory Board (CAB) of 10 persons with MS who completed 5 weekly meetings and provided feedback on the primary components of the program: exercise prescription, equipment, and behavioral coaching (2). Dr. Silveira updated the intervention materials based on feedback received during CAB meetings and in Phase II we convened three focus groups to refine and verify the stakeholder perceptions regarding the appropriateness of the exercise program

UTHealth Houston
IRB NUMBER: HSC-SPH-23-0719
IRB APPROVAL DATE: 06/17/2024

(3). The collective process yielded a novel wheelchair exercise training program that is ready to be examine for feasibility before testing within a formal clinical trial.

1. Silveira SL, Richardson EV, Motl RW. Informing the design of exercise programs for persons with multiple sclerosis who use wheelchairs: a qualitative inquiry of perceived components. Disability and Rehabilitation. 2019:1-11.
2. Silveira SL, Froehlich-Grobe K, Motl RW. Developing a community-engaged wheelchair exercise program for persons with MS: community advisory board formation and feedback. Disabil Rehabil Assist Technol. 2021 Dec 10:1-8. doi: 10.1080/17483107.2021.2010819. Epub ahead of print. PMID: 34892990; PMCID: PMC9215208.
3. Silveira SL, Froehlich-Grobe K, Motl RW. Formative evaluation of an exercise training program for persons with multiple sclerosis who are wheelchair users. Eval Program Plann. 2023 Apr;97:102243. doi: 10.1016/j.evalprogplan.2023.102243. Epub 2023 Jan 21. PMID: 36696872.

- Ultimately, the this study extends Dr. Silveira's line of research and may initiate a significant paradigm shift in rehabilitation research and practice by providing a critically needed home-based exercise training program for enhancing health, quality of life, participation, and independence of wheelchair user with MS.

Objectives

- To examine the feasibility, acceptability, and initial efficacy of a stakeholder-informed, home-based, remotely supported and supervised exercise training program for wheelchair users with multiple sclerosis (MS) compared to an attention/contact wellness control program.
- Feasibility will be operationalized using ongoing assessment of as recruitment, retention, and safety. We hypothesize that the intervention will be feasible in terms of reaching recruitment goals (n=24; 12 per group) within a one-year period, retaining ≥80% of those participants through the full 16-week study period, and safe in terms of <10% of participants reporting adverse events. We are defining our recruitment goals as participants who matriculate and are randomized, therefore we aim to consent up to 28 participants.
- Acceptability will be operationalized as participant satisfaction and perceptions measured in post-intervention formative surveys and interviews. We hypothesize that a greater proportion of participants in the SPIN exercise training condition will report high satisfaction and positive perceptions regarding the exercise training program compared with the attention/contactwellness control condition.
- The study will further examine changes scientific outcomes of interest (i.e., metabolic health, MS symptoms, and exercise behavior change) for determining effect size and sample size estimates in powering a larger clinical trial. We hypothesize that the SPIN exercise training interventionprogram will lead to greater improvements in metabolic health outcomes (i.e., HbA1c, cholesterol, glucose, and triglycerides), MS symptoms (i.e., fatigue, pain, depression, and quality of life) and exercise behavior compared to the attention/control wellness program.

Study Design

- Parallel group, randomized controlled trial

- The study is funded for a 2 year period and participants will be involved in study procedures for approximately 6 months.
- The primary outcome of interest is feasibility (i.e., recruitment, retention, and safety). The secondary outcome of interest is acceptability (i.e., participant satisfaction and perceptions).
- The tertiary outcomes of interest are scientific outcomes of initial efficacy(i.e., metabolic health, MS symptoms, and exercise behavior).
- Safety will be assessed in terms of incidence of participants reporting adverse events.

Study Population

- Eligibility criteria: (a) diagnosis of MS; (b) self-reported use of a wheelchair (i.e., manual wheelchair, power wheelchair, or scooter) ≥50% of the time; (c) age of 18 years or older; (d) relapse free for the past 30 days; and (e) being non-active defined as not engaging in regular physical activity (30 minutes accumulated per day) on more than 2 days of the week during the previous 6 months (i.e., not meeting current physical activity guidelines for MS). During telephone screening participants will complete an exercise pre-participation health screen and if participants report any symptoms or conditions contradictive of exercise then physician clearance will be required before enrollment.
- Inclusion/exclusion criteria align with the samples that were engaged in our community-engaged foundational studies and numerous clinical trials in persons with MS and other wheelchair users such as spinal cord injury.
- Participants will be recruited using clinic visits at UTHealth Houston and Harris Health MS clinics and flyers in the local community. Specifically, Dr. Lin will facilitate contact with potential participants in the UTHealth Houston and Harris Health clinics.

Study Procedures

- Interested participants will contact the Study Coordinator for a telephone screening, which includes a comprehensive description of the study followed by screening for inclusion criteria. Participants deemed eligible for the study will then be sent a consent form to review and sign using through REDCap. When the Study Coordinator receives the signed consent form, participants will be mailed a pre-test/baseline assessment packet. The pre-test assessment packet will include Actigraph GT3X+ accelerometer and instructions to wear the accelerometer on the non-dominant wrist for 7 days as well as an order for blood sample collection at a Quest Diagnostics/LabCorp location that is convenient for them. Participants will complete a battery of questionnaires online using REDCap. When the Study Coordinator receives the accelerometer and notification that a blood sample has been collected, participants will be randomized into the exercise training intervention condition or attention/contact control condition using the REDCap randomization module. Following randomization, participants will be mailed their condition-specific program materials as well as instructions for downloading Zoom. All participants will receive behavioral coaching, which is founded in Social Cognitive Theory (SCT) behavior change principles. Each participant will meet one-on-one with the same behavioral coach, the PI, weekly for the first 8 weeks of the program, and biweekly for the last 8 weeks (total of 12 meetings). Meetings will be recorded for auditing and training purposes as outlined in the consent form. The research team created 12 SCT-based, condition-specific newsletters that serve as the curriculum underpinning each program. Post-test assessment of tertiary outcomes following the 16-week intervention will mirror baseline

assessments. Participants will be asked to complete an additional evaluation questionnaire to assess satisfaction with the program and usability of intervention components. All participants will be invited to complete a post-test semi-structured interview via Zoom to provide feedback on their experiences and suggestions for refining the program. All participants will be compensated $75 for completing each assessment, and an additional $25 will be provided for those who complete the post-test interview.

- Informed Consent: Prior to completing any assessments we will review the Informed Consent document with each participant. The member of the research team will explain each section of this document and answer any questions. Participants will be asked to sign this document using REDCap before completing assessments and being enrolled in the study. Participants will be provided with a copy of the Informed Consent document for their records.
- Blood Draw (Assessment 1&2): Participants will be asked to complete a blood draw at a Question Diagnostics location in their local community that will take approximately 30 minutes. Biological samples will be collected and stored at Quest Diagnostics using their standardized clinical trial protocol. The samples will be disposed of immediately following analyses. They will draw 4mL of blood using a standardized protocol. This is about 1 teaspoon of blood. The biomarkers they will collect include HbA1c, cholesterol, glucose, triglycerides, and insulin.
- Questionnaires (Assessment 1&2): Participants will be asked to complete a battery of questionnaires online using REDCap at each assessment that will take 20-30 minutes. The battery of questionnaires includes a demographic and clinical characteristics questionnaire; the Patient Determined Disease Steps scale for assessing clinical disability status; the Godin Leisure Time Exercise Questionnaire; Fatigue Severity Scale; McGill Pain Questionnaire; Hospital Anxiety and Depression Scale; Multiple Sclerosis Impact Scale 29 as a quality of life measure; and the Leisure Time Physical Activity Questionnaire for People with Disabilities. Participants may skip any questions that make them feel uncomfortable.
- Physical Activity Assessment (Assessment #1&2): Participants will be asked to complete a standard 7-day accelerometery protocol using Actigraph wGT3X-bt) accelerometers (https://actigraphcorp.com/actigraph-wgt3x-bt/). Participants will be asked to wear the accelerometer on your non-dominant wrist during waking hours for 7 days.
- Coaching Sessions: You will be asked to join a Zoom call with your MS Behavioral Specialist coach throughout the study. The calls will consist of obtaining feedback on your progress and discussing topics relevant to your progress in the assigned program. These calls will be recorded and kept on a HIPAA compliant OneDrive folder for three years for future training and random auditing purposes then destroyed.
- Formative Evaluation (Assessment #2): Participants will be asked to complete a brief survey, online regarding your perceptions and experiences in the exercise training program that will take approximately 5-10 minutes. Participants may skip any questions that make them feel uncomfortable. We will also invite participants to complete an interview online, using Zoom that will last 20-30 minutes to provide feedback on the program they completed.
- Exercise Intervention: The exercise program includes both aerobic and strength training components to be completed over 16-weeks. The aerobic exercise prescription is progressive and individualized. Each participant starts with a goal of 10 minutes aerobic training the first 2-week period (i.e.,

accommodation period). Participants are then assigned to one of three trajectories of progression over the remaining 14-week period to reach a final goal of at least two, 30-minute aerobic workouts per week. Fifteen resistance training exercises were developed that include body weight movements and use of study-provided resistance bands or wrist weights for targeting upper body, core muscle groups, and lower body that are adaptable for manual or power wheelchair users. During the proposed program, participants will choose the resistance training exercises those that best suit their functional capabilities and goals. The resistance training prescription begins with 1 set of 10 repetitions of 5 exercises performed 2 days a week. Similar to the aerobic exercise prescription, three trajectories of progression for the resistance training will be used (i.e., sets, repetitions, and exercises) over the remaining 14 weeks to reach a final goal of at least 2 sets of 15 repetitions of 10 exercises. The participant manual includes instructions on precautions and safety for exercise that will be reviewed with all participants during the first coaching call. Coaches will check-in regularly with each participant to assess safety and report any adverse events to IRB.

- Wellness Intervention: The attention/contact wellness control condition will mirror the exercise training intervention condition, but focuses on implementing health behaviors other than physical activity (e.g., diet and emotional wellbeing) over 16 weeks. This program is an adapted version of the WellMS program from Prof. Motl's Phase III clinical trial (NCT03490240) that Dr. Silveira delivered and coached during an initial postdoctoral fellowship. The program is based on SCT principles of behavior change and integrates wellness resources from the NMSS. The research team has created 12 Newsletters split into six different topics, with each topic addressed in two newsletters. The topics include Stress Management, Emotional Regulation, Diet, Sleep, Balance and Fall Risk, and Fatigue. All coaching chats and newsletters will occur with the same frequency as in the exercise training intervention condition. Participants will be provided with a participant manual, logbook, and calendar. Participants will work with their behavioral coach on goal setting specific to wellness behaviors.

Data and Safety Monitoring

- All testing will be performed by trained personnel and all equipment will be calibrated daily before testing. If an individual indicates discomfort or the desire to discontinue testing, tests will be terminated immediately. All adverse events will be reported to the UTHealth Houston IRB and reviewed by the investigative team. Should any of these individuals and/or the IRB identify that any adverse event may be related to the study protocol, testing will be suspended and the protocol will be amended accordingly. Adverse events will be tracked using a REDCap database for assessing the primary study outcomes.

Statistics

- The planned enrolled sample size of 28 participants (i.e., 12 per group that matriculate and are randomized) is justified for pilot clinical trials when there is no prior information for sample size estimation.
- Dr. Silveira (PI) will lead the data analyses given her expertise in both quantitative and qualitative data analyses. Participant characteristics will be reported using means/medians and standard deviations/interquartile ranges for continuous variables. Categorical measures will be presented as counts and percentages. The analysis will use the intent-to-treat principle where patients will be

analyzed in their randomization assignment. Descriptive statistics including frequencies and percentages will be utilized to assess the feasibility metrics for the primary and secondary outcomes (*Hypothesis 1 & Hypothesis 2*). The scientific outcomes in *Hypothesis 3* (i.e., metabolic health outcomes, MS symptoms, and exercise behavior) will be examined using 2 time by 2 group mixed factor ANOVA with estimation of Cohen's d values for effect sizes. Participant's change in scientific outcomes will be further examined and compared with the ≥0.5 SD will be considered meaningful change based on benchmarks established in previous research.

Ethics

- First, following screening all participants deemed eligible for the study will then be sent a consent form to review and sign using through REDCap. The PI will review the consent document to ensure participants understand study procedures and sign the document prior to enrollment. During consent process the research team will emphasize the voluntary nature of all research procedures and assess consent at each following contact as consent is an ongoing process.

Data handling and record keeping

- All paper and electronic data collected from this study will be stored in a secure location on the UTHealth Houston campus and/or a secure UTHealth Houston server for at least three (3) years past the end of this research in a locked filing cabinet behind a locked door or password protected computer in PI's campus office as appropriate. Research records will be labeled with a code and the master key linking names with codes will be maintained in a separate and secure location.
- All participants will be assigned an identification number and all data collection, as well as data analyses, will be conducted with the coded non-identifiable data; there will be no link between the ID number and the subject's name. All data will be kept in a locked file cabinet and only aggregated data will be used for presentation or publication purposes. There will not be a link between the identification number and participant for purposes of tracking participants over time. We will not maintain a link between identification number and the subject's name after completion of the study procedures, and there is no intention of linking data collected in the current project with data collected in another project. We will retain screening data for those who qualify and volunteer, and destroy the screening data for those who are excluded or do not volunteer.
- Only the members of the research team listed on the IRB application will have access to the data. Any members of the research team who are added during the study period will be submitted as an amendment to the IRB prior to having access to study data or interacting with any human subjects.

Quality control and assurance

- A data and safety monitoring plan is established to ensure the safety of all participants involved in the study and ensure validity and integrity of the collected data. The PI will be responsible for execution of this plan and data collection methods using HIPAA compliant software including REDCap. Our laboratory currently has protocols in place for participant safety and data integrity, however should the need arise a report of a serious adverse event, the appropriate forms for the UTHealth IRB will be completed with copies provided to the funder. Participants will be asked to

contact the research team via telephone or e-mail in occurrence of an adverse event or any other problem. Life-threatening adverse events will be reported within 24 hours and serious, but non-life-threatening adverse events will be reported within three days.

Publication Plan

- The research team will submit a protocol manuscript prior to initiating recruitment and primary outcomes manuscript outlining results from this study. The final results from the study will be presented at a national rehabilitation conference.
- Aggregated data will be used for presentation or publication purposes related to reporting of results and subsequent grant proposals. Data will be reported such that the identity of all participants will be protected in all publications and presentations.
- A report of the overall study findings in lay terminology will be provided to all participants following the completion of data analyses.